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For whom the bell tolls…

This issue of the journal is dedicated to the evergreen memory of two Editors-in-Chief of the journal who recently passed on to the great beyond: Professors Olufemi Williams and Babatunde Osotimehin, the first and sixth Editors-in-Chief respectively. Prof. Williams, internationally renowned Professor of Pathology, served as the Editor between April 1971 and December 1980. During the period, he "shephered and nurtured" the journal through the formative years and worked tirelessly to ensure that the journal attained international recognition. He left Ibadan to serve as the Foundation Dean and Chief Medical Director of University of Calabar College of Medicine and was visiting Professor of Pathology to many universities in the United States. He was also Scholar in Residence at the National Institutes of Health, Bethesda, Maryland, USA for many years. He died on 16th July 2017.

Prof. Osotimehin served as Assistant Editor of the journal from March 1989 to June 1996 (while he was the Provost, College of Medicine, University of Ibadan, 1990-94) and later became the substantive Editor-in-Chief from September 1996 till December 2003. He revamped the Journal and upheld high standards. He effectively applied information technology in the business of the journal and expanded the content. During his tenure, the Journal published its first supplement on HIV/AIDS. He left the position of Editor-in-Chief on being appointed as the Director General of the National Agency for the Control of AIDS (NACA) and subsequently, Minister of Health, Federal Republic of Nigeria. He was appointed Under-Secretary General of the United Nations and the Executive Director of the United Nations Population Fund Agency (UNFPA) in New York in November 2010. He was a strong advocate of reproductive rights of women and safe births. He died on 4th June, 2017 at the age of 68 years.

Henry Wadsorth Longfellow (1807-1882), the American poet, wrote in *A Psalm of Life* that "Lives of great men all remind us, we can live our lives sublime, and departing leave behind us footprints on the sands of time" The two Editors were great scholars, mentors who epitomized integrity. They made their marks and were internationally recognized for their excellence. Their names will certainly be written in gold for their invaluable contributions to the growth of the Journal. We mourn their losses and may their souls rest in perfect peace.

A. Ogunniyi
Editor-in-Chief

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Assessment of family function in perimenopausal women in Ibadan

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Abstract
Background: The perimenopause is often accompanied by distressing symptoms which may take their toll on the woman and her family. This study aimed to assess the possible association of the perimenopause with poor family functioning.
Methods: It was a cross-sectional, descriptive study of 132 women aged >40 years, carried out at the Department of Family Medicine of the University College Hospital, Ibadan, Nigeria. The questionnaire included the General Functioning Scale of the Family Assessment Device, a self-report measure of family functioning that describes emotional relationships and functioning within the family. Explanatory variables were demographic data parameters and onset of menstrual irregularities, outcome variables were presence or absence of good family functionality. Categorical and continuous variables were analysed with chi-square test and students't-test, respectively. Data analysis was with IBM SPSS Statistics 20. Ethical approval was obtained from the institutional ethical committee.
Results: Most (80.3%) of the 132 respondents were already experiencing irregular menses. The General Functioning scale scores ranged from 1.08 to 3.08. The modal score was 1.92 which was within the range of good function. Applying a standard cut-off point of 2.17, 92 (69.7%) reported good family functioning, while 40 (30.3%) reported poor family functioning. Of all socio-demographic variables assessed, being in a monogamous marriage was the only observed one significantly associated with good family functioning ($p<0.01$).
Conclusion: These middle-aged women mostly had good family functioning. Monogamy was a significant association; the reasons for this may be further explored.

Keywords: *Perimenopause, climacteric, family*

Résumé
Contexte: La péri ménopause est souvent accompagnée de symptômes pénibles qui peuvent porter atteinte à la femme et à sa famille. Cette étude visait à évaluer l'association possible de la péri ménopause avec un fonctionnement familial médiocre.
Méthodes: Il s'agissait d'une étude transversale et descriptive de 132 femmes âgées de plus de 40 ans, menées au Département de Médecine Familiale du Collège Hospitalier Universitaire, Ibadan, Nigeria. Le questionnaire comprenait l'Echelle de Fonctionnement Générale du Dispositif d'Evaluation Familiale, une mesure d'auto-évaluation du fonctionnement de la famille qui décrit les relations émotionnelles et le fonctionnement au sein de la famille. Les variables explicatives étaient les paramètres de données démographiques et l'apparition d'irrégularités menstruelles, les variables de résultat étaient la présence ou l'absence de bonnes fonctionnalités familiales. Les variables catégorielles et continues ont été analysées respectivement avec le test du chi-carré et le test t- d'élève. L'analyse des données a été effectuée avec IBM SPSS Statistiques 20. L'approbation éthique a été obtenue auprès du comité d'éthique institutionnel.
Résultats: La plupart (80,3%) des 132 répondants connaissaient déjà des règles irrégulières. Les scores de l'échelle des fonctions générales variaient de 1,08 à 3,08. Le score modal était de 1,92 qui était dans la gamme de bonne fonction. En appliquant un point de coupure standard de 2,17 ; 92 (69,7%) ont déclaré un bon fonctionnement de la famille, tandis que 40 (30,3%) ont signalé un fonctionnement familial médiocre. De toutes les variables sociodémographiques évaluées, l'existence d'un mariage monogame était la seule observée qui était significativement associée au bon fonctionnement de la famille ($p<0,01$).
Conclusion: Ces femmes d'âge moyen avaient surtout un bon fonctionnement familial. La monogamie était une association importante; Les raisons de cela peuvent être explorées d'avantage.

Mots clés: *Péri ménopause, climatérique, famille*

Introduction

Menopause is a life-changing event. The reproductive changes of menstrual irregularity followed by

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amenorrhoea are obvious and often anticipated; however, the emotional and psychological changes may be unexpected, bewildering and extreme [1, 2], affecting the balance of the entire family. Puberty is noted to affect these other aspects [3, 4]; similarly, this can also be the experience at menopause, the other extreme of reproductive life. Furthermore, about the time of menopause, middle-aged women may also develop concurrent medical disorders that require long-term lifestyle changes or may have poor prognosis [5]. There may also be family changes [5] such as loss of a spouse, children leaving home or getting married, which leads to them becoming grandmothers. All these happening at the same time may constitute a stress to perimenopausal women and their families [6, 7].

Perimenopause is the period 'prior to the menopause (when the endocrinological, biological and clinical features of the approaching menopause commence) and the first year after menopause' [8]. The prevalent symptoms of the perimenopause and menopause are well-described [2, 9]; they are often discomfiting and women may respond in a variety of ways, which may take its toll on their family life. The psychological and emotional symptoms include anxiety, depression and easy irritability [2]. The latter will expectedly affect people in close proximity to the woman, which includes their families.

In comparison to other gynaecological conditions, anecdotal experience shows there are not many menopause-related hospital consultations in Nigeria. This may be due to the fact that women who perceive menopause as being normal are not likely to seek medical attention [10] while those who see it as being abnormal or as a result of a supernatural force may be inclined to seek help from the traditionalist [11] or from patent medicine dealers [10]. The authors did not find any indexed research on the impact of menopause on the well-being of the Nigerian family.

Researchers have noted from focus group discussions, the fears of women about post-menopausal sexual intercourse causing ill health. The discussants mostly agreed that menopausal women should abstain from sex [11, 12]. Some also feel sex during this phase can harm their husbands, while others state that their husbands feel that sex with a menopausal wife would harm them [11]. A husband, who still desires sexual activity may find other partners, or marry a younger woman. This may cause strife and rancour in the family. For a woman to function well in her traditional role as a family care-giver, she ought to be as healthy as possible at every stage of her life.

The Family Assessment Device (FAD) is a validated self-administered tool directed at assessing family functioning; based on the McMaster Model of Family Function [13-16]. The model identifies six dimensions of family functioning: problem solving, communication, roles, affective responsiveness, affective involvement and behaviour control. A seventh scale (general functioning) assessed general health or pathology of the family. It is recommended that the FAD is administered to all family members older than 12 years [13]. However, it has also been used with only one family member in clinical settings [13, 17]. The FAD consists of 53 items [13]. The FAD has been assessed for use by family physicians; with a conclusion that these doctors have sufficient skills to carry out the process [14]. The tool used in this study was modified from the original FAD—it is the 12-item General Functioning Scale (GF) of the FAD [17]. The GF has been validated for use in survey research. As described above, it is the portion of the FAD that assesses the general health or pathology of the family. The GF has been used in several settings: patients with medical or psychiatric disorders and their families [18], children [19], and in non-clinical college undergraduates [20] and adolescents [21].

The study aims to determine the effect of the perimenopause on the families of women attending a family practice clinic, and therefore assess the need for anticipatory care and counselling to these women.

Materials and method

The study employed a cross-sectional, descriptive design. It was carried out at the Family Medicine Department of the University College Hospital, Ibadan, located in South-west Nigeria. It is situated in the central, urban area of the city, and also serves peri-urban and rural communities of Ibadan and its environs. A minimum sample size of 98 was calculated from a formula for cross-sectional studies, using a prevalence of 6.8%. This was derived from the proportion of women who were unhappy about the menopause [22] in a previous study in Ibadan. Women aged 41 years and over, who attended the clinic over a four-week period and gave written consent, constituted the study population. Women with debilitating illness were excluded. Ethical approval was obtained from the joint University of Ibadan/ University College Hospital Ethical Committee.

The interviewer-administered study questionnaire sought information on demographic and other characteristics, and included the 12-item

General Functioning Scale (GF) of the Family Assessment Device. The GF is a self-report measure of family functioning that describes emotional relationships and functioning within the family [17]. The possible range of scores for each item is from one to four points; representing 'strongly agree', 'agree', 'disagree' and 'strongly disagree', respectively. It utilizes the reverse scoring system for the negatively-worded items (which are also odd-numbered: 1, 3, 5, 7, 9 and 11). The total obtainable score ranges from 12 to 48 points. The participant's family functioning score is the average of the 12 items. On this scale, using a standard cut-off of 2.17, high mean scores depict unhealthy 'pathologic' family functioning, while lower scores depict healthy family function [17]. In an attempt to further assess the effect of the perimenopause on the participants' families, they were asked to recall their family life up till they were 40 years old and fill the GF retrospectively into a second copy of the tool.

The outcome variables were the presence or absence of good family functionality. The explanatory variables were demographic data such as family status parameters and onset of menstrual irregularities. Categorical variables were analysed with chi-square tests, while continuous variables were analysed with students' t-test. Data analysis was done with IBM SPSS Statistics 20.

Results

One hundred and thirty-eight eligible women filled the questionnaire. However, only the 132 (95.7%) that completed all 12 items of the GF were included in the analysis. Their demographic characteristics are depicted in Table 1. Most of the study population (81.1%) were already within the perimenopause, inferred by the onset of menstrual irregularity.

Twenty-four respondents (18.2%) reported being more irritable than usual within the past year. Ten (7.6%) of them feel it had affected their relationship with their partner, while 7 (5.3%) felt it had affected their relationship with their children. Twenty-seven (20.5%) reported having had sex within a week of the interview, 36 (27.3%) within a month, 26 (19.7%) within six months, and the rest (43; 32.5%) had abstained longer than that. Thirty-two of the women (24.2%) had previously been diagnosed with medical illnesses, of which hypertension (22; 16.7%) was the most prevalent.

The range of GF scores of these women were 1.08 to 3.08, with most of them scoring 1.92. On applying a cut-off of above 2.17 for poor functioning; 92 (69.7%) reported good family functioning, while 40 (30.3%) reported otherwise. Selected demographic characteristics were cross-tabulated with good versus poor family functioning to evaluate possible associations (Table 2). Being married, having children, medical co-morbidity or having transited into perimenopause were not associated with family functioning. Being in a monogamous marriage was the only observed variable significantly associated with good family functioning ($p<0.01$).

The previous and current GF scales were compared (Table 3). The mean scores were similar in both sets, with no statistical difference (t-test: 95%

Table 1: Demographic characteristics of respondents

Variable	N (%)
Age (years)	
41-45	73 (55.3)
46-50	41 (31.1)
51-55	18 (13.6)
Marital status	
Single	5 (3.8)
Married	108 (81.8)
Separated/divorced	6 (4.5)
Widowed	13 (9.8)
Type of marriage	
Monogamous	68 (51.5)
Polygamous	40 (30.3)
Parity	
0	1 (0.8)
1-2	18 (13.6)
3-4	47 (35.6)
e"5	66 (50.0)
Tribe	
Yoruba	81 (61.4)
Igbo	13 (9.8)
Hausa	34 (25.8)
Other tribes	4 (3.0)
Religion	
Christianity	71 (53.8)
Islam	59 (44.7)
Traditional	2 (1.5)
Occupation	
Unemployed	6 (4.5)
Unskilled	86 (65.1)
Skilled	34 (25.8)
Professional	6 (4.5)
Level of education	
None/informal	33 (25.0)
Primary	31 (23.5)
Secondary	25 (18.9)
Tertiary	43 (32.5)
Irregularity/cessation of menses	
Yes	107 (81.1)
No	25 (18.9)

Table 2: Possible explanatory factors for respondents' perception of family functioning

Variable	'Good' family function (N= 92)	'Pathologic' family function (N=40)	*P*
Marital status			
Married	74 (68.5)	34 (31.5)	0.53
Unmarried	18 (75.0)	6 (25.0)	
Type of marriage			
Monogamous	56 (82.4)	12 (17.6)	<0.01
Polygamous	18 (45.0)	22 (55.0)	
Has living children			
Yes	91 (70.5)	38 (29.5)	0.22*
No	1 (33.3)	2 (66.7)	
Medical co-morbidity			
Yes	22 (68.8)	10 (31.2)	0.89
No	70 (70.0)	30 (30.0)	
Presence of menstrual irregularities			
Yes	74 (69.8)	32 (30.2)	0.98
No	16 (69.6)	7 (30.4)	

**Fishers' exact test*

Table 3: Comparison of family function scores before and during the perimenopause

	'Good' family function N(%)	'Pathologic' family function N(%)	*P*
Before climacteric	82 (69.5)	36 (30.5)	0.67
During climateric	79 (66.9)	39 (33.1)	

CI= -0.05 – 0.01; *p*=0.19). There was no difference in chi-square test either, when categorized and 'good' or 'pathologic' functioning (*p*=0.67).

Discussion

The middle-aged women in this study reported good family functionality, which was not affected by the perimenopause. The only identified association was being in a monogamous marriage. The participants of this study had fairly well-distributed demographic characteristics. These middle-aged women were mostly already experiencing menstrual irregularities, so it may be reasonable to assume they are mostly perimenopausal—irregular periods are one of its main clinical features [23, 24]. Most families represented in this study were reported to have good functionality. Demographic data that may constitute confounders to these findings were not found to be associated: for instance, having a medical co-morbidity, being unmarried or being childless. Health issues during middle age have been shown to make the reproductive transition more challenging [5]; however, associated illnesses did not translate into poor family functioning in the index study. Studies also show that marriage and children improve women's experience of the menopause by providing social support [25, 26], but this does not extrapolate to improved family functioning in this study.

With regards to the unmarried respondents, it is unusual for older women to live alone in Nigeria, where strong family networks exist. Even if she was never married and never had children, she would likely have younger relatives she had fostered, or may live with a member of her extended family. This explains why these participants were able to complete the GF in the first place, and may also somewhat explain the lack of difference with married women. Monogamy was the only factor that was identified as an association to improved family function. This is not surprising, as the information was elicited from the woman's point of view. Several studies show that women in polygamous marriages are more likely to report reduced life satisfaction, less marital satisfaction, poorer family functioning, more mental health symptomatology and less self-reported health than monogamous women [27, 28,

29]. Social support reduced the chances of the last two problems listed [29].

About a fifth of respondents considered themselves having been more irritable in the past year. Easy irritability is an established symptom of the menopause [30], and is not unusual in the perimenopause. A significant proportion of women had also not been having sexual intercourse regularly, despite mostly being married. Research in the study area showed that many middle-aged women have diminished interest in sexual intercourse, and decreased sexual activity in direct proportion to increasing age [31]. Several reasons were proffered for this, including: reduced sexual desire, cultural beliefs about sex, dyspareunia and availability of other co-wives to satisfy their husbands' sexual needs. Despite the irritability and diminished sexual activity, few women felt that menopause affected their relationship with their husbands or children in this study. This finding was similar to an earlier study in Ibadan [22]. The latter study also found that 18% of sexual-abstaining respondents stopped having intercourse because they had no further desire for procreation [22]. Any or all of these reasons may partly explain the abstinence practiced by some of this study's respondents. Perimenopause does not seem to affect families remarkably either, probably showing the strength of family relationships in the locality, or that these families may have coping strategies which are effective.

Comparison of the family's current general functioning score to the recalled score showed a small, but statistically insignificant, change towards pathologic functioning over time. This change was also not clinically relevant, as the mean scores remained below the cut-off point. This implies that the perimenopause was not a significant family stressor in this survey. Families are often able to pull together and support each other through stressful events, so this might not be surprising. Nigerian women generally expect these changes as a rite of passage to old age, so appear to be well-adjusted to them [32]. This study also corroborates that women's perception of family functioning was not influenced with transition into the perimenopause (in this case, heralded by menstrual irregularity).

The interpretation of this study is limited by the recall bias and the fact that only one family member was interviewed for family functioning. The tool is however described for use if only one family member is available in a clinic setting [13,17]. Also, the clinic setting limits generalization of the study findings. However, a family practice clinic represents primary care, which is more likely to represent the community than a specialist clinic, and may thus make these findings more acceptable.

In conclusion, the middle-aged women in this study basically had good family functioning, irrespective of their varied demographics. Being in monogamous marriages was the only factor that influenced this. Perimenopausal changes did not affect function. The specific details that associate monogamy with good family function may be further explored. Counselling and support may ameliorate the effects of polygamy on women affected by this.

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Applicability and cross-cultural adaptation of the self-administered Child–OIDP in a rural Nigeria community

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Abstract
Background: The utilization of the Child Oral Impact on Daily Performances (Child–OIDP), one of the most widely used quality of life measures for children, in rural communities will require cross adaptation of the measure since rural communities in Africa are in no small way influenced by the prevailing cultural norms and values. The aim of this study was to assess the applicability of self-administered Child–OIDP measure in a rural community in Nigeria.
Methods: A cross sectional study was conducted among 403 secondary school students in Igboora, Nigeria using self-administered Child–OIDP questionnaire translated into the local language.
Results: The mean age of the study participants was 12.4 (±0.7) years. The impact of oral health on their daily performances scores ranged from 0 to 66. Higher OIDP scores were significantly associated with perceived need for dental treatment ($p < 0.001$), satisfaction ratings of oral health condition ($p = 0.001$), satisfaction ratings of tooth appearance ($p = 0.030$) and pain ($p < 0.001$). The use of frequency or severity scales separately or combined exhibited similar and acceptable validity and reliability; however, the frequency scale alone had the highest Cronbach's alpha value (0.876), while use of both frequency and severity scales was best for inter–item correlations (0.552-0.714).
Conclusion: The translated version of the Child–OIDP measure is a valid and applicable tool in a rural community. Use of either the frequency or severity scale of this version of Child–OIDP is valid, cross-culturally adaptable and recommended.

Keywords: *Child, community, child–OIDP, quality of life, reliability, rural, validity*

Résumé
Contexte: L'utilisation de l'impact oral sur les performances quotidiennes de l'enfant (IOPQ-enfant), l'une des mesures de qualité de vie les plus utilisées pour les enfants, dans les communautés rurales nécessitera une adaptation croisée de la mesure puisque les communautés rurales en Afrique ne sont pas en très peu manière influencé par les normes et les valeurs culturelles en vigueur. L'objectif de cette étude était d'évaluer l'applicabilité de la mesure auto-administrée de l'IOPQ-enfant dans une communauté rurale au Nigéria.
Méthodes: Une étude transversale a été menée auprès de 403 collégiens à Igboora, Nigeria, en utilisant un questionnaire auto-administré IOPQ-enfant traduit dans la langue locale.
Résultats: L'âge moyen des participants à l'étude était de 12,4 (± 0,7) ans. L'impact de la santé bucco-dentaire sur leurs scores de performance quotidienne variait de 0 à 66. Les scores supérieurs de l'IOPQ étaient significativement associés au besoin perçu de traitement dentaire ($p <0,001$), aux notes de satisfaction de l'état de santé bucco-dentaire ($p = 0,001$), aux notes de satisfaction de l'apparence de la dent ($p = 0,030$) et la douleur ($p <0,001$). L'utilisation d'échelles de fréquence ou de gravité séparées ou combinées présentait une validité et une fiabilité similaires et acceptables; cependant, l'échelle de fréquence seule avait la valeur alpha la plus élevée de Cronbach's alpha (0,876), tandis que l'utilisation des échelles de fréquence et de gravité était meilleure pour les corrélations inter-item (0,552-0,714).
Conclusion: La version traduite de la mesure d'IOPQ-enfant est un outil valide et applicable dans une communauté rurale. L'utilisation de l'échelle de fréquence ou de gravité de cette version d'IOPQ-enfant est valide, inter-culturellement adaptable et recommandée.

Mots-clés: *Enfant, communauté, IOPQ-enfant, qualité de vie, fiabilité, rural, validité*

Introduction

The Child–OIDP is one of the most commonly used Oral Health Related Quality of life ($OHRQ_oL$) measures for children world-wide [1-9]. This measure assesses the self-perceived oral health status of children and how it impacts on their daily performances. It is a useful tool in the planning of oral health programmes as well as in the monitoring and evaluation of such programmes [4]. $OHRQ_oL$ measures are also used to complement normative

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needs assessment as they provide the advantage of taking into consideration the individual's views of personal oral health needs and how it affects daily activities. In addition, they take into cognizance the social, psychological and the functional aspects of the effect of oral health [4]. The Child–OIDP has the advantage of being short, easy to administer and measures behavioral impacts on the quality of life. The original version of the Child–OIDP was developed in English and validated among Thai children [10]. Since then, it has been validated in several countries and found applicable in these countries, assessing the self-perceived needs of children and the impacts of oral health on their quality of life [1-3,5-15]. Nonetheless, the Child–OIDP has not been validated among children in resource challenged rural regions of developing countries like Nigeria where children have been noted to have poor oral hygiene and live with high unmet dental needs [16]. Promotion of oral health among children in these communities is therefore of paramount interest, which will only be meaningful if the impact of their oral health on daily activities is assessed using measures such as Child–OIDP along with normative evaluation needed in planning and evaluation of such programmes.

Utilization of the Child–OIDP in such communities will require cross adaptation of the measure since rural communities in Nigeria are in no small way influenced by the prevailing cultural norms and values. Therefore, introduction of a new instrument developed from an environment with a different cultural lifestyle as well as language will necessitate cross-cultural adaptation of that instrument [17]. As such, it is essential to validate this measure, determine its applicability in terms of its reliability and validity before utilization.

Furthermore, the peculiarity of this region as regards resource constrain and lack of personnel requires consideration of the self-administered version of this questionnaire as well as evaluation of the individual frequency and severity scale along with the combined use of these scales. If found applicable, the sole use of the individual scales of the Child–OIDP will further lessen the cost of its administration. The aim of this study, therefore, was to determine the applicability of the Child–OIDP questionnaire in a Yoruba speaking rural Nigerian community.

Materials and methods

The study, a cross sectional survey, was conducted between September and December 2014 in Igboora, Southwestern Nigeria. Igboora is a rural community, within the Ibarapa Central Local Government Area (LGA) of Oyo State, Nigeria. The study participants were 403 first year junior secondary school students (7^{th} grade equivalent) aged 10 to 13 years attending three public and three private schools that were selected using systematic random sampling technique from the lists of schools in the town. Students aged 10 to 13 years were recruited because they are young adolescents for whom the original version of the child-OIDP index was developed and validated [10]. A minimum sample size of 384 students was estimated to be adequate to power the study using the Kish-Leslie formula for cross-sectional studies [18] with a prevalence of 50%, a precision (d) of 5% and confidence interval of 95%. After selecting the schools, using systematic random sampling technique, all the students in the selected schools in the first year of junior secondary who were aged between 10 and 13 years were then approached for the study.

The study was approved by the Oyo State Ethics Review Board. Permission and approval for the study was also obtained from the Local Inspectorate of Education of the Ibarapa Central LGA and the head teachers of the various schools involved in the study. Negative consent was sought from parents of the participating students and positive consent obtained from each student before participation in the study. Only students who understood Yoruba language, could read and write it and who consented to participate in the study were recruited. Excluded from the study were: students with language barrier; students whose oral examinations might be difficult such as those who might not open their mouths properly for a complete oral examination e.g. due to temporomandibular joint ankylosis; or those with mental disability.

Data collection

The students had intra oral examination to determine their dental needs and completed the questionnaire under supervision in their various classes. Two dentists blinded to the aim of the study supervised the filling of the questionnaires. The principal of each school allocated a teacher to each participating class to assist with the organization of the study. The students with oral complaints were referred appropriately for treatment.

Instrument of measure and its cross-cultural adaptation

Data were collected using self-administered translated Yoruba Child–OIDP questionnaires. The self-administration of the Child–OIDP has been found comparable with the original interviewer

administered version [19,20]. For this study, the original English version of the Child–OIDP, which consists of questions on the impact of oral health on eight daily performances within the preceding three months, was used. The daily performances were: difficulty in eating and enjoying food, speaking and pronouncing words, cleaning teeth, sleeping and relaxing, emotional stability, smiling and showing teeth, studying and social contacts. The Child–OIDP was quantified on a response frequency scale and severity scale graded from "0 to 3". Each performance score was calculated by multiplying the frequency score with the severity score and a total score generated by the sum of the eight performance scores, with a minimum score of 0 X 0 X 8 = 0 and a maximum of 3 X 3 x 8 = 72. A standardized score was obtained for each participant by dividing this calculated total score by 72 and multiplying it by 100 to give a percentage score that ranged from 0 to 100. A total frequency score and severity score for each performance was also calculated by additive method to determine and compare the reliability of each of these components of the Child–OIDP scale if used singly.

Two experts well versed in English and Yoruba languages translated this English version of the Child–OIDP into Yoruba language. A different dentist who did not have any understanding of the objectives of the study then back translated the Yoruba questionnaire into English language. The translating team modified minor changes found accordingly. A pilot survey was conducted among 20 students who did not participate in the final study; discussion was held with them to ascertain the face validity and the feasibility of self-administration of the questionnaire without employing picture aids that was used in the first validation of the instrument among Thai children [10]. The face validity evaluates if the instrument of measure is actually assessing what it sets out to measure. The content validity on the other hand determines the extent to which the instrument or tool is addressing the subject of concern by a team of professionals. A team of dentists working in the community and community health assistants determined the content validity of the questionnaire.

Additional questions included in this questionnaire were on the satisfaction ratings of oral health, which asked if the children were satisfied with the present condition of their teeth and on satisfaction ratings of teeth appearance, which asked if the children were satisfied with the present appearance of their teeth; both with responses on a Likert scale ranging from "very satisfied to very dissatisfied". Other information sought included: presence or absence of pain and perceived need for treatment assessed by asking the children "Do you need dental treatment?" and the response options were "yes," "no" or "don't know". These questions evaluated the subjective ratings of oral health and since no gold standards existed for assessing the criterion validity of quality of life measures, these questions were used as "proxy" to determine the construct validity of the questionnaire.

The discriminate validity is the ability of an instrument to distinguish between those with oral conditions or unmet dental needs and those without such conditions. This was determined by the association between dental needs and Child–OIDP scores. Dental needs were assessed as present or absent, evaluated by intraoral examination conducted by a trained and calibrated dentist who examined each participant's mouth according to the basic oral health survey methods. Examination was done with the pupil seated upright on a chair and natural lighting served as the source of illumination. Unmet dental need was recorded when there was presence of untreated dental caries, untreated fractured teeth, periodontal disease, oral ulcer and malocclusion, which was assessed with the index of orthodontic treatment need. Those without these oral conditions or who required oral instruction and motivation only were considered as not having dental needs. The reliability of the questionnaire was determined using the test retest reliability of randomly selected students reassessed a week after the initial administration of the questionnaire. The internal consistency and corrected inter item correlation of this questionnaire were also evaluated.

Data management and analysis

The reliability of the Child–OIDP was analyzed using the Cronbach's alpha coefficient, intra class coefficient, item total and inter-item correlation. The test retest reliability was assessed using Kappa statistics. Construct validity was evaluated by testing for the association between the OIDP scores and the perceived need for treatment, pain and satisfaction ratings of oral health using Mann Whitney statistics. For this purpose; the satisfaction ratings of oral health was dichotomized; with "very dissatisfied", "dissatisfied" and "neither dissatisfied nor satisfied" in a group and "satisfied" and "very satisfied" in another group.

Results

In the study, 410 students were approached for recruitment and 403 consented to participate in the

study i.e. a response rate of 98.3%. The mean age of the study participants was 12.4 (Standard Deviation = 0.70) years and 207 (51.4%) were females. The majority 385 (95.5%) was of the Yoruba ethnic group, the predominant ethnic group in the community; 14 (3.5%) were Igbo and 4 (1.0%) were of Hausa extraction but all spoke the Yoruba language.

A total of 167 (41.4%) had at least an impact of oral health on their quality of life in the preceding three months of which 79 (38.2%) were females. The most prevalent activity affected was eating and enjoying food (Table 1). Ninety eight (24.3%) participants had an unmet dental need.

Table 1: Prevalence of oral impact on daily performances of the respondents

Child–OIDP inventory	Number	%
Eating and enjoying food	149	37.0
Speaking and pronouncing words	112	27.8
Cleaning teeth	136	33.7
Smiling	73	18.1
Relaxing /sleeping	104	25.8
Emotional stability	78	19.4
Doing school work	67	16.6
Social contact	82	20.3
At least an impact	167	41.4

Face and content validity

The face validity was good as established during the pilot survey and the main study. In addition there were no missing values for any of the questions despite the questionnaire being self-administered. The content validity as determined by the dentists and the community health assistants showed that each of the translated questions was appropriate and actually measured what it set out to assess.

Construct validity

The total Child–OIDP scores correlated significantly with the satisfaction ratings of oral health condition and teeth appearance and pain. Children with pain had higher OIDP scores than those without pain ($p < 0.001$). Similarly, those who were very dissatisfied, dissatisfied, or neither dissatisfied nor satisfied with the condition of their teeth had higher OIDP scores ($p < 0.001$). In addition, a higher proportion of children who perceived a need for dental treatment reported an impact on their daily performances compared with those who did not perceive a need for treatment, $p < 0.001$ (Table 2). The frequency and severity scales analyzed singly also similarly correlated significantly with the satisfaction ratings of oral health condition and teeth appearance, and pain in the expected direction ($p < 0.005$).

Discriminate validity

The combined scale was able to distinguish between those with unmet normative dental needs and those without dental needs. Those with unmet dental needs had more impacts on daily activities compared with those with no dental needs $p < 0.001$. The use of the frequency scale and severity scale, singly, also showed this significant relationship $p < 0.001$.

Reliability

Frequency scale

Assessing the corrected inter-item correlation of only the frequency scale gave a Cronbach's alpha value of 0.876. The inter-item correlations matrix ranged from 0.293 (eating and enjoying food) to 0.592 (studying and emotional stability). The corrected inter-item correlation ranged from 0.584 (eating and

Table 2: Relationships between satisfaction ratings of oral health, perceived need for treatment, pain, unmet dental need and standardized Child–OIDP scores

Variable	Categories	OIDP Scores			
		Median	U**	Z	p value
Satisfaction with teeth appearance	Satisfied	0.0	18446.0	-2.16	0.031*
	Dissatisfied	3.0			
Satisfaction with present condition of teeth	Satisfied	0.0	17329.5	-3.44	0.001*
	Dissatisfied	2.5			
Presence of pain	No	0.0	6266.0	-6.98	0.001*
	Yes	2.0			
Perceived need for dental treatment	No	0.0	13928.0	-4.83	< 0.001*
	Yes	2.3			
Unmet dental needs	No	0.0	10433.5	-5.27	<0.001*
	Yes	2.0			

* – Statistically significant, ** – Mann-Whitney U Test

enjoying food) to 0.684 (studying). The intra class coefficient was 0.875.

Severity scale

Assessment of reliability of the sole use of the severity scale gave a Cronbach's alpha value of 0.841. The inter-item correlations matrix ranged from 0.270 (sleeping and speaking) to 0.574 (contact and smiling). The corrected inter-item correlation ranged from 0.497 (sleeping) to 0.626 (eating). Intra class coefficient for the severity scale was 0.830.

Table 3: Correlations between items in the combined frequency and severity scales

Child–OIDP inventory	Correlation between items	p value
Eating and enjoying food	0.603	<0.001
Speaking and pronouncing words	0.574	<0.001
Cleaning teeth	0.578	<0.001
Smiling	0.399	<0.001
Relaxing /sleeping	0.583	<0.001
Emotional stability	0.456	<0.001
Doing school work	0.428	<0.001
Social contact	0.482	<0.001

Combined use of frequency and severity Child–OIDP scales

The standardized Child–OIDP score gave a Cronbach's alpha value of 0.864 and the items correlated significantly to the others (Table 3). The inter-item correlations matrix ranged from 0.276 (contact and cleaning) to 0.714 (sleeping and emotional stability). The corrected inter-item correlation (Table 4) ranged from 0.552 (speaking) to 0.714 (emotional stability). The intra class coefficient was 0.854. The test retest reliability gave a kappa score of 0.81.

None of the deleted Child–OIDP items generated a Cronbach's alpha score greater than the standardized Cronbach's alpha score when the frequency, severity and both scales together were considered (Table 4). This showed that each item was important for the questionnaire. Likewise the inter item correlation scores showed homogeneity of the items when any of the scales was used singly or in combination.

Discussion

The present study is the first to determine the applicability of the Child–OIDP in a Yoruba speaking as well as rural community. In addition, this study evaluated the use of self-administered version of the Child–OIDP in a population-based sample in a resource challenged setting. This is notable as this version of the Child–OIDP helped in cost reduction since there was no need for interviewers and time was also saved. The results from this study showed that the Yoruba version of the Child–OIDP has acceptable psychometric properties with good validity and reliability. The face and content validity of the Child–OIDP was found acceptable. The construct validity of the Child–OIDP showed that children with oral impacts on their daily activities more often had pain and were less satisfied with their oral health condition or appearance of their teeth and perceived a need or treatment. This has been documented previously [9] showing that these measures are significantly related. The ability of the Yoruba version of Child–OIDP to be able to distinguish between those with normative dental

Table 4: Corrected inter-item correlations of the Child–OIDP inventory

Child–OIDP inventory	Corrected item–total correlation			Alpha if item deleted		
	FS	F scale	S scale	FS	F scale	S scale
Eating and enjoying food	0.627	0.584	0.626	0.834	0.865	0.804
Speaking and pronouncing	0.552	0.642	0.540	0.843	0.858	0.818
Cleaning teeth	0.568	0.592	0.526	0.840	0.864	0.819
Smiling	0.659	0.655	0.497	0.835	0.858	0.821
Relaxing /sleeping	0.610	0.673	0.572	0.835	0.855	0.812
Emotional stability	0.714	0.666	0.595	0.822	0.856	0.809
Doing school work	0.582	0.684	0.597	0.842	0.854	0.815
Social contact	0.566	0.588	0.605	0.840	0.864	0.808
Standardized Cronbach's alpha				0.864	0.876	0.841

FS – Frequency and severity scale multiplication, F – Frequency scale only calculated by additive method, S – Severity scale only

needs and those with no dental needs was also established, providing added value for this instrument. The discriminative property of Child–OIDP being able to distinguish between those with clinical oral conditions has been documented by others [7,14].

The outcome of evaluating the reliability of the combined frequency and severity scales of the Child–OIDP showed that all the items in the index correlated significantly, likewise the internal consistency gave a Cronbach's alpha score of 0.86, which is above the recommended value of 0.7. This Cronbach's alpha value was comparable to, although slightly higher than, those reported by other authors [7,9,15]. Deleting any of the component items did not result in lowering the Cronbach's alpha value in the present study, thus reflecting the importance of all the items in the instrument.

The use of either the frequency scale or the severity scale individually yielded a Cronbach's alpha value of 0.88 and 0.84 respectively, which is also above the recommended 0.7. Similarly, deletion of any of the items in the severity or frequency scales when used singly did not result in lowering of the Cronbach's alpha value. This therefore shows that either the frequency or severity scale may be utilized to assess the oral health related quality of life of children, with the frequency scale appearing to be a better instrument based on the findings of this study. This was similarly observed in adults with the frequency component of the OIDP measure [17].

This finding will also be of enormous benefit in similar environments where resources for oral health care are limited coupled with the need to plan an effective intervention, which will require assessment of oral health and how it impacts on daily activities. The use of the single scale Child–OIDP will go a long way in assisting oral health researchers in this environment in terms of cost and time saved, which will translate to less financial burden and fewer personnel required. The corrected inter-item correlation ranged from 0.28 to 0.5, which is above the recommended 0.2. The Yoruba version of the Child–OIDP is a stable instrument, evidenced by the good test-retest reliability.

The results revealed that 41.4% of the respondents in this study had at least an impact of oral health on their daily activities as similarly reported by Yusuf et al., [9], however, the values here are lower than reported in Albania [7] and Tanzania [21]. The differences in the prevalence of impact on oral health related quality of life has been attributed to variations in and distribution of diseases across the globe as well as cultural variations [9]. Eating and enjoying food was the most often reported activity impacted upon by oral health status. Castro *et al.,*[3] have similarly reported this. The value associated with eating, as a major function of the mouth and teeth, is possibly responsible for this finding.

The Yoruba version of the Child-OIDP can be utilized in regions of the world, such as in West Africa and where there are immigrants with roots in the region, where Yoruba is a language spoken by the inhabitants. The strength of the present study included selection of a representative sample using a probability sampling technique, in addition to both private and public schools within the community being sampled, thus involving the two major school types that exist in the country.

In conclusion, the translated version of the Child–OIDP measure is a valid and applicable tool in a Yoruba speaking rural community. Use of either the frequency or severity scale of this version of Child–OIDP is valid, cross-culturally adaptable and recommended**.**

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Physical characteristics, body composition and physical performance profile of male youth football players

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Abstract
Background: Physical fitness is an important determinant of injury and team success in football (soccer). Data on physical characteristics, body composition and physical performance in male youth players are sparse. This study aimed at presenting reference values for selected physical characteristics, body composition and physical performance in male youth football players in the Nigerian setting.
Methods: A cohort of 706 male youth football league players was assessed at a pre-participation screening programme. Selected physical characteristics, body composition and physical performance measures were evaluated in all players using standardised protocols.
Results: Reference values for physical characteristics, body composition and physical performance measures were reported. Players' age, height and BMI ranges were 14 – 19 years, 1.5 – 1.9 m and 15.8 – 26.0 kg/m^2 respectively. Older players exhibited higher median scores in explosive leg strength (39.0cm vs. 34.0cm) and balance (3.0s vs. 2.1s) but lower median score in core stability (30.6s vs. 36.3s). Significant differences were found in the BMI and physical characteristics of players in the different positions wherein goalkeepers demonstrated significantly higher values compared to outfield players in other positions ($p < 0.05$). However, players were mostly homogeneous in body composition and physical performance in the different positions ($p > 0.05$) except for core stability ($p = 0.044$).
Conclusion: Reference data for physical characteristics, body composition and physical performance have been derived for male youth football players in Nigeria. The data presented may serve as a reference guide for youth football coaches, sports medicine clinicians, scientists and other stakeholders in this region.

Keywords: Soccer, *Pre-participation Screening, Injury Prevention, Physical Fitness, Return to Play*

Résumé
Contexte: L'aptitude physique est un déterminant important de blessure et de succès pour l'équipe au football. Les données sur les caractéristiques physiques, la composition corporelle et la performance physique chez les jeunes joueurs sont défaillantes. Cette étude visait à présenter des valeurs de référence pour certaines caractéristiques physiques, la composition corporelle et la performance physique parmi des jeunes joueurs de football dans le cadre nigérian.
Méthodes: Une cohorte de 706jeunes joueurs en ligue de football a été évaluée lors d'un programme de dépistage pré-participation. Les caractéristiques physiques sélectionnées, la composition corporelle et les mesures de performance physique ont été évaluées chez tous les joueurs en utilisant des protocoles standardisés.
Résultats: Les valeurs de référence pour les caractéristiques physiques, la composition corporelle et les mesures de performance physique ont été reportées. Les niveaux d'âge, de taille et d'IMC des joueurs étaient respectivement de 14 à 19 ans, 1,5 à 1,9 m et 15,8 à 26,0 kg/m^2. Les joueurs plus âgés ont affiché des scores médians plus élevés en vigueur de pied explosive (39.0cm contre 34.0cm) et équilibre (3.0s vs. 2.1s), mais un score médian inférieur dans la stabilité majeure (30.6s contre 36.3s). Des différences significatives ont été trouvées dans l'IMC et les caractéristiques physiques des joueurs dans les différentes positions d'où les gardiens de but ont démontré des valeurs significativement plus élevées par rapport aux joueursextérieurs dans d'autres positions ($p < 0,05$). Cependant, les joueurs étaient principalement homogènes dans la composition corporelle et la performance physique dans les différentes positions ($p > 0,05$), à l'exception de la stabilité majeure ($p = 0,044$).
Conclusion: Des données de référence pour les caractéristiques physiques, la composition corporelle et la performance physique ont été obtenues pour les jeunes joueurs de football au Nigeria. Les données présentées peuvent servir de guide de référence pour les entraîneurs de football des jeunes, les cliniciens de médecine du sport, les scientifiques et les autres intervenants dans cette région.

Mots-clés: *Football, dépistage pré-participation, prévention des blessures, condition physique, retour au jeu*

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Introduction

Inadequate physical fitness is an intrinsic risk factor for sports injury in young people and this has been well established [1-3]. Physical fitness has also been shown to be a predictor of team success in elite football (soccer) [4]. Baseline physical fitness assessment including body composition and physical performance evaluation in football players is an essential aspect of sports medicine and science as this provides essential data that can be used by sport medicine clinicians, scientists and coaches to enhance players' health and performance.

Studies on youth and adult football players have documented fitness profiles in many parts of Europe and America and data from these studies suggest that players vary widely in body composition and physical characteristics [5-10]. This indicates that there may be disparities in the requirements between different playing positions, levels of play and age but whether this is reflected by differences in physical fitness in male youth football is hitherto not clear.

Data on physical characteristics and fitness profiling in male youth players are generally limited and such data have not been documented at any level of football in Africa. Thus, this study was aimed at providing selected physical characteristics, body composition and physical performance reference data for semi-professional male youth football players in Nigeria.

Methods

Study design and participants

The study utilized a cross-sectional design and involved all 706 male youth football players - 416 players in Division I (20 teams) and 290 players in Division II (16 teams) of the Lagos Junior League (LJL) registered for the 2012/2013 season. The LJL is a youth football league incorporated in 2010 by the Lagos State government. The league involves youth football clubs from the 20 Local Government Areas and 37 Local Council Development Areas in Lagos State with players from the various states across Nigeria. It runs yearly for a period of 6 months (September to February). The study was conducted at the LJL's secretariat located at the In-door Sports Hall of the Teslim Balogun Stadium, Surulere, Lagos, Nigeria.

Study procedure

A pilot study was conducted on two Division III teams (41 players) of the LJL to test all the instruments and procedures used for this study. This enabled the lead author (physiotherapist) and research assistants (eight physiotherapy students) to get acquainted with the data collection procedures. Necessary modifications arising from the pilot tests were made prior to final assessment and fitness testing. Teams/players who participated in the pilot study were not involved in the main study.

All registered players were invited to a pre-season fitness-screening programme prior to the commencement of the 2012/2013-league season. The fitness assessment for players was team-based with the league administrators officially inviting all teams in the two divisions. Team coaches (head coach and assistant) or/and sports officers were on ground to present registered players for assessment. Ethical approval for the study was obtained from the Health Research and Ethics Committee of the Lagos University Teaching Hospital, Idi-Araba, Lagos (ADM/DCST/HREC/487) prior to its commencement. Approval to carry out the study was also obtained from the LJL for official access to the various football clubs/teams. Informed consent was sought from individual players after the purpose and procedure of assessment had been carefully explained to them in a team setting. A clear indication of full comprehension and acceptance to participate was received from all the players.

Players from each team were made to undergo a face identification screening process by the league officials to confirm their registration status before fitness testing. A pre-assessment education and demonstration session was held for each participating team in order for players to understand the protocols for assessment after which players had their names written and heights measured and recorded in a pre-designed fitness data form. Height was measured using a non-elastic measuring tape, glued to a vertical wall, with the player standing barefooted. Each player was afterwards asked to proceed on the fitness testing protocols with their data forms. Each player went through four assessment stations (Figure 1). Twelve players were asked to quit after the assessment of their body composition in station 1 due to lower extremity injuries that precluded physical performance testing. All tests and measurements were performed over the course of three weeks (10 testing sessions) with an average of four teams per session.

Body composition assessment

Players' body composition parameters were measured by bioelectrical impedance analysis using the Omron Body Composition Monitor in station 1. The monitor assessed players' weight, BMI, body-fat percentage and skeletal muscle percentage.

Physical performance assessment

The performance-related fitness of players was assessed in stations 2 – 4 using validated and cost-effective testing protocols. Players were asked to perform 3 different football-specific fitness activities - standing stork (station 2), prone hold (station 3) and vertical jump height (station 4) for balance, core stability and explosive leg strength assessments respectively according to standardized protocols [11, 12]. Three trials of each assessment, except the prone hold (single trial), were performed and the mean of the trials was determined and used for analysis. To improve reliability, one practice trial prior to each test was permitted. The procedures for assessments are described below:

Balance assessment

The standing stork test was used to assess players' balance performance in a static position. The player stood comfortably barefooted on both feet with his hands on the hips. The player was asked to lift the non-dominant leg and place the sole of the non-dominant foot against the side of the kneecap of the dominant leg. The assessor then gave the command "go", started the stopwatch and the player raised the heel of the dominant foot to stand on his toes. The player was instructed to hold this position for as long as possible. The assessor stopped the stopwatch when the player's heel touched the ground or the non-dominant foot moved away from the knee of the dominant leg. The entire procedure was then repeated. The time taken to the nearest 0.1s for each player to trip off this posture described above was noted for 3 trials. The average of the trials was then documented [12].

Core stability assessment

The prone hold test was used to measure the core stability of players. Players were required to maintain a prone hold (commonly known as the plank) position for as long as possible. Players were monitored during the trial to ensure that the right posture was maintained. A linear horizontal position was desired throughout the test for all players. To ensure consistency, the same research assistant conducted this procedure for all players. The duration for which the required position was held was recorded as the test score in seconds [11].

Explosive leg strength assessment

This was done using players' vertical jump height. The following resources were used: a smooth wall, pieces of wide white papers (23 by 28 inches), a tape measure and an inkpad. The fingertip (middle finger) of the dominant hand (identified through verbal inquiry) of the player was marked with ink and the player was instructed to stand with the side next to the wall, keeping both feet on a marked ground and then asked to reach up as high as possible with one hand thereby marking the wall with the tip of the middle finger (M1). Each player was then asked to position his feet approximately shoulder width apart on the marked jumping spot and assume a starting position before attempting the jump. Steps or run-ups into the jumping action were not permitted and the landing had to occur on the marked spot. Participants were instructed to jump as high as possible and mark the wall with the ink on their fingertip (M2). The distance from M1 to M2 was then measured. Subjects performed 3 jump trials in succession, with approximately 15 to 30s recovery period between jumps. Jumps were considered void if the participant a) went into extreme (>45 degrees) hip flexion during the flight time of a jump; b) flexed the knees to the extent that the heel nearly touched the gluteal muscles; and/or c) did not land centrally on the marked ground spot. The average of the 3 trials was recorded to the nearest 0.1 cm for the jump height, which was taken as the explosive leg strength of players [11].

Data analysis

Descriptive statistics of frequencies, percentages, percentiles, median (for data with high variability) and means (±SD) were used to present data as appropriate. One-way ANOVA was used to explore the differences among players' positions. Level of statistical significance was set at an alpha of 0.05.

Results

The overall mean age of players was 17.67 ± 1.11 years (range = 14 – 19 years). Players' height and BMI ranged from 1.5 – 1.9m and 15.8 – 26.0kg/m^2 respectively. The descriptive characteristics of the players are presented in Table 1.

The mean (± SD), median (25th and 75th percentiles) and range of the physical characteristics and fitness profile of players by age categories and overall values are presented in Table 2. Older players (17 – 19 years) exhibited higher median scores in explosive leg strength (39.0cm vs 34.0cm) and balance (3.0s vs 2.1s) but lower median score in core stability (30.6s vs 35.8s) than younger players (14 – 16 years) (Table 2).

Table 3 presents the physical performance scores of the players from the 5th through the 95th percentiles by age group. Table 4 shows the comparisons of physical characteristics, body

Table 1: Descriptive characteristics of players

	Division I (n = 416)	Range	Division II (n = 290)	Range	Overall (N = 706)	Range
Physical characteristics (Mean ± SD)						
Age (year)	17.6 ± 1.1	14.0 – 19.0	17.7 ± 1.2	14.0 – 19.0	17.7 ± 1.1	14 – 19
Height (m)	1.72 ± 0.06	1.50 – 1.92	1.71 ± 0.06	1.51 – 1.88	1.72 ± 0.06	1.50–1.92
Weight (kg)	63.5 ± 6.78	43.60 – 93.30	62.65 ± 6.22	43.90 – 81.60	63.16 ± 6.57	44 – 93
Playing position **[n (%)]**						
Goalkeepers	38 (9.3)		25 (8.7)		63 (9.0)	
Defenders	126 (30.9)		91 (31.5)		217 (31.1)	
Midfielders	136 (33.3)		97 (33.6)		233 (33.4)	
Strikers	108 (26.5)		76 (26.3)		184 (26.4)	
Total	408		289		*697	
Limb dominance **[n (%)]**						
Right lower limb	272 (67.3)		189 (66.3)		461 (66.9)	
Left lower limb	61 (15.1)		34 (11.9)		95 (13.8)	
Ambidextrous	71 (17.6)		62 (21.8)		133 (19.3)	
Total	404		285		**689	

*Missing data for 9 players
**Missing data for 17 players

Table 2: Physical characteristics, body composition and physical performance of players by age group

Physical fitness parameters	14-16 years (n = 106)	17-19 years (n = 600)	Overall (N = 706)*	Range
Physical characteristics				
Height (m)	1.70 ± 0.06	1.72 ± 0.07	1.72 ± 0.06	1.50 – 1.90
Weight (kg)	60.99 ± 7.36	63.54 ±6.38	63.16 ± 6.57	43.60– 93.30
Body composition				
BMI (kg/m^2)	20.99 ± 1.77	21.49 ± 1.59	21.43 ± 1.62	15.8 – 26.0
Body fat (%)	12.56 ± 3.69	13.25 ± 3.42	13.15 ± 3.46	5.00 – 27.30
Skeletal muscle (%)	43.42 ± 2.56	44.54 ± 3.05	44.38 ± 2.97	11.6 – 56.0
Physical performance				
Explosive leg strength (cm)	34.0 (18.3, 46.8)	39.0 (21.0,48.0)	38.0 (21.0, 48.0)	7.0 – 70.0
Balance (s)	2.1 (1.5, 4.5)	3.0 (2.0, 4.8)	2.9 (1.8, 4.6)	0.7 – 48. 3
Core stability (s)	35.8 (26.0, 54.1)	30.6 (20.0, 47.5)	31.7 (20.7, 48.5)	1.1 – 158.3

Values are mean ± SD for physical characteristics, body composition and median (25th, 75th percentiles) for physical performance
**N = 694 for physical performance testing; BMI – Body Mass Index*

composition and physical performance of players with regards to playing position. Significant differences were found in the physical characteristics and BMI of players in the different positions ($p < 0.05$). Goalkeepers were significantly taller and heavier than out-field players ($p < 0.001$). Midfielders were the shortest and lightest ($p < 0.001$). No significant difference existed in the body fat ($p = 0.205$), skeletal muscle composition ($p = 0.294$) and the physical performance parameters ($p > 0.05$) of players in the different positions except for players' core stability ($p = 0.044$). Defenders recorded the highest core stability measure among the players ($p = 0.044$), with post-hoc analysis indicating that the defenders had significantly greater stability than the strikers.

Table 3: Percentile Norms for Physical Performance of Players by Age Group

Percentile	14 – 16 Years			17 – 19 Years		
	Explosive leg Strength (cm)	Balance (s)	Core Stability (s)	Explosive leg Strength (cm)	Balance (s)	Core Stability (s)
5th	13.1	1.1	13.7	15.0	1.1	10.2
10th	15.0	1.3	17.4	16.3	1.2	12.0
25th	18.3	1.5	26.0	21.0	2.0	20.0
50th	34.0	2.1	35.8	38.0	3.0	30.6
75th	46.8	4.5	54.1	48.0	4.8	47.5
90th	52.9	6.2	69.5	54.0	7.2	64.1
95th	55.0	8.1	79.4	59.0	9.3	80.1

Table 4: Physical Characteristics, Body Composition and Physical Performance of Players by Playing Positions

Physical Fitness Parameters	Goalkeeper (n = 63)	Defender (n = 217)	Midfielder (n = 230)	Striker (n = 184)	F-Value	P-Value
Physical Characteristics						
Height (m)	$1.76 \pm 0.06^{D,M,S}$	1.72 ± 0.06^{M}	1.70 ± 0.06	1.72 ± 0.06^{M}	16.36	<0.001*
Weight (kg)	$65.92 \pm 6.27^{D,M,S}$	64.07 ± 6.31^{M}	61.29 ± 5.67	63.57 ± 7.38^{M}	12.19	<0.001*
Body Composition						
BMI (kg/m^2)	21.37 ± 1.56	21.58 ± 1.60^{M}	21.19 ± 1.59	21.52 ± 1.66^{M}	2.53	0.049*
Body Fat (%)	12.60 ± 3.23	13.20 ± 3.78	12.95 ± 3.25	13.54 ± 3.41	1.53	0.205
Body Muscle (%)	44.40 ± 2.16	44.13 ± 3.58	44.67 ± 2.72	44.30 ± 2.75	1.24	0.294
Physical Performance						
Explosive Leg Strength (cm)	36.53 ± 14.62	34.82 ± 15.03	35.56 ± 14.68	36.30 ± 14.93	0.42	0.737
Balance (s)	3.54 ± 2.07	3.86 ± 3.34	3.90 ± 3.51	3.63 ± 4.03	0.34	0.797
Core Stability (s)	38.75 ± 21.90	39.28 ± 24.79^{S}	35.68 ± 21.57	33.50 ± 20.54	2.56	0.044*

**Significant at $p < 0.05$*
Values are mean ± SD
G denotes significant post-hoc differences when compared to Goalkeepers; D denotes significant post-hoc differences when compared to Defenders; M denotes significant post-hoc differences when compared to Midfielders; S denotes significant post-hoc differences when compared to Striker

Discussion

This study provides data for the physical characteristics and fitness profile of male youth football players in a Nigeria setting; the first time, to our knowledge, that any such data will be reported at any level of football in Nigeria. Monitoring of football-specific physical performance of players is important as it relates to levels of strength, core stability and balance which are all associated with injury risk in football and influences overall team success.

Values found in the present study for height, body weight and BMI are comparable with values found in similarly aged players [6, 13, 14]. The average percentage body fat for this cohort of male youth Nigerian football players was 13.2%. This finding is similar to the value reported by Matkovic *et al* [6] among Croatian elite players (14.9%) and Silvestre *et al.* [13] in a National Division I youth team (13.9%) Players were mostly homogeneous in their body composition parameters and physical performance. However, goalkeepers had significantly higher values in height and weight than players in other playing positions; which is consistent with findings from other studies [6, 15]. Defenders were the second heaviest and midfielders were the lightest, which again is congruent with findings from other studies [6, 16]. This characteristic of heavy body mass in defenders and lightness in midfielders could be considered an advantage in defensive actions and swiftly linking the defence to the attack for defenders and midfielders respectively.

Studies specifically relating to physical performance indices in male youth football are

sparse. Hence comparison with other studies especially recent studies from other parts of the world for similar age range is limited to data for explosive leg strength (vertical jump height) as presently available in the literature for male football. Values recorded for explosive leg strength is lower than those reported for elite adult players [5, 16]. This is likely because of the differences in the levels of play as the study population involved in the present study were semi-professional youth football players.

Physical performance values of players at the 5th through 95th percentiles by age group were generated from documented data to derive a normative range for players. Normative data for physical performance are essential to allow sports medicine clinicians to interpret how injured players are functioning relative to their age-matched healthy peers; which is an important element in monitoring treatment progression during rehabilitation of lower extremity injuries and return to play decisions. This may also serve as reference data for youth football coaches and managers in training progression, screening and stratification of players during selection trials. Furthermore, the results of this study provide a standard for evaluating the physical performance level of a player or the progression of rehabilitation within the context of normal age-adjusted values and can be used to assign a percentile rank to a given player's score within his age group. For example, an 18-year old player who reports an explosive leg strength value of 21cm has a percentile ranking of 25% relative to other players between the ages of 17 and 19 years.

A limitation of this study is that the reference data presented is specific to youth (under 20 years) football players in Nigerian; thus, its application in other countries and settings or levels of football participation is limited and should be with caution. Nevertheless, this study presents invaluable information on baseline fitness measures that would be generally relevant in advancing research relating to the health and physical performance of football players.

Conclusion

Normative data for physical characteristics, body composition and physical performance has been derived for male youth football players in Nigeria. The data presented may serve as a reference guide for youth football coaches, sports medicine clinicians, scientists and other stakeholders in this region and others with similar demographics.

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Honey and Vitamin E protect the developing cerebellum against alcohol-induced oxidative damage in rat

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Abstract
Background: Prenatal and postnatal exposure to ethanol induces oxidative stress by generation of free radicals. The protective effect of honey and vitamin E on alcohol-induced oxidative stress in the developing rat cerebellum was studied.
Method: Twenty five pregnant Wistar rats were divided into five groups. Group I animals served as the Controls and received distilled water, Group II received only alcohol, Group III received honey only, Group IV received honey with alcohol and Group V received Vitamin E with alcohol. Ten percent (10%) alcohol at a dose of 1.6 g/kg body weight, vitamin E at 500 mg/kg body weight and honey at 1.5 ml/kg body weight were administered orally in pre- and postnatal life. The pups were sacrificed on days 1, 7, 14, 21 and 28. Haematological, behavioural, oxidative stress, gross morphometric as well as histomorphometric evaluations were done.
Results: Results showed decreased cerebellar weights, alteration in behaviour, decreased percentage neutrophil and eosinophil numbers, increased white blood cell count, increased lipid peroxidation (LPO) and a decreased glutathione (GSH) levels in the alcohol-treated rats compared with the control group at $p<0.05$. Histologically, there was a thicker External granular layer (Egl) on postnatal day 14 which persisted after weaning and a decreased thickness of the Molecular layer (Ml) in the alcohol group at $p<0.05$. Co-treatment with honey and vitamin E improved the changes observed above.
Conclusion: From the study, honey and vitamin E appeared to ameliorate the effects of alcohol-induced oxidative stress and structural damage on the developing rat cerebellum. The antioxidant activities of honey and vitamin E were found to be similar.

Keywords*: Alcohol, honey, vitamin E, oxidative stress, cerebellum*

Résumé
Contexte: L'exposition prénatale et postnatale à l'éthanol induit un stress oxydatif par génération de radicaux libres. L'effet protecteur du miel et de la vitamine E sur le stress oxydatif induit par l'alcool dans le cerveleten développement de rat a été étudié.
Méthode: Vingt-cinq souris Wistar enceintes ont été divisés en cinq groupes. Les animaux du groupe I ont servi de contrôle et ont reçu de l'eau distillée, le groupe II a reçu uniquement de l'alcool, le groupe III a reçu du miel uniquement, le groupe IV a reçu du miel avec de l'alcool et le groupe V a reçu de la vitamine E avec de l'alcool. Dix pour cent (10%) d'alcool à une dose de 1,6 g / kg de poids corporel, de vitamine E à 500 mg / kg de poids corporel et de miel à 1,5 ml / kg de poids corporel ont été administrés par voie orale en vie prénatale et postnatale. Les souriceaux ont été sacrifiés aux jours 1, 7, 14, 21 et 28. Le stress hématologique, comportemental, oxydatif, les évaluations morphométriques grossières ainsi que les évaluations histomorphométriques ont été effectuées.
Résultats: Les résultats ont montré une diminution des poids cérébelleux, une altération du comportement, une diminution du pourcentagedes nombres de neutrophiles et d'éosinophiles, augmentation du nombre de globules blancs, augmentation de la peroxydation lipidique (LPO) et une diminution des taux de glutathion (GSH) chez les rats traités par alcool par rapport au groupe témoin à $p <0,05$. Histologiquement, il y avait une couche granulaire externe plus épaisse (Egl) le jour postnatal14 qui a persisté après le sevrage et une épaisseur réduite de la couche moléculaire (Ml) dans le groupe alcool à $p <0,05$. Le co-traitement avec le miel et la vitamine E a amélioré les changements observés ci-dessus.
Conclusion: A partir de l'étude, le miel et la vitamine E semblent améliorer les effets du stress oxydatif induit par l'alcool et des dommages structurels sur le cerveleten développement de rat. Les activités anti-oxydantes du miel et de la vitamine E se sont révélées similaires.

Mots-clés: *Alcool, miel, vitamine E, stress oxydatif, cervelet*

Introduction

Ethyl alcohol (ethanol) is one of the most widely consumed psychoactive substances all over the world. Its abuse and dependence remains among the greatest substance abuse problems worldwide and has also become one of the largest public health problems [1]. Ethanol is the principal type of alcohol found in alcoholic beverages and is produced by the

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fermentation of sugars by yeasts [2]. The risk of brain injury and related neurobehavioural deficits are some of the important consequences of chronic ethanol consumption and abuse [3]. Ethanol consumption has been reported to induce pro-inflammatory factors, resulting in the generation of additional reactive oxygen species (ROS) and increased cellular oxidative stress and consequent lipid peroxidation in the rat brain [4]. Oxidative stress has been implicated in a number of disease conditions including Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), cancer, aging, memory loss and depression [5].

The mechanisms underlying the cellular toxicity of ethanol is poorly understood, however studies have implied that oxidative stress could be a potential mechanism for ethanol-induced brain injury [6]. Alcohol has been reported to cross the blood-placenta barrier (BPB) as well as the blood-brain-barrier (BBB), resulting in lethality or congenital malformations in the embryo [7]. Other studies have shown that prenatal ethanol exposure interferes with the synaptogenesis phase of brain development, especially within the cerebellum and leads to various impairments in brain function [8].

The cerebellum, which develops from the rhombencephalon, lies in the posterior cranial fossa behind the cerebrum and is separated from the pons and medulla by the fourth ventricle. It coordinates complex motor activity, maintains balance and equilibrium, and has been reported to be highly susceptible to ethanol teratogenicity [9]. In the face of alcohol teratogenicity, supplementation with antioxidants can ameliorate ethanol-induced oxidative stress [10]. In this study, honey and vitamin E which are known to possess antioxidant activity were used as antioxidant supplements.

Honey is a natural liquid that is reported to contain at least 181 substances [11]. The composition of honey is rather variable and primarily depends on the floral source; however, certain external factors also play a role, such as seasonal and environmental factors and processing [12]. Honey is a supersaturated solution of sugars, of which fructose (38%) and glucose (31%) are the main contributors. A wide range of minor constituents are also present in honey, many of which are known to have antioxidant properties. These include phenolic acids and flavonoids [13], certain enzymes (glucoseoxidase, catalase), ascorbic acid, carotenoid-like substances, organic acids, Maillard reaction products, amino acids and proteins [14]. Honey consumption has been reported to ameliorate the defense mechanism against oxidative stress and mitigated free radical-mediated molecular destruction [15]. Furthermore, honey decreased the number of degenerated neuronal cells in the hippocampal CA1 region, a region that is known to be highly susceptible to oxidative insult [16].

Within the body, the primary role of vitamin E (a fat soluble vitamin) is to function as the major chain-breaking antioxidant in membranes [17]. Vitamin E also acts as a cell-membrane stabilizer, which is postulated by some researchers to be the primary mechanism for its prevention of muscle damage [18]. The vitamin possibly stabilizes the membrane by increasing the "orderliness of membrane lipid packaging. This effect allows for a tighter packing of the membrane and in turn greater stability to the cell especially in the face of oxidative stress [18]. This study therefore, highlights the morphological, behavioural, haematological and biochemical changes observed in the use of honey and Vitamin E in alcohol-induced oxidative stress in the developing rat cerebellum.

Materials and methods

Experimental animals

Twenty-five healthy adult female Wistar rats weighing between 140 and 180 g were obtained from the Animal house of the Faculty of Basic Medical Sciences, University of Ibadan. The rats were housed in plastic cages at room temperature with a 12 hours light/dark cycle, fed with pelleted chow obtained from Ladokun Feeds, Ibadan and drinking water provided *ad libitum.* Sawdust beddings were changed daily to maintain a hygienic environment. The animals were mated, vaginal smear test was conducted to confirm that mating occurred and the presence of vaginal plug indicated the possibility of pregnancy and was taken as the first day of conception.

Grouping of animals

The pregnant rats were divided into five groups:

Group I: received distilled water and served as the control group

Group II: received 1.6 g/kg body weight dose of 10% ethanol orally.

Group III: received 1.5 ml/kg body weight of honey orally.

Group IV: received 1.6 g/kg body weight of 10% ethanol and 1.5 ml/kg body weight of honey.

Group V: received 1.6 g/kg body weight of 10% ethanol and 500 mg/kg body weight of vitamin E.

Group VI: received 500 mg/kg body weight of vitamin E.

The drugs were administered orally with an intra-gastric gavage.

Preparation and administration of honey

The honey administered, Bee forever honey was purchased at Kuto market in Abeokuta, Ogun State, South-West Nigeria. The dose of honey was calculated as 1.5 ml/kg body weight and administered orally in pre and postnatal life. The dose of honey used was based on the works of Abdulmajeed *et al.* [19].

Preparation and administration of Vitamin E

Each capsule contains 100 mg of DL-á-tocopheryl acetate as 100 mg vitamin E acetate (G.A. Pharmaceuticals, Athens, Greece). The oily formulation of vitamin E was then neatly and completely aspirated out with the syringe. Each aspirate measured 0.2 ml containing 100 mg vitamin E. The insulin syringe was thereafter attached to a clean oral gavage through which each experimental animal was administered the measured dose of 500 mg/kg body weight per day one hour prior to ethanol administration, in pre- and post-natal life.

Preparation and administration of alcohol

Ethanol was purchased at Julimax chemical pharmaceutical company (product of BDH limited, Poole, England). The ethanol sample was diluted to 10% and each preparation was made fresh every time before the commencement of the experiment. The insulin syringe was attached to a clean intra-gastric gavage through which each rat was administered orally the measured dose of 1.6 g/kg body weight daily in pre- and post-natal life. The dose of alcohol used was based on the works of Das *et al.* [20].

Sacrifice and sample collection

The pups were weighed and behavioural assessment done on day 21. Blood samples were collected from pups of day 21 for haematology (full blood count) and the rats were killed at different stages on days 1, 7, 14, 21 and 28. The cerebri and cerebelli were dissected out, weighed and some of the cerebella tissues preserved in phosphate buffer at a temperature of 4^{o}C and pH 7.4 for biochemical analysis, and some were fixed in 10% formol-saline for histomorphometric studies.

Parameters studied

Behavioural assessment

This includes Forelimb grip (motor function test), negative geotaxis (balance and equilibrium) and open field test (locomotor and anxiety).

Forelimb grip strength test

This test involves the forepaws of the rats being placed on a horizontally suspended metal wire (measuring 2 mm in diameter and 1 m in length), placed one meter above a landing area filled with soft bedding. The length of time each rat was able to stay suspended before falling off the wire was recorded. Each rat was allowed up to 2 minutes of suspension before removal. This test reflects muscular strength in the animals [21].

Negative geotaxis

A plank was put at an angle of 45^0 to the wall and the rat was placed on the highest point facing downwards. The time it takes the rat to turn 180^0 was recorded. This test measures the motor re-orientation and equilibrium [22].

Open field test

Rats were taken to the test room in their home cages and were handled by the base of their tails at all times. Rats were placed in the centre of the open field and allowed to explore the apparatus for 5 minutes after which rats were returned in their home cages and the open field was cleaned with 70 % ethyl alcohol and allowed to dry between tests. A video camera connected to a computer was used to analyse the open field images.

Haematological analysis

Blood samples were taken from the retro-ocular plexus of the rats using heparinized capillary tubes into Ethylene Di-amine Tetra Acetic (EDTA) acid treated sample bottles for the determination of full blood count. The procedure was performed at the Veterinary Pathology Laboratory of the University of Ibadan.

Biochemical assays

The following markers of oxidative stress were assayed for, Superioxide dismutase (SOD) [23], Gutathione peroxides (GSH-Px) [24], reduced Gluthathione (GSH) [25], Catalase (CAT) [26] and lipid peroxidation (LPO) [27].

Histomorphometry

Cerebellar tissues of pups of days 1, 7, 14, 21 and 28 were processed employing routine paraffin embedding techniques and stained with Haematoxylin and Eosin (H and E) for histomorphometric evaluation.

Statistical analysis

The data obtained was statistically analysed using one-way analysis of variance (ANOVA) followed by Dunnett's test. A value of $P<0.05$ was considered as statistically significant. All the data were processed with Graph Pad Prism version 6.0.

Results

Cerebellar weight

A decreased cerebellar weight was observed in the ethanol-treated pups on days 7, 14, 21 and 28, and in the honey + vitamin E pups on days 7, 21 and 28 compared with the controls at $p<0.05$. Co-treatment with honey increased the cerebellar weights of pups on days 7 and 14 ($p<0.05$), and better than vitamin E (Table 1) compared with the ethanol group.

Line crossing

The alcohol and alcohol plus honey pups had reduced exploratory movements, much less movements and was statistically significant when compared with control group ($p<0.05$).

Grooming

The alcohol plus honey, and alcohol plus vitamin E group showed a high significant difference in

Table 1: Mean cerebellar weight of control and treated pups on day 1, 7, 14, 21 and 28.

Days/groups	Day 1	Day 7	Day 14	Day 21	Day 28
Control	0.07±0.01	0.26±0.05	0.40±0.07	0.44±0.05	0.50±0.07
Alcohol	0.08±0.01	0.10±0.00a	0.22±0.04a	0.32±0.04a	0.38±0.08a
Honey	0.07±0.01	0.36±0.05a,b	0.30±0.07	0.34±0.05	0.44±0.08
Alcohol+honey	0.07±0.01	0.36±0.05a,b	0.34±0.05b	0.34±0.05	0.40±0.00
Alcohol+vit E	0.08±0.01	0.14±0.05a	0.40±0.07b	0.24±0.05a	0.32±0.04a

Values (n=5) are taken as mean±SD and expressed in gram. vit E – vitamin E. ap<0.05 versus with control, bp<0.05 versus alcohol.

Haematology

An increased white blood cell (WBC) count and a decreased percentage neutrophil and eosinophil was seen in the alcohol-treated pups on day 21 compared with the control at $p<0.05$. Co-treatment with honey and vitamin E improved the blood parameters significantly when compared with the alcohol treated rats (Table 2).

Behavioural assessment

Open field test

Center square

Pups in the honey and alcohol plus honey group were found to be less inclined to move about in the open field and spent much time at the centre square. This was significantly higher when compared with control group ($p<0.05$).

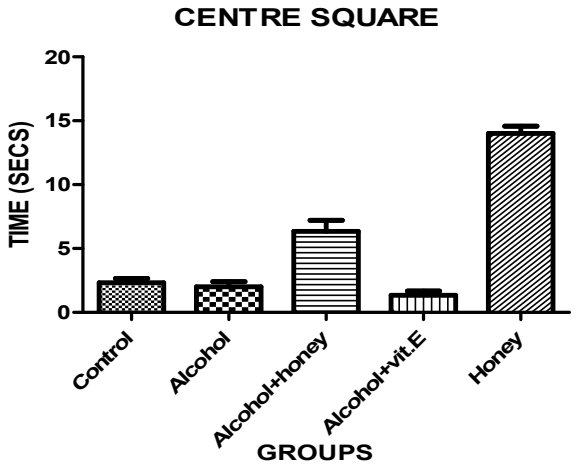

Fig. 1: Time spent in seconds at centre square between the groups. Values (n=5) are taken as mean±SD and expressed in seconds. vit E – vitamin E.

Table 2: Blood parameters of the control and treated pups on day 21

Days/groups	WBC 10^3/ µL	Neutrophil %	Eosinophil %
Control	3517±505.2	40.75±4.03	2.20±0.83
Alcohol	5188±283.9[a]	24.33±3.51[a]	1.40±0.54[a]
Honey	5500±866.0[a]	36.00±6.55[b]	2.00±1.00
Alcohol+honey	3388±500.6[b]	35.50±4.65[b]	2.20±0.83[b]
Alcohol+vit E	3883±108.0[b]	26.60±3.28[a]	2.20±1.10[b]

Values (n=5) are taken as mean±SD. vit E – vitamin E. [a]p<0.05 versus with control, [b]p<0.05 versus alcohol-treated .

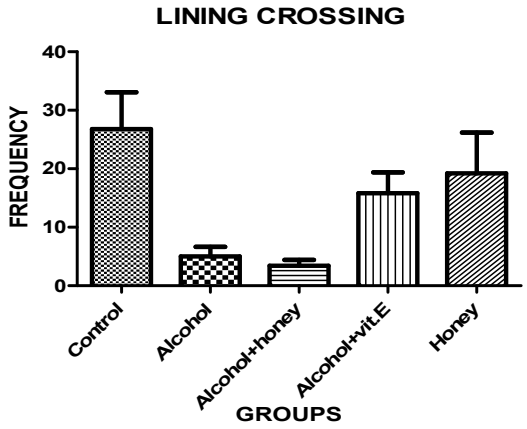

Fig. 2: Number of squares crossed between the groups. Values (n=5) are taken as mean±SD and expressed in numbers. vit E – vitamin E.

grooming when compared with the alcohol group at $p<0.05$.

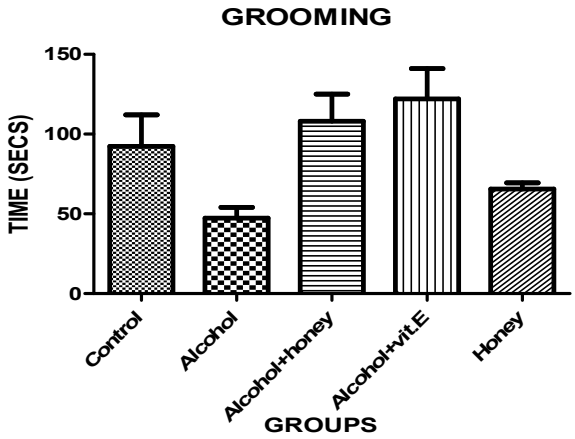

Fig. 3: Time spent in seconds for grooming between the groups. Values (n=5) are taken as mean±SD and expressed in seconds. vit E – vitamin E.

Freezing: Pups in the alcohol group spent most time freezing compared with the control and honey groups at $p<0.05$.

Stretch posture: The alcohol and honey group showed high statistical significant in the stretch posture compared with the control, alcohol plus honey group, alcohol plus vitamin E group at $p<0.05$.

Forelimb grip: The alcohol group had increased muscular strength with a longer drop-off time compared with control, honey and alcohol plus vitamin E groups at $p<0.05$.

Negative geotaxis: An increased time for negative geotaxis was seen in the alcohol plus vitamin E group compared with the control, alcohol and alcohol plus honey group at $p<0.05$.

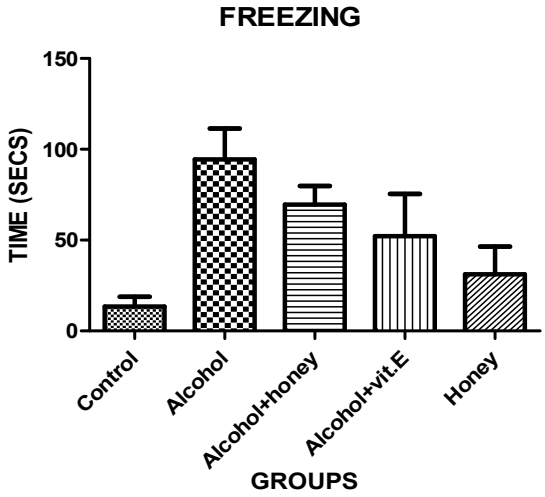

Fig. 4: Time of freezing in seconds between the groups. Values (n=5) are taken as mean±SD and expressed in seconds. vit E – vitamin E.

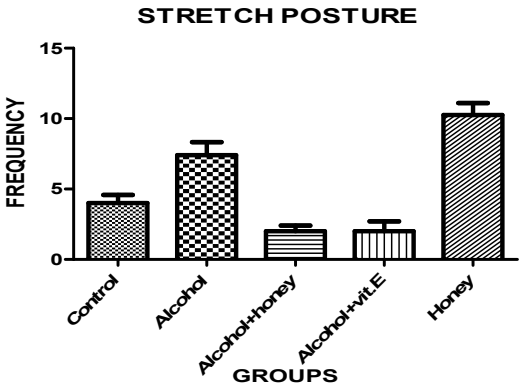

Fig. 5: Number of stretch posture between the groups. Values (n=5) are taken as mean±SD and expressed in numbers. vit E – vitamin E.

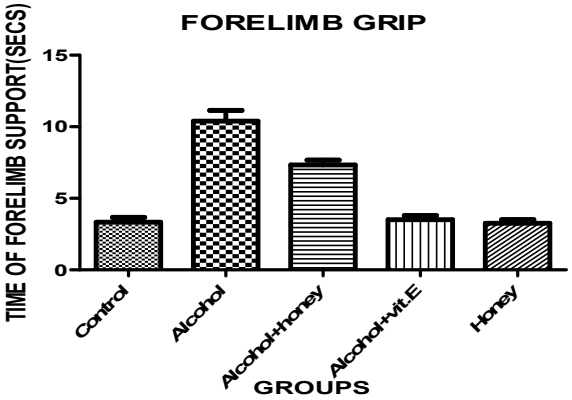

Fig. 6: Length of time in seconds of forelimb support between the groups. Values (n=5) are taken as mean±SD and expressed in seconds. vit E – vitamin E.

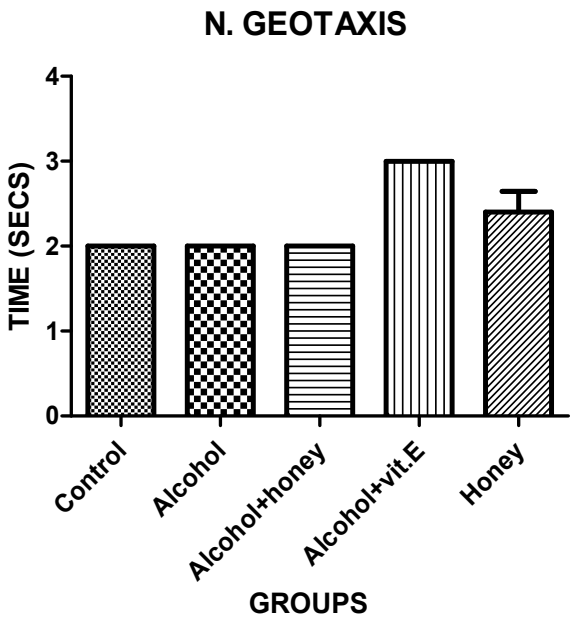

Fig. 7: Time of re-orientation in seconds between the groups. Values (n=5) are taken as mean±SD and expressed in seconds. vit E – vitamin E.

pups on day 21 compared with the control group at $p<0.05$. Honey and vitamin E decreased the rate of lipid peroxidation and increased the glutathione level compared with the alcohol group at $p<0.05$ (Table 3).

Histological and histomorphometric assessment of the cerebellar cortex

Histologically, the cerebellar cortex in the weaning phase (between postnatal days 1 and day 20) showed the normal four layers of external granular layer, molecular layer, Purkinje layer and granular layer. However, in the alcohol-treated pups on day 21, the external granular layer persisted (Figure 10).

Thickness of the External granular layer (EGL) and molecular layer (ML)

A significantly thicker EGL was seen in the alcohol-treated pups on day 14 compared with the control, honey and vitamin E treated groups at $p<0.05$ (Table 4, Figure 9). The ML was reduced in the alcohol-treated pups on days 21 and 28 compared with the control at $p<0.05$ (Table 4, Figures 10 and 11). There was persistent EGL in the alcohol-treated pups on day 21 (Figure 10). Treatment with honey and vitamin E improved the ML compared with the alcohol-treated pups on days 21 and 28.

Table 3: Effect of treatment on the LPO, SOD, CAT, GSH, and GSH-Px values on day 21 pups.

Groups	LPO (µmol/mg)	SOD (µ/mg)	CAT (µmol/mg)	GSH (µg/ml/mg)	GSH-Px (µ/mg)
Control	1.47±1.15	1.08±0.13	0.15±0.20	1.32±0.29	7.56±6.86
Alcohol	2.28±1.13[a]	0.86±0.16	0.05±0.01	0.92±0.22[a]	6.77±6.99
Alcohol+honey	1.84±1.19[b]	0.92±0.01	0.06±0.01	1.12±0.29	6.23±1.46[a]
Alcohol+vit.E	1.52±1.80[b]	0.91±0.01	0.05±0.01	1.68±0.37[b]	6.36±5.05[a]
Honey	1.85±2.57	0.61±0.35	0.06±0.01	1.07±0.05	6.11±2.54[a]

Values (n=5) are taken as mean±SD and expressed in gram. vit E – vitamin E. [a]compared with control $p<0.05$, [b]compared with alcohol $p<0.05$.

Table 4: Mean thickness of the EGL of cerebellar cortex on day 14 and the ML on days 21 and 28 pups in µm.

Groups	EGLday 14	ML day 21	ML day 28
Control	4.13±0.20	77.20±4.24	84.63±3.17
Alcohol	9.16±1.15[a]	59.33±9.58[a]	65.63±12.38[a]
Alcohol+honey	4.83±0.85[b]	63.30±1.96	69.83±3.17[a]
Alcohol+vit. E	5.93±0.68[b]	98.93±2.34[ab]	70.87±1.95[a]
Honey	4.20±1.08[b]	73.37±8.19[b]	82.30±7.20

Values (n=5) are taken as mean±SD and expressed in µm. vit E – vitamin E. [a]compared with control $p<0.05$, [b]compared with alcohol $p<0.05$.

Biochemical assessment

An increased lipid peroxidation and a decreased glutathione levels was observed in the alcohol-treated

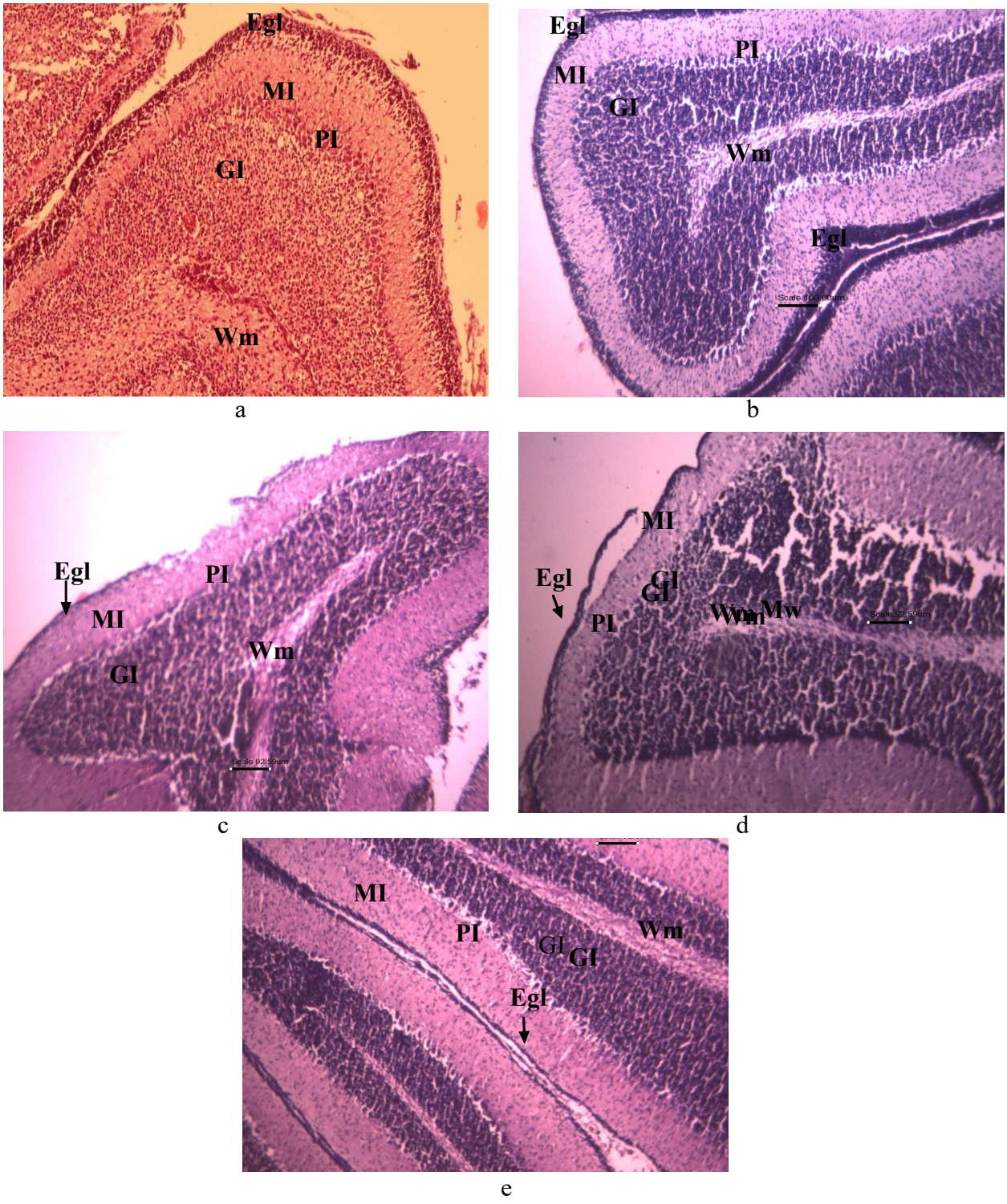

Fig. 9: Photomicrograph of the cerebellar cortex of pups of day 14. a) control, b) alcohol- treated with thicker Egl, c) alcohol+honey, d) alcohol+vit E. and e) honey alone. The Egl was thinner in c, d and e pups. Molecular layer (Ml), Purkinje layer (Pl), Granular layer (Gl), External granular layer (Egl) H&E. X100.

Discussion

The cerebellar weight of the rats compared in this study showed a significant reduction in the alcohol treated group compared with the control rats. This reduction may be due to the degree of brain atrophy which correlates with the rate and amount of alcohol consumed over a lifetime [28]. The honey group, alcohol plus honey and alcohol plus vitamin E all showed a significant increase in their cerebellar weight when compared with alcohol and this might suggest that the potent antioxidant activity of honey and vitamin E have ameliorated the oxidative damage of alcohol.

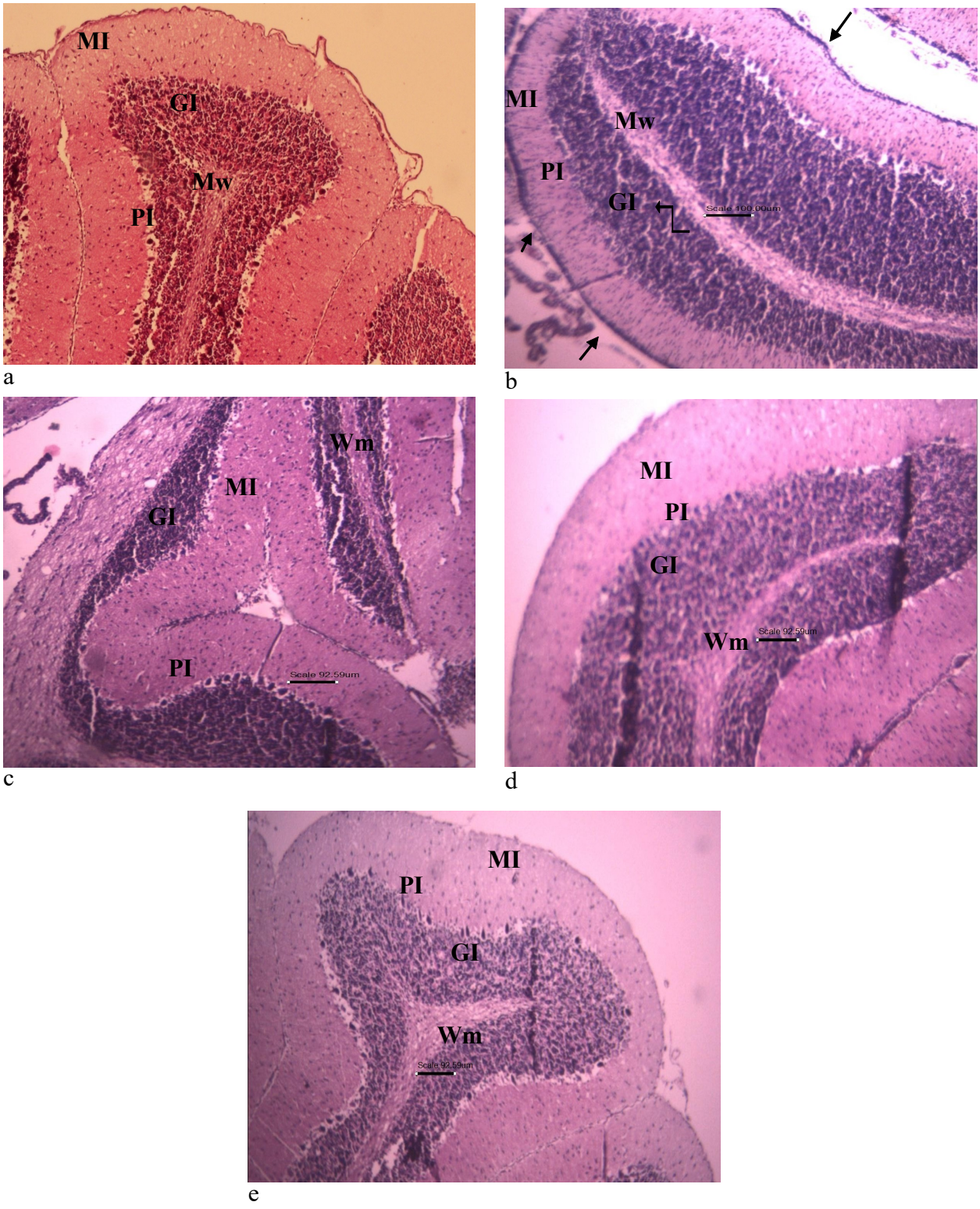

Fig.10: Photomicrograph of the cerebellar cortex of pups of day 21. a) control, b) alcohol- treated with decreased Ml thickness and persistent Egl (arrow), c) alcohol+honey, d) alcohol+vit E. and e) honey alone. Molecular layer (Ml), Purkinje layer (Pl), Granular layer (Gl), External granular layer (Egl) H&E. X100.

In this study, maternal alcohol consumption increased oxidative stress in the pups by decreasing the glutathione (GSH) level and increasing Lipid peroxidation (LPO) in brain, thereby generating more free radicals. The decrease in GSH levels (an endogenous antioxidant which helped in mopping up oxygen free radicals) represents increased utilization due to oxidative stress [29]. Reduced GSH and oxidative damage have been suggested to constitute early possible signalling events in apoptotic cell death [30, 31]. Macho *et al.* [32] reported that decreased GSH and disruption of the

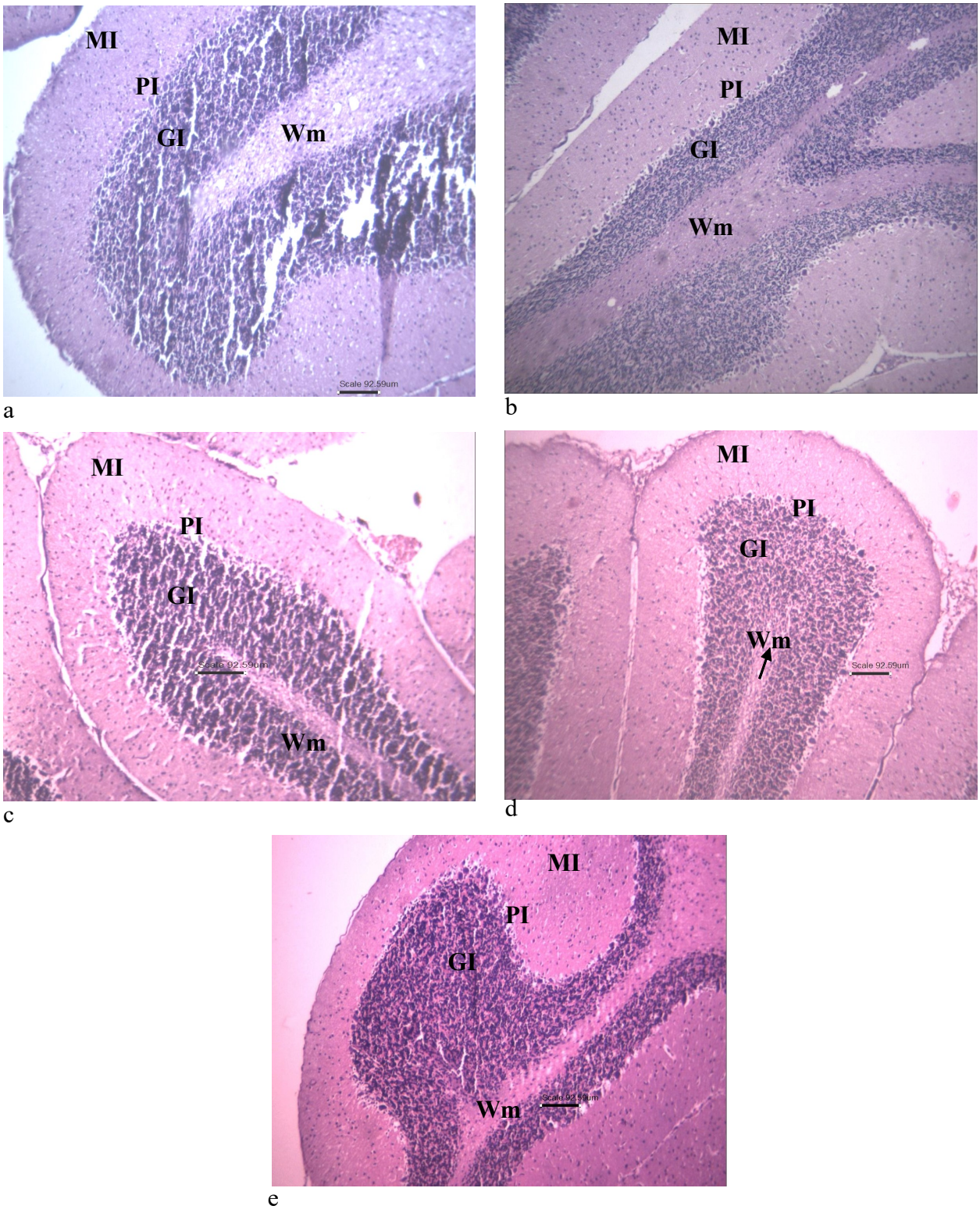

Fig.11: Photomicrograph of the cerebellar cortex of pups of day 28. a) control, b) alcohol- treated with decreased Ml thickness, c) alcohol+honey, d) alcohol+vit E. and e) honey alone. Molecular layer (Ml), Purkinje layer (Pl), Granular layer (Gl), External granular layer (Egl) H&E. X100.

mitochondrial trans-membrane potential preceded the onset of apoptosis. In this study, decreased GSH levels indicated that there was more production of free radicals to be mopped up and GSH is now acting to reduce the level of H_2O_2 produced due to alcohol that has generated free radicals. The significant incease in the levels of GSH in the honey and honey plus alcohol groups at $p<0.05$, implies that honey has potent antioxidant property. Li *et al*., [6] reported in a cell culture studies that glutathione depletion resulted in cell death by triggering the activation of neuronal 12-lipoxygenase which leads to production

of peroxides, the influx of Ca^{2+} resulting ultimately in cell death. Treatment of pups with honey and vitamin E, increased the levels of GSH, thereby decreasing free radical generation and preventing oxidative damage. The alcohol-treated pups showed a significant increase in the levels of malondialdehyde (MDA) in the brain homogenates, an indication of lipid peroxidation. Increased lipid peroxidation is the evidence of much free radical that might have led to cellular damage and previous studies have shown that increased lipid peroxidation plays a role in pathogenesis of several neurodegenerative diseases [33]. The onset of lipid peroxidation within biological membrane is associated with changes in their physicochemical properties and with alteration of biological functions of lipid and proteins [34]. In this study, honey and vitamin E significantly decreased the levels of MDA by mopping up free radicals generated by alcohol consumption, thereby exhibiting their antioxidant property.

Alcohol has been reported to exert a direct toxic effect on the bone marrow resulting in vacuolization of the bone marrow precursor cells as well as leukocyte and platelet functions [35]. The pups in the alcohol-treated group showed a significant increase in the white blood cell count and a decrease in percentage neutrophil and eosinophil. The cellular elements of the blood are particularly sensitive to oxidative stress because their plasma membranes contain a high percentage of polyunsaturated fatty acids (PUFA) [36]. Therefore the decrease in white blood cells differential count recorded in the alcohol-treated group might be the consequence of alcohol-induced lipid peroxidation and damage of their cell membranes. This result correlates with the findings of Awe *et al*., [37], where they reported that decreased percentage neutrophil and eosinophil following consumption of different grades of alcohol, reflect increased oxidative stress on the immune system and thus, decreasing resistance to infectious agents.

The Open Field Test provides simultaneous measures of locomotion, exploration, stress and anxiety [38]. In this study, the alcohol-treated rats showed significantly reduced line crossing values when compared with the controls and this indicates decreased locomotion and exploration and less anxiety. In stretch posture, the alcohol only showed significant increase when compared with the control group and this indicates that the animal is hesitant to move from one location to a new position [39] and thus a high frequency of these postures indicates a higher level of anxiety. The frequency of line crossing and the duration in the central square are measures of exploratory behaviour and anxiety. The alcohol only group showed no significant difference in the time spent in the central square when compared with the control rats but a significantly decreased frequency in line crossing, an indication of low exploratory behaviour and a decreased locomotor activity. This finding is consistent with the report of Valcheva-Kuzmanova *et al.*[40], in which consumption of high dose of ethanol reduced the frequency of horizontal movement thereby decreasing locomotor activity in rats.

The negative geotaxis which measured the re-orientation ability of the rats showed no significant difference in the time spent on re-orientation in alcohol, honey and control groups. This implied that, there was no effect of maternal alcohol consumption on the ability or latency to complete the negative geotaxis task. Some studies have reported severe impact of alcohol on negative geotaxis [41] (Hannigan; Thomas *et al.*), while other workers have not [42] (Vaglenova *et al*.,). These studies used a variety of doses, implying that the difference in the result obtained from this study and other studies may likely be due to methodological difference in the experiments. The forelimb grip test, which measures the muscular strength of rat, supported the observation in the open field test. The alcohol group had increased muscular strength (as measured by the duration of the grip), in contrast with the report of Steiner *et al*. (2011)[43] who reported a decreased grip strength in rat in a dose-dependent manner, with the grip strength strongest 15 minutes after alcohol injection and faded over the remaining 2.5 hours of the test period. The difference in our result may either be due to the age of the rats used because while we used weaned rats (postnatal day 21), they used adult rats, or the duration of the test period, as we used a short duration of grip. The honey group and the alcohol plus vitamin E group had lower drop-off durations when compared with the control group, but these were not statistically significant.

Histologically, a thicker Egl of the cerebellar cortex was seen in the alcohol-treated pups on Day 21 indicating persistence of this layer after weaning. Hatten *et al*., [44] reported that the Egl disappeared on day 20 after birth in rats. High metabolic activity occurs in the Egl which results in the differentiation, maturation and migration of cells of the cerebellar cortex during early development [45] (Malomo *et al*.). The persistent Egl seen in alcohol-treated pups after weaning (day 21), may be due to delayed migration of the cells of the Egl. The Ml thickness was reduced in the alcohol-treated group after weaning compared with the control pups. The mechanism for this reduction is unknown but

previous studies have shown that the decreased levels of antioxidants in the brain (especially in the cerebrum, cerebellum and hippocampus) increase their susceptibility to ethanol's teratogenicity [46]. The migration, differentiation, and maturation of cerebellar neurons are also affected by exposure to alcohol [47]. Treatment with Vitamin E and honey appeared to have a significant neuroprotective effects on Ml of cerebellar cortex.

In conclusion, this study has demonstrated that prenatal and postnatal ethanol consumption induced oxidative stress in the developing cerebellum of Wistar rat, evidenced by delayed maturation of the cerebellar Egl, reduction in thickness of Ml, as well as behavioural, haematological and biochemical alterations. However, treatment with honey and vitamin E was found to be effective in protecting the cerebellum against alcohol-induced oxidative damage.

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Respiratory diseases morbidity and mortality in two tertiary health institutions in South West Nigeria: incidence, pattern and referral for physiotherapy care

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Abstract

Background: There are several respiratory diseases (RDs) in the Nigerian populace. However, reports on the incidence and physiotherapist's involvement in the care and management of RDs is scarce. This study investigated the incidence, pattern of RDs and referral for physiotherapy care in two Nigerian teaching hospitals.

Methodology: A 10-year retrospective audit of RDs was conducted at two Nigerian University teaching hospitals, Osun State, South-west, Nigeria. A total of 2,637 case files of patients with RDs from January, 2005 to December 2014 were reviewed. Types of RDs, socio-demographic information, duration of hospitalization, referral for physiotherapy care, and status at the point of discharge (dead or alive)] were recorded. Data were summarised using descriptive statistics and graphical representations.

Results: The frequency of RDs was 12.4% in both hospitals. Pneumonia and respiratory tract infections (RTI) 1446(54.8%), tuberculosis 460(17.4%) and chronic obstructive pulmonary diseases (COPD) 296(11.2%) were the predominant forms of RDs. More males than females were affected especially children whose ages ranged between 0 – 9 years constituting 58.2%. Pneumonia/ RTI and COPD were the leading causes of death, 42.1% and 23.3% respectively. Majority of the patients, 77.9% were discharged within the first week of admission while only 4(0.2%) of all cases of RDs were referred for physiotherapy.

*Conclusion***:** The frequency of respiratory diseases in two tertiary health institutions in South-west, Nigeria from a 10 year review was high. Pneumonia and COPD were the leading causes of hospitalisation while male children were more vulnerable with high mortality and referral for physiotherapy was extremely poor.

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Key words: *Incidence, Pattern, Respiratory disease, Tertiary health institution, Physiotherapy*

Résumé

Contexte: Il existe plusieurs maladies respiratoires (MR) dans la population nigériane. Cependant, les rapports sur l'incidence et la participation du physiothérapeute dans les soins et la gestion des MR sont rares. Cette étude a étudié l'incidence, le schéma des MR et le renvoi pour les soins de physiothérapie dans deux hôpitaux d'enseignement nigérian.

Méthodologie: Une vérification rétrospective de 10 ans sur les MR a été menée dans deux hôpitaux d'enseignement de l'Université nigériane, Etat d'Osun, Sud-Ouest, Nigeria. Un total de 2637 dossiers de cas de patients atteints de MR de janvier 2005 à décembre 2014 a été examiné. Les types de MR, les données sociodémographiques, la durée de l'hospitalisation, le renvoi pour les soins de physiothérapie et le statut au point de décharge (mort ou vivant)] ont été enregistrés. Les données ont été résumées à l'aide de statistiques descriptives et de représentations graphiques.

Résultats: L'fréquence des MR a été de 12,4% dans les deux hôpitaux. La pneumonie et les infections de la trachée respiratoire (ITR) 1446 (54,8%), la tuberculose 460 (17,4%) et les maladies pulmonaires obstructives chroniques (MPOC) 296 (11,2%) étaient les formes prédominantes de MR. Plus de mâles que de femmes ont été affectés, en particulier les enfants dont les âges variaient entre 0 et 9 ans, représentant 58,2%. La pneumonie/ITR et la MPOC ont été les principales causes de décès, respectivement 42,1% et 23,3%. La majorité des patients, 77,9% ont été libérés au cours de la première semaine d'admission alors que seulement 4 (0,2%) de tous les cas de MR étaient référés pour la physiothérapie.

Conclusion: l'frequency des maladies respiratoires dans deux établissements de santé tertiaire dans le sud-ouest, du Nigeria à partir d'une évaluation de

10 ans était élevée. La pneumonie et la MPOC ont été les principales causes d'hospitalisation, tandis que les enfants masculins étaient plus vulnérables avec une mortalité élevée et le renvoi pour la physiothérapie était extrêmement médiocre.

Mots clés: *Fréquence, Schéma, Maladie respiratoire, Institution de santé tertiaire, Physiothérapie*

Introduction

The prevalence of respiratory diseases is on the increase globally [1]. According to the British Thoracic Society [2], approximately 1 in 7 individuals are affected by some forms of chronic lung disease, most commonly chronic obstructive pulmonary disease (COPD), which includes asthma, chronic bronchitis and emphysema. Data from the Centres for Disease Control and Prevention indicated that 16.2 million adults and 6.7 million children had asthma leading to more than 10.6 million visits to office-based physicians and a minimum of 444,000 hospital stays [3, 4]. Similarly, acute respiratory infections in children under 5 years of age are the most frequent cause of death from lung disease causing more than 4 million deaths annually. Furthermore, pulmonary tuberculosis (TB) constitutes the most frequent cause of death from a single pathogen in persons aged 15 to 49 years accounting for a total of 2 – 3 million deaths annually [5].

According to Lozano *et al* [6] when the top ten leading causes of death worldwide are considered, four belong to respiratory diseases namely chronic obstructive pulmonary disease (COPD), lower respiratory tract infections, pulmonary TB and lung cancer. Lower respiratory tract infection (RTI) and pulmonary TB are ranked second and eighth respectively as major causes of mortality in Africa [6]. In Nigeria, lower RTI constituted the second leading cause of death in all age brackets in 2002 and pulmonary TB was the seventh leading cause of death accounting for 4% of all deaths [7]. It is now evident that rates of death from lower RTI is more than double for each decade of life, whereas rates of death from pulmonary TB remain relatively constant [8]. Respiratory diseases have thus remained major public health concern and may continue to put heavy burden on the health care system if urgent actions are not taken.

Although national immunisation programme for the prevention and control of childhood communicable diseases has led to substantial reduction in the prevalence of major killer diseases among children, respiratory diseases are still among important leading causes of morbidity and mortality in sub-Sahara Africa (SSA) [9]. Several factors but not limited to poor nutritional status among children, persistent air pollution and increasing smoking habit among young adults as well as increasing aged population have been identified as risk factors for the increasing incidence of respiratory diseases in SSA [9, 10]. Unfortunately, there are few studies investigating the incidence of respiratory diseases in the south-west of Nigeria and also Nigeria as a whole.

Management of respiratory diseases has always been domiciled in tertiary health institutions due to inadequacy of specialised healthcare practitioners and facilities at primary and secondary health care centres. In Osun State, south-western Nigeria, there are only two tertiary health institutions providing medical services to a huge population of patients in the cities. However, larger numbers of inhabitants in Osun State are living in the rural communities with limited access to medical services. Treatments of respiratory diseases using pharmacological approaches have been reported to be effective for controlling infections, airway clearance and efficient breathing. However, many patients remain burdened with respiratory disability due to easy fatigability and poor exercise tolerance.

There is evidence that exercise plays significant role in reducing the burden of respiratory diseases through improvement in exercise capacity and quality of life [11, 12]. However, there is dearth of empirical data on pattern and involvement of physiotherapists in the management of respiratory diseases in Nigeria despite the prevailing evidence of its importance in the literature. This study conducted a 10 - year retrospective audit on the frequency and pattern of respiratory diseases and referral for physiotherapy care in two tertiary health institutions in Osun State, South west, Nigeria.

Methodology

This retrospective study was conducted in Ladoke Akintola University of Technology Teaching Hospital (LAUTECH), Osogbo and Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) Ile-Ife Osun State, Nigeria. The LAUTECH is a state government owned institution established about 20 years ago. It is located in Osogbo, capital city of Osun State. The hospital has more than 350 bed spaces and receives referral from all the neighbouring cities and states close to Osun State. The hospital is well developed with modern facilities for respiratory care and a good number of experts in pulmonology and respiratory care.

The Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) Ile - Ife Osun State,

Nigeria was founded more than four decades ago and is being funded by the Federal government of Nigeria. It was founded on integrated comprehensive health care services based on a pyramidal structure designed to secure excellent and efficient services. The institution has more than 850 bed spaces and provides health-care services to more than 10 million Nigerians in South West Zone of Nigeria. The services cover neighbouring states including Ondo, Oyo, Ekiti, Edo and part of Kwara State [13].

Procedure

The ethical approval for this study was obtained from the Health and Research Ethics Committee of the Institute of Public Health, Obafemi Awolowo University, Ile – Ife, Nigeria. Permission to examine case files of patients with respiratory diseases within period of years under review (January, 2005 to December, 2014) was sought and obtained from both institutions. The procedures for data collection were in two stages. Stage 1 included obtaining records from the health information technology units of the medical record of LAUTECH and OAUTHC to assess the total number of patients diagnosed and admitted for various respiratory diseases during the period under review. Furthermore, the case file number and other relevant information needed to facilitate the retrieval of case file in the medical record library were obtained. Data that were obtained covered January, 2005 and December, 2014. Stage 2 involved selection of case files of patients with various respiratory diseases over the period under review and individual case notes were traced out and scrutinised to obtain data including gender, age, types of various respiratory diseases, number of patients referred for physiotherapy and status at discharge (dead or alive) and yearly distribution of various respiratory diseases. Other relevant information to this study was obtained from the case file. The data were organised and tabulated. Age group was classified into ten years interval and duration of hospitalisation. Information obtained were recorded and stored in a storage device.

Data analysis

Data were analysed using descriptive statistics of frequency, percentage and graphical representations. The Statistical Package of Social Sciences (SPSS version 19) was used to perform statistical analysis.

Results

Table 1 showed annual distribution of respiratory diseases at Ladoke Akintola University of Technology Teaching Hospitals (LAUTECH), Osogbo and Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile–Ife, Osun State, South west, Nigeria over a period of ten years 2005 to 2014. The incidence rates of respiratory diseases in LAUTECH and OAUTHC were 33.0 and 67.0% respectively. Highest incidence of respiratory diseases was witnessed in year 2010 with a prevalence rate of 12.4% and a distribution rate of 40.5 and 59.5%. However, year 2011 recorded the lowest incidence of respiratory diseases with 6.6%. The incidence rate of pneumonia/ respiratory tract infection (RTI) during the years under review at both teaching hospitals was 54.8% followed by pulmonary tuberculosis, 17.4% and chronic obstructive pulmonary diseases (COPD) with 11.2 %. Pleural effusion and pulmonary oedema were the least respiratory diseases (Table 2).

Table 1: Annual distribution of respiratory diseases at both teaching hospitals

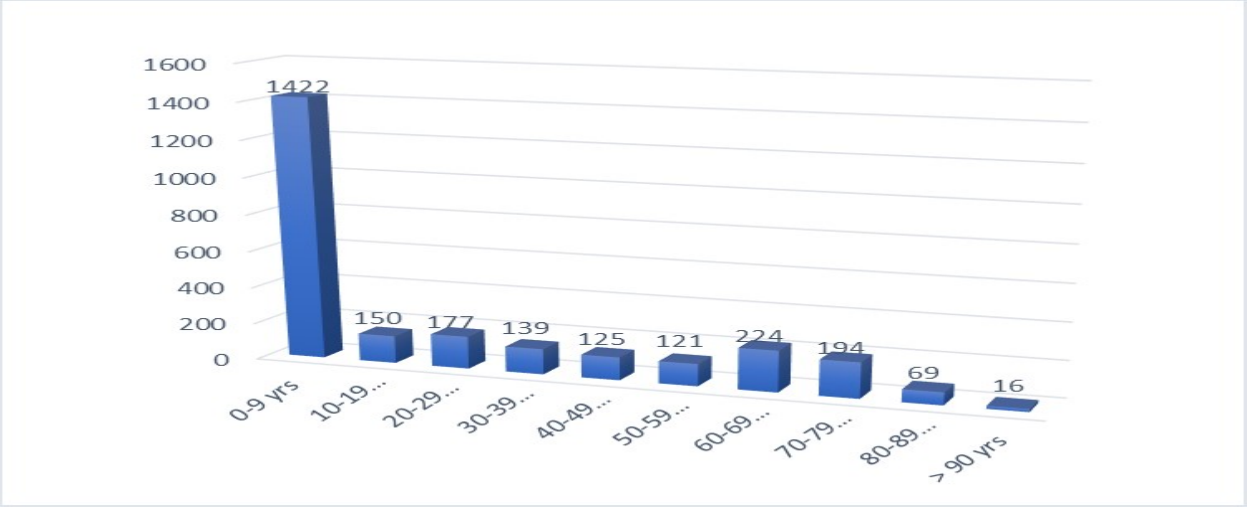
Year	LAUTECH n(%)	OAUTHC n(%)	All N(%)
2005	104(33.1)	210(66.9)	314(11.9)
2006	101(39.3)	156(60.7)	257(9.7)
2007	85(32.1)	180(67.9)	265(10.0)
2008	104(35.5)	189 (64.5)	293(11.1)
2009	104 (35.7)	187(64.3)	291(11.0)
2010	87(31.0)	194(69.0)	281(10.7)
2011	101(40.4)	149(59.6)	250(9.5)
2012	64(26.7)	176(73.3)	240(9.1)
2013	100(40.0)	150(60.0)	250(9.5)
2014	84(42.9)	112(57.1)	196(7.4)
Total	934(35.4)	1703(64.6)	2637(100.0)

Key: LAUTECH – Ladoke Akintola University of Technology Teaching Hospital
OAUTHC – Obafemi Awolowo University Teaching Hospitals Complex

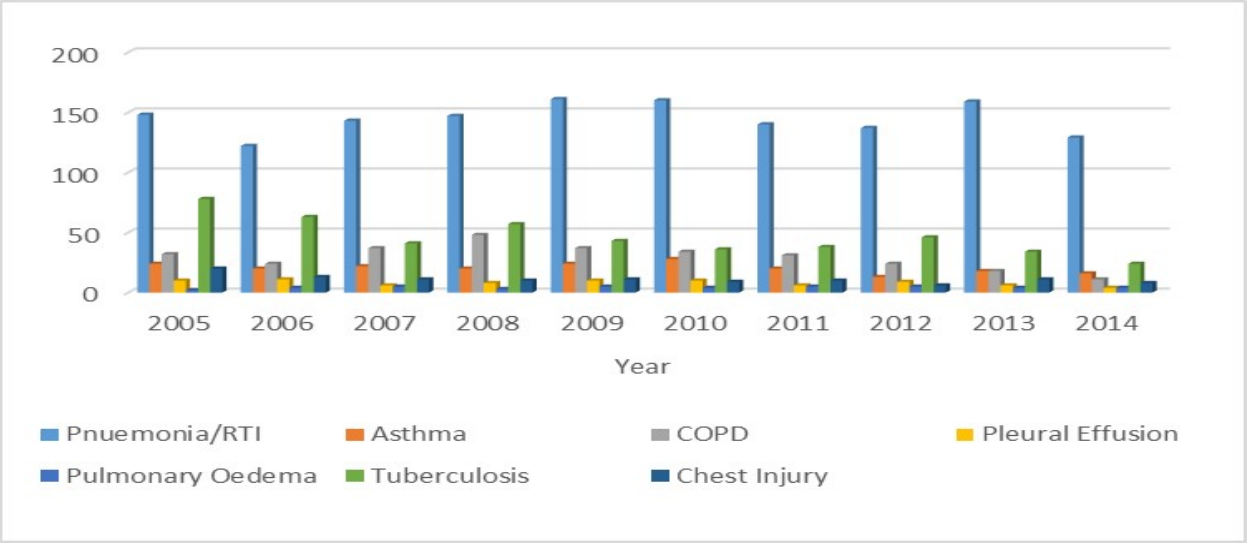
Table 2: Frequency and pattern of various respiratory diseases recorded at both teaching hospitals

Respiratory Diseases	No. of cases	Percentage
Pneumonia/RTI	1446	54.8
Pulmonary TB	460	17.4
COPD	296	11.2
Asthma	205	7.8
Chest Injury	109	4.1
Pleural Effusion	80	3.1
Pulmonary Oedema	41	1.6
Total	2637	100.0

Key: RTI – Respiratory tract infection, COPD – Chronic obstructive pulmonary diseases, TB - Tuberculosis



Key: Yrs: years
Fig. 1: Age distributions of respiratory diseases at both teaching hospitals



***Key**: RTI – Respiratory tract infection, COPD – Chronic obstructive pulmonary diseases*
Fig. 2: Annual distribution of all respiratory diseases at both teaching hospitals

The age distribution of patients with various respiratory diseases showed that individuals within age group of 0 – 9 years were mostly affected with a total prevalence of 53.9%. However, individuals older than 90 years recorded least prevalence of 0.6% (Figure 1). Table 3 shows gender distribution of respiratory diseases by age at both teaching hospitals during the years under review. The total prevalence of respiratory diseases was 57.4%. Male children within the age group of 0–9 years constituting 53.9% recorded highest prevalence of respiratory diseases. Males also recorded higher prevalence except in the age group of 20–29 years with a prevalence rate, male to female of 46.6% and 55.4% respectively.

The annual distribution of respiratory diseases showed that pneumonia had the highest prevalence rate.. Highest prevalence rates of pneumonia/RTI were recorded in years 2009, 2010 and 2013 respectively (Figure 2). The mortality rate resulting from all respiratory diseases was 10.1%. The highest mortality rate -15.3% from respiratory diseases occurred in 2005 while the lowest- 3.3% occurred in year 2013. Findings from this study also showed that there was progressive but inconsistent decline in mortality between years 2005 to 2014 (Table 4). Table 5 shows the mortality rate resulting from various respiratory diseases during the years under review. Pneumonia/RTI remained consistently the

Table 3: Gender distribution of respiratory diseases by age at both teaching hospitals

Age (year)	Male n (%)	Female n (%)	All N (%)
0 – 9	828(58.2)	594(41.8)	1422(53.9)
10 – 19	79(52.7)	71(47.3)	150(5.7)
20 – 29	79(46.6)	98(55.4)	177(6.7)
30 – 39	70(50.4)	69(49.6)	139(5.3)
40 – 49	65(52.0)	60(48.0)	125(4.7)
50 – 59	68(56.2)	53(43.8)	121(4.6)
60 – 69	135(60.3)	89(39.7)	224(8.5)
70 – 79	130(67.0)	64(33.0)	194(7.4)
80 – 89	45(65.2)	24(34.8)	69(2.6)
>90	10(62.5)	6(37.5)	16(0.6)
Total	1509(57.2)	1128(42.8)	2637(100.0)

Table 4: Distribution of death and live cases recorded per annum at both teaching hospitals

Year	Death n (%)	Alive n (%)	All N (%)
2005	48(15.3)	266(84.7)	314(11.9)
2006	38(14.8)	219(85.2)	257(9.7)
2007	32(12.1)	233(87.9)	265(10.0)
2008	23(7.8)	270(92.2)	293(11.1)
2009	24(8.3)	267(91.7)	291(11.0)
2010	23(8.2)	258(91.8)	281(10.7)
2011	24(9.6)	226(90.4)	250(9.5)
2012	8(3.3)	232(96.7)	240(9.1)
2013	30(12.0)	220(88.0)	250(9.5)
2014	16(8.2)	180(91.8)	196(7.4)
Total	266(10.1)	2371(89.9)	2637(100.0)

Table 6 shows the duration of hospitalization for various respiratory diseases and referral physiotherapy care at both teaching hospitals. Most patients were discharged from hospitals within the first week of admission with a prevalence rate of 77.9% while fewer patients were hospitalized more than nine weeks. However, the rate of referral showed that only 0.2% of all cases of respiratory diseases were referred for physiotherapy care throughout the years under review.

Table 6: Duration of hospitalisation and referral for physiotherapy care at both teaching hospitals

Duration (week)	No. of cases	Percentage
0 – 1	2054	77.9
1 – 2	389	14.8
2 – 3	132	5.0
3 – 4	47	1.8
4 – 5	1	0.0
5 – 6	3	0.1
6 – 7	3	0.1
7 – 8	5	0.2
> 9	3	0.1
Total	2637	100.0
Referral for physiotherapy care	n	%
Yes	4	0.2
No	2633	99.8
Total	2637	100.0

Table 5: Mortality distribution from various respiratory diseases at both teaching hospitals

Respiratory condition	No. of case	No. of death	Percentage
Pneumonia/RTI	1446	112	42.1
COPD	296	62	23.3
Pulmonary TB	460	40	15.6
Chest Injury	109	17	6.4
Pleural Effusion	80	14	5.3
Pulmonary Oedema	41	12	4.5
Asthma	205	9	3.4
Total	2637	266(10.1)*	100.0

*Total Death Rate = 10.1%

Key: COPD – Chronic obstructive pulmonary diseases, RTI – Respiratory Tract Infection, TB – Tuberculosis

leading cause of mortality throughout the years. The prevalence of death rate from pneumonia/RTI alone was 42.1% followed by COPD (23.3%) and pulmonary TB (15.6%) while the least cause of death from respiratory diseases was asthma with 3.4%.

Discussion

This study investigated the prevalence, pattern and referral for physiotherapy care for respiratory diseases in two government owned tertiary health institutions during a ten year period - 2005 to 2014.

The result indicated a high incidence of respiratory diseases such that Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile–Ife had higher cases of respiratory diseases compared to Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Osun State. The plausible explanation for the difference between the two teaching hospitals could be that the OAUTHC receives larger number of patients, more medical facilities and had presence of a large number of experts in the field of respiratory medicine. Furthermore, the hospital is one of the leading centres for care of respiratory diseases being funded by the Federal government of Nigeria.

Findings from our study also show that a prevalence ratio of male to female was 1.3: 1, implying more males than females were affected by respiratory diseases. This finding is also similar to a study by Rogerson *et al,* [14] who reported higher incidence of respiratory diseases in men. However, this is contrary to the findings of Desalu *et al,* [15] who reported male to female ratio of 1:1.4. The gender bias in the incidence of respiratory diseases may be due to hormonal differences between male and female. It has been reported that oestrogen might confer a protective mechanism on women from respiratory diseases until after menopause [16]. Furthermore, male gender might possibly be at higher risk of respiratory diseases due to risky lifestyle including smoking and alcohol abuse. However, Ibeh and Ele, [17] were of the opinion that the rate of respiratory disease might be changing without gender difference perhaps due to an increasing prevalence of smoking habit among women in the recent time.

Highest incidence of respiratory diseases was found among children within the age group of 0–9 years. This is in agreement with the findings of Kumar *et al,* [18] who reported that incidence of respiratory diseases decreases with increasing in age. The reason for high incidence in this age group could be adduced to low immune status in this age category. Furthermore, studies have reported that children with low socio-economic status are more prone to respiratory diseases [19, 20]. Poor nutritional status and poor neighbourhood environment including air pollution may lead to development of respiratory diseases among children and adults [10, 20]. Considering the pattern of respiratory diseases in the two health institutions, pneumonia/RTI, COPD were the leading causes of morbidity and mortality in this study. This is consistent with the findings of previous studies that pneumonia and COPD were the leading causes of death as a result of respiratory diseases [21, 22].

We found that death rate from respiratory disease was high. Similarly, reports from Ireland [23] also indicated that respiratory disease is the second leading cause of death accounting for 42% of all deaths, however, this figure has fallen by almost a quarter [23]. Our finding was also similar to that of Menezes *et al*, [24] who reported that mortality from respiratory diseases was high but is gradually on the decline. Although, findings from our study show that there was progressive decline in the mortality rate from 2004 (18.1%) to 2007 (8.7%), nonetheless reduction in death rate appears not yet satisfactory. The reduction in mortality rate could be explained from the view point of improvement in health care services, national immunization programme against killer diseases such as whooping cough, tuberculosis and increasing awareness against the risk factors such as smoking and changes in lifestyles that predispose to respiratory diseases. Furthermore, availability of anti – retroviral drugs for the treatment of HIV could also contribute to the reduction in the incidence of TB and other chest conditions.

Treatment of respiratory disease involves multi-disciplinary approach. The use of pharmacological intervention such as antibiotics, corticosteroids and expectorants helps to control infections, relief of breathlessness, suppresses immune reactions, lessen acute exacerbation and lower mortality [25, 26]. Furthermore, patients with respiratory diseases usually experience dyspnea, fatigue and impair exercise tolerance. Exercise has been found to be capable of enhancing aerobic performance and improve exercise capacity. Exercise is one of the core physiotherapy practices for improving strength, dyspnea and functional capacity, strengthening of breathing muscles and thoracic cage compliance, exercise tolerance, and quality of life [12, 27]. Various physiotherapy procedures and techniques including postural drainage, relaxation methods and breathing control are important in improving respiratory care.

Findings from our study show that referral for physiotherapy care is poor. Previous studies have shown that patients with respiratory diseases improved significantly following physiotherapy intervention [25 – 27]. Similarly, physiotherapists also use different methods to help clear excessive secretion along airway and breathing techniques to lessen energy expenditure during labored breathing. In addition, increased physical activity and improved health-related quality of life has direct link with reduction in all-cause mortality [26, 27]. Systematic reviews and meta-analyses also showed that patients with COPD and acute hypercapnic respiratory

failure, physiotherapy care including non-invasive ventilation reduced mortality compared to usual care and reduced the need for intubation [28, 29]. Several factors not limited to lack of multidisciplinary team approach, communication barrier and lack of knowledge of physiotherapists' role in the management of respiratory diseases among experts in respiratory care might account for the poor referral for physiotherapy care.

The outcome of this study should be interpreted with caution due to some inherent limitations. This report was mainly hospital-based findings which might not be true reflection of what is obtainable at community level. This might limit the generalizability of our findings to other settings. Furthermore, the actual causes of death in patients with respiratory diseases were not ascertained as not all cases of death had post mortem reports.

Conclusion and recommendations

In conclusion, incidence of respiratory diseases is high among patients attending government owned tertiary health institutions in Osun State, south-west, Nigeria. Pneumonia and chronic obstructive pulmonary diseases were the leading causes of morbidity and mortality and children below ten years old were more vulnerable especially males. Referral of patients with respiratory diseases for physiotherapy care was extremely poor. There is an urgent need to increase awareness about the importance of physiotherapy in respiratory care in Nigeria to enhance effective management and reduce morbidity and mortality associated with respiratory diseases. Government should formulate policies against tobacco smoking, air pollution by industries, good environmental hygienic practices, reduction in biomass materials for cooking and tarring of roads to reduce inhalation of dust that can easily predispose individuals to respiratory diseases. Children less than 10 years should be given greater attention in the care for respiratory diseases. Furthermore, referrals of respiratory diseases for physiotherapy care should be emphasized in our hospitals. In addition, community physiotherapy should be intensified to educate the populace about the havoc of indoor and outdoor biomass pollutants in the aetiology of respiratory diseases.

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Sociocultural beliefs and sexual activity among postmenopausal women in an urban community in Ibadan, Nigeria.

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Abstract

Background: Sexual activity after menopause is often considered to be a taboo in some Nigerian societies and the attendant problems are currently assuming publichealth importance. However, few studies done on Nigerian women have brought to the forefront many sociocultural beliefs about sexual activity after menopause.The study therefore examined sociocultural beliefs and sexual activity of postmenopausal women.

Methods: A cross-sectional study was conducted among 514 postmenopausal women aged 40 to 65years. An interviewer-administered questionnaire was used to obtain data on sociodemographic characteristics, attitude to sociocultural beliefs regarding sexual activity and current sexual activity of respondents. Chi-square test and logistic regression were used to test for associations and determine predictors of outcome variables.

*Results***:** The mean age of the respondents was 54.0 ±5.6 years and the mean age at menopause was 47.3±4.4 years. Overall, 54.3% agreed with at least one of the stated sociocultural beliefs. Among those who currently had partners, 68.4% and 30.7% reported pre and postmenopausal sexual activity respectively. The significant predictors for cessation of postmenopausal sexual activity were no formal education (O.R =4.1, 95% C.I from 2.0 to 8.3), supportive attitude towards sociocultural beliefs (O.R =5.6, 95% C.I from 3.4 to 9.4) and older age group (O.R =4.1, 95% C.I from 2.4 to 7.0).

Conclusion: Sociocultural beliefs adversely affected postmenopausal sexual activity among these women, which has implications on the partners seeking alternative sexual partners with the attendant problems of sexually transmitted infections /HIV. Educational interventions targeted at changing these erroneous beliefs should be developed.

Keywords: *Sociocultural beliefs, postmenopausal women, sexual activity*

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Résumé

Contexte: L'activité sexuelle après la ménopause est souvent considérée comme un tabou dans certaines sociétés nigérianes et les problèmes qui en découlent sont en train de prendre en compte l'importance de la santé publique. Cependant, peu d'études réalisées sur les femmes nigérianes ont porté à l'avant-garde de nombreuses croyances socioculturelles concernant l'activité sexuelle après la ménopause. L'étude a donc examiné les croyances socioculturelles et l'activité sexuelle des femmes ménopausées.

Méthodes: Une étude transversale a été réalisée chez 514 femmes ménopausées âgées de 40 à 65 ans. Un questionnaire administré par un intervieweur a été utilisé pour obtenir des données sur les caractéristiques sociodémographiques, l'attitude à l'égard des croyances socioculturelles concernant l'activité sexuelle et l'activité sexuelle actuelle des répondants. Le test chi-carré et la régression logistique ont été utilisés pour tester les associations et déterminer les prédicteurs des variables de résultat.

Résultats: L'âge moyen des répondants était de 54,0 ± 5,6 ans et l'âge moyen à la ménopause était de 47,3 ± 4,4 ans. Dans l'ensemble, 54,3% étaient d'accord avec au moins une des croyances socioculturelles déclarées. Parmi ceux qui avaient actuellement des partenaires, 68,4% et 30,7% avaient déclaré une activité sexuelle pré et post-ménopausée respectivement. Les prédicteurs significatifs pour la cessation d'activité sexuelle post-ménopausée étaient l'absence d'éducation formelle (OR = 4.1, IC 95% de 2.0 à 8.3), attitude de soutien à l'égard des croyances socioculturelles (OR = 5.6, IC 95% de 3.4 à 9.4) et groupe d'âge plus âgé (OR = 4,1, IC à 95% de 2,4 à 7,0).

Conclusion: Les croyances socioculturelles ont eu une incidence négative sur l'activité sexuelle post ménopausique chez ces femmes, ce qui a des implications sur les partenaires qui cherchent des partenaires sexuels alternatifs avec les problèmes de transmission d'infection sexuelle / VIHqui en découlent. Des interventions éducatives visant à modifier ces croyances erronées devraient être développées.

Mots-clés: *Croyances socioculturelles, femmes ménopausées, activité sexuelle*

Introduction

Menopause is currently receiving global attention due to a progressive increase in life expectancy. About 15-30% and 5-8% of the population are postmenopausal women in the industrialized and developing countries respectively [1] with an increasing trend in developing nations.

The health of women within the reproductive age group is currently a source of significant concern. The challenges faced by women in this age group are further worsened by the culture of silence that envelops reproductive health matters.Women who eventually survive the childbearing years go on to face yet another challenging phase of their lives.As women age; they experience both physical and sociocultural challenges that may hinder the attainment of optimal health. Just as there is a need to focus on women of reproductive age ; there is also a need to ensure that the health needs of older women are met [2]. Apart from medical problems associated with the menopause, women are also likely to have feelings of insecurity and low self esteem which may be compounded by sociocultural beliefs about sexual activity after menopause passed down from hand to hand [2].

Menopause is defined as the cessation of the normal monthly menses as a result of the normal decline in ovarian function. It is a time in a woman's life when menstrual period ceases and the ovaries permanently stop releasing eggs. Menopause is said to be complete when a woman has experienced amenorrhoea for 12 consecutive months. Usually, age of onset varies from 47 years to about 55 years; however, in rare cases,menopause can occur in the early 30s and sometimes as late as the 60s [3].

Menopausal symptoms experienced by women vary, many notice no symptoms other than a gradual cessation in their periods while others suffer from a myraid of symptoms; as these menopausal symptoms vary among women ,so also do the sociocultural beliefs associated with sexual activity and menopause [3].

Sociocultural belief is the acceptance by the mind that something relating to or involving cultural and social factors is true or real, often underpinned by an emotional or spiritual sense of certainty.

Across various cultures, a lot of sociocultural beliefs exist regarding postmenopausal sexual activity. In Bolivia, menopausal women are of the the opinion that sex should be less frequent or not engaged in at all after menopause [4]. Among the Hausas of Nothern Nigeria, postmenopausal women gain physical freedom from confinement (Purdah, a practice imposed on them when they are married, whereby the women are restricted indoors and if they must go out then, they must be veiled from head to toe), while in some other cultures, menopausal women are stripped of their identity, as they are no longer seen as women and they are denied the right to have sexual intercourse[4].

In a study on Nigerian women, sociocultural beliefs about sexual activity after menopause were brought to the forefront as many of their respondents opined that having sexual intercourse after menopause would lead to possible chronic stomach pain for women and "weakness of manhood for men".Postmenopausal women who still wanted to have sexual intimacy were considered sex maniacs [5].

Another study conducted in Ibadan revealed that attitudes to menopause were generally positive as the majority of respondents saw menopause as a naturally physiologic process. However; there is some misinformation that menstruation is cleansing and thus the absence of this cleansing process would increase the propensity for sexually transmitted diseases when postmenopausal women have sex [6].

Several other sociocultural beliefs and wrong notions about sexual activity after menopause have been revealed. Some women maintained that sexual activity after menopause would likely lead to death of the woman; while some others believe that having sex after menopause could contaminate the man's sperm, thereby preventing him from being able to impregnate another woman; it was reported that many of the natural physical changes associated with old age including body weakness, loss of eyesight and urinary incontinence are attributed to sexual activity after menopause [5].

Adekunle *et al* documented that the cessation of menstrual flow was associated with the likelihood of acquiring diseases following intercourse in the erroneous view that the menstrum drains away impurities. For these women, sexual life ended with the menopause due to the cultural belief stipulating abstinence at menopause [7]. How much influence these beliefs have on sexual activity of postmenopausal women can be further revealed by indepth research.This study examined these sociocultural beliefs and sexual activity among post menopausal women in Ibadan North East LGA, Nigeria.

Materials and methods

Study area

The study was carried out in Ibadan, the capital of Oyo State in Nigeria. Ibadan is an urban city with a projected population of 3.5 million people [15]. Ibadan municipality is made of five local government

areas, namely, Ibadan North East, North West, South East, South West, and Ibadan North, each consisting of several health wards. Ibadan North East which was used for the study, has 12 health wards and health care facilities.

Study population

All women aged 40 to 65 years, who had not menstruated for 12 consecutive months and who resided within the selected areas were enrolled in the study, provided they gave their consent to participate.

Study design

This study is a community-based, cross-sectional descriptive study. Data were collected from women to determine socio demographic characteristics, attitude to socio cultural beliefs regarding sexual activity and current sexual activity of respondents.

Sampling technique

A four-stage sampling technique was used for data collection. Ibadan North East has 12 political ward. In the first stage, a political ward was selected using simple random sampling.

In the second stage, street and household listings were obtained with the assistance of local government staff and immunization tour guide officers and 10 streets were selected through simple random sampling. In the third stage, 50 households with at least one postmenopausal woman were selected using systematic random sampling. In the fourth stage, in each household, one postmenopausal woman aged 40-65 years was selected through balloting and was interviewed using the pretested questionnaire.

Instruments

A semi-structured questionnaire was used to collect data on the respondent's characteristics. Information was obtained on sociodemographic variables, attitude to sociocultural beliefs regarding postmenopausal sexual activity and current level of sexual activity of respondents. Menopause status was assessed based on responses to the questions about whether or not they had menstruated in the preceding 12 months and if not, the age at menopause. A five - point Likert scale was used to score attitudes of the respondents to the selected sociocultural beliefs. Total obtainable attitudinal scores ranged from 0 to 11. The score for each item decreases from 5 to 1 with strongly agree having the highest score and strongly disagree having the lowest score. By indicating any of these five possible options for each item, the respondent provides her attitude to each sociocultural belief. Scores of 0 to 5 and 6 to 11 were rated as nonsupportive and supportive attitudes respectively. Current level of sexual activity was assessed based on responses to the questions on frequency of sexual activity before and after onset of menopause .To validate the study instruments, they were translated toYoruba, the local language, and back translated to English and then pretested outside the ward selected for the study.

Data collection

Four research assistants were employed after three days of training to assist the researchers in data collection. To ensure that the data gathered were of high quality, one of the researchers (a community health physician trainee) was in the field with trained research assistants throughout the period of data collection.

Data analysis

Data gathered were entered into SPSS 15.0 software package. Chi square test was used to test for association between variables of interest. Logistic regression was performed on variables found to be significantly associated against the outcome variable (cessation of postmenopausal sexual activity). The level of statistical significance was set at $P < 0.05$.

Ethical Issues

Ethical approval to conduct the study was obtained from the Ethical Review Committee of the Oyo State Ministry of Health.

Results

Socio-demographic characteristics

A total of 522 women were potentially eligible to be interviewed. Eight of the proposed respondents were not available (due to travel, hospitalization, or being missed at home on two consecutive visits). Consequently, 514 respondents (98.4%) constituted the study population.The mean age of the respondents was 54.0 ±5.6 years and the mean age at menopause was 47.3±4.4 years. Most of the respondents 403(78.4%) were married, 453 (89.2%) were of Yoruba ethnicity.and the majority 369 (71.8%) had formal education. The details of sociodemographic characteristics of respondents are shown in table 1.

Attitudes towards socio-cultural beliefs associated with menopause and sexual activity

The women agreed with the following sociocultural beliefs regarding postmenopausal sexual activity: menopause makes a woman biologically manlike (61.7%), sex after menopause: is evil (54.8%), causes

Table1 : Socio Demographic Characteristics of the respondents

	Frequency	Percentage
Age Group		
Below 50 years	116	22.6
Above 50 years	398	77.4
Age at menopause		
40-44	215	41.1
45-49	224	42.9
50 and above	83	16.0
Marital Status		
Married	403	78.4
Single/Never married	43	8.3
Widowed	68	13.2
Level of Education		
No formal Education	145	28.2
Primary Education	157	30.5
Secondary Education	116	22.6
Tertiary Education	96	18.7
Ethnicity		
Yoruba	453	88.0
Igbo	44	8.6
Hausa	10	2.0
Others	7	1.4
Husband's Level of Education		
No formal Education	106	26.4
Primary Education	105	26.0
Secondary Education	99	24.5
Tertiary Education	93	23.1

Respondents' attitude to postmenopausal sexual activity

Mean attitudinal score was 4.1± 3.2 with a little above half of the respondents being against postmenopausal sex (54.3%) and agreed with at least one of the stated sociocultural beliefs (Table 4), while the remaining (45.7%) were supportive of postmenopausal sex.

Association between postmenopausal sexual activity and some variables

Among those who currently had partners, only 30.7% reported postmenopausal sexual activity. Significantly higher proportions of those with no formal education (78.6%), those aged ≥50 years (69.9%) and with supportive attitude towards the sociocultural beliefs (83.8%) reported cessation of postmenopausal sexual activity ($p<0.05$).

Predictors of cessation of post-menopausal sexual activity

On logistic regression, the significant predictors for cessation of postmenopausal sexual activity were no formal education (O.R =4.1, 95% C.I from 2.0 to 8.3), supportive attitude towards sociocultural beliefs (O.R =5.6, 95% C.I from 3.4 to 9.4) and older age group (O.R =4.1, 95% C.I from 2.4 to 7.0).

Table 2: Respondents' attitude to socio-cultural beliefs associated with menopause and sexual activity

Variable	Agree n (%)	Don't know n (%)	Disagree n (%)
Sex after menopause transmits curses to oneself	186(36.2)	134(26.1)	194(37.7)
Sex after menopause is evil	282(54.9)	93(18.6)	139(27.0)
Sex after menopause transmits curses to children	15(2.9)	129(25.1)	370(72.0)
Sex after menopause indicates promiscuity	223(43.4)	97(18.6)	194(37.7)
Sex after menopause transmits curses to partner	60(11.7)	144(28.0)	310(60.3)
Having sex after menopause will cause swollen abdomen from accumulated semen	260(50.6)	129(25.1)	125(24.3)
Having sex after menopause makes one sick	255(49.6)	141(27.4)	118(23.0)
Having sex after menopause will cause blindness	99(19.3)	172(33.5)	243(47.3)
With menopause, a woman can no longer enjoy sex	206(40.1)	186(36.2)	122(23.7)
Women are less sexually attractive after menopause	317(61.7)	159(30.9)	138(26.8)
Women are more sexually attractive after menopause	122(23.7)	79(15.4)	233(45.3)
Onset of menopause makes a woman to be like a man biologically	186(36.2)	134(26.1)	118(23.0)

swollen abdomen due to accumulated semen (50.6%), makes one sick (49.6%), indicates promiscuity (43.4%), and women are less sexually attractive after menopause (41.8%). Overall, 45.7% agreed with at least one of the stated sociocultural beliefs and the mean attitudinal score was 4.1±3.2.

Discussion

The study identified various socio cultural beliefs associated with menopause and sexual activity as well as socio demographic and socio cultural factors that influence postmenopausal sexual activity. For many women, menopause is considered synonymous with the time women no longer see their monthly

Table 3: Respondents characteristics and post menopausal sexual activity

Variable	Post menopausal sex Yes n %	No n %	Chisquare/ fishers exact	P value
Age (years)				
< 50	69 (59.5)	47 (40.5)	32.600	<0.001*
50 and above	121 (30.1)	277 (69.9)		
Attitude to sociocultural beliefs				
Not Supportive	152 (54.5)	127(45.5)	8.346	<0.001*
Supportive	38 (16.2)	197(83.8)		
Religion				
Christianity	140 (43.5)	182 (56.5)	16.807	<0.001*
Others	47 (25.3)	139 (74.7)		
Ethnicity				
Yoruba	150 (33.1)	303 (66.9)	24.312	<0.001*
Others	40 (65.6)	21 (34.4)		
Marriage Type				
Monogamous	128 (43.0)	170 (57.0)	11.583	0.001*
Polygamous	51 (27.6)	134 (72.4)		
Educational status				
Formal education	160 (42.8)	214 (57.2)	19.932	<0.001*
No formal education	30 (21.4)	110 (78.6)		
Occupation				
Skilled	23 (65.7)	12 (34.3)	12.671	<0.001
Semiskilled/Unskilled	161 (35.5)	293 (64.5)		

**P <0.005*

Table 5: Adjusted predictors of cessation of postmenopausal sexual activity

Variable	Odds ratio	95%CI	P value
Marital status			
Married	1.411	0.237-2.545	0.125
Others (ref)			
Age (years)			
50+	4.109	2.432-7.231	<0.001*
<50(ref)			
Family setting			
Monogamous	0.665	0.412-1.073	0.095
Polygamous (ref)			
Educational status			
No formal education	4.138	2.067-8.357	0.001*
Formal education (ref)			
Ethnicity			
Yoruba	3.213	0.323-3.950	0.319
Others (ref)			
Occupation			
Skilled	1.198	0.578-3.775	0.934
Semiskilled/Unskilled (ref)			
Attitude to socio cultural beliefs			
Supportive	5.620	3.409-9.438	<0.001*
Non supportive (ref)			

**P value <0.05*

period and can therefore no longer get pregnant [5]. It is difficult to make comparisons with other studies because views on menopause and sexual activity vary from culture to culture. A woman who belongs to a culture that perceives menopause as symptom free may not experience menopausal symptoms related to physical changes in midlife such as hot flushes and depression. These women may pass through the menopause without difficulties.

In this study, the mean age at menopause was found to be similar to other numerous studies conducted in different parts of the world which showed that the mean age at menopause largely lies between age 45-57 years.[7-9,16,].

Generally, more than half of the study population agreed with at least one of the socio-cultural beliefs and this may be due to the fact that there is a strong interplay between cultural beliefs and how a woman views the symptoms associated with menopause. As reported by Mcmaster *et al*, there is a strong indication that menopause is not regarded as negative in some African cultures as it is in most Western countries [10]. Subsequently, women who see menopause as a medical condition have more negative perceptions of menopause compared to those who view it as a life transition or a symbol of aging [11].

More women in this study perceived menopause as a normal event and this is consistent with previous findings which showed that women regarded menopause as a normal physiological event [9].

About one third of the respondents reported post menopausal sexual activity, this finding may be indicative of the beliefs and attitude of the respondents to the issue as reflected in the decrease in frequency of sexual activity pre and post menopause. It may also be due to separation or spouse/partner death as about 21.5% of the study population were either separated or widowed. Correspondingly, earlier studies in Ibadan and Ile-Ife reported a prevalence of post menopausal sex of 27.42% and 42% respectively [7, 8].

The study observed a decrease in post menopausal sexual activity with an increase in age and age at onset of menopause. More women less than 50 years of age reported post menopausal sexual activity compared to those 50 years and above. Women 50 years and above were four times more likely not to engage in post menopausal sexual activity. This may be due to the fact that there is reduced libido with onset of menopause and with increasing age. Also a higher proportion of women whose age at onset of menopause was below 50 years of age reported having post menopausal sexual activity compared to those whose age at menopause was 50 years and above. This finding agrees with a similar study in the United States where a high proportion of women whose age at menopause is between the ages of 45-54 years were more sexually active compared to those that fall between the ages of 56-64 years [12]

As expected, a higher proportion of women that were married also reported having post menopausal sexual activity compared to those in other categories. Also, those in monogamous unions had a higher proportion engaging in post menopausal sexual activity compared to those in polygamous unions. This higher number of respondents who were married and in monogamous unions may be due to the fact that their spouse/partner is still alive or that they are in stable unions and do not have to share their spouse/partner with someone else. A previous study in Benin, Nigeria also identified death of spouse, separation and the presence of younger co-wives who could satisfy their husbands better as factors that affect postmenopausal sexual activity [9].

A higher proportion of Christian women reported having postmenopausal sexual activity compared to those of other religions. A study in the northern part of Nigeria indicated that postmenopausal women are no longer classified as women and are hence allowed to leave the puddah if they had been confined to it in the past [13]. Also, in this same study, it was highlighted that Muslim postmenopausal women are free to participate in all religious activities as opposed to menstruating women who cannot participate in the obligatory prayers and fasting during menstruation [13]. A higher proportion of women from other ethnic groups reported having post menopausal sexual activity compared to those of Yoruba ethnicity.More respondents who had formal education and whose husbands had formal education also reported having post menopausal sexual activity compared to those with no formal education.

Respondents with no formal education were about four times more likely to have stopped engaging in sexual activity compared to those with formal education. This finding points out the importance of education in issues of sexuality and this is in keeping with another study which showed an association between education and attitude to sex [14].

There were significant associations between postmenopausal sexual activity and religion, level of education, marital status, as well as family type (monogamous versus polygamous). This is similar to various studies in Nigeria and the United States [9,13,14,16].

Limitations

This study faced certain limitations which should be acknowledged. It was difficult to verify some of the information given by the respondents. There was also recall bias as some of the respondents' could not remember clearly what happened during and after the menopause. Their responses may also have been influenced by socio cultural beliefs about privacy of sexual issues peculiar to our environment. However, this study was able to provide some baseline information that supports the existence of sociocultural beliefs and its association with postmenopausal sexual activity.

Conclusion

This study identified the different sociocultural beliefs associated with menopause and sexual activity among post-menopausal women. Furthermore, women's attitudes to socio cultural beliefs on menopause and sexual activity were also highlighted. Socio cultural beliefs influenced these women regarding postmenopausal sexual activity and this may have far reaching effects on their partners as they may seek alternative means of solving this problem. This finding has a great implication on family life and health as the partners of these women with these beliefs may seek alternative sources of sexual gratification thereby being at risk for sexually transmitted diseases and HIV.

Recommendation

Women generally, and postmenopausal women in particular should be encouraged to speak out regarding sexual issues and ask for advice from the health personnel, instead of suffering in silence. Educational interventions targeted at changing these erroneous beliefs should be developed and made available to women groups across communities. This will help to dispel the myths surrounding menopause and sexual activity.

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A prospective analysis of indications, pattern of tooth extraction and predictors of multiple extractions in an urban adult population in Southwestern Nigeria

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Abstract

Background: Tooth extraction constitutes the bulk of procedures in oral surgery clinics. The recent trend seems to indicate a change regarding the indications and the pattern of tooth extraction. We prospectively evaluated the indications, pattern of tooth loss and the predictors of multiple extractions among a cohort of adult patients.

Methods: This is a prospective cohort study of adult patients tooth extraction between December 2014 and August 2015. Patients' demographics and clinical data were collected with a structured questionnaire. Data analysis was done using statistical package for social sciences (SPSS) version 19.0. Variables were subjected to univariate and multivariate logistic regression to evaluate predictors of multiple tooth loss

Results: A total of 446 adults had 557 tooth extractions with 412 (88.4%) single extractions and 54 (11.6%) multiple extractions. Maxillary teeth (231) and mandibular teeth (326) were extracted in 203 and 263 patients respectively. Predominant indications were dental caries (61.8%) and periodontal disease (19.1%) with minor indications consisting of eruption/impaction problem, trauma, endo-periodontal lesions and endodontic failure. Univariate analysis showed that older age group (p-value 0.0001), lower educational level (p-value 0.0001), regular consumption of sugar contents (p-value 0.025) and irregular teeth brushing (p-value 0.0001) were associated with multiple extractions. The independent predictors of multiple tooth loss identified were older age group, lower educational level and irregular brushing of teeth.

Conclusions: The predominant indication for tooth extraction was dental caries. Older age group, patients with lower educational level, poor oral hygiene and regular consumption of sugar contents predispose to multiple tooth extractions.

Keywords: *Tooth extraction, changing pattern, multiple tooth extractions, caries, periodontitis*.

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Résumé

Contexte: L'extraction des dents constitue l'essentiel des procédures dans les cliniques de chirurgie buccale. La tendance récente semble indiquer une modification concernant les indications et le schéma d'extraction dentaire. Nous avons évalué prospectivement les indications, le schéma de perte de dent et les prédicteurs d'extractions multiples chez une cohorte de patients adultes.

Méthodes: Ceci s'agit d'une étude de cohorte prospective d'extraction dentaire de patients adulte entre décembre 2014 et août 2015. Les données démographiques et les données cliniques des patients ont été recueillies avec un questionnaire structuré. L'analyse des données a été effectuée en utilisant le logiciel statistique pour les sciences sociales (SPSS) version 19.0. Les variables ont été soumises à une régression logistique uni-variée et multi-variée pour évaluer les prédicteurs de la perte de dent multiple.

Résultats: Un total de 446 adultes ont eu 557 extractions dentaires avec 412 (88,4%) d'extractions simples et 54 (11,6%) d'extractions multiples. Les dents maxillaires (231) et les dents mandibulaires (326) ont été extraites respectivement chez 203 et 263 patients. Les indications prédominantes étaient les caries dentaires (61,8%) et la maladie parodontale (19,1%) avec des indications mineures consistant en un problème d'éruption / impaction, des traumatismes, des lésions endopéridontaires et une insuffisance endodontique. L'analyse uni-variée a montré que le groupe d'âge plus élevé (valeur p 0.0001), le niveau d'éducation inférieur (valeur p 0,0001), la consommation régulière de sucre (valeur p 0.025) et le brossage dentaire irrégulier (valeur p 0,0001) étaient associés à de multiples extractions. Les prédicteurs indépendants de la perte de dent multiple identifiés étaient un groupe d'âge plus élevé, un niveau d'éducation inférieur et un brossage irrégulier des dents.

Conclusions: L'indication prédominante pour l'extraction dentaire était la carie dentaire. Le groupe des personnes âgées, les patients ayant un niveau d'éducation inférieur, une mauvaise hygiène bucco-dentaire et une consommation régulière de sucre prédisposent à des extractions multiples de dents.

Mots-clés: *Extraction dentaire, changement de modèle, extractionsdentaires multiples, caries, parodontite.*

Introduction

Tooth extraction is the most prevalent procedure in the oral surgery clinics despite the increasing knowledge about adequate oral hygiene, the wide understanding of oral diseases, evidence-based dentistry and advanced prevention strategies [1]. Factors leading to tooth loss remains essentially the same worldwide but the pattern varies between and within countries [2-4]. However, tooth loss etiology is in transition since many communities are still undergoing modifications in dietary patterns, socioeconomic configurations, and health care development. These factors have significant impact on oral health and changes in their pattern have a significant impact on the oral health burden in practice with a significant health care cost implication. Therefore, the epidemiological trend monitoring over time is essential at improving oral health care, even in the communities where significant decline in oral health problems has been observed.

The periodic verification of causes and pattern of tooth loss can help in the assessment of the oral health needs, evaluation of adequacy of current oral care strategies, the choice of the intervention strategies and the appropriate policies which are affordable, sustainable and appropriate to the local situations. Comparing such data with those from the western world will enhance the standardization of global best practices.

There are few published studies that have examined the trends in the pattern of tooth extraction in a given country over a period of time. In the light of this, our aims were to prospectively evaluate the indications and identify the predictors of multiple tooth loss in an urban adult population in southwest Nigeria.

Materials and methods

This is a prospective cross-sectional study conducted on a cohort of adult patients presenting for tooth extraction at the University College Hospital (UCH) dental clinic and Oyo state Government dental centre, Ibadan between December 2014 and August 2015. Included were patients 16 years of age and above that had extraction of one or more teeth at any of the study centres and consented to participate in the study while excluded were patients below 16 years of age and patients that refused to give consent to participate in the study. The data were collected following informed consent obtained from the patients for study participation and extraction. The ethical approval for the study was obtained from the University of Ibadan UI/UCH Ethical Review Committee. (Ethical clearance registration number: NHREC/05/01/2008a)

The study participants included 446 consecutive adult patients (16 years and above) that had either single or multiple permanent tooth extraction at the study centres and who consented to participating in the study. Data collected included the age, gender, socioeconomic status, educational attainment, types and number of teeth removed, indications for tooth removal, oral hygiene practice and the pattern of previous dental clinic attendance.

All the extraction procedures were done aseptically under local anaesthesia. Tooth delivery was by intra-alveolar forceps extraction for fully erupted teeth and trans-alveolar extraction (surgical disimpaction) for impacted teeth.

Statistical analysis

Data analysis was performed using the SPSS for windows version 19.0, Inc., Chicago, IL, USA for descriptive statistics with median for continuous variables and frequency for categorical data. Categorical variables were tested using the Pearson Chi-square test to examine relationship between multiple tooth loss and specific patients' characteristics. Univariate and multivariate logistic regression analysis was used to identify factors that may predict multiple teeth extraction and variables achieving a p-value of ≤ 0.05 are considered statistically significant.

Outcome measures

The primary outcome measures were indications for tooth extraction, pattern of tooth extraction as well as the predictors of multiple tooth extraction.

Results

A total of 466 adult patients with 557 extractions were included in the study. There were 217 males and 249 females with a median age of 42.5 (16-86) years. More than two-third of the patients were below the age of 60 years and 65 (14%) patients had associated comorbidities. Table 1 represents the primary presenting complaints of the patients who presented for tooth extraction during the study period. Four hundred and twelve (88.4%) patients underwent single tooth extraction while 54 (11.6%) had multiple teeth extracted with the number ranging between 2-9 teeth. Maxillary teeth were extracted in 203 patients while 263 patients had 326 mandibular teeth removed. The distribution of quadrants of extraction included maxillary right (113), maxillary left (117), mandibular right (191) and mandibular left (135). There was a single case of mesiodens extraction.

Table 1- Primary complaints of patients who presented for dental extraction

Primary complaints	Frequency	Percentage
Toothache	399	85.7
Discolouration	2	0.4
Tooth mobility	29	6.2
Swelling	3	0.6
Pus discharge	2	0.4
Broken tooth/retained root	17	3.8
Toothache and mobility	4	0.9
Fractured tooth	1	0.2
Impacted tooth	3	0.6
Mal-aligned teeth	3	0.6
Extra tooth	1	0.2
Replacement of teeth	2	0.4
Total	466	100.0

Table 2- Indications for tooth extraction in 466 patients

Indications	Frequency	Percentage
Dental caries and its sequelae	288	61.8
Periodontal disease	89	19/2
Endoperiodontal lesions	8	1/7
Prosthetic reasons	2	0.4
Impaction/eruption problems	23	4.9
Endodontic failure/failed root canal problems	8	1.7
Trauma	38	8.2
Supernumerary/supplemental teeth	5	1.1
Orthodontic reasons	3	0.6
Patient request	2	0.4
Total	466	100.0

The commonest indication for tooth extraction was dental caries in 61.8 % of the patients and this was followed by periodontal disease in 19.1%. Table 2 shows the indications for tooth extraction in this study while table 3 shows the clinical characteristics of the patient in relation to the indications for extraction. The analysis of the indications for tooth extraction when related to the age groups shows that dental caries predominated in the younger age groups while periodontal disease was the commonest reason for tooth extraction in the older age groups with a significant p-value of 0.0001 (Figure 1). Most of the patients in the study had regular tooth brushing habit and only 4.5% had tooth-brushing irregularity. Of the 466 patients, 11.4% exhibited parafunctional habits and these include bruxism, teeth clenching, lip/cheek chewing and object or nail biting.

Table 3- showing clinical characteristics of 466 patients

	DC	PD	EPL	PS	IP/ER	EF/FRC	Trauma	SN/SMT	ODR	PR
Age Group										
16-59 yrs	247	38	4	1	23	8	26	4	3	2
60-86yrs	41	51	4	1	0	0	12	1	0	0
Educational level										
No education	5	6	1	0	0	0	1	0	0	1
Primary	16	11	1	1	0	0	5	0	0	0
Secondary	94	38	3	0	4	1	10	1	0	0
Higher	173	34	3	1	19	7	22	4	3	1
Consumption of sugar:										
Regularly	92	17	2	0	12	2	11	2	0	1
Occasionally	193	60	5	2	11	5	26	3	3	1
None	3	12	1	0	0	1	1	0	0	0
Presence of cormobidity:										
Yes	31	22	1	0	0	1	10	0	0	0
No	257	67	7	2	23	7	28	5	3	2
Tobacco use:										
Yes	7	2	0	0	0	9	2	0	0	0
No	281	87	8	2	23	8	36	5	3	2
Gender:										
Male	125	49	5	1	11	1	19	3	1	2
Female	163	40	3	1	12	7	19	2	2	1

DC, Dental caries; PD, periodontal disease; EPL, endoperidontal lesions; PS, prosthetic reasons; IP/ER, impaction/ eruption problems; EF/FRC, endodontic failure/failed root canal; SN/SMT, supernumerary/supplemental teeth, ODR, Orthodontic reasons; PR, patient request

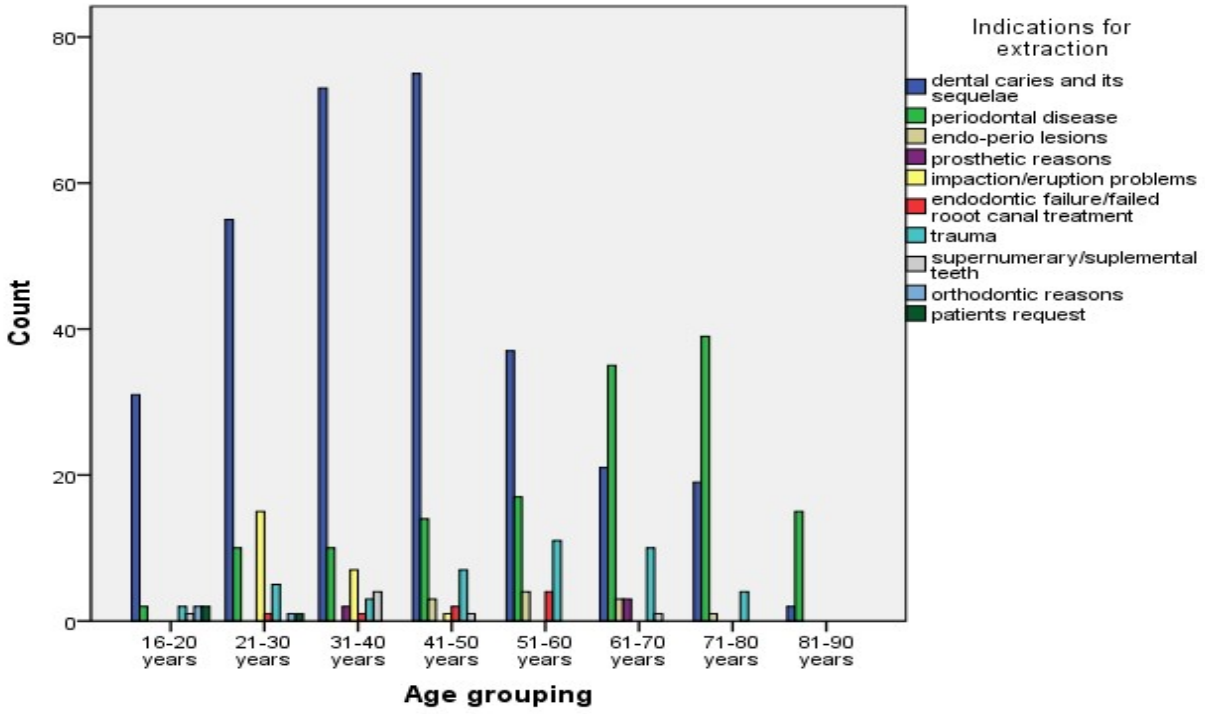

Fig. 1: Indications for extraction compared with age group

Table 4- showing clinicopathological factors predicting multiple tooth extraction on univariate analysis

Factors	Single Extraction (416)	Multiple Extraction (50)	P-value
Gender			
Male	188	29	0.086
Female	228	21	
Age group			
16-59 years	329	27	0.0001 (in
60-86 years	87	23	favour of
Educational level			the older
No formal education	9	5	age group)
Primary education	24	10	
Secondary education	140	11	0.0001
Tertiary education	243	24	
Consumption of sugar contents			
Regularly on daily basis	129	10	0.025
Occasionally	274	35	
Non-consumption	13	5	
Tooth brushing habit			
Irregularly	6	5	0.0001
Regularly	410	45	
Use of tobacco			
Yes	11	0	0.245
No	405	50	
Presence of comorbidity			
Yes	57	8	0.658
No	359	42	

The analysis of variables for susceptibility to multiple tooth extraction with Pearson correlation coefficient shows significant factors to be the older age group, lower educational level, regular consumption of sugar contents in diets and beverages and irregular teeth brushing with p-values of 0.0001, 0.0001, 0.025 and 0.0001 respectively (Table 4). Factors such as gender, relationship status, occupational earnings, parafunctional habits, use of tobacco products and presence of comorbidities showed no significant impact on number of tooth extracted. Multivariate logistic regression analysis of various variables showed older age group, lower educational level and irregular brushing of teeth as the independent predictors of multiple tooth extraction.

Discussion

The pattern of tooth loss reflected in this study confirms caries as the leading cause of tooth mortality in a developing world. Saheeb *et al*. [5] in a previous study in southeast Nigeria also found dental caries as the predominant cause of tooth loss in 86.2% of their patients similar to the finding of another study from Northwestern Nigeria. Other studies from the Northwestern part of Nigeria have also reported a similar finding [6]. Until recently, the burden of dental caries as the cause of tooth loss

used to be low compared to periodontal disease in the developing nations [7]. Aderinokun and Dosumu previously reported that the leading cause of tooth loss was periodontal disease (61.9%) and followed by caries (31.4%) [8]. However, over the years dental caries seems to have progressively increased while periodontal disease has decreased relatively in the developing world.

The reduction in the prevalence of periodontal disease could be a reflection of the fact that the various oral preventive measures have actually achieved more positive results for periodontal disease than for caries over the past years. Another reason that may be considered is that the oral preventive measures for periodontal disease are more accessible, available and affordable than the preventive and restorative treatments for caries. However, the trend in this study suggests that there are still more to be done for both caries and periodontal disease in the South Western part of Nigeria.

Tooth mortality due to trauma in the present study is higher than that reported by an earlier similar study from Nigeria [9]. The discrepancy could be related to traumatic dental injuries resulting from maxillofacial injuries. In Nigeria with the advent and increasing use of the motorcycle as a means of transportation, coupled with poor compliance and implementation of strict road safety measures, increasing incidence of maxillofacial injuries has been reported [10]. This could also explain the wide disparity between our finding and findings from Saudi Arabia, Scotland and Wales where the proportion of tooth loss due to trauma is less than 1% [11-14]. This may be due to the fact that the preventive and well implemented road safety measures in these environments have led to a marked reduction in tooth mortality due to trauma.

Contrary to the reports by various authors from other populations where orthodontic considerations are assuming a significant cause of tooth loss [11,15], only 0.6% of the extractions in this study were for orthodontic reason. Orthodontic treatment is expensive and therefore usually sought by persons in the affluent societies. Nigeria has a significantly high poverty level and therefore, such interventions are not largely affordable. Other possible reasons may be poor awareness and lack of motivation by the general population.

The molars were the most extracted teeth (67.5%), followed by premolars (15-5%), incisors (12.0%), with the canines being the least extracted teeth (3.8%). This pattern of extraction is similar to one reported in the previous studies [9]. Alesia and Khalil however reported that the lateral incisor was the least extracted tooth type in their study [11]. The tooth morphology, the positions in the arch as well as the pattern of eruption have been previously suggested to be responsible for this extraction pattern [16].

The peak ages of tooth loss due to dental caries and periodontal disease in this study are higher than those reported in most other earlier studies [9,17,18]. The availability of oral care aids, improved oral health awareness, improved oral self care practices, easy availability, affordability and accessibility of analgesics and antibiotics may delay patients' presentation to the dental institution and hence keep the teeth longer in the mouth.

The present study has shown that older age group, lower educational level, regular consumption of sugar contents in diets and beverages as well as irregular tooth brushing were the significant factors responsible for the multiple tooth extractions. There are several studies which have shown that older age group is associated with poor oral health [19,20]. Generalized poor oral health can predispose to several oral pathologic conditions that can severely affect the health of several teeth at the same time and warrant their extraction. Various studies have shown that the oral health of individuals from low socioeconomic class is worse than that of the individuals from the upper class of the socioeconomic strata [21,22]. The present study also showed that the individuals with lower educational levels have higher tendency towards multiple extractions which may be attributable to the poor oral health promoting habits and affordability. Buchwald *et al*. [23] in their study also reported a direct proportional relationship between tooth loss and the educational level

Irregular tooth brushing was a significant factor for multiple tooth loss in this study. The cumulative effect of poor plaque control will eventually culminate in tooth loss [24]. Regular tooth brushing is considered to be the single most effective means of plaque control and overall the most effective way of promoting oral health [25]. Tooth plaque bacteria are equivocally known to also be responsible for other oral diseases like caries [25].

Frequent consumption of sugar contents in diets and beverages was also a significant factor for multiple extractions in the present study. Various previous studies have shown sugar to be the most important dietary agent in the etiology of dental caries [26,27]. Increased access to sugar without adequate protective or caries preventive measures is usually associated with an increase in caries experience. Increased caries experience coupled with restricted access to dental restorative facilities may

explain why multiple teeth may have to be extracted in the developing nations. We found no significant relationship between co-morbid conditions, smoking and multiple tooth loss contrary to previous studies reporting association between smoking as well as co-morbid conditions and tooth loss [28,29]. This may be due to the small number of the participants with associated comorbidities and smoking habit.

Conclusion and recommendation

The upward trend in tooth loss due to caries is yet to be halted in our environment. The elderly, patients with lower educational level, poor oral hygiene and regular consumption of sugary contents have a higher preponderance to multiple tooth extractions. There is the need for an improved enlightenment and education on adequate oral health care. We also need to develop effective strategies with appropriate caries preventive and restorative care which are readily accessible, affordable and sustainable in our environment.

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Pre-deposit autologous blood donation in blood conservation: perspective from a resource poor country

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Abstract

*Background***:** The transfusion service in developing countries is bedeviled with the challenges of perennial shortage of allogeneic blood and the need for safe blood. The perceived risk of transfusion-transmitted disease led to the incorporation of autologous blood transfusion (ABT) as an integral component of elective surgical protocol in many institutions in the 1980s. The improvement of viral safety of allogeneic blood products following the introduction of molecular techniques has led to a decline in the use of autologous blood use. Therefore a literature search was performed to examine current evidences and motivate the utilization of autologous blood in developing countries to increase blood availability and safety

*Materials and methods***:** A literature search on autologous blood donation and transfusion was carried out using PubMed, high wire press and google scholar. Article from 1991 to 2016 on the provision of autologous blood with its challenges, merits and demerits were reviewed.

Results: Provision of adequate units of blood is not a major issue in developed countries. With the advent of nucleic acid testing, the risk of HIV, HCV, HBV infections with receiving transfusion of allogeneic blood is considerably small. The cost incurred by the execution of autologous blood transfusion service in the developing countries is less than in the developed countries. The majority of the population in developing countries do not have access to adequate blood supply and the risks of transfusion transmitted viruses is much higher than in developed countries

Conclusion: The Hospital Transfusion Committee should encourage surgeons to offer autologous blood donation/transfusion to patients who are fit. Guideline should also be developed to establish criteria for perioperative blood donation and there should be a policy in place that allows crossover of autologous blood units to homologous blood units which will convert the autologous blood wastage reported from the studies in developed countries to gain for patients in poor resource countries.

Keyword: *Autologous, allogeneic, blood, shortage, developing countries*

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Résumé

Contexte: Le service de transfusion dans les pays en voie de développement est confronté aux défis de la pénurie perpétuelle de sang allogénique et au besoin de sang sain et sauf. Le risque perçu de maladie transmissible par transfusion a conduit à l'incorporation de transfusion sanguine autologue (TSA) en tant que composante intégrale du protocole chirurgical électif dans de nombreuses institutions dans les années 80. L'amélioration de la sécurité virale des produits sanguins allogéniques suite à l'introduction de techniques moléculaires a entraîné une diminution dans l'utilisation de sang autologue. Par conséquent, une recherche documentaire a été effectuée pour examiner les preuves actuelles et motiver l'utilisation du sang autologue dans les pays envoie de développement pour accroître la disponibilité et la sécurité du sang.

Matériaux et méthodes: Une recherche de la littérature sur le don et la transfusion de sang autologue a été effectuée à l'aide de Pub Med, de la presse à fil haut et du GoogleScolaire. Article de 1991 à 2016 sur la fourniture de sang autologue avec ses défis, mérites et démérites ont été examinés.

Résultats: La fourniture d'unités adéquates de sang n'est pas un problème majeur dans les pays développés. Avec l'avènement des tests d'acide nucléique, le risque d'infection par le VIH, VHC, VHB avec transfusion de sang allogénique est considérablement réduit. Le coût engagé par l'exécution du service de transfusion sanguine autologue dans les pays en voie dedéveloppement est inférieur à celui des pays développés. La majorité de la population dans les pays envoie de développement n'a pas accès à un approvisionnement sanguin adéquat et les risques de virus transmissibles par transfusion sont beaucoup plus élevés que dans les pays développés.

Conclusion: Le Comité de Transfusion Hospitalière devrait inciter les chirurgiens à offrir une donation ou transfusion autologue de sang aux patients qui sont en forme. Une ligne directrice devrait également être élaborée selon les critères établis pour le don de sang peropératoire et il devrait y avoir une politique qui permette le passage des unités de sang autologues aux unités de sang homologues qui convertiront le gaspillage de sang autologue rapporté par les études dans les pays développés pour gagner aux patients des pays à ressources appauvrie.

Mot-clé: *Autologue, allogénique, sang, pénurie, pays envoie de développement*

Introduction

Blood transfusion is an important component of an effective health care system. The need for blood continues to increase globally due to improvement in diagnostic and treatment options as well as advances in surgical and medical procedures requiring blood transfusion. Allogeneic blood transfusion is the commonly used approach in transfusion of individuals who need blood transfusion. Allogeneic blood transfusion is the transfusion of blood from a donor to another person who is the recipient. However, two major problems plague the supply of allogeneic blood in sub-Saharan Africa. These include provision of safe blood free from transfusion transmitted infections and adequate amount to overcome the perennial shortage of blood [1]. Whole blood donor rate in low and middle-income countries is 4.6 per 1,000 population and 11.7 donations per 1000 peoples compared with 33.1 donations per 1000 peoples in high income countries [1]. The report for Nigeria in 2010 was 0.2 units/1,000 population [2] while WHO recommends 10/1000 population to meet clinical demand in resource-limited settings [3].

The organisation of Blood Transfusion Service in some developing countries is a combination of centralized, decentralized and informal system [4]. Family replacement donors constitute 75% of the blood donors [4]. It behoves the transfusion services to search for means of reducing the impact of these major challenges on morbidity and mortality. Timely access to the right quantity and quality of blood is an important tool for performance of surgery in many patients. There is increasing concern on availability of blood for surgical patients. Even though, the best practice is to manage any bleeding without blood transfusion or use a blood alternative, there are patients who are best treated with blood transfusion due to the amount of perioperative blood loss. Access to safe and adequate blood for surgery remain a mirage for both surgeons and patients. In developing countries, the patient and blood transfusion services are responsible for maintenance of blood supply. With an average donation rate of 0.37% in developing countries, the balance between the impact of measures to contain known and unknown threats, and the adequacy and accessibility of blood and blood components is not within acceptable limit [5].

In order to expand the sources of blood, it is imperative to seek additional source of blood supply to the allogeneic blood to meet present blood needs. Autologous blood can be rationally considered to provide an alternative source of blood supply to allogeneic blood products for some patients undergoing surgical procedures. In cases of unused blood, where criteria for allogeneic blood collection are met and infectious marker screening is negative, consent of donor could be obtained for the blood to be given to patients in dire need of transfusion. The provision of autologous blood will improve availability, safety and quality of blood for transfusion in some surgical patients. Therefore this review is carried out to improve the supply and safety of blood to surgical patients and promote the utilization of autologous blood transfusion in low income countries in order to conserve the limited allogeneic blood stock.

What is blood conservation?

Blood Conservation is a global concept engulfing all possible strategies aimed at reducing patients' exposure to allogeneic blood products. It is patient blood management by: Correcting preoperative anaemia; Minimizing perioperative blood loss through blood-sparing perfusion and surgical techniques; The administration of agents to diminish blood loss (aprotinin, tranexamic acid, epsilon aminocaproic acid, fibrin sealant) or to promote red blood cell production (erythropoietin); Using minimal haemoglobin-based transfusion triggers and the use of autologous blood. An individualized strategy based on patient specific risk factors, such as preoperative haemoglobin level, anticipated difficulty of the procedure, anticipated blood loss and comorbidities are useful in getting good outcome.

Autologous blood donation as a strategy in blood management can conserve the use of allogeneic blood reducing the pressure on these limited resources. In addition to reducing the demand on allogeniec blood, any unused blood units can be transferred to the homologous pool. While the proportion of such units of blood may be few, the impact on the blood reserve in emergencies could be significant. There are unique sets of challenges pertaining to blood conservation in different surgical procedures and age of patients which determine the strategy to engage. The direction of blood conservation is towards bloodless surgery because of safety and efficacy concerns of allogeneic blood transfusions, their impact on patient outcomes and associated staggering costs. In patient going for

cardiac surgery, blood is certainly required and higher haematocrit will be required for surgery because of cardiopulmonary by pass circuit [6]. Autologous blood donation (ABD) can be carried out in children older than 3 years of age or with weight more than 15 kg in which case a volume of 10 ml/kg may be collected per phlebotomy using femoral vein, while replacing the volume and electrolyte deficit with 0.9% saline or colloid. Supplemental iron, Vitamins (A, C, K), folic acid and B12 may be required [6]. In elective surgical patients who are fit, when multimodal preventive measures are not adequate for a safe surgery, autotransfusion may be explored.

Current status of autologous blood donation and transfusion

Autologous blood donation is the donation of blood for self. Autologous blood transfusion (ABT) is the reinfusion of blood or blood components to the same individual from whom they were taken [7]. It is a process in which the blood donor and recipient are the same. It is the safest type of blood transfusion and is important in the strategy of blood conservation. The perceived risk of transfusion-transmitted disease led to the clamour for ABT in the 1980s [8]. In 1987, Pre-deposit autologous donation (PAD), which is the banking of red cell units from the patient before planned surgery accounted for 11% of the total transfusion volume at Saint Cloud Hospital in Minnesota [9]. In Europe, predeposit autologous blood units collected in year 2000 was 3.3% of the allogeneic units compared to 4.2% in 1997. The predeposit collection was commonest in Italy (7.8%) and Germany (6.4%) [10].

There is dearth of data on its use in developing countries, a study from Kenya reported 5% of patients from general surgery and orthopaedic ward: 98.4% deposited only one unit while 1.6% deposited four units of blood [11]. In an African setting, autologous donation and transfusion have been administered to patients aged 13-80 years. Predeposit haemoglobin was 11.7gm/dl and post operative haemoglobin was 10.2gm/dl a day after surgery [12]. Intra-operative cell salvage was observed to be financially comparable to purchasing an equivalent number of red cell concentrate (RCC) from the South African National Blood Service (SANBS) and have potential benefit by reducing allogeneic blood transfusion [13]. With the development of effective viral screening test, the number of patients offered ABT has steadily declined and pre-operative donation of autologous blood is a practice that is now being abandoned [14]. However, its use is expanding in Japan [15] to improve patient management. Given the current remote risk of viral transfusion-transmitted infection by donor blood in developed countries, the rationale, safety and cost-effectiveness of routine PAD has been severely questioned. In the 1990s, Saint-Louis' Regional Hospital, Senegal introduce the delayed autologous transfusion due to prevailing transfusional risks and blood shortage [16]. The procedure helped to optimize the use of the limited allogeneic blood stock.

Autologous transfusion in Nigeria

Autologous blood accounts for 9% and 0.5% of blood transfused in North Eastern and South Western, Nigeria respectively [17, 18]. A prospective study on obstetric and gynaecological patients at the University of Maiduguri Teaching Hospital, Maiduguri over an 8 year period showed that 20.7% and 22.1% of blood received by obstetrics and gynaecological patients respectively were autologous blood [19]. Induction of labour in 53.9% constitutes the major reason for the autologous blood donation in obstetric while the major indication in gynaecology patients was myomectomy (25.7%). In an audit of spinal surgery in Eastern Nigeria, 3 out of 70 patients were offered autologous transfusion [20] The proportion of patients being offered autologous blood donation in our hospital, University College Hospital Ibadan, Nigeria has reduced from 0.5% in 2008 to 0.2% by 2015 [unpublished data]. Factors responsible for the utilization of the program include donor acceptance, clinician referrals, and perceived lack of conflict with the homologous donation process [9].

In a study conducted in Benue state of Nigeria where HIV prevalence rate was reported as 12.7% according to the 2010 sentinel survey, 85.1% patients were willing to have autologous transfusion in the event of an elective Surgery [21]. Another study conducted in south western Nigeria with a lower HIV seroprevalence showed that knowledge of ABT among patients for surgery was poor, 69% of elective surgical patients have never heard of ABT; 74% were willing to participate in ABT if offered by their physician [22]. The challenges identified are lack of information about ABT and patients are not being offered the option [21,22]. Autologous blood donation was mainly carried out for orthopaedic, otorhinolargnngological and gynaecological procedures [23]. A study showed that allogeneic blood transfusion in a Nigerian hospital is significantly more expensive than autologous transfusion mainly due to greater infective morbidity

in homologous blood recipients [24]. Autologous blood can be used to make blood available to patients within the context of available resources to reduce morbidity and mortality.

Types of autologous blood donation

Four types of autologous blood donation and transfusion are available to patients. These are predeposit / preoperative autologous blood donation (PABD), acute normovolemic hemodilution, intraoperative blood salvage, postoperative blood salvage. Predeposit (pre-operative) blood donation (PAD) is the process in which the patient donates blood prior to surgery and the blood is stored for an anticipated need during or after surgery. In acute normovolemic hemodilution (ANH), blood is collected immediately prior to surgery in the operating room and the patient's blood volume is maintained by the simultaneous infusion of crystalloid or colloid fluids. The blood is stored in the operating theatre at room temperature and reinfused at the end of surgery or if significant bleeding occurs. ANH is most often used in cardiac bypass surgery where the immediate postoperative transfusion of 'fresh whole blood' containing platelets and clotting factors is seen as an advantage. Reported hazards of ANH include fluid overload, cardiac ischemia and wrong blood into patient.

Intraoperative blood salvage is the process in which blood is collected from the surgical field and is reinfused after being washed. Blood lost into the surgical field is filtered to remove particulate matter and aspirated into a collection reservoir where it is anticoagulated with heparin or citrate. If sufficient blood is collected and the patient loses sufficient blood to require transfusion, the salvaged blood can be centrifuged and washed in a closed, automated system. Red cells suspended in sterile saline solution are produced, which must be transfused to the patient within 4 hours of processing. It is not recommended when bowel contents contaminate the operation site and in patients with malignancies. Automated devices are available for elective and emergency surgery. Postoperative blood salvage is the process in which shed blood is collected from surgical drains and reinfused to the patient [8]. It is mainly used in orthopaedic procedures, especially after knee or hip replacement and in correction of scoliosis. The simple filtration systems for reinfusion of unwashed red cells are mainly used when expected blood losses are between 500 and 1000 ml. Automate devices are available. It remains unclear whether it adds significantly to a comprehensive blood conservation programme

When there is a potential requirement for transfusion in elective surgical procedures, pre-deposit autologous donation can be used in selected cases to conserve blood for the blood transfusion services and reduce the potential complications of allogeneic blood transfusion. Despite this advantages it is underutilized for medically eligible patients undergoing elective operation [25].

Benefit of autologous blood transfusion over allogeneic transfusion

The inherent risks in allogeneic transfusions persists despite all efforts to ensure safety in recipients. The well-known risks are the transmission of infections and immunological complications. Even though the risk of transfusion transmissible infections have reduced significantly in the developed countries as shown in table 1[26]. The risk in developing countries is of major concern because of high seroprevalence (Table 2). In developed countries, transfusion of blood products is now very safe with respect to viral transfusion-transmissible infections (TTIs). This is due to the combined effect of careful selection of donors on the basis of their history and clinical information and increased sensitivity of pathogen testing, which reduces infectious window periods with high transfusion standard. The estimated residual transfusion risk for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) were 1, 4.5, and 2.5 infections per 1000 transfused units, respectively in sub Saharan Africa [35]. The presence of paid and replacement blood donors is compounded by inadequate pathogen testing, inconsistent testing strategies and suboptimal quality assurance. Therefore, high level of blood safety is not guaranteed. Autologous blood transfusion would eliminate the risk of these infections and also emerging pathogens while reducing patient anxiety about TTIs. Autologous blood donation stimulates erythropoiesis, though the red blood cell (RBC) mass regenerated by PABD is smaller than the RBC mass pre-deposited [36].

Report on the incidence of immunological complications are sparse due to poor documentation and lack of haemovigilance in most developing countries. The immunological complications include ABO incompatibility, febrile transfusion reaction, transfusion-related acute lung injury, allergy, urticarial, alloimmunization and immunomodulation. A study from Nigeria reported an incidence of 8.7%. [37]. In Norway, Denmark and United Kingdom immunological transfusion reactions occurred 96.7 times per 100 000 red cell transfusion [38]. Febrile

Table 1: Risk of Transfusion Transmitted Viruses for Mandatory Screening in Selected Countries

Viruses	Country	Rate (100,000 units)
Hepatitis B Virus	UK	1:2.8 million
	USA	1:300,000
	Canada	1:1.7million
	Australia	1:720,000
	Netherland	<1:620,000
Hepatitis C	UK	<1:2.8million
	USA	1:1.1million
	Canada	1:6.7million
	Australia	1:1million
	Netherland	<1:620,000
HIV	UK	1:2.8million
	USA	1:1.5million
	Canada	1:8million
	Australia	<1:1million
	Netherland	<1:620,000c

Adapted from Rogers M.A.M., Rohde J.M. and Blumberg N. Haemovigilance of reactions associated with red blood cell transfusion: comparison across 17 countries. 2015 ISBT International Society of Blood Transfusion. 2015 Doi:10.1111/vox.12367.

Table 2: Prevalence of transfusion transmitted viruses for mandatory screening in selected developing countries

Viruses	Country	Prevalence (References)
Hepatitis B Virus	Nigeria	10-20% [27,28,29]
	Burkina Faso	13.4% [30]
	Ghana	9.6 – 21% [31,32]
	Cameroon	12.6% [33]
	Mozambique	10.6 % [34]
Hepatitis C	Nigeria	0.5-6% [27,28,29]
	Burkina Faso	6.3% [30]
	Ghana	5.6% [31, 32]
	Cameroon	3.6% [33]
	Mozambique	0% [34]
HIV	Nigeria	3.0-7.2% [27,28,29]
	Burkina Faso	1.8% [30]
	Ghana	4.9% [31, 32]
	Cameroon	3.3% [33]
	Mozambique	8.5% [34]

non-haemolytic (FNHTR) and delayed serologic transfusion reactions were the most frequent adverse events reported after RBC transfusion, occurring in 26 patients per 100 000 RBC units and 25 patients per 100 000 RBC units administered, respectively (26). Febrile non-haemolytic transfusion (FNHTR) is not life-threatening but could be distressful. The study from Nigeria showed that 5.6% of 462 transfusions had FNHTR. [37]. Leukocyte-depleted blood products may minimize this problem but leucoreduction of RBC units is not carried out in the developing countries. Most delayed haemolytic transfusion reactions (DHTR) are unpreventable because the blood is serologically compatible at the time of transfusion, but some cases are due to antibodies to minor red cell antigens that were simply not detected by the routine pre-transfusion antibody screening assay. The incidence of DHTR is likely to be higher in transfusion practice without facility to screen for antibodies outside the routine ABO and Rhesus D blood group which is the situation in many developing countries.

In a tertiary care hospital in Ohio, USA, allergic transfusion reactions accounted for 17% of the transfusion reactions [39]. Severe allergic reactions (anaphylaxis, anaphylactoid signs and symptoms, and/or hypotension) were observed in 7.7% of allergic reactions, or 1.3% of all transfusion reactions [39]. Immunomodulation is unusual in autologous blood transfusion. It is an allogeneic blood transfusion related immunosuppression, which is thought to increase the incidence of postoperative infections (up to six times), delay healing of postoperative wounds, and thereby prolong hospitalization. Newman *et al* reported that re-operation for infection was higher in cases with allogeneic blood exposure (1.67%) than in patients without blood transfusion (0.72) (p=0.013) and autologous –only transfusion [40].

Disadvantages of autologous blood transfusion

Even though ABT is a useful procedure to reduce most of the complications of blood transfusion, it is not without risks. Record-keeping, collection, and transfusion errors are occasional risks of autologous transfusions [41]. The risk of bacterial contamination and clerical error must be taken into account for both autologous and homologous blood. There is a 1-2% risk of possible clerical errors in labelling of unit and identifying patient [9]. The risks associated with any blood donation is not eliminated in ABT. This include bruising and tenderness at venipuncture site, syncope attack, [1,16], 783 risk of a complication requiring hospitalization [8]. Anaemia that may compromise the patients' health is another disadvantage because the patients provide safe blood for themselves at the expense of the risk of developing iron deficiency anaemia [42]. Time commitment by patient is required from the patient to donate. A donated unit of blood may be discarded if there is complication during storage such as clots in blood or leakage of blood bag. In hospitals, where surgery is scheduled 3-5 weeks in advance, blood may go out of date if surgery is postponed.

Although ABT donation reduces the risk of receiving allogeneic transfusion by 43%, but it increases the overall risk of receiving any blood transfusion (allogeneic and/or autologous) [43]. The increased rate of exposure to any transfusion was attributed to two factors: (1) patients who donate autologous blood in general have lower preoperative haemoglobin levels than those patients who do not predonate autologous blood, and therefore have an increased probability of requiring an intra-operative and/or postoperative blood transfusion; (2) the availability of predonated autologous blood engenders a more liberal transfusion policy. ABT donors are vulnerable to being over- transfused or re-transfused due to less conservative transfusion threshold than allogeneic since microbiological safety is not an issue. Autologous blood is more costly than homologous blood [14] largely due to collection of units not subsequently transfused. The wastage of unused PAD units varies from 18% to greater 50% [14]. In cases of unused blood, where the circumstances of blood collection and infectious marker screening meet the criteria for allogeneic blood collection, consent of donor could be obtained for the blood to be given to patients in dire need of transfusion. This wastage may be converted to an advantage in developing countries particularly sub Saharan Africa where the blood donor rate is low. It should also be borne in mind that patients may not be able to pre-donate all the blood they require for surgery because the complete donor criteria must be met.

Since PABD is not without potential risks to the donor, who is also the patient, the supposed benefit of PABD has to be weighed against the risks of donation and re-transfusion of autologous blood on one hand and against the risk of allogeneic transfusion on the other hand [44].

Cost of autologous blood transfusion

The cost implication of ABT is an issue of concern and varies from country to country depending on guidelines for the implementation of the ABT. The post donation cost is determined by the extent of processing that the guideline requires. The increased protection afforded by donating autologous blood is no longer seen as an advantage that justifies the increased cost given the improved safety of allogeneic transfusions in countries incorporating stringent criteria and sophisticated technique to select blood donors. [45]. In our hospital, University College Hospital, Ibadan, Nigeria, an autologous blood unit costs $8 while an allogeneic blood unit costs $30. The cost of labour or input of the managing physician is not often included in the cost of autologous blood in our hospital as it is donated at the hospital based blood bank. The cost for autologous blood is exclusive of the search for replacement donors. The cost incurred by patients who choose to predonate blood (e.g., inconvenience, time, travel costs, expense of additional medication) [46] may be comparable to the stress and cost of getting two or more replacement donors.

The costs associated with administering the preoperative autologous donation program by the hospital, physician fees for conducting assessments of prospective autologous donors, and the procurement, processing and storage of the blood by the Red Cross may not be an issue in an hospital based blood bank. Some people are of the opinion that allogeneic blood transfusions are expensive. Reported cost per unit of packed red cells has varied between $270 and $780, depending on further costs for storage, laboratory analyses (cross match tests, antibody tests, etc.), and other post donation processing. Actual figures in Switzerland show that the cost for one RBC unit in surgery is $500, without taking into consideration transfusion-related complications [47]. Only approximately half of autologous units collected are actually used [48]. Previous report from Nigeria suggested that homologous blood transfusion is significantly more expensive than autologous transfusion and the rate of infection was 85.7% for homologous blood recipients compared to 14.3% for autologous blood recipients [24]. Autologous blood may improve availability of blood without unnecessary burden on family members to source blood and also reduce anxiety about transmission of infections

Indications for pre deposit autologous blood donation

According to Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee and Italian Society of Transfusion Medicine and Immunohaematology [10], the following are the indications for autologous blood donation: patients with rare blood groups for whom it is difficult to obtain allogeneic blood, patients with multiple alloimmunisation for whom it is difficult to obtain compatible allogeneic blood, patients who refuse consent to allogeneic transfusion for personal reasons, scoliosis surgery in children and surgical procedures where blood transfusion is anticipated

Eligibility

There are no generally accepted criteria for predeposit autologous donation [49]. Three categories of patients are considered for PABD:

Patients who meet normal donor health criteria; Patients who are well and ordinarily able to withstand the blood collection procedure but who do not meet normal donor selection criteria and patients who are unwell. The donor should be between 10 and 65 years of age who could be either a male or female and should have a haematocrit greater than 35%. If patient is <50kg, the amount of blood removed at a time should not be more than 8ml/kg of the body weight, and for peadiatric patients, not more than 10% of the blood volume should be removed at a time. The ABT patient must be screened and found negative for HIV, HCV and HBV.

Contraindications

Appropriate donor selection is essential. The incidence of adverse reactions is no greater in properly selected autologous donors than in homologous donors [9]. Administration of oral ferrous sulfate allows many patients to meet all of their perioperative transfusion requirements [9]. In order to avoid wastage, autologous blood donation should not be considered in patients without a definite surgical date. Other conditions in which it is contraindicated include: Current systemic infection which could either be viral, bacterial or fungal, anaemia with haemoglobin <110 g/L or packed cell volume < 33% prior to commencement of autologous collection, disorders such as haemoglobinopathies, pre -eclampsia, chronic obstructive way disease, diabetes mellitus, severe hypertension, psychiatric illness/epilepsy, cerebrovascular disease including transient ischaemic attacks or a stroke, cardiac disease especially ischaemic heart disease, such as angina and myocardial infarction and patient on B brokers or ACE inhibitor (isovolaemic replacement). Blood donors with poor venous access and those who had sustained a delayed faint (weakness or loss of consciousness) several hours after collection, should not be considered.

Procedure

Patients considered suitable for elective surgical procedures and are in good general health to tolerate phlebotomy are generally suitable for autologous blood collection. However, only patients with a reasonable expectation that blood will be transfused should be selected and counselled for the procedure. Therefore, the hospital should have a maximum blood ordering schedule for each surgical procedure to engage in PABD. Patients with any cardiovascular, cerebrovascular or respiratory diseases which will preclude them from allogeneic blood donation should not be considered for autologous blood donation. The doctor with clinical responsibility towards the patient should determine if patient is fit to undergo the PABD. The documentation used to refer a patient for autologous blood collection should be signed by the medical practitioner and be accompanied by a signed patient consent form. The patient must be aware that it may be necessary to transfuse allogeneic blood. A standard questionnaire administered for allogeneic blood donor which include questions about high risk factors for transmission of blood transmissible disease and medical suitability should be completed by the patient at the time of each collection. Patients who weigh less than 50 kg should have 8ml/kg collected and the volume of anticoagulant should also be adjusted accordingly:

The total blood volume of the patient can be calculated using a figure of 80ml/kg.
Example: Weight of patient 35kg
Total blood volume 35kg x 80ml/kg = 2800 ml
Volume of blood to be collected 2800 x 10% = 280ml
To calculate the amount of anticoagulant required for a given volume and hence the amount of excess anticoagulant to be removed, use the following equation.

$$\frac{\text{Volume of blood collection} \times 63}{450} = \text{volume of anticoagulant}$$

Example: volume of blood collection; 280 ml

$$\text{Volume of anticoagulant: } \frac{280 \times 63}{450} = 39 \text{ ml}$$

Excess anticoagulant: 63 - 39 = 24 ml A double collection pack is required so that, transfer the excess anticoagulant into attached plasma bag prior to blood collection without breaching the closed system could be performed.

At least 4-5 units of blood can be collected before surgery. Haemoglobin level must be determined before each donation which should not be less than 110g/l. The blood is collected weekly within the four [4] weeks prior to the date of the operation. Blood should not be drawn more than once a week, the last donation at least 4-7 day before surgery. Occasionally a leap – frog technique can be performed in which the oldest blood unit is returned to patient to allow another unit (fresher unit) to be withdrawn. Intravenous fluids should be considered if systolic blood pressure becomes less than 100mm/hg following blood collection. Traceability of all autologous units must be possible, consequently transfusion records must permit tracking of each unit

from the patient, through all procedures performed on the unit, to transfusion to the patient, or disposal. Autologous collections must be stored and transported in a manner similar to that of allogeneic blood but stored in a different fridge from allogeneic blood.

Pedipack which allows collection of 250mls while containing 35mls of anticoagulant are appropriate for children and adults less than 50kg. Patients who pre-deposit should have oral iron prescribed before the first donation and continue until surgery. Labelled blood bags and sample tubes should not be placed on a shared table or trolley between two adjacent donors to reduce the risk of transposition. The tests of markers for transfusion transmitted infections should be carried out on the first and last donations. Pre-transfusion testing including a group and antibody screen should be performed on the patient prior to surgery, as allogeneic blood may be required in addition to the autologous blood previously collected

The labels on the donated blood unit must clearly state:

1. Autologous Blood
2. Unique blood pack number.
3. Blood group.
4. Collection and expiry date.
5. Place of collection.
6. Patient details (name, date of birth, Hospital number).
7. Patient's signature.
8. Final destination (ward or theatre at which blood will be stored/transfused).
9. Summary of the test results for infectious disease markers
10. The blood group (ABO / Rh D) and any compatibility tests

With a red cell storage-life of 35 days at 4°C, most healthy adult patients can donate up to three red cell units before elective surgery. Patients may be given iron supplements, sometimes with erythropoietin, to prevent anaemia or allow more donations to be collected. Although recombinant human erythropoietin can stimulate red blood cell production before autologous donation and decrease the need for transfusion, it is not clear whether this strategy, which can cost thousands of dollars per patient, will be cost-effective [42]. Its use is generally not recommended. The Blood Safety and Quality Regulations (BSQR, 2005) require that donations for PAD must be performed in a licensed blood establishment, rather than a routine hospital setting. The donations must be processed and tested in the same way as donor blood and are subject to the same requirements for traceability.

A very high level of blood safety is guaranteed by the combined effect of careful selection of donors on the basis of their history and clinical information, serological tests and genomic amplification to screen for transfusion-transmissible infections.

Decision on Unused Autologous Blood unit

The issue of disposition of pre-donated blood which is not transfused to donor-patients remains unresolved. In some transfusion centres, all units are discarded. In others, the blood can be administered to other patients if the donor met all the criteria for homologous donors and the blood tested negative for infectious disease markers [9]. Controversy exists concerning whether the costs and potential risks outweigh the potential benefits of "crossover" use in the general blood supply of unutilized blood that was donated for autologous transfusion. Individuals with high pre-operative haematocrit are able to tolerate more blood loss during surgery and have less need for re-transfusion of PABD units and may be responsible for increased wastage of PABD units [36].

The additional cost of autologous blood is a function of the discarding of units that were donated but not transfused. The first theoretical advantage of ABD is prevention of transfusion-transmitted disease namely viral infections such as HIV or hepatitis virus or emerging virus. Actually, the very low residual risk that remains from allogeneic transfusion after appropriate selection of donors, leuko-reduction and nuclear acid testing in developed countries does not argue for allogeneic blood in developing country. The effectiveness of autologous blood donation and transfusion may not be marked but the difference it make in different contexts may be significant. Autologous donation programs would have the additional advantage of boosting the blood bank stock. There is therefore a need to develop a clinical-organizational protocol to encourage PABD as it may hold promise of increase availability of blood in low income countries.

Conclusion

Considering the tremendous pressure on blood supply in sub-Saharan Africa, there is a need for individual hospital transfusion committees to set up standard guidelines for the use of autologous transfusion that would be synchronized with the transfusion policies to improve availability of safe blood. Once there is an effective collaboration between the blood bank and the attending surgeons, blood donors may be recruited and screened at a hospital-based blood bank in contrast to the

centralized transfusion centre in the developed countries. Patients' families are burdened with the responsibility of finding replacement blood donors and there are concerns about blood safety. The tremendous cost incurred by the execution of autologous blood transfusion service in developed countries may not be replicable in the developing countries.

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Endocrine Disruptors-Arsenic, cadmium and lead in pre and postmenopausal black women with breast cancer.

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Abstract
Background: The involvement of toxic metals in adiposity has been suggested to be contributory to the high incidence of breast cancer, particularly in sub-Saharan Africa. This study is aimed at evaluating serum arsenic, cadmium and lead in relation to adiposity and blood pressure in Nigerian women with breast cancer.
*Methodology***:** The study comprised 85 women newly diagnosed with breast cancer pre-therapy (cases) matched with 84 apparently healthy women without breast cancer (controls) according to age and menstrual phase. Arsenic (As), cadmium (Cd) and Lead (Pb) levels were determined by atomic absorption spectrophotometry. Blood pressure and anthropometry were determined by standard methods. Data analysed by Student's t-test and Pearson correlation coefficient were considered statistically significant at $p<0.05$.
Results: Cd and Pb levels were significantly higher in cases, compared with controls ($p<0.05$). Waist circumference (WC), hip circumference (HC), weight, height, waist hip ratio (WHR), waist height ratio (WHtR) were significantly higher in cases compared with controls ($p<0.05$). Cadmium positively correlated with diastolic blood pressure while FT_4 inversely correlated with arsenic in the cases ($p<0.05$).
Conclusion: Observations in this study suggest the involvement of these toxic metals in adiposity which could be involved in breast carcinogenesis.

Keywords: *Lead, cadmium, arsenic, breast cancer, blood pressure, adiposity*.

Résumé
Contexte: L'implication des métaux toxiques dans l'adiposité a contribué à la forte incidence du cancer du sein, en particulier en Afrique subsaharienne. Cette étude avisée à évaluer l'arsenic sérique, le cadmium et le plomb par rapport à l'adiposité et à la tension artérielle chez des femmes nigérianes atteintes de cancer du sein.

Méthodologie: l'étude comprenait 85 femmes nouvellement diagnostiquées avec le cancer du sein, prétraitement (cas) égalée avec 84 femmes apparemment en bonne santé sans cancer du sein (témoins) selon l'âge et la phase menstruelle. Les niveaux d'arsenic (As), de cadmium (Cd) et de plomb (Pb) ont été déterminés par la spectrophotométrie d'absorption atomique. La pression artérielle et l'anthropométrie ont été déterminées par des méthodes standard. Les données analysées par le test t d'étudiant et le coefficient de corrélation de Pearson ont été jugées statistiquement significatives à $p<0,05$.
Résultats: Les niveaux de Cd et de Pb étaient significativement plus élevés dans les cas, par rapport aux témoins ($p<0,05$). La circonférence de la taille (CT), la circonférence de la hanche (CH), le poids, la hauteur, le rapport de la taille et de la hanche (RTH), le rapport de taille de la hauteur (RTHt) étaient significativement plus élevés dans les cas comparés aux témoins ($p<0,05$). Le cadmium s'est corrélé positivement avec la pression sanguine diastolique tandis que le FT_4 était inversement corrélé avec l'arsenic dans les cas ($p<0,05$).
Conclusion: Les observations dans cette étude suggèrent l'implication de ces métaux toxiques dans l'adiposité qui pourraient être impliqués dans la carcinogenèse du sein.

Mots-clés: *Plomb, cadmium, arsenic, cancer du sein, pression sanguine, adiposité.*

Introduction

Breast cancer is the most frequent cancer among women and also the leading cause of cancer mortality in women globally. An estimated 1.5 million new cases of breast cancer worldwide was reported in 2002 [1]. In Nigeria, an increase in incidence of breast cancer has been reported [2]. Recent findings have suggested the contribution of environmental factors to the high incidence of breast cancer [3]. This is due to the increased use of various metals in industry, agriculture and medicine brought about by the current industrial revolution which has invariably led to wide spread environmental pollution [4].

Toxic metals-arsenic (As), cadmium (Cd) and lead (Pb) have been reported to adversely affect the endocrine signalling system and are referred to as endocrine disruptors (EDs). Endocrine disruptors are

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almost impossible to eliminate in the environment, because they do not decompose, hence, they are absorbed into the human system through different routes. Arsenic and cadmium compounds are lipophilic, hence, they readily penetrate cell membranes [5]. On the other hand, cadmium can bind to protein to form a complex (cadmium-metallothionein) which is actively taken into the cell by endocytosis [6]. Lead may be absorbed by passive diffusion [7].

These toxic metals are a major source of oxidative stress, which is involved in the development of breast cancer [8]. Emerging reports indicate that these toxicants could influence adiposity, however, the exact mechanisms involved is not clear. Visceral adiposity has been strongly associated with an adverse metabolic risk including insulin resistance and a strong aetio-pathogenic factor for the development of type 2 diabetes mellitus [9]. These systemic effects could be involved in cancer biology [10]. Arsenic is a metalloid that is ubiquitous in the environment. Human exposure includes ingestion of contaminated food and water, inhalation of contaminated air and by dermal contact. Arsenic compounds are lipid soluble and within 24 hours of absorption are distributed throughout the body where they can bind to sulfhydryl (-SH) groups on proteins. Arsenic may also replace phosphorus in bone tissue and be stored for years [11]. Methylation efficiency in humans appears to decrease at high arsenic dose. Studies show that aging is associated with a diminishing capacity to methylate inorganic arsenic, resulting in increased retention of As in soft tissues [12] including breast tissues. Chronic exposure to As compounds has been associated with several types of cancer [13]. Arsenic interferes with oestrogen receptor, its non-cytotoxic concentrations significantly inhibited oestradiol receptor-regulated effects in human breast cancer MCF-7 cells [14].

Cadmium ranks close to lead as a metal of current toxicological concern [15]. It occurs in nature in association with zinc and lead. Extraction and processing of these metals often lead to environmental contamination with Cd. Although, smoking is a well-established source of cadmium exposure, the major route of cadmium exposure is ingestion of shellfish and certain food, particularly root vegetables, potatoes and grains (rice and wheat) grown on cadmium-rich soils [16]. Cadmium is a known cumulative toxicant with a biological half-life of more than 10 years in humans [17]. Cadmium accumulation occurs in the adipose tissue, liver and kidneys [18]. Only a small fraction of inhaled or ingested Cd is excreted, resulting in increased body burden over time [19]. Chronic low Cd exposure will eventually result in accumulation to toxic levels [18]. Women tend to have higher Cd levels than men presumably because of lower iron stores, which increase Cd absorption. Thus, comparable environmental exposures to Cd may disproportionately affect women compared to men [20]. Significantly higher Cd levels were observed in breast tissue and biological media from women with breast cancer compared with controls, suggesting that exposure to Cd could be interpreted as a potential risk factor for breast cancer [21].

Lead has been reported as a metal that can be found in drinking water, which is of great public health concern [15]. Lead contamination in the environment, resulting in toxicity in several body organs and systems has been documented [22]. This is in spite of the fact that Pb in gasoline, food cans and in paints was banned in the United States between 1980 and 1990. Recent reports showed that enamel paints with very high levels of Pb were sold freely in Nigeria [23]. The association of Pb with breast cancer is inconsistent [24].

There is paucity of information regarding the association of As, Cd and Pb with adiposity in breast carcinogenesis in sub-Saharan Africa. This study was therefore designed to determine the serum levels of As, Cd and Pb in relation to adiposity in Nigerian women with breast cancer who have not started treatment.

Materials and methods

Study design

This study was a case-control study conducted in the Surgical Oncology Clinic of the Department of Surgery, University College Hospital, Ibadan. The study protocol was approved by the University of Ibadan and University College Hospital Health Review Committee (UI/EC/10/0193). Informed consent was obtained from the participants before their recruitment. Semi-structured pre-test questionnaire was administered to each participant to obtain data on demography, social, diet and reproductive history.

Study participants

One hundred and sixty-nine women aged 28-80 years were consecutively recruited for this study. Eighty-five were histologically confirmed breast cancer patients who had not commenced treatment (Cases). They were recruited from the Surgical Oncology Clinic of the Department of Surgery, University College Hospital, Ibadan, by a Consultant Surgical Oncologist. Eighty-four non-pregnant, apparently healthy women aged 28-80 years were recruited as controls. The controls were recruited at three Primary

Health Clinics (PHC) in Ibadan North Local Government Area of Oyo state (PHC, Idi Odundun, Agodi, PHC, Agbowo and Elderly Women/Widows Clinic, Agodi-gate). Their breasts were examined by trained nurses for the presence of any breast lump. They were asked if they felt any pain or had any discomfort in their breasts. Those that complained of pain, discomfort and/or had lump in their breasts were excluded from the study. Each of the cases was matched for age and menstrual phases (follicular, luteal and menopausal status) with the controls. Participants were reported as postmenopausal if they had stopped menstruating over the last twelve months [25]. Participants that had bilateral oophorectomy were also considered postmenopausal.

Inclusion criteria

Non pregnant, non- hypertensive participants with histologically confirmed breast cancer who had not commenced treatment and gave informed consent.

Exclusion criteria

Pregnant women and those who reported being on hormonal drugs (i.e. contraceptives), had other types of cancers and/or chronic diseases were excluded from the study. Postmenopausal women on hormone replacement therapy were also excluded.

Anthropometric indices

Anthropometric indices: weight, height, body mass index, waist circumference, hip circumference, waist-hip ratio, waist-height ratio were measured by standard methods described elsewhere [26].

Blood pressure (BP) measurement

Blood pressure was determined using a mercury sphygmomanometer and recorded to the nearest mmHg [28]

Sample collection

10mL of venous blood was aseptically obtained by venepuncture from participants and dispensed into plain bottle in the controls, and after diagnosis and histological confirmation of invasive ductal carcinoma pre-therapy in the cases. All samples were centrifuged at 500g for 5 minutes, the serum obtained was aspirated into clean vials and stored at -20^{o}C until analyses were done.

Toxic metals estimation

Serum arsenic, cadmium and lead were determined by atomic absorption spectrophotometry (Buck Scientific, 210 VGP. Atomic Absorption Spectrophotometer. Connecticut, USA).

Serum oestradiol, progesterone, FT_4 and TSH were determined by enzyme immune assay on TOSOH AIA System Analyzers (Tosoh Corporation, Tokyo 105-8623, Japan). Values for hormones; oestradiol, progesterone, FT_4 and TSH have been previously reported [27]. The reference intervals of hormonal assays are Oestradiol (E_2): Follicular Phase: 90-1100 (pmol/L), Luteal Phase: 90-1200 (pmol/L), Postmenopausal: $\leq$170 (pmol/L). Progesterone: Follicular: $\leq$2.8 (nmol/L), Luteal: 15-80 (nmol/L), Postmenopausal: $\leq$ 1.59 (nmol/L). Free Thyroxine (FT_4):10.6-21.0 (pmol/L). Thyroid Stimulating Hormone (TSH):0.38-4.31 (mIU/L). The limits of detection were 0.318 nmol/L for progesterone, 52.85 pmol/L for oestradiol, 1.29 pmol/L for FT_4 and 0.01 mIU/L for TSH. The intra-batch coefficients of variation were 11.3% for progesterone, 4.1% for oestradiol, 5.3% for FT_4 and 5.0% for TSH.

Statistical analysis

Data were analysed using Statistical Package for Social Scientists (SPSS) software, version 18. Student's t-test was used for comparison of quantitative variables. Pearson correlation coefficient was used to find relationships between the quantitative variables. Two-tailed independent t-test of significance at 95% confidence limit with $p<0.05$, was considered significant.

Results

Table 1 shows age, anthropometric indices, blood pressure and toxic metals in premenopausal women with breast cancer (pre cases) and premenopausal women without breast cancer (pre controls). Waist circumference, hip circumference, weight, height, waist hip ratio, waist height ratio, systolic blood pressure, lead, cadmium and arsenic were significantly higher in premenopausal women with breast cancer compared with the controls ($p<0.05$).

. Table 2 shows age, anthropometric indices, blood pressure and toxic metals in postmenopausal women with breast cancer (post cases) and postmenopausal women without breast cancer (post controls). Weight, height, lead, cadmium and arsenic were significantly higher in postmenopausal women with breast cancer ($p<0.05$)

Table 3 shows age, anthropometric indices, blood pressure and toxic metals in women with breast cancer (cases) and women without breast cancer (controls). Waist circumference, HC, weight, height, WHR and WHtR, systolic blood pressure, lead, cadmium and arsenic were significantly higher in women with breast cancer ($p<0.05$).

Table 1: Comparison of Age, blood pressure and toxic metals in premenopausal women with breast cancer and controls.

Variable	Cases (n=54)	Control (n=53)	t	*P*
Age (years)	40.91±0.7	40.74±0.6	0.19	0.852
Toxic Metals				
Lead (µg/dL)	5.4±0.2	1.8±0.1	18.35	<0.001*
Cadmium (µg/dL)	0.04±0.00	0.01±0.00	18.79	<0.001*
Arsenic (µg/dL)	0.30±0.01	0.04±0.00	17.59	<0.001*
Hormones				
Oestradiol (pmol/L)	452.8±43.3	430.8±46.5	0.35	0.729
Progesterone (nmol/L)	12.3±2.6	8.8±2.2	1.02	0.309
FT_4 (pmol/L)	17.8±0.6	14.9±0.3	4.51	0.000*
TSH (mIU/L)	1.8±0.2	1.5±0.1	1.36	0.178
Anthropometric Indices				
Waist Circumference (cm)	88.5±1.4	78.3±1.3	5.32	<0.001*
Hip Circumference (cm)	100.5±1.5	95.9±1.0	2.51	0.014*
Weight (Kg)	68.0±1.9	60.1±1.3	3.44	0.001*
Height (m)	1.63±0.0	1.57±0.0	4.35	<0.001*
Body mass index (Kg/m^2)	25.7±0.7	24.5±0.5	1.40	0.164
Waist hip ratio	0.88±0.0	0.81±0.0	6.07	<0.001*
Waist height ratio	54.6±1.0	49.9±0.9	3.52	0.001*
Blood pressure				
SBP(mmHg)	122.96±1.4	119.04±1.2	2.06	0.042*
DBP (mmHg)	82.4±1.1	80.9±1.0	0.97	0.336

*Values are mean±SEM (Standard error of mean), n=number of subjects, t=Student's t-test, p=significance level, *=significant at p<0.05, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, µg/dL=micrograms per decilitre, nmol/L=nanomole per litre, pmol/L=picomole per litre, mmHg=millimetre mercury*

Table 2: Comparison of age, blood pressure and toxic metals in postmenopausal women with breast cancer and controls.

Variable	Cases (n=31)	Control (n=31)	t	*P*
Age (years)	61.23±1.5	61.65±1.5	-0.19	0.843
Toxic metals				
Lead (µg/dL)	5.76±0.24	1.75±0.06	15.98	<0.001*
Cadmium (µg/dL)	0.05±0.00	0.01±0.00	15.99	<0.001*
Arsenic (µg/dL)	0.31±0.02	0.04±0.00	15.22	<0.001*
Hormones				
Oestradiol (pmol/L)	156.5±12.4	90.4±3.6	5.04	0.000*
Progesterone (nmol/L)	2.1±0.4	1.0±0.1	2.92	0.005*
FT_4 (pmol/L)	17.7±0.6	14.3±0.4	4.79	0.000*
TSH (mIU/L)	1.6±0.2	1.3±0.1	1.36	0.181
Anthropometric indices				
Waist circumference (cm)	92.2±1.7	89.8±1.5	0.97	0.337
Hip circumference (cm)	103.9±1.7	102.7±1.7	0.50	0.619
Weight (Kg)	71.4±2.2	65.6±1.7	2.10	0.010*
Height (m)	1.63±0.0	1.59±0.0	2.34	0.023*
Body mass index (Kg/m^2)	26.8±0.7	25.7±0.7	1.25	0.217
Waist hip ratio	0.89±0.0	0.88±0.0	0.09	0.480
Waist height ratio	56.6±1.2	56.5±0.9	0.09	0.930
Blood pressure				
Systolic BP (mmHg)	122.26±1.8	120.00±1.6	0.93	0.360
Diastolic BP (mmHg)	80.32±1.3	80.32±1.2	0.00	1.000

*Values are mean±SEM (Standard error of mean), n=number of subjects, t=Student's t-test, p=significance level, *=significant at p<0.05, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, µg/dL=micrograms per decilitre, nmol/L=nanomole per litre, pmol/L=picomole per litre, mmHg=millimetre mercury.*

Table 3: Comparison of age, anthropometric indices and blood pressure measurements in women with and without breast cancer.

Variable	Cases (n=85)	Control (n=84)	t	*P*
Age (years)	48.3±1.3	48.45±1.27	- 0.07	0.941
Toxic metals				
Lead (µg/dL)	5.5±0.2	1.8±0.0	24.17	<0.001*
Cadmium (µg/dL)	0.04±0.0	0.01±0.0	24.60	<0.001*
Arsenic (µg/dL)	0.3±0.0	0.04±0.0	23.21	<0.001*
Hormones				
Oestradiol (pmol/L)	344.8±31.9	307.8±34.7	0.79	0.433
Progesterone (nmol/L)	8.6±1.8	5.9±1.4	1.17	0.245
FT_4 (pmol/L)	17.8±0.4	14.7±0.3	6.37	0.000*
TSH (mIU/L)	1.7±0.1	1.4±0.1	1.88	0.062
Anthropometric indices				
Waist circumference (cm)	89.9±1.1	82.6±1.2	4.54	<0.001*
Hip circumference (cm)	101.8±1.1	98.5±1.0	2.21	0.028*
Weight (kg)	69.2±1.4	62.1±1.1	3.98	<0.001*
Height (m)	1.63±0.0	1.58±0.0	4.88	<0.001*
Body mass index	26.1±0.5	24.9±0.4	1.83	0.070
Waist hip ratio	0.9±0.0	0.8±0.0	4.86	<0.001*
Waist height ratio	55.3±0.7	52.4±0.7	2.81	0.006*
Blood pressure				
Systolic BP(mmHg)	122.7±1.1	119.4±1.0	2.22	0.028*
Diastolic BP (mmHg)	81.7±0.9	80.7±0.8	0.81	0.418

*Values are in mean±SEM (Standard error of mean), n=number of subjects, t=Student's t-test, p=significance level, *=significant at p<0.05, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, µg/dL=micrograms per decilitre, nmol/L=nanomole per litre, pmol/L=picomole per litre, mmHg=millimetre mercury*

Table 4: Correlation of biochemical parameters, anthropometric indices and blood pressure in women with breast cancer

Index	Index	r	*P*
Progesterone	Oestradiol	0.692	0.000
	Diastolic blood pressure	0.218	0.045
Oestradiol	Diastolic blood pressure	0.214	0.050
FT_4	Arsenic	-0.346	0.001
TSH	Height	0.324	0.002
Lead	Cadmium	0.953	0.000
Cadmium	Diastolic blood pressure	0.238	0.028
Waist circumference	Hip circumference	0.803	0.000
	Waist hip ratio	0.473	0.000
	Waist height ratio	0.933	0.000
	Body weight	0.372	0.000
Hip circumference	Waist height ratio	0.741	0.000
	Body weight	0.476	0.000
Waist hip ratio	Waist height ratio	0.455	0.000
Waist height ratio	Height	-0.391	0.000
Systolic blood pressure	Diastolic blood pressure	0.426	0.000
Height	Body weight	0.409	0.000

r= Pearson correlation coefficient, P= probability, p<0.05=significant

Table 4 shows the correlation of biochemical parameters, anthropometric indices and blood pressure in women with breast cancer. Progesterone positively correlated with oestradiol and diastolic blood pressure (p<0.05). Oestradiol also positively correlated with diastolic blood pressure (p<0.05).

Table 5: Correlation of hormones, endocrine disruptors, anthropometric indices and blood pressure in women without breast cancer

Index	Index	r	*P*
Progesterone	Oestradiol	0.538	0.000
Oestradiol	Waist circumference	-0.368	0.001
	Hip circumference	-0.289	0.008
	Waist hip ratio	-0.298	0.006
	Waist height ratio	-0.286	0.009
	Height	-0.280	0.010
	Body weight	-0.263	0.016
Lead	Cadmium	0.869	0.000
Arsenic	Waist circumference	0.253	0.020
	Waist hip ratio	0.322	0.003
	Waist height ratio	0.266	0.014
Waist circumference	Hip circumference	0.820	0.000
	Waist hip ratio	0.725	0.000
	Waist height ratio	0.957	0.000
	Body weight	0.628	0.000
Hip circumference	Waist height ratio	0.766	0.000
	Body weight	0.657	0.000
Waist hip ratio	Waist height ratio	0.715	0.000
	Body weight	0.298	0.006
Waist height ratio	Body weight	0.505	0.000
Diastolic blood pressure	Height	-0.265	0.015
	Body weight	0.242	0.027
Height	Body weight	0.398	0.000

r= Pearson correlation coefficient, P= probability, p<0.05=significant

FT_4 inversely correlated with arsenic ($p<0.05$). TSH positively correlated with height ($p<0.05$). Lead correlated positively with cadmium, cadmium correlated positively with diastolic blood pressure ($p<0.05$). There were positive correlations between waist circumference, hip circumference, waist hip ratio, waist height ratio, and body weight ($p<0.05$). Hip circumference positively correlated with waist height ratio and body weight ($p<0.05$). Waist hip ratio positively correlated with waist height ratio, while waist height ratio inversely correlated with height ($p<0.05$). Height correlated positively with body weight ($p<0.05$). Systolic blood pressure positively correlated with diastolic blood pressure ($p<0.05$).

Table 5 shows the correlation of biochemical parameters, anthropometric indices and blood pressure in women without breast cancer. Progesterone correlated positively with oestradiol. Oestradiol correlated inversely with waist circumference, hip circumference, waist hip ratio, waist height ratio, height and body weight $p<0.05$. Lead positively correlated with cadmium ($p<0.05$). Arsenic positively correlated with waist circumference, waist hip ratio and waist height ratio ($p<0.05$). Waist circumference positively correlated with hip circumference, waist hip ratio, waist height ratio and body weight ($p<0.05$). Hip circumference positively correlated with waist height ratio and body weight ($p<0.05$). Waist hip ratio positively correlated with waist height ratio and body weight ($p<0.05$). Waist height ratio positively correlated with body weight. Height positively correlated with body weight ($p<0.05$). Diastolic blood pressure inversely correlated with height but positively with body weight ($p<0.05$).

Discussion

Breast cancer incidence in women has been related to industrialization consequent upon the widespread contamination of the soil, air and water by the toxic metals [29]. In this present study, serum Cd level was significantly higher in premenopausal cases, postmenopausal cases and cases compared with their respective controls ($p<0.05$). The ability of cadmium to induce cell proliferation, differentiation, apoptosis and signal transduction by enhancement of protein phosphorylation, activation of transcription and translation factors suggests its ability to induce breast cancer [30]. Moreover, Cd has the potential to disrupt endocrine function by behaving like sex hormones

[31]. At low concentrations, the metal mimics the effects of oestradiol and binds with high affinity to the hormone-binding domain of oestrogen receptor alpha (ERá). This binding involves several amino acids, suggesting that Cd activates the receptor through the formation of a complex with specific residues in the hormone-binding domain [32]. Hypermethylation and repression of DNA repair genes appear to be an early signature of cadmium-induced cancer and may constitute part of the mechanisms by which the toxicant induces tumourigenesis [33].

Lead is of concern due to its wide use [34]. However, results of epidemiologic studies investigating the association of Pb with cancers are inconsistent and vary according to the type of cancers reported [35, 24]. Direct DNA damage as a result of oxidative stress, clastogenicity, inhibition of DNA synthesis or repair have been reported as the mechanisms of Pb carcinogenicity [36, 3]. In this present study, serum Pb was significantly higher in premenopausal cases, postmenopausal cases and cases when compared with their corresponding controls ($p<0.05$). This is consistent with the findings of Siddiqui *et al.* [37] in which blood Pb level was significantly higher in breast cancer cases than controls. There are reports that Pb adversely affects steroidogenesis by substituting for zinc in the DNA binding zinc (Zn^{2+})-finger motif of steroidogenic enzymes. These enzymes are Steroidogenic Acute Regulatory Protein (StAR), Cytochrome P450 side chain cleavage enzyme (CYP450cc) and 3 beta hydroxysteroid dehydrogenase (3β HSD). This results in decrease in the expression of these enzymes [38].

Arsenic exposure constitutes one of the most wide-spread environmental carcinogens and is associated with increased risk of different types of cancers [39]. However, few studies have focused on the association of environmental exposure to arsenic and breast cancer risk. Prior to this study, information on the association of arsenic with breast cancer in sub-Saharan Africa is sparse. In this present study, the serum level of arsenic was significantly higher in premenopausal cases, postmenopausal cases and cases than their respective controls ($p<0.05$). Transcription factors in human MDA-MB-435 breast cancer and rat H4IIE hepatoma cells were reportedly sensitive to low dose arsenic [40]. Arsenic is thought to induce carcinogenicity by inducing DNA hypomethylation leading to aberrant gene expression [41, 42] or by DNA methylation silencing genes associated with controlling tumourigenesis [43]. Arsenic competes with DNA methyl transferase genes (DNMT) for S adenosylmethionine (SAM), potentially limiting the availability of SAM to be used by DNMT to catalyze methylation of CpG. This could result in hypomethylation and reactivation of silenced tumour suppressor genes [44, 45]. Altered histone modification associated with arsenic-induced gene expression in carcinogenesis has been suggested [33].

Our observations show the contribution of environmental factors/endocrine disruptors-lead, cadmium and arsenic to breast cancer. Our previous study showed the contribution of adiposity and other endocrine disruptors-polychlorinated biphenyls and bisphenol-A levels to breast cancer in Nigeria [26]. In this present study, WC, HC, height, weight, WHR and WHtR were significantly higher in cases when compared with controls ($p<0.05$). Height and weight were significantly higher in both pre and postmenopausal women compared with their respective controls ($p<0.05$). This is in tandem with reports of an association between higher body weight and increased breast cancer risk in postmenopausal women [46]. Although, height has also been linked to increased breast cancer risk in postmenopausal women, this association is not clear in premenopausal women [48, 49]. Ogundiran *et al.* [47] demonstrated that height was a significant risk factor for female breast cancer in both pre and postmenopausal women. The underlying mechanism could be that childhood energy balance is associated with mammary gland mass and increased insulin-like growth factors [50]. Attained height is determined by genetic makeup and environmental factors, including energy intake during childhood and adolescence. In societies with an insufficient food supply, caloric intake plays a more important role in determining height than in societies with an abundant food supply [50]. Thus, energy intake in earlier life may play an important role in breast carcinogenesis.

Body mass index is a measure of overall adiposity. It has been shown to have a significant role in the identification of obese and overweight individuals [51]. There was no difference in the BMI between cases and controls ($p<0.05$) in this study. Similar observation was observed in the pre and postmenopausal cases compared with their respective controls. Charles-Davies *et al* [9] reported that the metabolic complications of overweight and obesity could be more related to the location of body fat rather than to the amount of total body fat which is measured by BMI. Visceral obesity has been strongly associated with metabolic dysfunctions including metabolic syndrome and type 2 diabetes mellitus and could predispose individuals to breast

cancer [10, 52]. In this present study, determinants of visceral obesity (WC, WHR, WHtR and subcutaneous obesity (HC) were significantly higher in only premenopausal cases than controls ($p<0.05$). Our observations corroborate the study of Fagherazzi *et al*. [53]. The association of visceral and subcutaneous obesity with breast cancer in premenopausal cases is therefore suggested. However, similar observations were made in a previous study in premenopausal apparently healthy Nigerian women with metabolic syndrome without breast cancer [52]. It is therefore possible that visceral adiposity and subcutaneous adiposity alone may be not be involved in premenopausal breast carcinogenesis.

Arsenic correlated positively with waist circumference, waist hip ratio and waist height ratio in controls in this study**.** This could be explained by the fact that arsenic is lipophilic and probably have preference for subcutaneous fat. Studies have shown that obesity is marked by alteration in the production of adipocytokines; leptin and adiponectin. Increased leptin levels and decreased adiponectin levels promote breast carcinogenesis [53]. Leptin is strongly angiogenic and may increase tumour angiogenesis by directly acting on the endothelium or by increasing local vascular endothelial growth factor (VEGF) secretion [54, 55]. Studies in Ibadan showed elevated leptin levels in apparently healthy premenopausal women with metabolic syndrome compared with those without metabolic syndrome. Leptin levels were similar in both pre and postmenopausal women with metabolic syndrome [51]. Earlier study showed that elevated levels of leptin in individuals with metabolic syndrome might reflect adiposity and could be a compensatory mechanism for maintaining weight/fat loss and blood pressure [51]. An inverse correlation was observed between FT_4 and As in cases in this study. This suggests the possible interference of thyroid hormones by arsenic in women with breast cancer. This could be due to the binding of As to the thyroid hormone receptors which blocks the binding of the thyroid hormones.

In this present study, the mean values of SBP and DBP in the cases and controls reflect normal blood pressure. However, SBP was significantly higher in cases and premenopausal cases than their respective controls ($p=0.028$; $p=0.042$, respectively). This might reflect the mild increase in visceral obesity in premenopausal cases compared with their controls. Reports of the relationship of steroid hormones with blood pressure have not been clearly defined [56, 57]. Positive correlation was observed between oestradiol, progesterone and diastolic blood pressure in cases in this study. Oestradiol in contraceptives may increase salt and water retention [58]. Moreover, progesterone has a tendency to antagonize the actions of aldosterone, thereby supporting an increase in blood pressure [58]. The positive correlation observed between cadmium and diastolic blood pressure in the cases was in tandem with the observation of Gallagher and Meliker [59]. The inhibition of endothelial nitric oxide synthase protein in blood vessels, which suppresses acetylcholine-induced vascular relaxation to induce hypertension is a possible mechanism [60].

Conclusion and recommendation

Findings in this study implicate Cd, Pb and As in breast carcinogenesis. Therefore, routine screening for these toxic metals as well as reduction of environmental pollution by advocacy and education may significantly reduce the incidence of the disease.

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Scope and determinants of practice of surgical oncology among maxillofacial surgeons in Nigeria

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Abstract
Background: Head and neck cancers are associated with significant morbidity and mortality. Previous report suggested a low level of practice of maxillofacial oncology in Nigeria, even in the face of significant burden of head and neck cancers in our environment.
Material and methods: This study was a questionnaire based cross sectional survey of known maxillofacial surgeons in Nigeria with regards to the scope and determinants of the practice of cancer surgical care.
Results: A total of fifty three oral and maxillofacial surgeons participated in this survey. All respondents were involved in cancer surgery, however, 18 of the respondents only managed between 6-10 cases per year. An overwhelming majority of the respondents (39, 73.6%) worked in teaching hospitals. Thirty six (67.9%) of the respondents managed cancer patients without a multidisciplinary care team. Multimodal treatment including radiotherapy was only rarely available. Capacity for reconstruction was limited as only 4 of the respondents were competent to carry out microvascular tissue transfer.
Conclusion: This cross-sectional study has revealed the relative weakness and deficiency in the scope of oncologic maxillofacial surgery in Nigeria. Although these findings may be a reflection of our status as a developing nation, urgent steps need to be taken to address the deficiencies in view of the poor outlook of head and neck cancers even in the developed world.

Keywords: *Scope, determinants, practice, maxillofacial, oncology, Nigeria*

Résumé
Contexte: Les cancers de la tête et du cou sont associés à une morbidité et à une mortalité significative. Les rapports précédentssuggèrent un faible niveau de pratique de l'oncologie maxillo-faciale au Nigéria, même en raison d'un fardeau important du cancer de la tête et du cou dans notre environnement.
Matériel et méthodes: Cette étude était une enquête transversale basée sur un questionnaire sur les chirurgiens maxillo-faciaux connus au Nigeria en ce qui concerne la portée et les déterminants de la pratique des soins chirurgicaux cancéreux par les chirurgiens maxillo-faciaux.
Résultats: Un total de cinquante-trois chirurgiens bucco-dentaires et maxillo-faciaux ont participé à cette enquête. Tous les répondants ont participé à une opération de cancérologie, mais 18 répondants seulement ont réussi à gérer entre 6 à 10 cas par an. Une majorité accablante des répondants (39; 66%) travaillaient dans les hôpitaux d'enseignement. Trente-six (67; 9%) des répondants gèrent des patients atteints de cancer sans une équipe de soins multidisciplinaires. Le traitement multimodal, y compris la radiothérapie, n'était que rarement disponible. La capacité de reconstruction était limitée car seulement 4 des répondants étaient compétents pour effectuer le transfert de tissu micro-vasculaire.
Conclusion: Cette étude transversale a révélé la faiblesse relative et la carence dans le cadre de la chirurgie oncologiquemaxillo-faciale au Nigeria. Bien que ces résultats reflètent notre statut de pays en voie de développement, des mesures urgentes doivent être prises pour remédier aux carences en raison de la mauvaise visibilité des cancers de la tête et du cou, même dans le monde développé.

Mots-clés: *Portée, déterminants, pratique, maxillo-faciale, oncologie, Nigéria*

Introduction

Oral and maxillofacial surgery in Nigeria is an evolving specialty, and includes ablative and reconst ructive surgeries in the management of orofacial tumours. Orofacial tumours are common worldwide with associated challenges and prospects for both the oncology patient and the oral and maxillofacial surgeon. Head and neck cancers constitute the 6th most common cancers in the world and are important causes of morbidity and mortality [1]. They occur mainly in the oral cavity, oropharynx, hypopharynx and the larynx. Despite improved treatment modalities, the diseases remain poor in outcome with a 50% five year survival rate that has not improved in the last two decades [2].

The scope of practice in maxillofacial surgery has been previously reported to be limited in Nigeria relative to what obtains in the developed world, coupled with the absence of sub specialization and

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oncology is one of the least covered areas [3]. Although the burden of orofacial malignancies in our environment could be difficult to ascertain, it is perhaps significant.

The study aimed to investigate the scope and determinants of practice of surgical oncology among maxillofacial surgeons in Nigeria.

Materials and method

Study type: Cross sectional survey

Participants

Eligible participants included all maxillofacial surgeons in Nigeria and on the mailing list of Nigerian Association of Oral and Maxillofacial Surgeons. The study was carried out in accordance with the Declaration of Helsinki and participants' anonymity was guaranteed.

A self-administered questionnaire was developed and pre-tested to assess the factors influencing the practice of oncology among maxillofacial surgeons in Nigeria. Information was collected on demographics, years of practice, type and location of practice, training in oncology, level of involvement in management of oncology, multidisciplinary team management, factors influencing ability to provide oncological care as well as factors discouraging practice of oncology.

The questionnaire with a covering note was delivered to all the maxillofacial surgeons by hand or electronically. Non-responders were contacted by phone, email or personal contact four times. Data was entered into a personal computer and descriptive statistical analysis performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Table 1: Age and sex distribution of respondents

Age	Sex distribution		
	Male	Female	Total
36-40	5	0	5
41-45	14	2	16
46-50	13	3	16
51-55	4	2	6
56-60	2	2	4
>60	6	0	6
Total	44	9	53

Results

A total of fifty three oral and maxillofacial surgeons participated in this survey. Majority were in the 41-50 age range (32, 60.4%). None of the respondents was less than 36years of age while 6(11.3%) were above 60 years of age. Forty four (83.0%) were males while 9 (17.0%) were females (Table 1). Majority (52.0%) were ten years or less as specialist. Eleven (20.8%) had been in practice for over 20years. An overwhelming majority of the respondents (39, 73.6%) worked in teaching hospitals. This was followed by nine (17.0%) in federal medical/ specialist centres (Figure1). Thirty nine (73.6%) of

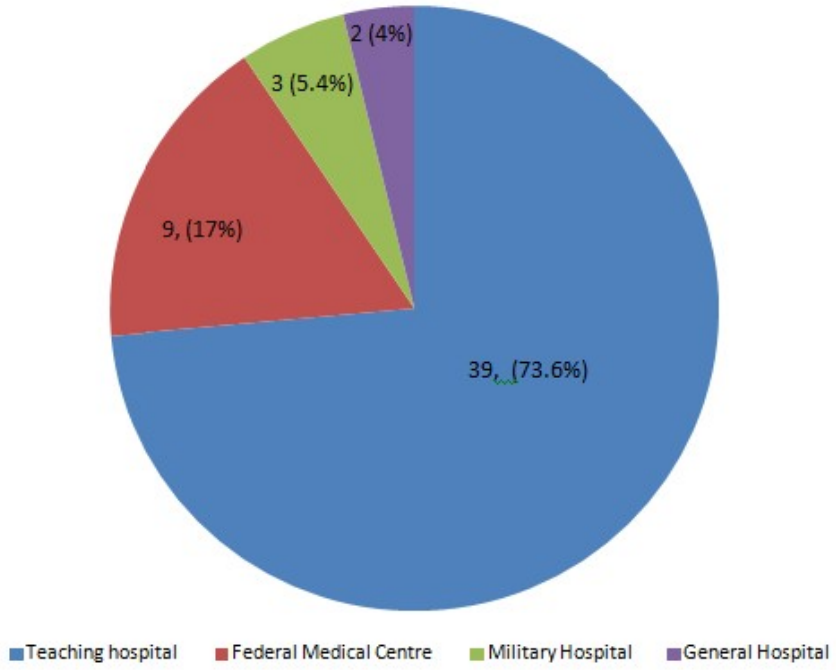

Fig. 1: Status of the hospital of practice of respondents

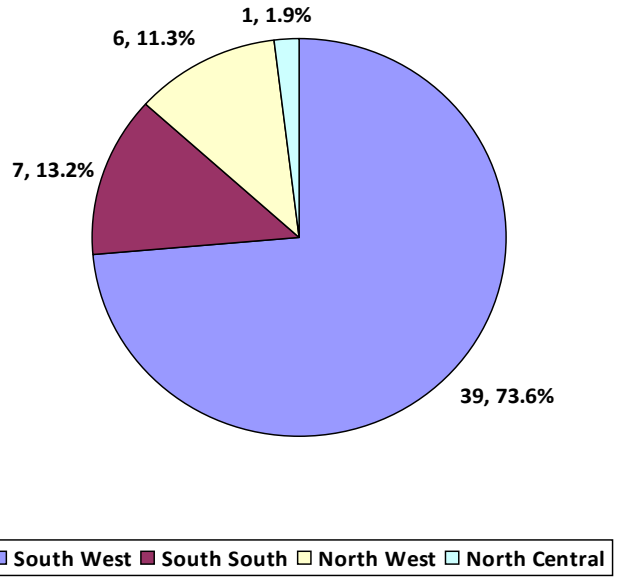

Fig. 2: Location of practice of respondents within the geopolitical zones of the country

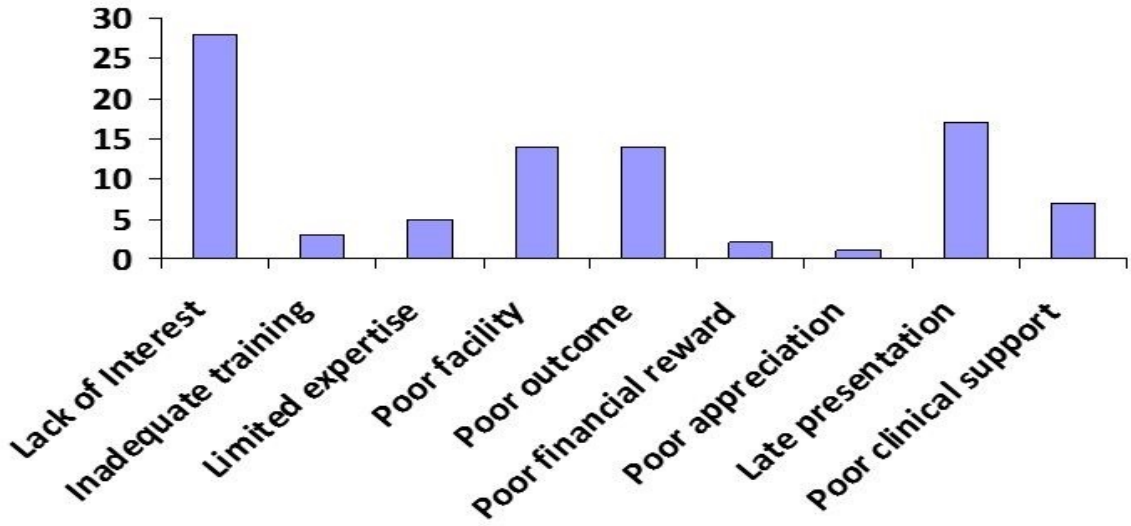

Fig. 3: Factors limiting scope of practice of oncology

the respondents practiced in the Southwest, this was followed by 7(13.2%) from the south-south geopolitical zone of the country (Figure 2). With regards to training in oncology, 10 respondents (18.9%) were involved in the management of 10-15 cases of head and neck malignancies per year during their training. Others gave the figure as 16-20 (9, 17.0%), 21-25, (7, 13.2%) and 5(9.4%) gave a figure of 30cases per year. However, only 21 respondents had an oncology-biased exposure of between 3-12months. In terms of current practice, all the respondents manage cancer cases. However, 18 of the respondents manage between 6-10 cases per year. Others put the figure at 11-15 (7, 13.2%), 16-20(8, 15.1%). Thirty six (67.9%) of the respondents who manage cancer patients do not operate within a multidisciplinary care team, with 16 of those within teams having irregular clinical team meetings. With

regards to capacity for reconstruction, only 4 were competent in carrying out microvascular transfer.

Radiotherapy was always available in the centre of only two of the respondents. For those without radiation facilities, distances of up to 400km needed to be covered to access radiotherapy. Although all respondents carry out oncological surgery only 19 were keen practitioners. Others who were not keen gave reasons for lack of keenness as late presentation, usually poor outcome/poor quality of life of patients, poor facilities/support, limited expertise, and poor financial reward (Figure 3). With regards to further training in oncology by way of a fellowship, 38 of the respondents indicated interest in such a programme.

Discussion

The report of a national survey of the scope and determinants of practice of surgical oncology among maxillofacial surgeons in Nigeria is presented. Previous study [3] had shown a distribution of maxillofacial surgeons along the Nigerian geopolitical zones to be largely skewed toward an obvious southern predominance as well as the federal institutions. This was also replicated in this study as 39 (73.6%) of the respondents were from the southwest and federal institutions. This imbalance continues to be a major issue as other parts of the country remains grossly underserved.

The area of interest and scope of practice of the surgeon is generally influenced by both prequalification (during training) and post qualification (after training) experiences. As observed by Brennan [4], insufficient exposure affects the competence and hence area of interest and practice. In the present study, although surgeons appear to have had decent oncologic exposure during the residency training, only 21(40%) of respondents had any oncology-biased training with only three spending up to 12 months in such training positions.

The practice of oncology, globally, is multidisciplinary [5]. Each member of the team brings a perspective and a skill that will ensure optimum care and outcome. Given the complexity of management of head and neck cancers, patients with advanced disease (more likely in our environment) require multidisciplinary team (MDT) management by a collaborative team comprising of multiple specialties and disciplines with reported positive and significant impact [6,7]. An additional attraction is the continuity of care for all patients for each stage in the treatment process, as well as the offer of adequate information and supports a MDT setting [7].

Thirty six of the respondents in this study did not operate within a multidisciplinary team, while 16 of those did reported that team meetings were rather irregular. MDT approach ensures that patients benefit from vast expertise, professional perspective and knowledge [5, 8]. MDT also incorporates holistic and personalized patient care [9] which is beneficial. Reports have also demonstrated improved treatment outcomes and survival rates in head and neck cancer patients managed through MDT [10-12]. Reasons for many not operating within a team may be dearth of specialists needed for the formation of such teams or perhaps, negative attitudes towards MDT.

It is equally important to also consider the volume of cases treated as available body of evidence suggests that high-workload or specialist teams had better outcomes than their low-workload solitary counterparts [13-15]. Designated centres are more likely to have the infrastructure and expertise and more likely to apply multidisciplinary and multimodal treatment approach than low volume centres. In this study, 18 respondents treat less than 10 cases per year. This undoubtedly will have significant effect on the experiences brought to bear in the management of the patients and subsequently treatment outcome. Reconstruction has become an essential part of the surgical skills of the current maxillofacial oncologic surgeons with practitioners trained in the areas of microvascular tissue transfer [16].

Advances in head and neck reconstruction have made significant improvement in the quality of life and resectability of head and neck cancer. Reconstruction options for defects of the head and neck include primary closure, local flap, pedicle flap and free flap transfer. The use of pedicle flaps and microvascular tissue transfer should be part of the competences of the maxillofacial surgeon involved in the management of malignancies [12]. This is certainly an area that requires attention in this environment as only four of the respondents reported having the competences. This will undoubtedly limit the extent of surgery, cases that could be taken up and by extension, the quality of treatment provided and quality of life of the patients. However, where free tissue transfer skills may be difficult to acquire, pedicle flaps, the workhorse of the reconstructive surgeon should be widely available.

Radiation oncology is an integral part of the management of the oncology patient. It is an important part of the multimodality treatment of the head and neck cancer [11, 17]. Availability and accessibility of expertise as well as facilities can significantly determine how and where a patient is managed and affect disease outcome. Non

availability could discourage surgical intervention and result in outright referral of patients. Anecdotal report suggests the presence of only seven radiation facilities in Nigeria at the moment. This mode of treatment was only usually available in centres where two of the respondents worked.

Although all respondents were involved in the surgical management of the cancer patient, only 19 were keen practitioners. Those who were not keen gave reasons for lack of keenness as late presentation, usually poor outcome/poor quality of life of patients, poor facilities/support, limited expertise and poor financial reward. These reasons have been identified and will need urgent and comprehensive attention in view of the burden of head and neck cancers in our environment [18].

With regards to further training in oncology by way of a training fellowship, efforts should be directed towards facilitating both local and international exposures in oncology by the training institutions and relevant professional and regulatory bodies. Regional centres with adequate manpower and infrastructure could be established in the various geopolitical zones to act as centres of excellence, providing core specialist training in maxillofacial oncology.

Conclusion

This cross-sectional study has revealed the relative weakness and deficiency in the scope of oncologic maxillofacial surgery in Nigeria. The factors contributing to the current state have been highlighted; ranging from inadequate exposure to poor state of infrastructure and manpower deficits. Although these findings may not be peculiar to Nigeria, but a reflection of our status as a developing nation, urgent steps need to be taken to address the deficiencies in view of the poor outlook of head and neck cancers even in the developed world.

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Responses of selected haematological and biochemical parameters to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

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Abstract
*Background***:** Severe malaria affects several haematological and biochemical parameters with vast clinical manifestations which may lead to death. However, the rate at which these respond to artesunate/artemether-lumefantrin combination therapy as monitoring tools for therapeutic response and recovery in children with severe malaria is not documented.
Objective: The aim of the study was to determine the responses of selected haematological and biochemical parameters to artesunate/artemether-lumefantrin combination therapy in children with severe malaria with the goal of identifying parameters with very fast response for early monitoring of therapeutic response and recovery.
Materials and methods: The level of selected haematological parameters [haemoglobin (Hb), packed cell volume (PCV), total leucocytes (TWBC), neutrophils (N), lymphocytes (L), monocytes (M), eosinophils (E), basophils (B) and platelets (P)] and serum level or activity of some biochemical parameters [malondialdehyde (MDA), protein carbonyls (PCO), nitric oxide (NO), glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), vitamins A, C, and E, C-reactive proteins (CRP), bicarbonate (HCO_3^-) and glucose] were measured using standard methods in 100 children (1-10 years) with severe malaria before treatment (day 0), 48 hours of treatment (day 2) and 48 hours after treatment (day 7) according to WHO recommended dosage of artesunate/ artemether-lumefantrin combination therapy, using 200 clinically healthy children as control.
Results: Eosinophils, monocytes, basophils, HCO_3^-, PCO/SOD, CRP/SOD and HCO_3^-/glucose in case children were normalised during treatment (day 2) indicating fastest response while the level or activity of TWBC, N, L, SOD, GR, GPx and glucose was normalised after treatment (day 7) depicting fast response. The level or activity of PCV, Hb, P, MDA, PCO, NO, CAT, GSH, vitamins A, C, E and CRP in case children were significantly different ($p<0.05$) compared to control after treatment (day 7) indicating slow response.
Conclusion: This study showed that eosinophils, monocytes, basophils, HCO_3^-, PCO/SOD, CRP/SOD and HCO_3^-/glucose have the fastest responses to treatment in severe malaria, and may be used as additional parameters for early monitoring of therapeutic response in children with the disease.

Keywords: *Severe malaria, haematological and biochemical parameters, monitoring, children, Artesunate-lumefantrine combination*

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Résumé
Contexte: Le paludisme sévère affecte plusieurs paramètres hématologiques et biochimiques avec de nombreuses manifestations cliniques pouvant entraîner à la mort. Cependant, le taux auquel ils répondent à la thérapie combinée par l'artésunate/ artéméther-lumefantrine comme outils de surveillance pour la réponse thérapeutique et le rétablissement chez les enfants atteints du paludisme grave n'est pas documenté.
Objectif: Le but de l'étude était de déterminer les réponses de certains paramètres hématologiques et biochimiques à la thérapie combinée d'artésunate/ arteméther-lumefantrine chez les enfants atteints du paludisme sévère dans le but d'identifier des paramètres avec une réponse très rapide pour un suivi hâtif de la réponse thérapeutique et de la récupération.
Matériaux et méthodes: Le niveau de paramètres hématologiques sélectionnés [hémoglobine (Hb), volume cellulaire emballé (PCV), leucocytes totaux (TWBC), neutrophiles (N), lymphocytes (L), monocytes (M), éosinophiles (E), basophiles (B) et les plaquettes (P)] et le niveausérique ou l'activité de certains paramètres biochimiques [malondialdéhyde (MDA), protéines carbonylées (PCO), oxyde nitrique (NO), glutathion (GSH), super-oxyde dismutase (SOD), catalase (CAT), La glutathion réductase (GR), la glutathion peroxydase (GPx), les vitamines A, C et E, les protéines C-réactives (CRP), le bicarbonate (HCO_3-) et le

glucose] ont été mesurées en utilisant des méthodes standard chez 100 enfants (1-10 ans) avec un paludisme grave avant traitement (jour 0), 48 heures de traitement (jour 2) et 48 heures après traitement (jour 7) selon la posologie recommandée par l'OMS pour la thérapie combinée avec l'artésunate/ artéméther-lumefantrine, en utilisant 200 enfants cliniquement sains comme témoins .
Résultats: Eosinophiles, monocytes, basophiles, HCO_3-, PCO/SOD, CRP/SOD et HCO_3-/glucose dans le cas où les enfants étaient normalisés pendant le traitement (jour 2) indiquant la réponse la plus rapide alors que le niveau ou l'activité de TWBC, N, L, SOD , GR, GPx et glucose ont été normalisés après traitement (jour 7) représentant une réponse rapide. Le niveau ou l'activité de PCV, Hb, P, MDA, PCO, NO, CAT, GSH, vitamines A, C, E et CRP dans le cas où les enfants étaient significativement différents ($p < 0,05$) par rapport au contrôle après traitement (jour 7) indiquant réponse lente.
Conclusion: Cette étude a montré que les éosinophiles, les monocytes, les basophiles, le HCO_3-, PCO/SOD, CRP/SOD et HCO3-/glucose ont les réponses les plus rapides au traitement contre le paludisme sévère et peuvent être utilisés comme paramètres supplémentaires pour le suivi hâtif de la réponse thérapeutique chez les enfants atteints de la maladie.

Mots-clés: *Paludisme sévère, paramètres hématologiques et biochimiques, surveillance, enfants, combinaison Artesunate-Lumefantrine*

Introduction

Malaria, caused by the bite of Plasmodium carrying female anopheles mosquito, remains a major cause of morbidity and mortality worldwide. Globally, malaria accounts for 350 to 500 million cases with 100 to 300 million deaths, the majority of whom are young children in sub-Sahara Africa particularly Nigeria, Congo, Ethiopia and Uganda [1]. *P. falciparum* is the predominant Plasmodium specie in sub-Sahara Africa, and the major cause of malaria cases and death [1].

Due to increase in resistance of malaria parasite to conventional anti-malaria drugs, the World Health Organization (WHO) developed a treatment approach recommending intramuscular or intravenous artesunate as the first line of treatment in severe malaria [2]. Artesunate is a semi-synthetic derivative of artemisinin and the mechanism of action is based on its hydrolysis to dihydroartemisinin with the release of carbon-centered reactive species which attack and destroy the sarcoplasmic endoplasmic reticulum ATPase gene of the malaria parasite leading to the parasite death [3]. However, due to their short half-life (2-3 hours), and to prevent development of resistance, artemisinin compounds are combined with one or two long-acting antimalarial drugs such as lumefantrine (half-life; 4-6 days in falciparum malaria patients), amodiaquine, mefloquine or sulfadoxine/pyrimethamine as artemisinin-based combination therapy (ACT) [4,5]. Artesunate/ artemether-lumefantrin combination therapy is one of the most common combination therapy used in the treatment of severe malaria [6]. Lumefantrine is a synthetic aryl-amino alcohol antimalarial and functions by interfering with the haem polymerization process; a critical detoxifying pathway for the malaria parasite [7].

Uncomplicated malaria, when not promptly and properly diagnosed and treated, may progress to severe malaria which is characterised by hyperparasitaemia, anaemia, jaundice, respiratory distress, renal insufficiency, convulsion, unconsciousness, coma and a host of other symptoms and could result in death [2]. Once diagnosed accurately, effective treatment and management of severe malaria especially in children require precise and accurate monitoring of therapeutic response. The use of parasite density in monitoring therapeutic response has been a common practice. This however, is limited by the effect of sequestration especially in *falciparum* malaria and inter-microscopists variation in reporting the parasite density [8,9]. Likewise, the use of clinical presentations for this purpose is flawed by inter-clinician variation in interpreting clinical presentations [10]. With these noted shortcomings, coupled with the high fatality rate of falciparum malaria in children, there is a need to explore more accurate, objective and fast-response methods for monitoring therapeutic response in children with severe malaria.

Severe malaria affects several haematological and biochemical parameters with vast clinical manifestations which may lead to death [11]. However, information on the rate of responses of these parameters to treatment is not documented. Therefore, this study was carried out to determine the rate of responses of selected haematological and serum biochemical parameters to artesunate/ artemether-lumefantrin combination therapy in children with severe malaria.

Materials and methods

Study population

One hundred children with severe malaria (case children) aged 1 to 10 years, treated at the paediatrics' wards of Jos University Teaching Hospital; a

reference tertiary hospital in Jos, and 200 clinically healthy children (1-10 years) without malaria attending the hospital for medical check- ups and routine immunization (serving as control) were recruited for this study from 28th April 2014 to 15th February, 2016. Jos is the capital city of Plateau state in Nigeria, located between latitude 80° 24'N and longitude 80°32' and 100°38' E.

Children who met the study's inclusion criteria were recruited consecutively for the study. The inclusion criteria for the case children were: (i) assent of the child and of the parent/caregiver's consent; (ii) children aged 1 to 10 years clinically presenting with severe malaria without any other ailment as diagnosed by the paediatrician; (iii) children with one or more symptoms of malaria complications such as fever, anaemia, respiratory distress and jaundice; (iv) children microscopically confirmed of hyperparasitaemia; (v) children confirmed by laboratory tests as presenting with only severe malaria after excluding other disease conditions such as septicaemia, helminthiasis, typhoid, shigellosis, glucose-6-phosphate dehydrogenase deficiency (G6PDD), sickle cell disease, human immune-deficiency virus (HIV) and hepatitis B; (vi) children on admission in the hospital using mosquito bed-net; (vii) children on artesunate/artemether-lumefantrine combination therapy; and (viii) children that recovered and were discharged by the 7th day of admission.

The inclusion criteria for the control children were: (i) children aged 1-10 years diagnosed as clinically healthy by the paediatrician; (ii) assent of the child and parent/caregiver; (iii) children confirmed by laboratory tests as clinically healthy; and (iv) all children enrolled as control were negative for malaria parasite thick-smear examination (for malaria). They were without febrile episodes in the past 6 months and were not on antimalarial drugs for the past 2 weeks or on paracetamol in the past 24 hours and without any sign of anaemia or neurological involvement.

Study design

This was a prospective longitudinal hospital-based case-control study.

Sample size determination

In determining the minimum sample size, the prevalence rate of 57.7% reported by Angyo *et al*. [12] among children with severe malaria attending JUTH was used as the reference.

Using a prevalence of 57.7%, the sample size needed to achieve a precision of 1% at 95% confidence level was obtained from the equation below (Falade *et al.*) [13]:

$$n = \frac{p(1-p)}{(d/Z\alpha/2)^2}$$

Where n= sample size; d=0.01; Zα=1.96; p-value=0.57

$$n = \frac{0.57(1-0.57)}{(0.01/1.96/2)^2}$$

n =100 (i.e 100 cases and 100 controls)

Ethical statement

This study was carried out in line with the ethics guiding research undertakings on human subjects as approved by the ethical committees of University of Ilorin (reference No. UERC/ASN/2014/013) and Jos University Teaching Hospital (reference No. JUTH/DCS/ADM/127/XIX/5933). Informed consents of the children's parent (s) or caregivers were obtained before enrolment, after due explanation of the aims and procedures of the project.

Malaria diagnosis

Malaria parasite test was determined by microscopy using duplicate slides of Giemsa stained thick and thin blood films [14]. Malaria parasite density was determined by the number of parasites/µl of blood (thick film) method using respective patient's total white blood cell count [13]. Hyperparasitaemia in children was defined as parasite count >200 x 10^3 parasites/µl [15].

Administration of drugs

Case children were given 2.4 mg/kg of artesunate intravenously at 0 hours, then 1.2 mg/kg at 12, 24 and 48 hours (if the patient was able to swallow, the daily dose was given orally). This was followed by oral administration of artemether-lumefantrin as 5 to 24mg/kg of artemether and 29 to 144mg/kg of lumefantrin as fixed dose over 3 days [2].

Samples collection and methods of laboratory analysis

After clinical assessment, stool samples were collected once into transparent stool containers from both case and control children. This was used for exclusion of helminthiasis and pathological enteric bacterial infection, using stool microscopy and culture tests. Normal saline method was used for microscopy and Selenite-F and dextrose-citrate agar for culture as was described by Cheesbrough [16].

Five millilitres (5ml) of blood was aseptically collected from both case and control subjects using needle and syringe. In the control, this was done once while in the case children this was done before initiation of treatment on the day of admission (day 0), then 48 hour after initiation of treatment (day 2) [17]. Another sample was collected 48 hours after the last dose of the combination therapy i.e. 7th day of initiation of treatment [18].

Two millilitres (2ml) of the blood was dispensed into EDTA tube for screening tests for exclusion of other abnormalities, malaria parasite and haematological tests. Screening tests for exclusion of other abnormalities carried out include: Haemoglobin genotype for exclusion of sickle cell disease using electrophoresis as described by Roberts and Williams [19]; glucose-6 phosphate dehydrogenase (G6PD test for exclusion of G6PD deficiency using the meth-haemoglobin qualitative method described by Brewer *et al*.,[20]; hepatitis B surface antigen test for exclusion of viral hepatitis using rapid diagnostic test (RDT) kit from Standard Diagnostics, Korea; and blood culture for exclusion of septicaemia by direct aseptic injection of the blood into brain heart infusion broth and thioglycollate broth (at 1:20 dilution) as was described by Cheesbrough [16].

The remaining 3ml of the blood was dispensed into screw-caped plain sample tube for biochemical assays. It was allowed to clot and retract at room temperature (22-27 ^{o}C) for about 20 minutes. The serum was separated after centrifuging at 3000 revolutions per minute (RPM) for 5 minutes in a clinical bench top centrifuge (MSE minor England) using Pasteur pipette and divided into three different aliquots into pre-cleaned, dried, metal and steroid free cryo-vials for immediate HIV screening using the immunochromatographic technique (RDT; Standard Diagnostics, Korea) and then stored at -20 ^{o}C for analysis of biochemical parameters.

Unless otherwise stated, all the reagents used for this study were of analytical grade and were prepared in distilled-deionized water. Tests were carried out in duplicate tubes.

Haematological analysis

Packed cell volume (PCV) was determined using Hawskley haematocrit centrifuge by centrifuging the sealed blood filled capillary tube at 3000 revolutions per minute for 5 minutes [21]. Haemoglobin level was determined colorimetrically using Drabkins solution as stated by Facer [22]. Total differential leucocytes and platelets counts were done manually [21].

Biochemical assays

Malondialdehyde (MDA), protein carbonyl (PCO) and nitric oxide (NO) concentrations were determined by the methods of Satoh [23], Reznick and Packer [24], and Griess [25] respectively. Superoxide dismutase (SOD) activity was determined by measuring the level of inhibition of epinephrine according to the method of Hara and Irwin [26]. Catalase (CAT) activity was determined by measuring the rate of decomposition of hydrogen peroxide to water and oxygen according to the method of Sinha [27]. Glutathione peroxidase (GPx) activity was determined by measuring the rate of oxidation of glutathione according to the method of Paglia and Valentine [28]. Glutathione reductase (GR) was determined by monitoring the reduction of oxidized glutathione to glutathione in the presence of β-nicotinamide adenine dinucleotide phosphate (NADPH) which is oxidised to $NADP^{+}$ following the procedures of Goldberg and Spooner [29]. Glutathione (GSH) concentration was determined using the method of Beutler *et a*l. [30]. Vitamins A, C and E concentrations were determined by the method of Hasan *et al.* [31]. The serum levels of bicarbonate, glucose and C-reactive protein (CRP) were determined following the methods of Tietz [32], Barham and Trinder [33] and Black *et al*. [34] respectively.

Data analysis

Results were expressed as mean ± standard error of the mean (S.E.M.) for case and control children. Data were analysed using One-way analysis of variance (ANOVA) followed by post hoc Duncan multiple range test and paired t-test, differences were considered signiûcant at $P<0.05$ when compared with control. The procedures were performed using SPSS software (version 19.0, SPSS Inc., Chicago, IL).

The responses of the parameters were categorised as: Fastest response (those that their mean levels increased or decreased steadily such that there was no significant difference between their day 2 through day 7 levels when compared with the mean control values, fast response (those that increased or decreased steadily and their mean levels by day 7 were not significantly different with the control), slow response (those that increased or decreased steadily and their mean levels by day 7 were significantly different with control).

Results

Age and gender distribution of the case and control children

Out of the 100 case and 200 control children recruited for this study, 72 (72.0%) and 123 (61.5%) were aged

1 to 5 years respectively and, following the same order, 43(43.0%) and 90 (45.0%) were males. There were no significant differences in age (p=.181) and sex (p =.880) distribution of the children with or without malaria (Table 1).

Table 1: Age and gender distribution of the case and control children

	Control N (%)	Case N (%)	p-value
Age			
1 to 5 years	123(61.5)	72 (72.0)	0.181
5.1 to 10 years	77 (38.5)	28 (28.0)	
Total	200 (100.0)	100 (100.0)	
Gender			
Male	90 (45.0%)	43 (43.0)	0.880
Female	110 (55.0)	57 (57.0)	
Total	200 (100.0)	100 (100.0)	

presented three or more signs of severe malaria before treatment which resolved progressively with treatment. Fever, anaemia, jaundice, respiratory distress and prostration were the most common signs before treatment. None had cerebral malaria. One hundred percent (100%) of the children recovered and were discharged by the 7th day of admission (Table 2).

Responses of selected haematological parameters to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

The levels of packed cell volume (PCV), haemoglobin and platelet count were significantly lower ($p<0.05$) in case children before treatment compared to control but were significantly increased ($p<0.05$) during and after treatment (Table 3). However, the blood counts of total leucocytes, neutrophils, lymphocytes, eosinophils, monocytes and basophils counts were significantly higher

Table 2: Clinical presentations in children with severe malaria; before, during and after treatment

Clinical presentations	Day 0 N (%)	Day 2 N (%)	Day 7 N (%)
Fever + vomiting + jaundice + hepatomegaly + anaemia	13(100.0)	0 (0.0)	0 (0.0)
Fever + anaemia + prostration + jaundice + respiratory distress	29(29.0)	0 (0.0)	0 (0.0)
Fever + prostration + jaundice	21 (21.0)	0(0.0)	0 (0.0)
Fever + prostration + anaemia + respiratory distress + diarrhoea + vomiting	12 (12.0)	0 (0.0)	0 (0.0)
Fever + unconsciousness + respiratory distress + diarrhoea + bleeding + anaemia	6 (6.0)	0 (0.0)	0 (0.0)
Fever + anaemia + jaundice	10(10.0)	0 (0.0)	0 (0.0)
Fever + convulsion + diarrhoea+ anaemia	5 (5.0)	0 (0.0)	0(0.0)
Fever + jaundice	0(0.0)	8 (8.0)	0 (0.0)
Fever + anaemia	0 (0.0)	5 (5.0)	0 (0.0)
Fever + anaemia + hepatomegaly + jaundice	0 (0.0)	4 (4.0)	0 (0.0)
Fever	0 (0.0)	34 (34.0)	0 (0.0)
Anaemia	0 (0.0)	5(5.0)	2 (2.0)
Jaundice	0 (0.0)	5 (5.0)	0 (0.0)
Anaemia + hepatomegaly	0 (0.0)	0 (5.0)	2(2.0)
Improving	0 (0.0)	11(11.0)	0 (0.0)
Stable	0 (0.0)	28(28.0)	96 (96.0)
Others (uncommon signs presented by few of the children include: cyanosis, dysuria and oliguria)	4 (4.0)	0 (0.0)	0 (0.0)
Total	100(100.0)	100(100.0)	100 (100.0)

Day 0= before treatment; Day 2= 48 hours of treatment; Day 7= 48 hours after treatment.

Clinical presentations in children with severe malaria before, during and after treatment

We documented the clinical presentations of children with severe *P. falciparum* malaria; before treatment, 48 hours of treatment and 48 hours after treatment. One hundred percent (100%) of the children

($p<0.05$) in case children before treatment compared to control. Total leucocytes, neutrophils count and lymphocytes count levels were significantly reduced ($p<0.05$) in case children during treatment and normalised after treatment (Table 3). The eosinophils, monocytes and basophils counts were

normalised in case children during treatment and after treatment (Table 3).

Table 3: Haematological parameters of children with severe malaria treated with artesunate/artemether-lumefantrin combination therapy

Haematological indices	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
PCV (%)	36.68 ± 0.27[a]	26.59 ±0.50[d]	31.11± 0.16[c]	34.16 ± 0.22[b]
Haemoglobin (g/dl)	12.15 ± 0.09[a]	8.86 ±0.17[d]	10.36 ± 0.05[c]	11.28 ± 0.08[b]
Total leucocytes (x10^9/L)	6.14 ± 0.10[a]	9.50 ± 0.30[c]	8.23 ± 0.23[b]	6.63 ± 0.18[a]
Neutrophils count (x10^9/L)	2.25 ± 0.06[a]	4.91 ±0.23[c]	3.76 ± 0.18[b]	2.54 ± 0.12[a]
Lymphocytes count (x10^9/L)	3.85 ± 0.09[a]	4.49 ±0.17[b]	4.44 ± 0.11[b]	4.03 ± 0.09[a]
Eosinophils count (x10^9/l)	0.0003 ± 0.00006[a]	0.056 ±0.010[b]	0.008 ± 0.002[a]	0.006 ± 0.003[a]
Monocytes count (x10^9/L)	0.006 ± 0.001[a]	0.15 ± 0.03[b]	0.02 ± 0.004[a]	0.000 ± 0.000[a]
Basophils count (x10^9/L)	0.00 ± 0.00[a]	0.0001 ± 0.00006[b]	0.00 ± 0.000[a]	0.00 ± 0.000[a]
Platelets count (x10^9/L)	283.17 ± 1.71[a]	178.64 ± 3.95[d]	215.62 ± 1.11[c]	240.74 ±1.40[b]

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment.

Table 4: Serum levels of selected oxidative biomarkers of children with severe malaria treated with artesunate/ artemether-lumefantrin combination therapy

Oxidative Biomarkers	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
MDA (µmol/ml)	7.46 ± 0.25[a]	23.50 ± 0.55[c]	10.34 ± 0.42[b]	10.97 ± 0.40[b]
PCO (nmol/ml)	35.24 ± 0.48[a]	223.22 ± 6.55[d]	141.22 ± 3.16[c]	50.22 ± 2.24[b]
NO(µmol/L)	222.74 ± 1.77[a]	183.49 ± 5.36[c]	203.78 ± 2.25[b]	239.71 ± 4.60[d]

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment.
MDA = malondialdehyde; PCO = protein carbonyls; NO = nitric oxide

Table 5: Serum levels of selected enzymatic antioxidants of children with severe malaria treated with artesunate/ artemether-lumefantrin combination therapy

Enzymatic Antioxidants	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
SOD (U/ml)	2.88 ±0.14[a]	0.76 ± 0.08[b]	1.04 ± 0.08[b]	3.01 ± 0.20[a]
CAT (U/ml)	44.41 ± 1.05[a]	9.71 ± 0.46[d]	14.73 ± 0.81[c]	20.13 ± 0.62[b]
GPx (U/l)	19.49 ±0.46[a]	392.62 ± 32.43[c]	164.41 ± 2.54[b]	29.84 ± 1.00[a]
GR (U/l)	63.04 ± 0.80[a]	183.94 ± 5.81[c]	106.74 ± 1.55[b]	68.18 ± 1.12[a]

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment.
SOD = superoxide dismutase; CAT= catalase; GPx = glutathione peroxidase; GR= glutathione reductase

Responses of selected serum oxidative biomarkers to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

The responses of serum levels of malondialdehyde (MDA), protein carbonyls (PCO) and nitric oxide (NO) in case children before treatment (day 0), 48 hours of treatment (day 2) and 48 hours after treatment (day7) showed that MDA and PCO levels were significantly higher ($p<0.05$) in case children before, during and after treatment compared to control (Table 4). However, treatment with artesunate/artemether-lumefantrin combination therapy significantly reduced ($p<0.05$) the levels of MDA and PCO (Table 4). NO level was significantly lower ($p<0.05$) before and during treatment, but was significantly increased ($p<0.05$) after treatment in case children compared to control. Treatment with artesunate/artemether-lumefantrin combination therapy significantly increased ($p<0.05$) NO level (Table 4).

Responses of selected serum antioxidants to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

The responses of some serum enzymatic antioxidants to artesunate/artemether-lumefantrin combination therapy in children showed that the activity of SOD was significantly lower ($p<0.05$) in case children before and during treatment with artesunate/artemether-lumefantrin combination therapy compared to control but was normalised after treatment (Table 5). Catalase activity was significantly lower ($p<0.05$) in case children before, during and after treatment with artesunate/artemether-lumefantrin combination therapy compared to control but the activity was significantly increased ($p<0.05$) by treatment. The activities of GPx and GR were significantly higher ($p<0.05$) in case children before and during treatment with artesunate/artemether-lumefantrin combination compared to control but were normalised after treatment (Table 5). The levels of GSH, vitamins A, C and E were significantly lower ($p<0.05$) in case children before, during and after treatment with artesunate/artemether-lumefantrin combination therapy compared to control but their levels were significantly increased ($p<0.05$) by treatment (Table 6).

Responses of serum bicarbonate, glucose and C-reactive protein to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

The responses of serum bicarbonate, glucose and C-reactive protein (CRP) concentrations to artesunate/artemether-lumefantrin combination therapy in children with severe malaria showed that the level of bicarbonate was significantly lower ($p<0.05$) in case children before treatment compared to control but was normalised during and after treatment (Table 7). Also, glucose concentration was significantly increased ($p<0.05$) in case children before treatment compared to control, but was normalised after treatment (Table 7). The level of CRP was significantly higher ($p<0.05$) in case children before treatment compared to control but was reduced significantly ($p<0.05$) by treatment (Table 7).

Responses of selected combined serum parameters to artesunate/artemether-lumefantrin combination therapy in children with severe malaria

The levels of some combined biochemical parameters to artesunate/artemether-lumefantrin combination therapy in children with severe malaria were investigated in this study. The levels of HCO_3/Glucose, GSH/NO and GSH/PCO ratios were significantly lower ($p<0.05$)in case children before treatment compared to control while the levels of

Table 6: Serum levels of selected non-enzymatic antioxidants of children with severe malaria treated with artesunate/artemether-lumefantrin combination therapy

Non-enzymatic Antioxidants	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
Glutathione (mg/l)	395.72 ± 9.55[a]	171.94 ± 6.18[d]	248.34 ± 5.82[c]	344.92 ± 3.37[b]
Vitamin A (µg/dl)	45.50 ± 0.48[a]	21.13 ± 0.51[d]	26.60 ± 0.59[c]	34.80 ± 0.39[b]
Vitamin C (mg/dl)	7.52 ± 0.31[a]	2.51 ± 0.13[c]	3.93 ± 0.11[b]	3.78 ± 0.06[b]
Vitamin E (mg/dl)	5.63 ± 0.43[a]	2.92 ± 0.11[c]	3.04 ± 0.05[c]	4.61 ± 0.07[b]

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment.

PCO/SOD and CRP/SOD ratios were significantly higher ($p<0.05$) in case children before treatment compared to control (Table 8). During treatment, the levels of HCO_3/glucose, PCO/SOD and CRP/SOD ratios were normalised and sustained after treatment. The levels of GSH/NO and GSH/PCO ratios in case children were significantly increased ($p<0.05$) during and after treatment (Table 8).

Table 7: Serum levels of bicarbonate, glucose and C-reactive protein of children with severe malaria treated with artesunate/artemether-lumefantrin combination therapy

Parameters	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
Bicarbonate (mmol/l)	24.55 ± 0.25^a	22.28 ± 0.51^b	25.13 ± 0.61^a	24.15 ± 0.40^a
Glucose (mmol/l)	3.85 ± 0.05^a	4.40 ± 0.13^b	4.36 ± 0.11^b	4.02 ± 0.11^a
C-reactive protein (mg/l)	6.05 ± 0.24^a	120.54 ± 4.65^d	80.69 ± 4.65^c	20.21 ± 8.47^b

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment

Table 8: Serum levels of selected combined biochemical parameters of children with severe malaria treated with artesunate/artemether-lumefantrin combination therapy

Combined Parameters	Control	Cases		
		Day 0	Day 2	Day 7
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M
HCO_3^-/Glucose	$6.05 \pm .12^a$	$4.85 \pm .20^b$	5.60 ± 0.21^a	6.07 ± 0.24^a
GSH/NO	$1.30 \pm .05^a$	0.41 ± 0.06^d	0.80 ± 0.04^c	1.12 ± 0.04^b
GSH/PCO	$11.17 \pm .32^a$	0.35 ± 0.06^d	1.37 ± 0.07^c	7.30 ± 0.24^b
PCO/SOD	65.59 ± 13.40^a	2880.66 ± 413.04^b	255.39 ± 19.96^a	26.71 ± 2.73^a
CRP/SOD	$4.63 \pm .55^a$	1705.21 ± 249.43^b	163.99 ± 17.34^a	11.37 ± 1.40^a

Each value is a mean of n determinations ± S.E.M. (n is 100 for case children and 200 for control children). Values carrying different superscripts along the same row are significantly different ($p<0.05$).
Day 0 = before treatment; Day 2 = 48 hours of treatment; Day 7 = 48 hours after treatment.
GSH = glutathione, NO = nitric oxide; PCO = protein carbonyl; SOD = superoxide dismutase; CRP = C-reactive protein

Discussion

In this study, we demonstrate that the blood count of eosinophils, monocyte, basophils and serum level of HCO_3^-, PCO/SOD, CRP/SOD and HCO_3^-/Glucose respond quickly to artesunate/artemether-lumefantrin combination therapy in children with severe malaria.

Severe malaria is associated with alterations in the normal ranges of haematological parameters [12]. The fastest response of the blood count of eosinophils, monocytes and basophils to artesunate/artemether-lumefantrin combination therapy in children with severe malaria could be due to fast redistribution of these leucocytes from peripheral circulation to their primary resident tissues following the introduction of effective antimalarial drug, destruction of the parasites and subsequent fall in inflammatory reactions [35-38]. This finding corroborates the report of Ayodele [39] that these haematological parameters (eosinophils, monocytes and basophils) have direct response to the malaria parasite and anti-malarial drug. The fast response of TWBC to treatment as observed in this study could have been influenced by the fast responses of N and L which are the predominant leucocytes in peripheral circulation even in the control subjects [37]. The rates of responses of TWBC, N and L could be related to increased splenic sequestration of leucocytes following antimalarial therapy [39] and haemoglobin are markers of erythropoietic function [40]. The slow responses of PCV and haemoglobin as observed in this study could be explained on the premise that artemisinins act by lysing parasite infected erythrocytes and clearance of the parasites

from circulation elicits the red blood cells to divide gradually and replenish the host blood [40] thus, causing the slow response of these indices to treatment. This observation is in agreement with the report of Camacho *et al.* [41] which showed that anaemia was resolved on day 28.

Severe malaria induces oxidative stress which is associated with alterations in the normal ranges of oxidative biomarkers in the serum [42, 43]. In this study, the slow response of serum levels of the oxidative parameters (malondialdehyde, protein carbonyls and nitric oxide) to artesunate/artemether-lumefantrin combination therapy in children with severe malaria makes them unfit for early monitoring of therapeutic response and recovery in children with severe malaria. Artemisinin drugs are oxidative drugs which cause increase in reactive species and oxidation of lipids and proteins [45, 46]. Thus, the effect of artemisinin could account for the slow responses of the oxidative parameters to treatment. Fabbri *et al*. [46] reported that oxidative stress biomarkers resolved and were not significantly different from control by day 14 in treated patients with *P. vivax* infection.

The normal serum levels or activities of both enzymatic and non-enzymatic antioxidants were altered in patients with severe malaria [47-50]. The fast response of SOD to the treatment in this study may be due to the enzyme's high catalytic efficiency. It has been reported that SOD has a very large catalytic efficiency (kcat/K_M) of ~7 x10^9 $M^{-1}S^{-1}$ [50]. The fast responses of serum GR and GPx activities to the treatment in this study could be related to the fast oxidation of GSH to GSSG and reduction of GSSG to GSH by these enzymes due to rise in reactive species as a result of the oxidative action of artemisinins [44]. Serum catalase activity unlike the other antioxidant enzymes showed a slow response to treatment in this study despite its reported high catalytic efficiency of 4.0x$10^8$$M^{-1}s^{-1}$ [51]. This could be due to the binding of artemisinin to the enzyme's heme protein [52], thereby retarding the activity of the enzyme [53] and hence response to treatment and patient's recovery. The slow responses of all the non-enzymatic antioxidants (GSH, vitamins A, C and E) to treatment could be related to the increase in reactive species due to the oxidative artemisinin drug [44, 45].

Severe malaria also alters the normal level of bicarbonate [54], glucose [54] and C-reactive protein [55] in the serum. Serum bicarbonate is a marker of respiratory and renal functions [56]. The fastest response of serum bicarbonate to artesunate/artemether-lumefantrin combination therapy in children with severe malaria observed in this study may be attributed to the fast rise in pH due to decreased lactic acid production because of parasite destruction and clearance [57]. The fastest response of serum bicarbonate could also be due to the very fast response of carbonic anhydrase; the enzyme responsible for interconversion of carbondioxide and bicarbonate with catalytic efficiency (kcat/K_m) of 10^8 $M^{-1}S^{-1}$ [58]. The fast response of serum glucose to treatment observed in this study could be related to the hyperinsulinaemic effect of artemisinin drugs and the short half-life of these drugs [59]. CRP is one of the most widely used acute phase protein because of its fast rise and rapid kinetics [60,61]. From this study, the slow response of serum CRP to treatment could suggest that some inflammatory reactions were still on in the children even though they had recovered [62].

The serum levels of the selected combined serum parameters that are associated with severe malaria can be helpful for monitoring therapeutic response in children with the disease [63]. The fastest responses of combinations of some of the parameters such as PCO/SOD, CRP/SOD and HCO_3^-/glucose to treatment as obtained in this study were in consonance with the finding that combining parameters from distinct pathological pathways improve predictive accuracy over individual biomarkers and each marker may independently contribute information regarding the nature of disease and therapeutic response [63]. This implies that the fastest response parameters are useful in early detection of treatment success or failure and recovery in children with severe malaria as well as early detection of uncommon adverse drug side effect that may be applicable to few individuals.

In conclusion, this study shows that the level of eosinophils, monocytes, basophils, HCO_3^-, PCO/SOD, CRP/SOD and HCO_3^-/glucose have the fastest responses to treatment in severe malaria and can therefore be employed for early monitoring of therapeutic response in children with the disease.

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Occlusal presentations of individuals with sickle cell disease

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Abstract
*Objective***:** To determine the occlusal presentations of individuals with sickle cell disease.
*Materials and methods***:** One hundred and thirty five subjects with sickle cell anaemia and who had not previously received any form of orthodontic treatment were recruited from the sickle cell clinic/ Haematological out patient's clinics in four tertiary health care institutions in the south western part of Nigeria. Ethical approval was sought and gotten from each tertiary institution Ethical Committees involve in the study. All eligible subjects were seated on a comfortable chair had their oral examination done by a single author under natural lighting illumination for both dental intra – arch and occlusal parameters and all the data gotten were entered into a spread sheet and analyzed with SPSS version19 computer software. The level of confidence was set at $p < 0.05$.
Results: The age range was 10 - 49 years with majority of the sample falling into the age range 10 – 29 years. The sample comprised of 61 males and 74 females. Eighty nine percent of the samples were phenotypically positive for HbSS and also commoner among the female samples (57.0%). Occlusal anomalies such as increase overjet, anterior maxillary arch spacing and maxillary prognathism were observed in 40.7%, 58.5% and 45.2% respectively.
Conclusion: There is a high prevalence rate of malocclusion among HbSS individuals and they present with a variety of occlusal anomalies which will require the attention of the orthodontist in order to improve their aesthetics, function and psychological wellbeing.

Keywords: *Sickle cell anaemia, occlusion, orthodontics*.

Résumé
Objectif: Pour déterminer les présentations occlusales de personnes atteintes de drépanocytose.
Matériaux et méthodes: Cent trente-cinq sujets atteints d'anémie falciforme et qui n'avaient auparavant reçu aucune forme de traitement orthodontique ont été recrutés dans la clinique de drépanocytes/Cliniques hématologiques de patients non-hospitalisés dans quatre établissements de soins de santé tertiaires dans la région sud-ouest du Nigeria. L'approbation éthique a été cherchée et obtenue de chaquecomité d'éthique des institutions tertiairesparticipant à l'étude. Tous les sujets admissibles ont été assis sur une chaise confortable et ont eu leur examen oral par un seul auteur sous éclairage naturel pour les deux paramètres intracellulaires dentaires et occlusaux et toutes les données obtenues ont été entrées et analysées avec le logiciel SPSS version19. Le niveau de confidence a été fixé à $p < 0,05$.
Résultats: La tranche d'âge était de 10 à 49 ans avec la majorité de l'échantillon tombant dans la tranche d'âge de 10 à 29 ans. L'échantillon compris 61 hommes et 74 femmes. Quatre-vingt-neuf pourcent des échantillons étaient phénotypiquement positifs pour HbSS et aussi fréquent chez les femelles (57,0%). Des anomalies occlusales telles que l'augmentation du risque de surjet, l'espacement antérieur de l'arc maxillaire et le prognathisme maxillaire ont été observées respectivement dans 40,7% ; 58,5% et 45,2%.*Conclusion:* Il y a un taux de prévalence élevé de malocclusion chez les individus HbSS et ils présentent avec une variété d'anomalies occlusales qui nécessiteront l'attention de l'orthodontiste afin d'améliorer leur esthétique, fonction et bien-être psychologique.

Mots-clés: *Anémie falciforme, occlusion, orthodontique.*

Introduction

Sickle cell anaemia is a genetic disorder which results from point mutation of the beta chain of the haemoglobin gene resulting in abnormal haemoglobin variant referred to as haemoglobin S (HbS) [1]. This mutation causes the erythrocytes to change into sickle shape, which are destroyed more rapidly than normal red blood cells. Sickle cell anaemia results from the inheritance of the haemoglobin S gene from both parents, resulting in the homozygous state (HbSS) [2]. It is a hereditary and familial haemolytic disease, the most common genetic disorder amongst black people and one of the major chronic non-communicable diseases affecting man [3].

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Furthermore, the sickle-shaped haemoglobin loses their ability to undergo deformation which is required by them for navigating through the microcirculation. Hence, they cause obstruction in the capillaries bed and restrict blood flow to organs thereby resulting in ischemia, pain and often tissue damage.

It is the most common worldwide symptomatic haemoglobinopathy [4] and has an incidence of about 2% in Nigeria [5]. Although, the disorder has been documented in literature to be widely spread in Nigeria with a higher prevalence in the North (11.87%) [6]. Other variant of this disorder that also exists is the HbSC which occurs at a prevalence of 19% in the south and between 0.22 – 0.5 in the northern part of the country [6]

The prevalence of sickle cell anaemia in Nigeria is said to be on the increase, especially among the urban educated elite and in other communities with access to effective basic health care [7]. To compensate for the short life of the red blood cells, compensatory mechanisms associated with hyperplasia and expansion of bone marrow take place and these result in changes in bony structures. These changes can be observed on radiographs.

Studies have shown that individuals living with sickle cell anaemia may present with malocclusion in the form of maxillary gnathopathy [8], delayed tooth eruption and periodontitis [9], increased overjet and overbite [10]. Gnathopathy and excessive growth of the anterior part of the maxilla in the secondary dentition leads to prognathism, spacing and proclination of the incisor teeth [10]. These malocclusions results in psychosocial problems because of poor dental aesthetics, functional problems and susceptibility of teeth to trauma. It is believed that as the Nigerian population steadily grows, the likelihood of an exponential growth in the population of individuals with this disorder will be high hence many of them may likely seek orthodontic intervention to improve their smile, function and quality of life and self-esteem as a result of increasing awareness of the possibility of managing their occlusal discrepancies through the use of various orthodontic appliances.

This study therefore is aimed at determining the occlusal presentation of the sickle cell individuals of a Nigerian population with a view to ascertaining the level of their functional and psychosocial burden.

Materials and methods

The study was descriptive cross-sectional and carried out over a period of eight (8) months among consecutive sickle cell individuals aged 10 – 49 years attending sickle cell out clinics in four tertiary health care institutions in the south western part of Nigeria. The south western region of Nigeria is cosmopolitan and with various occupational groups hence, home to diverse ethnic groups and economic seat of Nigeria.

A total sample of 145 respondents was recruited out of which only 135 of them were analyzed due to incomplete data. The demographic record of each patient was retrieved from the case notes. Information not in the case note was either gotten from the patient, parents and or guardian. Ethical approval was sought and gotten from each tertiary institution Ethical Committees involved in the study (ADM/DCST/221/VOL.10, CHS/MMP/ERC/63, OOUTH/DA.326/T/7, 00005422). Also, verbal and written consent was sought and obtained from each subject involved in the study.

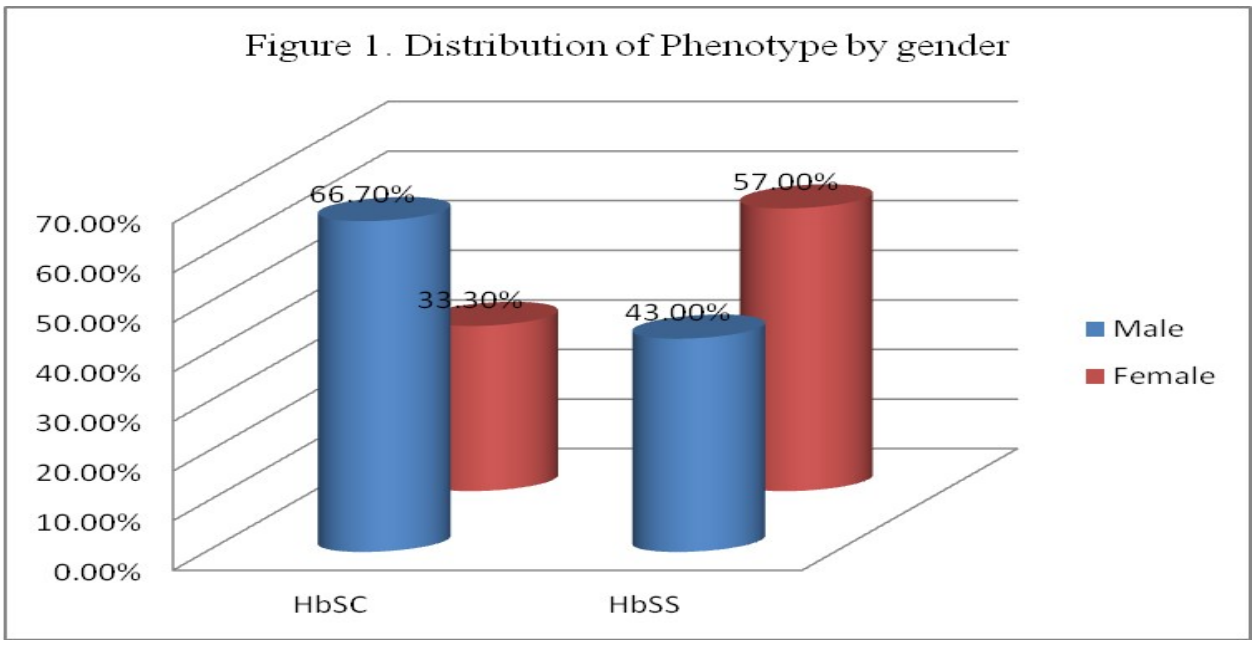
Inclusion criteria for subjects included; Subjects in steady health, no prior history of orthodontic treatment, full complement of teeth to avoid any confounding arch discrepancies as a result of tooth/teeth loss and an electrophoresis diagnosis of sickle cell anaemia. All eligible subjects had an oral examination done with gloved hands, facemask and a disposable dental explorer, dental mirror and a meter rule.

The information gotten was entered into a spreadsheet which consisted of two (2) sections. Section (A) recorded the demographic findings and the section (B) recorded the orthodontic oral findings.

Analysis was carried out using SPSS statistical software version 19. Data presentations were in the form of tables and charts (chi – square test and T – test was used to compare variables). An observation was considered to be statistically significant when the p value was less than 0.05.

Table 1: Demographic distribution of respondents

Age Range (years)	Gender		Total (count/%)
	Female (count/%)	Male (count/%)	
10 – 19	32	26	58
20 – 29	33	27	60
30 – 39	5	7	12
40 – 49	4	1	5
Total	74	61	135



Results

There were 135 samples examined and their ages ranged from 10 – 49 years. There were 61 males and 74 females with majority of the sample skewed around the age 10 – 29 years (Table 1). Only two main variants of the disorder were picked up during data collection and these were the HbSS (most common) and the HbSC variants. This study revealed that 89.0% of the samples were phenotypically positive for HbSS of which 57.0% of them were females while 11.0% were phenotypically positive for HbSC of which 66.7% of them were males. (Fig. 1)

Discussion

Nigeria is said to have the largest concentration of sickle cell anaemia individual worldwide [11, 12]. Numerous Nigerian studies have reported different prevalent rates for this genetic disorder which is put at between 2 – 2.9% [13, 14] in the southern part of the country to about 11.8% [6] in the north. Many of these studies are hospital based hence; the actual prevalence could be greater.

In this study, the most and least prevalent molar relations were Angle's Class I and Class III molar relationship which accounted for 61.5% and 11.1% respectively (Table 2). This is similar to a previous study in Lagos, Nigeria by daCosta *et al* [15] in 2005 among sickle cell individuals. Though, in their study they did not record any Angle's Class III molar relationship. Among the Angle's Class II molar relationship recorded in this study, it is very important to note that 97.3% of them presented

Table 2: Distribution of occlusal presentation in respondents

Occlusal presentation	Total count (%)
Anterior posterior relationship	
Angle's Class I	61.5
Angle's Class II	27.4
Angle's Class III	11.1
Asymmetrical molar relationships	0.04
Overjet	
Reduced/Reversed <2mm	11.9
Normal 2 – 4 mm	47.4
Increased >4mm	40.7
Mean overjet 3.96±2.15mm	
Overbite	
Anterior open bite (AOB)	8.1
Edge-Edge bite	8.9
Normal	73.3
Increased	9.6
Tooth:Arch relationshipUpper arch	
Anterior segmentNormal	17.8
Crowding	23.7
Spacing	58.5
Posterior segment	
Normal	80.7
Crowding	10.4
Spacing	8.9
Lower arch	
Anterior segment	
Normal	22.2
Crowding	34.8
Spacing	43.0
Posterior segment	
Normal	77.8
Crowding	16.3
spacing	5.9
Maxillary Prognathism	
Present	45.2
Absent	54.8

with Angle's Class II division 1 molar relationship. This might not be too surprising due to the presence of maxillary hyperplasia and expansion of bone marrow compensating for the short life span of erythrocytes [8, 10, 16] that is quite common in these individuals thereby often causing incompetence of the lips [8] and a proclination of the upper anterior teeth due to the lack of a lip seal [8].

Table 3: The incidence of malocclusion among respondents

Occlusion	Gender		
	Female count/%)	Male (count/%)	Total (count/%)
Malocclusion	48(51.6)	45(48.4)	93(68.9)
Normal occlusion	26(61.9)	16(38.1)	42(31.1)
Total			135(100)

management for their malocclusion. This assertion had been previously suggested by Okafor et al.(17) who recommended in their study that sickle cell anaemia individuals should have access to orthodontic management associated with phonoaudiologic support in order to alleviate their conditions.

The tooth size arch length ratio discrepancies (arch spacing) recorded in this study were quite high and comparable to other previous studies in this group of individuals [15]. The arch spacing was more common and pronounced in the upper arch as compared to the lower arch. Maxillary hyperplasia as a result of haemopoeitic need might be responsible for this observation.

Therefore, the overall occlusal characteristics of the sickle cell individuals placed them with a malocclusion prevalence of 68.9% with no gender predilection (Table 3).

Table 4: Comparative analysis of occlusal characteristic with other studies

Occlusal presentations	*Present study%	*daCosta *et al* 2005 %	Onyeaso 2002 %	Sanu 2000 %	Isiekwe 1989 %
Angle's Class I	61.5	88.5	76.5	90.3	76.5
Angle's Class II	27.4	11.5	15.5	4.8	14.7
Angle's Class III	11.1	0	8.0	2.1	8.4
OverjetReduced	11.9	13.4	0.7	40.0	19.1
Increased	40.4	48.2	16.2	11.1	24.1
OverbiteReduced	17.0	7.6	1.4	7.3	5.2
Increased	9.6	21.2	3.8	15.6	13.5
Tooth:Arch Crowding (Upper)	23.5	10.6	-	14.6	25.8
Crowding (Lower)	34.6	-	-	25.3	41.9S
pacing (Upper)	58.	49.0	-	36.1	-
Spacing (Lower)	42.6	30.8	-	24.7	-

*Sickle cell population study. Others were on general population

Other occlusal traits observed in these individuals from this study included the highly increased overjet of 40.4% (Table 2). This is also similar to the observations by Taylor et al [10] and daCosta *et al* [15] in their study. The prevalence of increased overjet is quite alarming when compared with previous studies carried out among the general population though with an HbSS prevalence rate of about 2.9%. The implication of this is that the anterior teeth of these individuals are prone to a fracture and its complications usually following trauma due to their conspicuousness. In order to avoid these and the burden that might be associated with it which could affect the quality of life in this group of individuals, many might require orthodontic

Conclusion

Sickle cell individuals presents with a variety and high prevalence of occlusal anomalies which affect aesthetics, function, psychological and self-esteem. The malocclusion characteristics they present with further add to the burden they undergo as individuals due to their condition by reducing their oral health quality of life hence, it will be imperative that in order to reduce these burden physicians should refer them to dentist for dental education talk and a correction of their malocclusion.

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Afr. J. Med. Med. Sci. (2017) **46,** 385-390 *Perspective/View point*

Empowering the future leaders against tomorrow's challenges

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Abstract
The world is rapidly evolving – culturally, economically, socially, ecologically, scientifically and demographically. The paper is devoted to leadership in the 21st century and beyond. Widespread disruption in business models and labour markets are predicted due to the fourth Industrial Revolution, which includes developments in artificial intelligence and machine-learning, robotics, nanotechnology, 3-D printing, genetics and biotechnology. Organizations also face globalization, deregulation, e-business, telecommunications and virtual teams' dynamics. There is therefore an enormous change in the skill sets needed to thrive in the new landscape. Leaders will need to develop a paradigm shift that favours adaptability, empowerment, collaboration, diversity, team work and open-mindedness. As technology races ahead, leaders will need to foster a culture that embraces technology while also emphasizing development of creative and social skills to counteract loss of jobs due to ever-increasing computerisation. Future leaders must move beyond managing to leading change, while practising the concept of personal leadership which includes taking responsibility and measuring their impact continually.

Keywords: *future challenges, change, adaptability, social skills, empowerment, personal leadership.*

Résumé
Le monde évolue rapidement - sur le plan culturel, économique, social, écologique, scientifique et démographique. Le document est consacré au leadership au XXIème siècle et au-delà. Des perturbations généralisées dans les modèles commerciaux et les marchés du travail sont prévues en raison de la quatrième révolution industrielle, qui comprend des développements en intelligence artificielle et en machine-apprentissage, en robotique, en nanotechnologie, en impression 3D, en génétique et en biotechnologie. Les organisations sont également confrontées à la mondialisation, à la déréglementation, à l'e-business, aux télécommunications et à la dynamique des équipes virtuelles. Il y a donc un énorme changement dans les ensembles de compétences nécessaires pour prospérer dans le nouveau paysage. Les dirigeants devront développer un changement de paradigme qui favorise l'adaptabilité, l'autonomisation, la collaboration, la diversité, le travail en équipe et l'ouverture d'esprit. Au fur et à mesure que la technologie avance, les dirigeants devront favoriser une culture qui englobe la technologie tout en mettant l'accent sur le développement de compétences créatives et sociales pour contrer la perte d'emplois à caused'une informatisation croissante. Les futurs leaders doivent aller au-delà de la gestion vers un leadership dechangement, tout en pratiquant le concept de leadership personnel qui inclut à prendre en charge et à mesurer continuellement leur impact.

Mots-clés: *Défis futurs, changement, adaptabilité, compétences sociales, autonomisation, leadership personnel.*

"The illiterate of the 21st century will not be those who cannot read and write but those who cannot learn, unlearn and relearn." - Alvin Toffler

Introduction

The world has become fast-paced. We all operate in a global arena which is constantly evolving – culturally, economically, socially, ecologically, scientifically and demographically. Hence, the topic 'Empowering the Future Leaders against Tomorrow's Challenges' is quite relevant. Questions that will be addressed in this paper are the following:

- What are the most pressing challenges that we will face as future leaders?
- As the next generation of leaders to confront such challenges, how do we best prepare and develop leadership abilities, qualities and skills?
- What are the next generations of technologies, methodologies, models and solutions we will need to overcome such challenges?

You all recall the recent story of the three-year-old boy who fell into Cincinnati zoo's gorilla enclosure, prompting keepers to shoot Harambe, 17-

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year-old 450lb silverback Gorilla who grabbed him [1]. Isiah Dickerson was with his mother Michelle Gregg at Cincinnati Zoo, Ohio, when he somehow made his way through a barrier, into a moat - and was lifted up by Harambe. Within minutes, the 17-year-old 450lb silverback was killed by zookeepers who feared for Isiah's safety. The decision sparked a backlash, with calls for the boy's parents to be prosecuted. Many people blamed the boy's parents for 17-year-old Harambe's death. Many people criticized the Zoo management for the decision taken. Let us reflect on the leadership questions inherent in the story:

What would you do if you were the one in charge? If you decided to use tranquilizers and they didn't work in enough time to save the child, how will you handle the fallout? What if he was your child? Will your decision be different?

Leaders face these types of unexpected scenarios when they must make far reaching decisions, sometimes in a split second. Therefore, preparation is key.

Before we move on, let us agree on what we define as empowerment. For us, can we agree that empowerment means the process of equipping future leaders, which we are, with the necessary tools, attitudes, perspectives and resources to become leaders who are ready for the challenges of tomorrow?

Inherent in the definition stated above is that the future is in fact not that distant – it may be interpreted as the next minute, the next hour or tomorrow! The emerging question is: what are the challenges?

Changing landscape of jobs and industry

The last World Economic Forum report – **'The Future of Jobs'** released in January 2016 predicted widespread disruption, not only to business models but also to labour markets over the next five years due to the fourth Industrial Revolution. The industrial revolution includes developments in previously disjointed fields such as artificial intelligence and machine-learning, robotics, nanotechnology, 3-D printing, genetics and biotechnology [2]. The conclusion therefore is that there is an enormous change in the skill sets needed to thrive in the new landscape.

Hence, the first challenge is that of 'change' and 'managing change'. Change is the natural law of life. As individuals, we all go through the stages of infancy, childhood, adolescence and adulthood where we seek identity and fulfillment. That change starts from maturation from a medical student to a medical doctor and for those who choose to continue on that path, change from a 'baby doctor' like one elder once called new medical graduates to future specialists. Is that the terminal end? No! of course not!, what about becoming a leading specialist with global recognition or a Professor and leading expert in a subspecialty, say Professor of militancy genomics! For while we all laugh about that, we must in fact introspect and ponder: is there a locus in some people's genes that predisposes them to becoming rebels or militants against their nation, communities and men? Why is a minority pursuing a destructive course while the overwhelming majority plods on legally? Gene or environment (or as some will say, nature or nurture?). Most certainly a debate for another day.

Managing change and adaptability

Many of us here will surely not pursue the medical specialist training path. Some graduates of this medical school have become musicians, fashion designers, business leaders and of course politicians! Therefore, our discourse today must choose the middle navigation course and remain applicable to all. How, then, do we manage change as they come into our lives? The central lesson is first of all to accept the fact that change is natural and will always occur. Hence, we must use our today well, to ensure that we can adapt to future changes. In fact, adaptability is the next strategy. Darwinian theories still hold sway in the affairs of men. In a speech delivered in 1963 by a Louisiana State University business professor, Leon C. Megginson, at the convention of the Southwestern Social Science Association [3], Megginson presented his interpretation of the central idea outlined in Darwin's "On the Origin of Species": I quote him:

"Yes, change is the basic law of nature. But the changes wrought by the passage of time affects individuals and institutions in different ways. According to Darwin's Origin of Species, it is not the most intellectual of the species that survives; it is not the strongest that survives; but the species that survives is the one that is best able to adapt and adjust to the changing environment in which it finds itself."

When we apply this theoretical concept at individual level, we can state that the individuals or the future leaders who will survive and thrive tomorrow are those that are able to adapt to the changing physical, social, political, moral, organizational and spiritual environment in which they find themselves. In today's rapidly changing, highly competitive environment, the ability to change rapidly, efficiently, and almost continually will distinguish the winners from the losers. Our winners

will not resist change, they will embrace change and say: "how do I make this work for me, for my team, for the institution where I serve and for the global village". Such individuals are active participants and contributors to the society. They live the dictum: "to serve is to lead."

Challenges of globalisation

Daft and coworkers tell us that the world of organizations is changing rapidly [4]. Organizations are no longer stable and settled. They face globalization, deregulation, e-business, telecommunications and virtual teams. Daft points out that people in organizations around the world are feeling the impact of these and other trends and are being forced to adapt to new ways of working [4]. In this context, leaders are facing really tough jobs to keep people grounded, focused and motivated toward accomplishing positive goals. As Daft sees it, shifts representing a transition from traditional to new paradigms are having a dramatic impact on organizations and presenting new challenges for leaders [4]. Comparing old and new paradigms of leadership, Daft contrasts stability with change and crisis management, control with empowerment, competition with collaboration, uniformity with diversity, self-centeredness with higher purpose and heroism with humility. Such unstable situations call for a continuous awareness of the changing human needs in the workplace, and effective leadership practices to encourage and support people in their achievement of organizational goals.

Under these new conditions, to make change work for you is the call. For all progress require change. We all have to adapt to new ways of working. Many in developed nations are already choosing to work from home. And you wonder how they do it with the TV, internet and social media clamoring for their attention? Leaders today already have a tough job trying to keep people focused and motivated towards accomplishing intended goals, how much more tasking will this be for future leaders?

We also have to remember the unsettled, challenging and constantly evolving economic situation and the increase of ethical scandals like that of the recent Global fund for AIDS/MALARIA and Tuberculosis grant recently suspended for Nigeria[5]. Reports stated that "grants to Nigeria have faced substantial systematic and operational risks and challenges" [5]. These identified risks are challenges we should develop strengths in to change the narrative about grant management in Nigeria. Further, we must not forget the increasing relativity in saying 'we live in a secure environment'. Yes, the question of security which is associated with terrorism, wars and crime are extant challenges we all must have answers to, to thrive in the future.

Leading change and innovation

Let me challenge you to go a step ahead of what we have been discussing so far. Move beyond managing change at a personal level to practicing 'leading change'. Leaders that organizations need henceforth are those who can guide people through the uncertainty and confusion, which periods of rapid change entail. Today's world is in a constant motion, and nothing seems certain anymore. It is now clear that managers who believe that stability is all they need to maintain in the twenty-first century, would surely be mistaken and unsuccessful. Initial success without innovation is a recipe for failure. How then do we become masters of change and innovation?

To master change, there are a myriad of things you must do and which I will discuss in some detail: societal understanding, embracing technology, cultivating an open mind, anticipation, emotional intelligence development and the concept of personal leadership.

We must understand the society of today – we are participants in a global knowledge economy. To "learn today is to live." A man who has stopped learning has embarked on the journey to the land of the dead. Utilise today to learn the best about your field, while not forgetting other areas of human endeavor. Read, read and read! Be a well-rounded person which people will be happy to stay with at a dinner table or during other social interactions. Be versatile in sports, philosophy, economics, politics, arts and other fields of science. Explore other areas that interest you outside of medicine. Let your mind be like a sponge soaking knowledge and enjoying it. Networking is easier when you have varied interests – some you will meet and they will get endeared to you because you are a versatile doctor who is at ease during conversations about diverse subjects. A sound mind attracts people. You should be one.

Open-mindedness and technology

Cultivating an open mind is paramount, this includes having wide interests, being imaginative and insightful and having a willingness to consider new ideas. People with such open minds are intellectually curious and often seek out new experiences through travel, the arts, movies, reading widely, or other activities. Open-mindedness is important to leaders because leadership is about change rather than stability. In an interesting study of three nineteenth-century leaders - John Quincy Adams, Frederick

Douglass, and Jane Addams; early travel experiences and exposure to different ideas and cultures were found to be critical elements in developing open-minded qualities in these leaders [6]. Travel during the formative years helped these leaders develop a greater degree of openness to experience because it put them in situations that required adaptability.

The next strategy is to embrace technology and you have to immerse yourself in it. None of you should be scared about coding and programming – that is the language of today and the future. Schools abroad and some even in Nigeria are already teaching primary school students coding. Coding is the thinking science. Can you imagine a doctor, a bank manager or a lawyer today who doesn't know how to use the computer and the internet becoming successful? Are you versatile in the use of Excel and other spreadsheets? What about SPSS? Take on the challenge and learn something beyond what medical school affords you. Several free online courses are available to empower you and give you that edge to be the chosen one – I just completed one on 'Project Management' with "EdX" – a Harvard-based online course - for we all have projects to manage – personal, family and organizational [7]. Your colleagues abroad are several years ahead – versatile in statistical software and already writing papers. *See yourself as being prepared for the global competition not the local survival rat race.*

Personal experience

Truly to be globally competitive is to anticipate. You have to ask yourself the following questions periodically as I do. What will I need in the future to function in the field I wish to pursue? Which certificates will I need to help boost my CV and make me qualified for future opportunities? Opportunities favor the prepared folks as chance favors prepared minds. The days I was expending my scholarship savings while on fellowship in Germany on writing Membership of Royal College of Physicians and Surgeons Glasgow(MRCS) exams; I never had an inkling that an opportunity for a fellow position in Cardiothoracic surgery in the UK for which I will need the MRCS qualification will emerge. I still remember my pensive mood while on the train taking me to the Frankfurt airport, Germany in March 2008, (after 18 months in Germany with only 170 Euros remaining in my pocket)! That expensive MRCS has added a lot more in material wealth and beyond to me. To be prepared for an uncertain future is to anticipate, make decisions and take action.

Social skills and emotional intelligence

Part of preparation for the future is what you are all engaging in today – involvement in extra-curricular activities to learn how to work in teams and develop leadership skills. By the time I was starting residency I already had about 4 papers published – of course in ***Dokita*** which prepared me for the future. How many of you are joining Dokita today and contributing articles to the journal? My writing skills were partly honed as a Dokita editorial board member with authorship and editorial experience. You also use these engagements to develop a key ingredient of success for leaders – emotional intelligence [8]. Emotional intelligence is the ability to control and identify emotions, and applying that ability to given tasks. Think of Emotional Intelligence in terms of specific competencies that you need to consciously develop.

Important components of emotional intelligence include self-awareness, self-management and regulation; social competence and relationship management. Empathy is a part of the social awareness cluster and deserves special mention in today's world. When you have empathy, you can walk in someone else's shoes to better understand what they are going through and why they are experiencing specific emotions. This allows you to be kinder and to more effectively communicate having looked at the situation through their perspective.

Good social skills enable you to cultivate positive emotions in other people. This helps you to build strong bonds with people that will last long-term. Another aspect of better social skills is knowing that emotions are like a virus. They spread quickly to everyone around. For example, if you are with a group of people and you are upset about something, this causes those in the group to feel down too. It is important to recognize this and then you are able to use your self-regulation to exert positive emotions to keep the people around you happy.

Once you master your social skills, you will be able to be an effective leader. You will be able to make negative people more positive and people will naturally respect you and what you have to say. The most successful people have solid social skills because they can adapt to a variety of situations with ease and maintain their poise. The social skills are much more important in this age of fourth industrial revolution [2] with relentless automation replacing people. Current findings suggest that as technology races ahead, workers will have to take on tasks that are non-susceptible to computerisation – i.e., tasks requiring creative and social intelligence. For

workers to win the race, however, they will have to acquire creative and social skills [9].

If you have already forgotten everything said so far, please make sure you keep the following points intact in your memory for life:
(i) Learn to build relationships from now on. (ii) Connect with key people in your life on a regular basis. (iii) Set dates in your calendar to touch base every few months. (iv) Find new relationships that might be able to connect you with key people some day in the future or who are authorities in their own right. (v)The relationships in your professional life are probably the most important asset you have. Now is the time, when you don't need it, to seek out and establish your professional support system so that it is there for you when you really do need it.

Mentoring is also a great way to develop your leadership potential. Find role models whom you want to emulate, who are doing what you want to do in the future or stand out as examples of the kind of leader you want to be. If you know them personally, foster that relationship, feed it, nurture it and make lots of notes. If they are a public personality and inaccessible in person, read everything they write, watch them on Youtube or on Ted Talks and attend any event that gets you closer to their thoughts, ideas, and dreams. It's important to realize that no one is going to pull our hands and drag us to the table but we must walk there ourselves. And part of this walk is through getting the right leadership skills and knowledge so that one earns a right to be at the table. Leadership is not given on a platter of gold, you have to claim it.

Leadership readiness qualities

To sum up, I will like to acquaint us all with the four qualities the future demands, well captured by a world renowned Consulting firm – Hays Group of the UK [10]. These four qualities identify an individual's readiness to extend himself/herself beyond current role and take on leadership positions successfully in the future. Tested against data from thousands of assessments conducted by Hay group around the world, these attributes are:

Eagerness to learn

The willingness to take a risk in exchange for the opportunity to learn something new. This factor reflects an individual's confidence in stretching beyond their comfort zone, as well as their ability to listen to – and learn from – others.

Breadth of perspective

The ability to include multiple perspectives and disciplines when evaluating and solving problems. This involves viewing a given job within the broader context of the organization.

Understanding others:

The capacity to accurately perceive other people's perspectives and experiences. This factor is a measure of an individual's motivation and ability to learn from others- particularly those with different outlooks- by listening with care and respect.

Personal maturity

The ability to see criticism and difficulties as opportunities for learning and growth. Every senior manager knows the path to leadership can be challenging, even painful, with setbacks along the way. The mature leader maintains emotional balance and keeps on learning in the face of turmoil.

In essence, ladies and gentlemen let us develop the skills needed for and beyond the 21st century – collaboration, communication, problem-solving, critical thinking, leadership and entrepreneurship – to prepare for tomorrow. The word 'discipline' means to sacrifice something immediate for something more meaningful later. It includes ability to delay gratification. Discipline is the price you pay for dreams to become reality.

Closing comments

Let me remind us of the three primary questions set at the beginning:

- What are the most pressing challenges that we will face as future leaders?
- As the next generation of leaders to confront such challenges, how do we best prepare and develop leadership abilities, qualities and skills?
- What are the next generation of technologies, methodologies, models and solutions we will need to overcome such challenges?

I have attempted to address these questions. As future leaders, we will need to continually reflect on them and answer them in our contexts and within our various spheres of influence.

Let us avoid being like those people who externalize or postpone leadership to that day when they are pronounced as President, Governor, Chief Medical Director, Vice Chancellor or Chief Executive Officer. Leadership does not always need a position or title. You are all leaders as you are sitting down, for to serve is to lead. Who are you leading? **Self**. Leadership is both an ART and an ACT. It is innate and at the same time corporate. It requires taking responsibility and being accountable. You are responsible and mature when you accept that the

world owes you nothing. You have to maximize all opportunities to develop yourself. Hold yourself accountable daily. As you lie on your bed to sleep, ask yourself the questions that define the quality of your impact in life. Let us subject ourselves to daily checks of whether we are making enough impact and helping to put smiles on others' faces as we plod on in life. These are integrity questions which are core to being a real success in life and a leader who is equipped for tomorrow challenges.

The questions:

- What difference did you make today?
- Who did you affect?
- What opportunities to inspire or help did you miss?
- What do you need to change?

For when we regularly hold ourselves so accountable can we develop our integrity and move beyond competence to emotionally intelligent leadership with character. And that is the seed for a great tomorrow.

Ladies and gentlemen, the world is rapidly changing and as future leaders we must move beyond managing to leading change, embracing technology, developing the requisite skills and abilities and regularly measuring the impact of our lives. Let us embrace the concept of personal leadership – taking responsibility, holding ourselves accountable and growing.

Take this Latin proverb to heart and live it: ***'Si präsens bene collocaveris, de futuro tibi dubium non erit.'***
(If you make good use of the present time, you need not be apprehensive about the future.)

I thank you for listening.

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Exophthalmometric values and periocular anthropometry among 10 to 18 year old Nigerians

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Abstract
Background: Exophthalmometry and palpebral dimensions measurements are important in ophthalmic, as well as facial reconstructive surgery practice and the range of normal values vary among different races and age groups.
Objective: To establish a set of exophthalmometric values and palpebral dimensions in a healthy Nigerian population of older children and young adults.
Methods: A descriptive cross sectional school survey was conducted among secondary school students aged 10 to 18 years in a Local Government Area, South-Western Nigeria. Exophthalmometry value and palpebral dimensions were measured using Hertel exophthalmometer and a non-stretchable transparent plastic millimeter ruler respectively.
Results: The mean exophthalmometric value was 15.95 ± 1.10 mm in both eyes, (right eye, 15.88 ± 1.01; left eye, 16.02 ± 1.04, t = -9.146, p <0.001) and it increased with age (r = 0.725, p < 0.001). In the right eye, the mean palpebral fissure height was 10.60 ± 0.71 mm, palpebral fissure width was 31.10 ± 1.18 mm, medial canthal distance was 8.8 ± 0.78 mm, lateral canthal distance was 10.8 ± 0.75 mm, and margin reflex distance-1 was 3.5 ± 0.50 mm. In the left eye, the mean palpebral fissure height was 10.50 ± 0.72 mm, palpebral fissure width was 31.20 ± 1.12 mm, medial canthal distance was 8.7 ± 0.79 mm, lateral canthal distance was 10.8 ± 0.77 mm and margin reflex distance-1 was 3.5 ± 0.50 mm. A statistically significant difference (p=0.014) was noted only in the palpebral fissure width between the two eyes.
Conclusion: This survey has established normative values for exophthalmometry and palpebral dimensions among 10- to 18-year-old Nigerians in our locality which can be compared with other parts of the country.

Keywords: *Anthropometry, Exophthalmometry, Palpebral dimensions, Nigerian*

Résumé
Contexte: Les mesuresde dimensions de l'exophtalmométrie et palpébrale sont importantes dans l'ophtalmie ainsi que lapratique de la chirurgie reconstructive faciale, et la gamme des valeurs normales varie selon les races et les groupes d'âge.
Objectif: Pour établir un ensemble de valeurs exophtalmométriques et de dimensions palpébrales dans une population nigériane saine d'enfants âgés et de jeunes adultes.
Méthodes: Une enquête transversaledescriptive sur les écoles a été réalisée chez des élèves du cycle secondaire âgés de 10 à 18 ans dans une commune, sud-ouest du Nigeria. La valeur de l'exophtalmométrie et les dimensions palpébrales ont été mesurées à l'aide de l'exophtalmètre d'Hertel et d'une règle millimétrique en plastique transparent non extensible respectivement.
Résultats: La valeurmoyenne exophtalmométrique était de 15,95 ± 1,10 mm dans les deux yeux, (oeil droit 15,88 ± 1,01 ; œil gauche 16,02 ± 1,04, t = -9,146, p <0,001) et elle a augmentée avec l'âge (r = 0,725 p <0,001). Dans l'œil droit, la taille moyenne de la fissure palpébrale était de 10,60 ± 0,71 mm, la largeur de la fissurepalpébrale était de 31,10 ± 1,18 mm, la distancecanthale médiale était de 8,8 ± 0,78 mm, la distance canthale latérale était de 10,8 ± 0,75 mm et la distance réflexe marginale-1 était 3,5 ± 0,50mm. Dans l'œil gauche, la taille moyenne de la fissure palpébrale était de 10,50 ± 0,72 mm, la largeur de la fissure palpébrale était de 31,20 ± 1,12 mm, la distance canthale médiale était de 8,7 ± 0,79 mm, la distance canthale latérale était de 10,8 ± 0,77 mm et la distance réflexe marginale-1 était de 3,5 ± 0,50mm. Une différence statistiquement significative (p = 0,014) n'a été notée que dans la largeur de la fissure palpébrale entre les deux yeux.
Conclusion: Ce sondage a établi des valeurs normatives pour l'exophtalmométrie et les dimensions palpébrales parmi les nigérians de 10 à 18 ans dans notre localité ce qui peut être comparés avec d'autres régions du pays.

Mots-clés: *Anthropométrie, Exophtalmométrie, Dimensions palpébrales, Nigérian*

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Introduction

The orbit is a bony cavity with an average volume of 45ml and houses the eyeball along with various other structures such as the extraocular muscles, retro-orbital fat, the lacrimal gland and the associated neural and vascular structures [1]. Exophthalmometry is the quantitative assessment of the position of the globe in the orbit [2] and many diseases of the orbit manifest with abnormal protrusion of the eye for which exophthalmometry is a routine test to evaluate the patients. The Hertel exophthalmometer is the most commonly used exophthalmometer in clinical practice because it is a handy and inexpensive device which produces consistently reproducible results, though, it cannot be used in individuals with defects in the lateral orbital wall [3]. Anthropology reveals that the skeletal build-up of humans is unique in different races, and that males and females have different bony framework [4]. The normal morphologic and functional values of eyelid positions also vary widely between race, sex, and age [4]. Therefore, knowledge of the average dimensions of periocular structures, facial proportions and the relationships between individual segments of the face is protean. Opinions differ on the effect of age on exophthalmometric value (EV) and palpebral dimensions (PD).

However, many authors [5-7] reported that EV increases during the first two decades of life, and stabilizes thereafter, thus, suggesting that EV at the end of the second decade is a true representation of EV in adulthood. Heterogeneity in EV and PD values and their correlates among different populations had been clearly demonstrated [5, 8-12]. Therefore, when evaluating the results of these measurements, the normal values specific to the population must be taken into consideration. However, only a few studies [13-15] have reported normative exophthalmometry data in the Nigerian population and these were conducted mainly among the older age groups, thus, values based on studies among Caucasians are used as reference in the country. This study thus aims to define normal EV and PD values in this select group of healthy Nigerian population.

Methods

A descriptive cross-sectional study was conducted among 1,018 secondary school students in Akinleye Local Government Area (LGA) of Oyo State, South Western Nigeria. Multistage sampling was used to recruit students from five public co-educational secondary schools out of the 35 government owned schools in the LGA. Sample size was estimated using the formula for calculating single proportions [16]. The senior arm of each school and one of the two junior arms were selected by simple random sampling and a class each was selected from junior class one to senior class six by balloting. All students in each selected class were included in the study. Excluded from the study were students with previous or present history of ocular and orbital trauma or surgeries, family history suggestive of thyroid eye disease, facial asymmetry or abnormalities, high refractive errors, and squint. Interviewer-administered questionnaires were administered to all the students participating in the study to elicit relevant past ocular, medical and family history.

Visual acuity was assessed with a Snellen's chart positioned at 6 meters in a well illuminated environment for all the students following which exophthalmometry was done with an accurately calibrated Hertel exophthalmometer (Keeler Instruments Inc., Broomall, PA, USA) using the standard method described by Kumari *et al*[1]. The mean of three readings was taken as the final reading.

Periocular anthropometric measurements taken were palpebral fissure height (PFH), the central vertical distance between the upper and lower lid margins at primary position of gaze; palpebral fissure width (PFW), the horizontal distance between the medial and lateral canthi; medial canthal distance (MCD), the horizontal distance between medial canthus and medial limbus while patient is at primary position of gaze; lateral canthal distance (LCD), the horizontal distance between lateral canthus and lateral limbus while patient is at primary position of gaze and margin reflex distance-1 (MRD_1), the vertical distance between the upper eyelid margin and cornea reflex while patient is at primary position of gaze. Palpebral measurements were taken in a well illuminated room with additional illumination from a rechargeable lamp. Measurements were taken with the use of non- stretchable transparent plastic millimeter ruler using the method described by Öztürk [17]. The mean of two readings was taken as the final reading.

Ethical approval was obtained from the University of Ibadan/University College Hospital Ethical Committee, and permission was sought and gotten from State Ministry of Education, LGA Education Board and the principals of selected schools. Written informed consent was obtained from the parent/guardian of each student and verbal assent was obtained from each student. The study was conducted according to the guidelines by Helsinki declarations on human research.

The collected data was entered into a data base, cleaned and analysed using the Statistical Package for Social Sciences version 20 software (SPSS Inc, Chicago IL, USA). Means and

frequencies were generated and comparison of the mean exophthalmometric values and palpebral dimensions between categories was done using the Student T-test and Pearson's correlation analysis. Level of significance was 0.05.

Results

A total of 1,018 students were studied, comprising 516 (50.7%) males and a mean age of 14.8 ± 1.9 years. The mean EV for both eyes was 15.95 ± 1.10mm (95% CI 15.89 to 16.01; range, 14mm to 19mm). The EV was significantly higher in the left eye (16.02 ± 1.04, 95% CI 15.96 to 16.09) compared to the right eye (15.88 ± 1.01, 95% CI 15.82 to 15.95) (t = -9.146, p <0.001), and increased with age (r = 0.725, p < 0.001, Fig. 1). The range of differences in exophthalmometric value between the right and left eyes of the participants was 0-2 mm. Following participants' categorization into two age groups of 10 to 14 years (younger age group) and 15 to 18 years (older age group), the mean EV was significantly higher among the 15-18 years age group (t = -25.596; p <0.001). However, no significant difference was found between males and females (p = 0.73). (table 1)

Table 1: Mean exophthalmometric values by age groups and gender

Age group (years)	Number	Mean (SD)	Both Eyes t-test (p-value)
10-14	493	15.31±0.59	-25.5964(<0.001)
15-18	525	16.56±0.92	
Gender			
Male	516	15.96±1.004	0.3426 (0.7319)
Female	502	15.94±0.994	

group (10.86±0.67mm) was significantly higher than in younger age group (10.27 ±0.61mm) (t = -14.609, p <0.001) (Table 2). No significant difference (p=0.245) was noted between the right eyes (10.60 ± 0.71 mm) and left eyes (10.50 ± 0.72 mm) of the students.

The mean LCD increased with age (r = 0.204, p <0.001) and was significantly higher in the older (15-18 years) age group (t = -5.180, p <0.001), but there was no significant difference between males and females (p = 0.46), and right eyes (10.8 ± 0.75 mm) and left eyes (10.8 ± 0.77 mm) of the students (p=0.595). The mean MCD however, increased with

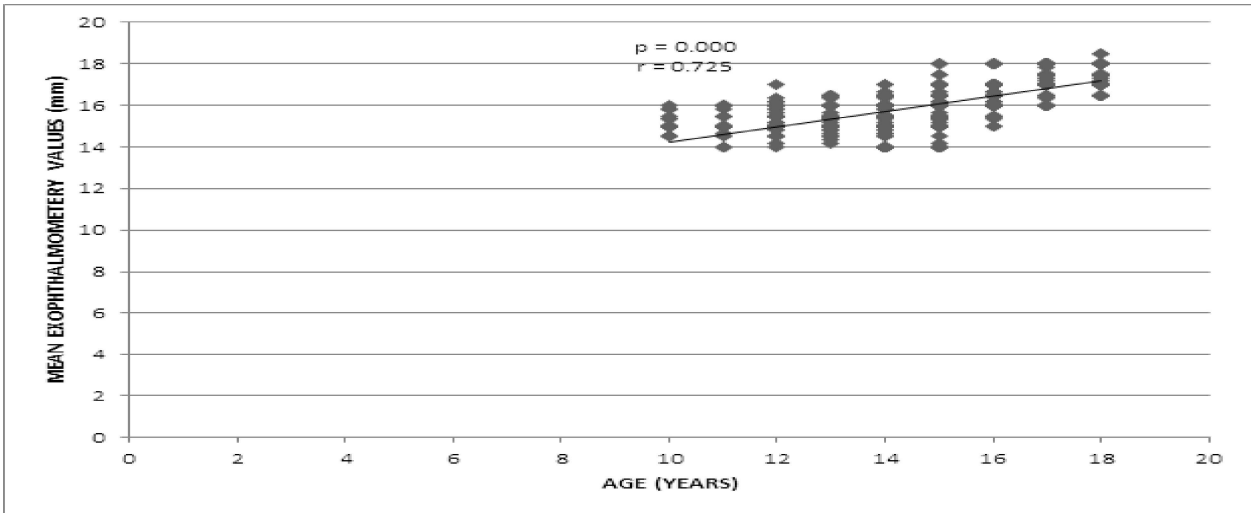

Fig. 1: Correlation of EV with age

The PFW increased significantly with age (r = 0.33, p <0.001), with the mean PFW in older age group (31.47±1.03mm) being significantly higher than in younger age group (30.84±1.15mm) (t = -9.220, p <0.001). A statistically significant difference (p=0.014) was noted in the mean PFW between the right eye (31.10mm ± 1.18 mm) and left eye (31.20mm ± 1.12 mm) of the students. Also, the PFH increased significantly with age (r = 0.45, p < 0.001), (Fig. 2), and the mean PFH in older age

age (r = 0.224, p <0.001) (Figure 3), but showed no significant difference between the age groups (t = -6.501, p = 0.054) and gender (p = 0.82). (Table 2). No significant difference was also noted between the right eyes (8.8 ± 0.78 mm) and left eyes (8.7 ± 0.79 mm) of the students (p=0.275).

The mean margin reflex distance 1 (MRD_1) in the right and left eyes was identical (3.50 mm ± 0.50 mm) and this did not differ significantly between the age groups in each eye, (right eye, t = -0.5978, p

= 0.5501; left eye, t= -0.1870, p = 0.8517) and gender (p > 0.05).

Discussion

The mean exophthalmometric value (EV) in this study was similar to an earlier study by Ibraheem *et*

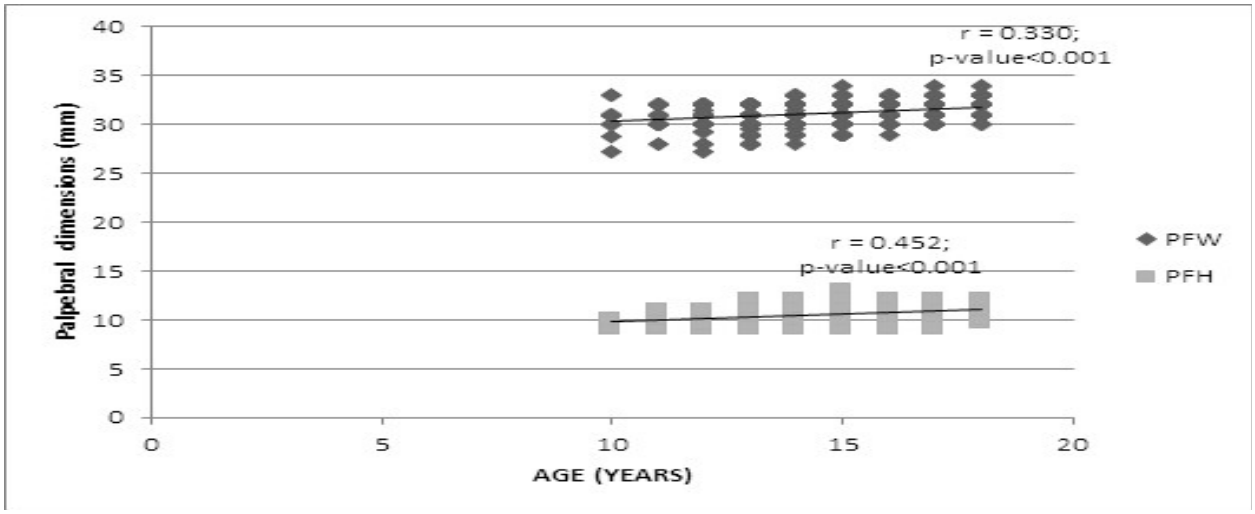

Fig. 2: Correlation of age with palpebral fissure width and height

Table 2: Mean PFW, PFH, LCD, MCD values between age groups and by gender

Age groups (years)	N	PFW (mm)	p-value	PFH (mm)	p-value	LCD (mm)	p-value	MCD (mm)	p-value
10 - 14	493	30.83	<0.001	10.27	<0.001	10.66	<0.001	8.61	0.054
15 - 18	525	31.48		10.86		10.91		8.92	
Gender									
Male	516	31.14	0.52	10.54	0.16	10.81	0.46	8.77	0.82
Female	502	31.18		10.61		10.77		8.76	

PFW=palpebral fissure width, PFH=palpebral fissure height, LCD=lateral canthal distance, MCD=medial canthal distance, N=number

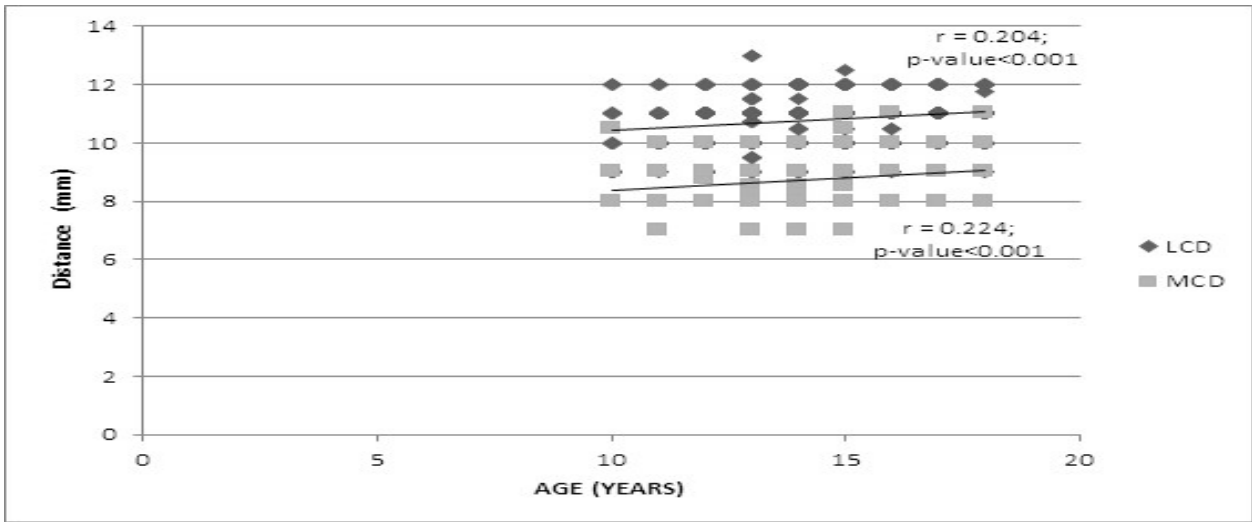

Fig. 3: Correlation of age and the lateral and medial canthal distance.

Table 3: Margin Reflex Distance (MRD_1) for Right & Left eye between age groups and gender.

Age groups (years)	N	Right eye		Left eye	
		Mean	t-test (p-value)	Mean	t-test (p-value)
10-14	493	3.533±0.507	-0.598 (0.550)	3.527±0.512	-0.187 (0.852)
15-18	525	3.552±0.501		3.533±0.503	
Gender					
Male	516	3.534±0.503	-0.535 (0.593)	3.509±0.504	-1.325 (0.186)
Female	502	3.551±0.506		3.551±0.509	

al [18] done in the same part of the country. They [18] however, studied mostly adults thus, suggesting that EV stabilizes and approximates adult values in the second decade of life as earlier reported by some authors [1,5,6]. Variations in EV with different racial groups had been documented by other authors [5,9,12,19] and the mean EV in this study is higher than those reported among Chinese, [5] Turkish, [19] and Iranian [9] teenagers, but lower than reported among Americans. [12] Osuobeni [20] had reported that Black youngsters had the highest EV followed by Arabs, Caucasians and Chinese, and opined that this may due to anatomic variations in the different racial groups. A significant strong positive correlation was noted between age and EV in this study, similar to previous reports [6,9,21]. Exophthalmometric value has been reported to increase with age, reaching a peak in the second decade of life, and subsequently starts to decline [5,22]. It is believed that EV increases from childhood to teenage years due to the disproportionate growth of the facial skeleton and orbital contents, eventually reaching its maximal level at adolescence [5,6]. The left eye had a statistically significant higher mean EV compared with the right eye in this study. However, this is not clinically significant as the difference is less than a millimeter. Previous researchers also varied in their report of the effect of laterality on exophthalmometry as some studies [9,13,18] found the left eye to have higher value, while other studies [1,10,19] reported higher value in the right eye. In agreement with previous studies, [9,12,23] males in this survey had higher EV than females, though, not statistically significant. Kaye *et al* [7] attributed the higher value in males to the bigger stature of males compared with females.

Palpebral fissure height and PFW significantly increased with age in this study, similar to findings of previous authors [24-26], which probably reflects the continued growth in facial bones and modeling of the facial soft tissues in this stage of life. Ibraheem *et al* [18] however, reported a slight decrease in the mean PFH and PFW with increasing age, though not statistically significant. It is noted however, that they studied mostly adults and elderly individuals. Erbagci *et al* [25] postulated that the shortening of PFW seen in older individuals may be due to progressive laxity of the medial and lateral canthal structures. Females had a higher PFH in this study, though not statistically significant, in agreement with Ibraheem *et al* [18]. Similarly, we found PFW to be higher in females in consonance with the report of Eze *et al* [27] but at variance with Ibraheem *et al* [18] who reported that males had a significant higher PFW than females and attributed this to a probable difference in the pattern of craniofacial growth with gender.

There is a weak positive correlation between the medial and lateral canthal distances and age in this study ($p < 0.001$). In the older age group, the mean MCD and LCD are lower than reported by Ibraheem *et al* [18] among the participants who were less than 30 years of age in their cohort. This also suggests a continuous growth of the facial bones and soft tissues with age, as the values of these parameters increased with age in our study. A weak positive correlation also exists between the palpebral fissure height and width and age in this study ($p < 0.001$) also, suggesting continued growth in facial bones and soft tissues in this stage of life. Of the palpebral dimensions, only the PFW showed a statistically significant, but not clinically significant difference between the right and left eyes similar to a previous report [27].

The mean MRD_1 in this study is slightly higher than the earlier report [18] in the region but lower than what was reported by Price *et al* [24]. This disparity could be attributed to the age differences in the studied populations as Ibraheem *et al* [18] included elderly individuals in their cohort, as well as racial differences [24].

A major limitation of this study is the school survey design which limits the age of the participants that were studied to the younger age group. However, there are existing studies among adults in the region and other parts of the country.

Conclusion

In conclusion, a different exophthalmometric value (range 14mm to 19mm, mean 15.95mm) than the present commonly used reference value for absolute exophthalmometry (range 10mm to 21mm, mean 16.20mm) was obtained in this study. The values for exophthalmometry and palpebral dimensions derived from this study are thus recommended as references for 10- to 18-year old patients in our region. Further studies in other parts of the country are suggested to determine variability of these values.

Acknowledgments

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Tribute
of
PROFESSOR BABATUNDE O. OSOTIMEHIN
(Editor, African Journal of Medicine and Medical Sciences - 1996 - 2003)

Gaudemus igitur, Gaudemus igitur!!

We are gathered here today in honour of a worthy Alumnus and a past Provost of this College of Medicine. I have the special privilege of welcoming to this occasion our special guests, who are connected in a special way with the deceased as we do.

I wish to recognise and welcome all our distinguished members of staff to this Special College Assembly Convened with the sole purpose of celebrating the life of a former Provost of the College of Medicine.

I warmly welcome the dear wife of the departed, Mrs. Olufunke Osotimehin, the children and indeed the entire family. We sincerely appreciate the opportunity given the College to play this part in paying respect to a man deserving honour. The news of death of this foremost Clinician came as a shock to the College, University and indeed the entire nation. Late Professor Babatunde O. Osotimehin who was much loved and fondly referred to as **'Bob'** will be greatly missed.

Ars longa, Vita brevis - For life is short, but art is long.

With this phrase Greek philosophers challenged our thoughts about life and death whenever it comes as it must, because in the end the essence of life is not how long it was, but how creative, or impactful, a life had been. From all we have heard about our much loved Professor since his demise, it is safe to say that, whilst it would appear that the length of his life was relatively short, his creativity in living it has ensured that the art of his life will indeed be long. This as he has left many legacies in the various stages of his life, in the places he worked, and with the people he met.

His spent his longest time in the College of Medicine, from his medical student days till death (50 years in all), and what a time. We have been told he was a brilliant student, who did not appear to be an 'effico'. We have heard that he not only acquired the competencies to diagnose the best life-partner for him with just one short-case sitting of the particular derrière on his knees, on the back seat of a crowded car in the dark; but also those with which he found, clerked and investigated that partner at the Scala laboratories one year later; as well as the skills he managed her with successfully for the next 44 years. What a guy!!! What a well-trained student!!

We have been reminded that Professor Babatunde Osotimehin was a brilliant man of 'molecules', an accomplished scholar and Provost before he 'found his calling' as international social scientist, civil servant and ambassador which position he had first desired at the age of 19. In those testimonies, one caught a hint that the various groups were trying espouse what their part of his life

Professor Babatunde O. Osotimehin
OON, MD, FWACP, FRCP, FAS
1948 - 2017

contributed to his legacy. But indeed, a closer look at molecules indicate that Bob was being Bob as he moved determinedly, from one effortlessly executed posting of life to the other. This is because from studying molecules you learn that all life is just a transformation of one type energy to another as is demonstrated by the cell cycle which is the basis of life. In this ever-continuing process, nature is at its best as it transforms cells from one stage to another without losing energy, and even when the cell dies the process of its demise is energy-efficient as all its components are resorbed and used by other cells - its progeny.

Tribute read at the Special College Assembly on Thursday, 20 July 2017

Late Professor Osotimehin had also learned from his time in the molecular laboratory that the life and death of a cell is determined by surrounding cells and is dependent on its environment. This theory was proven first by Schelhammer in 1904 when he showed that a cell isolated from others quickly died not matter the amount of nutrients in its immediate milleu. It was further elucidated by Chung, Cunha and others in the early 1990 when they showed that a normal cell placed amongst cancerous neighbors becomes cancerous, whilst a cancerous cell placed amongst normal neighbors reverts to a normal cell. Realizing his qualities, this understanding may have contributed in part to Professor Osotimehin's decision to redirect his efforts from the relatively small environment of the laboratory and the University to the larger field of international health in his quest to make his society better in as large a scale as possible and thus ensure his own well-being. His success at this task has of course been laid bare over the past month.

From the above and other testimonies we can conclude that this Professor's life was made up of a heterogeneous collection of Shakespearean acts with this world as his stage. From his birth in a country of the Tempest, his Macbethian pre-destination, through his emulation of the toasts of Romeo and the nimbleness of the elves of A Midsummer's night dream in his admirable waltzes through his academic and political careers; and finally his Hamlet-like exit from the stage. The art in his life, which has inevitably made him a legend, can only be admired but not copied, and this is perhaps a welcome comfort to his successors who would rather not be measured by the yard-stick his achievements.

Mrs. Osotimehin and the rest of the Osotimehin family and friends here present, distinguished audience of this Special Academic Assembly, the first of its kind for a departed Provost, it is true that Professor Osotimehin's candle has gone out and that his body will soon leave this institution for ever, we are however assured that through his works and deeds, the light of his legacy will continue to illuminate our hallowed chambers and corridor of academe eternally, and the name 'Bob' will be remembered in this citadel of learning for more than a life time.

We pray that his soul will rest in the peace of his Lord, and that that peace will abide with his family, friends, students and mentees forever.
Professor Babatunde Osotimehin, by the grace of God the 4th Provost of the College of Medicine, University of Ibadan, 1990-1994. *Requiescat* in Pace.

E. Oluwabunmi Olapade-Olaopa *Esq., FAS*
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Notes for Contributors

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