AFRICAN JOURNAL OF MEDICINE
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Aims

The aims of *The African Journal of Medicine and Medical Sciences* are: (1) to provide a medium for wide dissemination of information resulting from biomedical research in Africa and elsewhere; (2) to furnish a means whereby appropriate international medical and health organisations may transmit information to medical scientists throughout Africa; (3) to serve as a medium for publication of proceedings of international conferences on medical sciences in Africa; (4) to serve as a medium for the exchange of information and opinion among medical scientists in medical institutions of Africa and elsewhere; (5) to promote inter-regional cooperation amongst medical scientists in Africa.

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A call for novel approaches to patient management

Science thrives on innovation. Necessary change in diagnosis and management approaches can only come through "thinking outside the box". It will be unusual for things to change if the approach to diagnosis and treatment are static, unless by divine intervention. This journal is committed to bringing to readers' attention any innovative approach to management to improve the standard of care.

Nephrotic syndrome comprises anasarca, massive proteinuria, hypoalbuminaemia and hypercholestrolaemia. Treatment of the oedema involves use of diuretics and repeated paracentesis combined with the infusion of salt-poor albumin, where available and affordable. Over time, the oedema becomes unresponsive to therapy and this can be a challenge. Peritoneo-venous shunting is then considered at this stage. In the study by Hassan and colleagues in Ile-Ife, a modification was introduced whereby the ascitic fluid is drained intermittently into a sterile container and then infused into a peripheral vein using an infusion set as a one-way valve. Twenty six patients underwent the procedure and the authors reported significant changes in body weight, abdominal girth, urinary protein excretion, and serum albumin levels. There was no mortality. Although cost analysis was not carried out and the period of follow up of the patients appeared short, it can be assumed that this would be a very useful therapy for individuals with refractory oedema in nephrotic syndrome.

With the emerging problems of non-communicable diseases in developing countries, non-pharmacological methods are being employed in the form of physical exercises for health promotion. Martins and colleagues reported that supervised work-place exercise appeared superior to "unsupervised exercises-on-prescription" for the reduction of body weight and blood glucose levels in their patients that were followed up for 3 months. This agrees with the known benefits of exercise in preventing diabetes and obesity. Physical exercise has also been noted to improve cognitive performance. Once again, supervised exercise is being recommended as a great health promotion strategy.

Oxidative stress leads to cell death and may have a genetic basis but may be caused by vascular insufficiency, toxic exposure and metabolic damage. It occurs in many neurodegenerative conditions. Owoeye and colleagues, using Wistar rats, have reported on the beneficial effect of tomato pomace powder in the management of induced-sepsis. Tomato contains many active ingredients that promote health and it is available in abundance. It is anticipated that this finding would be translated for use in humans with sustained benefits. Three of the 15 manuscripts published in this issue of the journal have been highlighted. The others are no less interesting and contain one or two lessons that can improve patient management and/or be the subject of future studies.

Prof. A. Ogunniyi
Editor-in-Chief

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Comparative neuroprotective effects of Progesterone and vitamin E in induced traumatic brain injury in Wistar rat

O Owoeye, SO Agboola, IO Imosemi and AO Malomo
Department of Anatomy, College of Medicine,
University of Ibadan, Ibadan, Nigeria.

Abstract

Background: Traumatic brain injury (TBI) is an insult to the brain from external mechanical force whose effect is exacerbated by oxidative damage. This study investigated the possible neuroprotective effects of progesterone (P) and vitamin E (E) on traumatized rat brain.

Materials & Methods: Forty five adult male Wistar rats were randomized into nine groups: I: Non-traumatized control (NTC); II: Non-traumatized and P-treated (NTP); III: Non-traumatized and E-treated (NTE); IV: Blunt-traumatized control (BTC); V: sharp-traumatized control (STC); VI: Blunt-traumatized and P-treated (BTP); VII: Blunt-traumatized and E-treated (BTE); VIII: Sharp-traumatized and P-treated (STP) and IX: Sharp-traumatized and E-treated (STE) groups. Animals were treated with P (16 mg/kg body weight) and E (500 mg/kg body weight) via oral gavage daily for five days. On day six post-TBI, behavioural tests were conducted and rats euthanized after which brains were harvested for oxidative stress markers and histologically processed by paraffin method.

Results: Behaviourally, BTC significantly ($p<0.05$) elevated the forelimb grip strength and transitions while reducing the number of grooms and rearings when compared with the NTC. In the BTP and BTE groups these parameters were significantly increased when compared with BTC values. Similarly, both BTC and STC elevated MDA level and significantly ($p<0.05$) reduced the activity of GSH, whereas the activities of SOD, CAT, and GPx were upregulated ($p<0.05$). Histology showed degeneration of cortical neurons in all groups that had brain injury when compared with NTC group, though this was ameliorated by vitamin in the BTE and STE groups. Histomorphometry showed significantly ($p<0.05$) elevated red neuronal count in BTC and STC groups which were reduced in the BTE, STP and STE groups.

Conclusion: Both BTC and STC induced oxidative stress and cortical neuronal degeneration which was reduced in the BTE, STP and STE groups. However, co-treatment of trauma with vitamin E demonstrated better neuroprotection relative to progesterone in both blunt and sharp forms of trauma.

Keywords: *Traumatic brain injury, Blunt trauma, Sharp trauma, Progesterone, Vitamin E.*

Résumé

Contexte : La lésion cérébrale traumatique (LCT)est une injure du cerveau causée par une force mécanique externe, dont l'effets est aggravé par un dommage oxydatif. Cette étude a examiné les effets neuro-protecteurs possibles de la progestérone (P) et de la vitamine E (E) sur le cerveau traumatisé du rat.

*Matériaux et méthodes:*Quarante-cinq rats Wistar mâles adultes ont été randomisés en neuf groupes: I: contrôle non traumatisé (CNT); II: non traumatisé et traité avec P (NTP); III: non traumatisé et traité avec E (NTE); IV: Contrôle contondanttraumatisé (BTC); V: contrôle de traumatisme aigu (STC); VI: traumatisé contondant et traité avec P (BTP); VII: traumatisé contondant et traité avec E (BTE); VIII: groupes traumatisés aiguset traités avec P (IX) et groupes IX: groupes traumatisés aiguset traités avec E (STE). Les animaux ont été traités avec P (16 mg / kg de poids corporel) et E (500 mg / kg de poids corporel) par gavage oral quotidiennement pendant cinq jours. Le sixième jour après laLCT, des tests comportementaux étaient effectués et les rats ont été euthanasiés, après quoi les cerveaux ont été récoltés pour déterminer les marqueurs du stress oxydatif et traités histologiquement par la méthode de la paraffine.

Résultats: Sur le plan comportemental, le BTC a significativement ($p <0,05$) élevé la force de préhension et les transitions de la patte antérieure tout en réduisant le nombre de toilettages et d'élevages par rapport au CNT. Dans les groupes BTP et BTE, ces paramètres ont été significativement augmentés par rapport aux valeurs BTC. De manière similaire, BTC et STC ont élevés les taux de MDA et réduisaient significativement ($p <0,05$) l'activité de GSH, alors que les activités de SOD, de CAT et de GPx étaient régulées à la hausse ($p <0,05$). L'histologie a montré une dégénérescence des neurones corticaux dans tous les groupes ayant subi une lésion cérébrale par rapport au groupe CNT,

Correspondence: Prof. A.O. Malomo, Department of Anatomy and Surgery, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: aomalomo@yahoo.com; oowoeye2001@yahoo.com

bien qu'elle ait été améliorée par la vitamine dans les groupes BTE et STE. L'histo-morphométrie a montré une augmentation significative ($p < 0,05$) du nombre de neurones rouges dans les groupes BTC et STC, qui étaient réduits dans les groupes BTE, STP et STE.
Conclusion: BTC et STC ont tous deux induit un stress oxydatif et une dégénérescence neuronale corticale qui ont été réduits dans les groupes BTE, STP et STE. Cependant, le co-traitement des traumatismes avec la vitamine E a démontré une meilleure neuro-protection par rapport à la progestérone dans les formes de traumatismes contondants et aigus.

Mots-clés: *lésion cérébrale traumatique, traumatisme contondant, traumatisme aigu, progestérone, vitamine E.*

Introduction

Traumatic brain injury (TBI) is a preventable, non-congenital insult to the brain from external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical, and psychological functions with associated diminished or altered state of consciousness [1]. Besides the primary brain damage, secondary brain damage caused by mechanisms such as brain oedema, free radical formation or release of inflammatory mediators may exacerbate the injury [2] making it progress to be one of the main causes of death and disability. Varying causes of brain injury may have different effects for example: falls in older patients, high-velocity traffic accidents in younger patients, firearms in violence-related injuries [3, 4]. With methylprednisolone, once considered a main stay of treatment, now shown to be harmful [5] and without evidence to support the use of magnesium in patients with acute brain trauma [6], it becomes imperative to continue the search for alternatives that can mitigate or reduce the effects of secondary brain damage after TBI.

Although progesterone has long been considered a female reproductive hormone, previous studies show that it has substantial pleiotropic properties as a neuroprotective agent in both animal models and humans [7]. Progesterone receptors are widely distributed throughout the central nervous system [8] and its neuroprotective property against brain damage has been reported [9, 10]. Progesterone, a hormone which is both widely available and inexpensive, has steroidal, neuroactive and neurosteroidal actions in the central nervous system [11]. Its neuroprotective effect has been demonstrated in a variety of animal models, including ischemic and traumatic brain insult models [12]. Previous studies have shown that post-traumatic injury treatment with progesterone decreases brain oedema [13], attenuates free radical damage [14], reduces neuronal loss [15], inhibits the inflammatory response [16], restores the blood-brain barrier (BBB) function [17], increases the levels of endothelial progenitor cells [18] and promotes behavioural recovery [19]. After brain injury, steroids like progesterone and its metabolites can exert protective effects on neurons and glial cells by preventing cerebral oedema, necrosis, apoptosis, and inflammation, while enhancing neuro-regenerative mechanisms [15, 20]. The above reported protective features of progesterone makes it a candidate drug for further investigation for possible neuroprotective effect on induced brain injury in Wistar rats.

The natural form of vitamin E is synthesized only by plants and is found predominantly in plant oils. It is a fat soluble chemical compound found in the human diet in varying amounts and over 90% of the total body vitamin E is found in the adipose tissue [21]. It is the primary membrane bound lipid-soluble, chain-breaking antioxidant that protects cell membranes against lipid peroxidation [22, 23]. By reducing free radical attack, antioxidants break the chain reaction of lipid peroxidation and thus protect the cell membranes by lipid repair and lipid replacement. The preventive effect of vitamin E on cypermethrin or endotoxin-induced oxidative stress in rat tissues supported its antioxidative activity [24]. Since oxidative damage has been implicated in TBI, vitamin E's antioxidative property will also be investigated in this study.

This study aimed to investigate the possible ameliorative effect of progesterone in trauma-induced injury of brains of the adult male Wistar rat compared with that of vitamin E.

Materials and methods

Experimental animals

Forty-five adult male Wistar rats (150-180 g) were obtained from breeders in College of Medicine animal house, University of Ibadan. They were acclimatized at a freely ventilated and naturally illuminated animal house of the Department of Veterinary Physiology, University of Ibadan, for two weeks before being assigned randomly to experimental and control groups. The animals were housed in transparent plastic cages (39 x 29 x 27 cm) with wood shavings as bedding and were fed with standard pelleted rat diet produced by Vital Feeds, Jos, Nigeria and water provided *ad libitum*. The experimental protocols were carried out to conform with the acceptable guidelines on the ethical use of animals in research [21].

Preparation and administration of progesterone
Each 1 mL ampoule containing 25 mg of progesterone (Kwality Pharmaceuticals Ltd, Amritsar, India) was completely aspirated with a new 21 G size needle attached to a new 1 mL hypothermic syringe (Becton Dickinson, La Portde-Clair, France). The insulin syringe was thereafter attached to a new 27 G size needle through which each rat was administered intra-peritoneally.

Preparation and administration of α-tocopherol (vitamin E)
Each soft gelatin capsule containing 100 mg of DL-α-tocopheryl acetate as 100 mg vitamin E acetate (Gujarat Liquid Pharmacaps Limited, Gujarat, India) was punctured with a new size 21 G needle attached to a new 1 mL hypothermic syringe. The vitamin E content of each capsule was completely aspirated out with the syringe measuring approximately 0.2 mL. The syringe was thereafter attached to a clean intra-gastric gavage through which each rat was administered orally the measured dose of 500 mg/kg/body weight daily [23].

Research Design
The forty five adult male rats were divided into nine groups thus:
Group I (n=5): Non-traumatized control group that received 1 mL distilled water daily (NTC).
Group II (n = 5): Non-traumatized and Progesterone-treated, 16 mg/kg bwt, i.p. (NTP).
Group III (n=5): Non-traumatized and Vitamin E-treated, 500mg/kg bwt., per os (NTE).
Group IV (n=5): Blunt-traumatized control (BTC).
Group V (n=5): Sharp-traumatized control (STC).
Group VI (n=5): Blunt-traumatized and Progesterone-treated, 16 mg/kg, i.p. (BTP).
Group VII (n=5): Blunt-traumatized and Vitamin E-treated, 500 mg /kg, per os (BTE).
Group VIII (n=5): Sharp-traumatized and Progesterone-treated, 16 mg/kg bwt, i.p. (STP)
Group IX (n=5): Sharp-traumatized and Vitamin E-treated, 500 mg /kg bwt, per os (STE)

Progesterone was administered at 16 mg/kg body weight one hour-, six hours-, twenty-four hours post-injury and thereafter once daily for five days post-injury. The dosage and route of administration of progesterone were based on the method of Si *et al.* [22], whereas vitamin E was a single daily dose according to published report [23].

Experimental induction of traumatic brain injury (TBI)
To experimentally induce TBI, the animals were anaesthetized with Ketamine hydrochloride injection (Rotex Medica Trittan, Germany) at a dose of 100 mg/Kg and 0.5 g of Diazepam-Tranzite injection (Sirochem Ningbo Limited, China). Thereafter, the hair on the animal's head was shaved to expose the target area and methylated spirit applied to the shaved area for antiseptic function. Animals were then placed on a flat surface provided on the levered table (Figure 1). A spot of injury was located, 2.5 mm posterior and 2.5 mm lateral to the bregma [24]. A round metallic ball was fashioned to the end of Steinmann's pin used for blunt type of TBI. Another Steinmann pin was fashioned to induce Sharp type of TBI. The levered table was adjusted to accommodate 2.5 mm traumatic distance for each animal. A cortical injury device as described by Stahel *et al*. [25] and employed by Leinhase et al. [26] was followed using a standardized weight drop device. A metallic object of 425 g was dropped at a uniform height of 5 cm on the skull to induce brain injury. The equipment in figure 1 [27] was made of a retort stand and levered table, the retort stand held two clamps at a distance of 5cm interval, the upper clamp held a wooden block called "stopper" used to regulate the traumatic distance by stopping the Steinmann's pin. The lower clamp held a wooden block called "Guide" which was used to guide the Steinman's pin pathway over the rat's skull. The levered table was made from a modified car jerk with a flat board on it as shown in figure 1. Topical application of cotton wool soaked with methylated spirit on the bleeding spot prevented skin contamination. At the end of each procedure, each animal was removed from the levered table and gently placed in the cage to recover.

Behavioural tests
Behavioural tests were performed on five rats per group on day 6 post-trauma, after weighing each rat, as detailed below:

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 is recorded. A maximum time of 2 minutes is given to each rat after which it will be removed. This test reflects muscular strength in the animals [28].

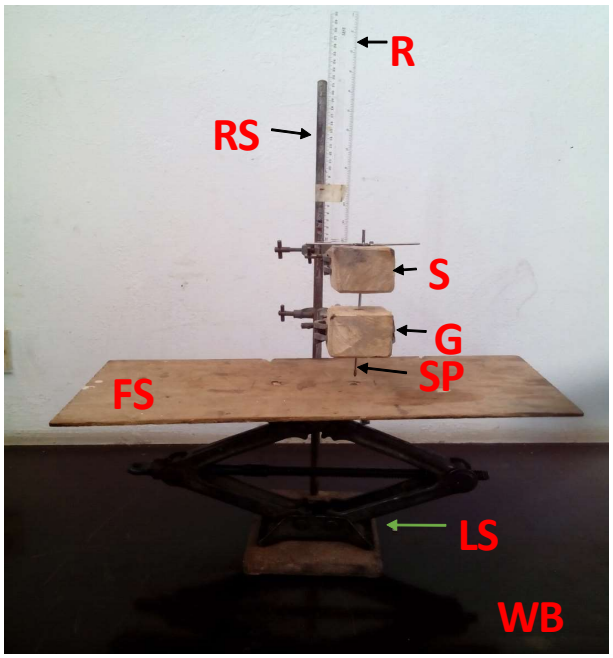

Fig. 1: Photograph of "weight drop apparatus" (Ajeleti, 2009) showing the ruler (R), retort stand (RS), lever stand (LS), work bench (WB), flat surface (FS), Steinmann's pin (G) and stopper (S).

Negative geotaxis

A plank was placed at an angle (45^0) to the wall and the rat was placed on the highest point facing downwards. The time it took for the rat to turn up, or start moving up the plank was measured. This test measures the motor re-orientation activities [29].

Open field tes

Rats were carried to the test room in their home cages and were handled by the base of their tails at all times. Rats were placed into the centre of the open field and allowed to explore the apparatus for 5 minutes. After the 5 minute test, rats were returned in their cages and the open field was cleaned with 70% ethyl alcohol and permitted to dry between tests. This test measured line crossing, that is, number of squares crossed, rearing and grooming [30].

Sacrifice and Sample collection

After completing the behavioural tests, rats were sacrificed by anesthetizing the animals with ketamine overdose followed by quick decapitation. Brain samples were dissected and removed, weighed and divided into two parts, one half was used for biochemical assay and the other half for histological analysis according to the method of Owoeye and Onwuka [31]. Thereafter, the half of cerebrum of each brain separated for histological processing was fixed in 10% formalin. The remaining half of brains for biochemical assay were kept in frozen state in freshly prepared phosphate buffered solution PBS at pH 7.4.

Biochemical assays

The brain samples were homogenized in 50 mMTris–HCl buffer (pH 7.4) containing 1.15% potassium chloride, and the homogenate was centrifuged at 10,000 g for 15 minutes at 4 °C. The supernatant was collected for the estimation of catalase (CAT) activity which was determined in erythrocyte lysate using Aebi's method [32]. Superoxide dismutase (SOD) was assayed by the method described [33]. Protein concentration was determined according to published method [34]. Reduced glutathione (GSH) was determined at 412 nm in a colorimeter using the method described by Beutler *et al*. [35]. Glutathione peroxidase (GPx) activity was determined by the method of Rotruck *et al*. [36]. Lipid peroxidation was quantified as malondialdehyde (MDA) according to the method described by Varshney and Kale [37].

Histological studies

The tissues were processed at the Histology Laboratory, Department of Anatomy, University of Ibadan, Nigeria. Samples of cerebral cortex tissues were processed for paraffin embedding and sectioning. The paraffin blocks were mounted, trimmed and sectioned at 5 microns thickness, mounted on adhesive slides and thereafter stained with Haematoxylin and Eosin.

Histomorphometry

Areas with injured cells were selected at low magnification power with light microscope, from these, five high power fields were selected and the number of red neurons was counted using an Olympus Japan CX 41 microscope with a DP 21 camera attachment by a pathologist blank to the treatment groupings.

Statistical analysis

Data were presented as mean ± S.D and then analyzed using one-way ANOVA with Graphpad Prism (Version 5.04; GraphPad Software, La Jolla, California, USA). Confidence interval was calculated at 95% and level of significance fixed at 5%.

Results

General observations

Rats in NTC, NTP and NTE groups remained active throughout the experimental period whereas all the traumatized animals were physically inactive immediately post-trauma but returned to normal activities forty-eight hours post-injury.

Forelimb grip test

As depicted in tables 1 and 2, the duration of forelimb grip in the BTC group was significantly ($p<0.05$) elevated compared with the control group whereas it was significantly lowered in BTP when compared with the BTC group. Although STC did not elicit such response compared with the NTC group, STE was significantly ($p<0.05$) elevated relative to ST.

Negative geotaxis

As shown in tables 1 and 2, negative geotaxis was significantly ($p<0.05$) increased in the BTE group relative to BTC group. In the sharp trauma groups, there were no significant differences between the groups.

Line crossing

Tables 1 and 2 show that while there was significant ($p<0.05$) reduction in rearing in the BTC group relative to NTC group, significant elevations occurred in the BTP and BTE groups relative to BTC. In contrast, there were significant ($p<0.05$) reductions in STP and STE values compared with STC.

Grooming

Both blunt and sharp trauma elicited significant ($p<0.05$) reduction in number of grooming as shown in tables 1 and 2 when compared with NTC group. There were level of significance elevations in values obtained for BTP, BTE and STE groups when compared with the BTC and STC groups.

Biochemical parameters

Table 1: Effect of blunt brain trauma on behavioural parameters of male Wistar rats.

Groups	Fore limb grip(s)	Negative geotaxis(s)	No.of grooms	No. of squares crossed	No. of rearing
NTC	5.50±0.58	1.80±0.45	108.67±15.58	37.00±2.45	11±1.73
NTP	2.60±0.89	2.20±0.84	67.67±11.50*	35.30±11.67	8.50±2.12
NTE	5.35±0.35	1.76±0.42	98.00±12.0	36.00±2.25	10.5±0.43
BTC	11.25±2.06*	1.75±0.5	30.00±5.00*	53.67±9.50*	6.00±0.82*
BTP	3.33±0.58**	2.00±0.00	55.33±11.02**	36.33±15.37	10.67±0.58**
BTE	4.80±0.84**	3.75±1.50**	57.00±27.87**	21.67±3.22**	9.33±2.52**

*Values are expressed as mean ± SD of five animals. Non-traumatized control (NTC); Non-traumatized and P-treated (NTP); Non-traumatized and E-treated (NTE); Blunt-traumatized control (BTC); Blunt-traumatized and P-treated (BTP); Blunt-traumatized and E-treated (BTE); Progesterone (P); Vitamin E (E). *p< 0.05 versus NTC group; **p< 0.05 versus BTC group.*

As depicted in tables 1 and 2, the number of squares crossed increased significantly ($p<0.05$) in the BTC and STC groups compared with the NTC for both blunt and sharp trauma. The values were reduced significantly ($p<0.05$) in the BTP, BTE, STP and STE groups when compared with BTC and STC groups.

Rearing

Effect of treatment on Malondialdehyde (MDA), Superoxide dismutase (SOD), Catalase (CAT) and Glutathione Peroxidase (GPx).

As shown in table 3 and 4, both BTC and STC elicited non-significant ($p>0.05$) rise in MDA levels, and the activities of SOD, CAT and GPX relative to

Table 2: Effect of sharp brain trauma on behavioural parameters of male Wistar rats.

Groups	Fore limb grip(s)	Negative geotaxis(s)	No. of grooms	No. of squares crossed	No. of rearing
NTC	5.50±0.58	1.80±0.45	108.67±0.58	37.00±2.45	11±1.73
NTP	2.60±0.89	2.20±0.84	67.67±9.50*	35.30±11.67	8.50±2.12
NTE	5.35±0.35	1.76±0.42	98.00±12.0	36.00±2.25	10.5±0.43
STC	5.00±0.82	2.00±0.82	42.67±6.43*	70.67±3.22a*	10.00±1.00
STP	2.20±0.84	1.75±0.50	36.75±6.45*	31.67±5.03*	6.33±2.52*
STE	18.67±4.73**	2.33±0.58	71.00±4.36**	42.00±7.21*	2.25±7.21*

*Values are expressed as mean ± SD of five animals. Non-traumatized control (NTC); Non-traumatized and P-treated (NTP); Non-traumatized and E-treated (NTE); Sharp-traumatized control (STC); Sharp-traumatized and P-treated (STP); Sharp-traumatized and E-treated (STE). Progesterone (P); Vitamin E (E). *p< 0.05 versus NTC group; **p< 0.05 versus STC group.*

Table 3: Effect of blunt brain trauma, progesterone and vitamin E on antioxidant parameters in male rats.

Groups	MDA(µmol/mg)	SOD(µ/mg)	CAT(µmol/mg)	GSH(µg/ml/mg)	GPX(µ/mg)
NTC	6.62±0.85	0.96±0.14	0.01±0.00	1.73±0.03	6.70±0.31
NTP	6.95±0.22	0.83±0.04	0.02±0.01	1.53±0.23	6.76±0.31
NTE	6.31±0.62	0.92±0.08	0.01±0.00	1.50±0.05	6.63±0.30
BTC	7.56±0.22	1.07±0.09	0.02±0.02*	0.81±0.13*	7.13±0.32
BTP	6.75±0.46	0.91±0.08	0.02±0.00	1.12±0.47	6.87±0.41
BTE	7.09±0.37	1.02±0.09	0.02±0.00	1.00±0.31	6.86±0.54

*Values are expressed as mean ± SD of five animals. Non-traumatized control (NTC); Non-traumatized and P-treated (NTP); Non-traumatized and E-treated (NTE); Blunt-traumatized control (BTC); Blunt-traumatized and P-treated (BTP); Blunt-traumatized and E-treated (BTE); Progesterone (P); Vitamin E (E). *p< 0.05 versus NTC group; **p< 0.05 versus BTC group.*

Table 4: Effect of sharp brain trauma, progesterone and vitamin E on antioxidant parameters in male rats.

Groups	MDA (µmol/mg)	SOD(µ/mg)	CAT (µmol/mg)	GSH (µg/ml/mg)	GPX(µ/mg)
NTC	6.62±0.85	0.96±0.14	0.01±0.00	1.73±0.03	6.70±0.31
NTP	6.95±0.22	0.83±0.04	0.02±0.01	1.53±0.23	6.76±0.31
NTE	6.31±0.62	0.92±0.08	0.01±0.00	1.50±0.05	6.63±0.30
STC	7.80±0.62	1.04±0.12	0.02±0.01*	0.91±0.34*	7.18±0.99
STP	6.72±0.42	0.76±0.11**	0.01±0.00	1.22±0.44	7.00±0.25
STE	6.99±0.61	0.79±0.05	0.01±0.01	1.12±0.32	6.97±0.51

*Values are expressed as mean ± SD of five animals. Non-traumatized control (NTC); Non-traumatized and P-treated (NTP); Non-traumatized and E-treated (NTE); Sharp-traumatized control (STC); Sharp-traumatized and P-treated (STP); Sharp-traumatized and E-treated (STE). Progesterone (P); Vitamin E (E). *p< 0.05 versus NTC group; **p< 0.05 versus STC group.*

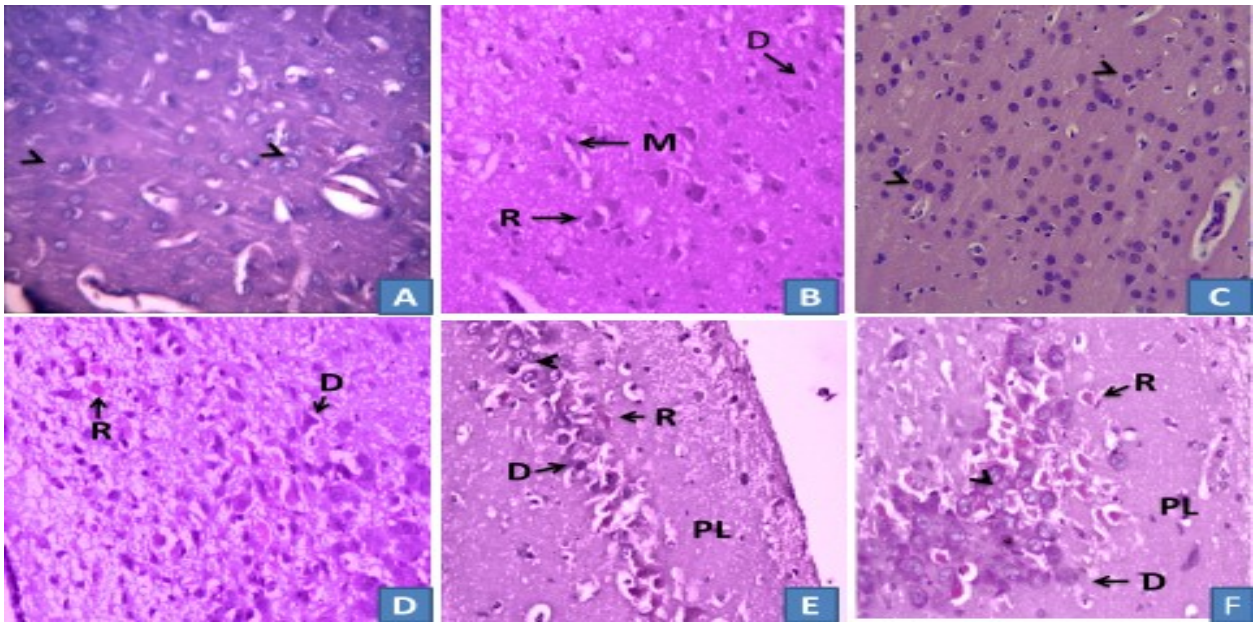

***Fig. 2**: Photomicrographs of the cerebral cortex of (A) non-traumatized control (NTC), (B) non-traumatized progesterone-treated (NTP), (C) non-traumatized vitamin E-treated (NTE), (D) blunt-traumatized control (BTC), (E) blunt-traumatized progesterone-treated (BTP) and (F) blunt-traumatized vitamin E-treated (BTE) groups of rats. Observe viable neurons (arrowheads) in groups A and C, and the red (R) and dark (D) degenerating neurons in groups B, D, E and F; M, Microglial cell; PL, Plexiform layer. Stain: H&E. Magnification: ×400.*

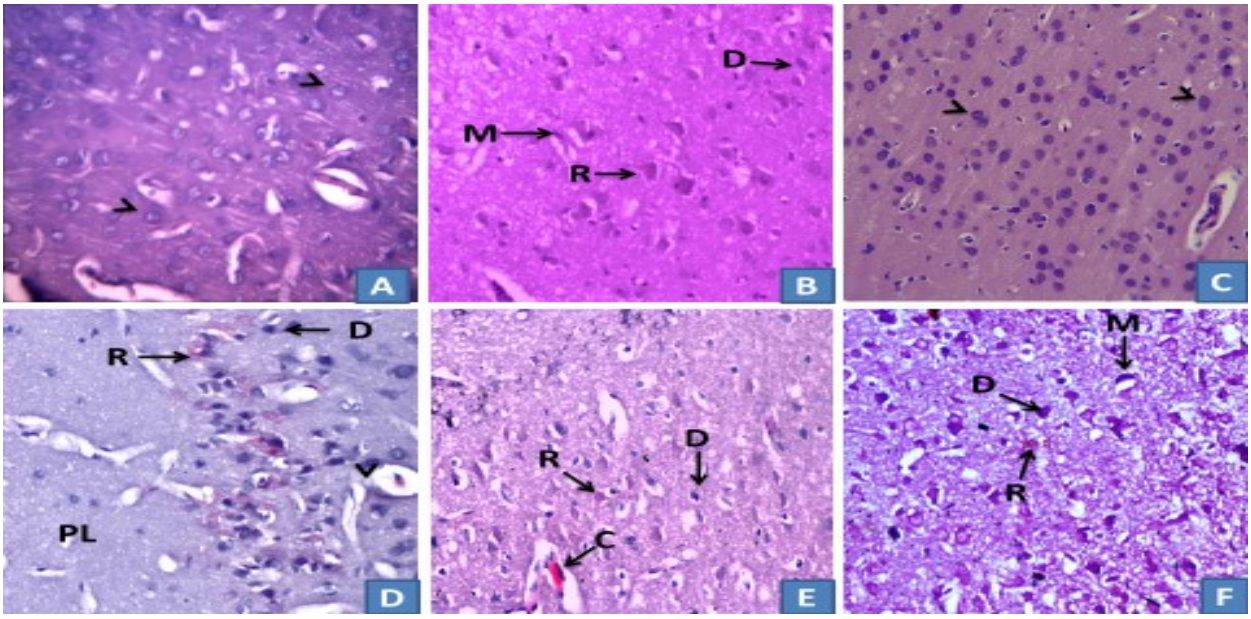

Fig. 3: *Photomicrographs of the cerebral cortex of (A) non-traumatized control (NTC), (B) non-traumatized progesterone-treated (NTP), (C) non-traumatized vitamin E-treated (NTE), (D) sharp-traumatized control (STC), (E) sharp-traumatized progesterone-treated (STP) and (F) sharp-traumatized vitamin E-treated (STE) groups of rats. Arrowheads, normal neuron; Dark (G) and red (R) degenerating neurons; M, Microglial cell; P, Plexiform layer; C, Capillary. Stain: H&E. Magnification: ×400*

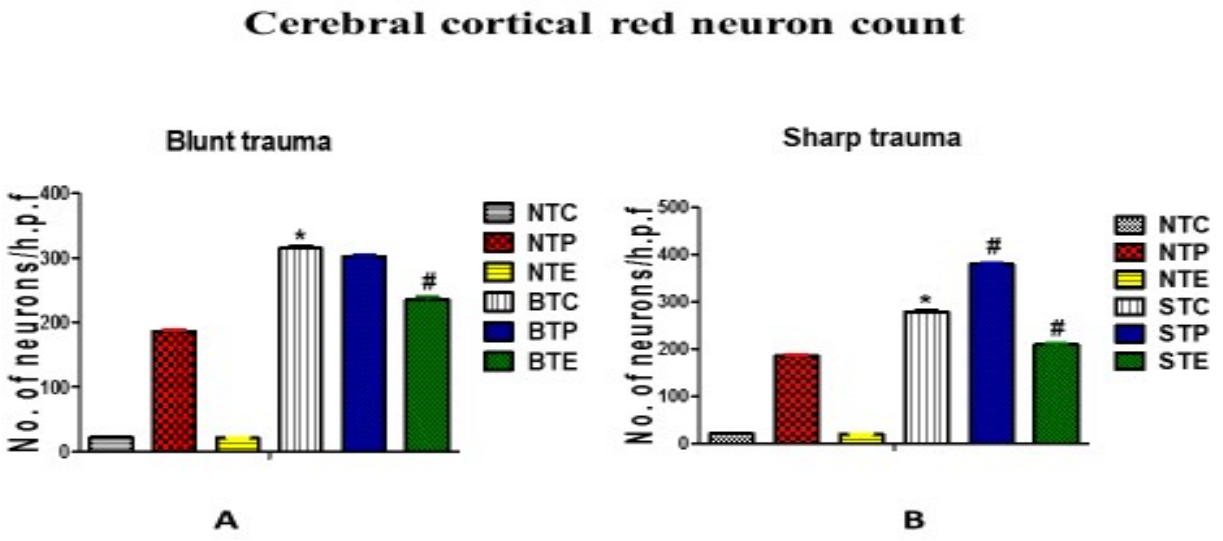

Fig. 4*: Mean±SD counts of red neurons per high power field (h.p.f.) of the cerebral cortex in the traumatized brain of the Wistar rat. Values are expressed as mean ± SD of five animals. Non-traumatized control (NTC); Non-traumatized and P-treated (NTP); Non-traumatized and E-treated (NTE); Blunt-traumatized control (BTC); Blunt-traumatized and P-treated (BTP); Blunt-traumatized and E-treated (BTE); Sharp-traumatized control (STC); Sharp-traumatized and P-treated (STP) and Sharp-traumatized and E-treated (STE) groups. Progesterone (P); Vitamin E (E). *p< 0.05 versus NTC group; #p< 0.05 versus BTC (A) and STC (B) groups.*

NTC. These values were reduced in the BTP, BTE, STP and STE groups when compared with BTC and STC trauma groups.

Effect of treatment on Glutathione (GSH)

Tables 3 and 4 show that both BT and ST elicited significant ($p<0.05$) reductions in GSH level compared with control, whereas these concentrations

were elevated in the BTP, BTE, STP and STE groups in a non-significant (p.0.05) manner when compared with trauma groups (BTC and STC) only.

Histological observations

Photomicrographs

Figures 2 and 3 show presence of viable neurons and absence of red and dark neurons in the cerebral cortical layers in the NTC and NTE groups. Red and dark neurons (evidence of degeneration) are observed in the NTP, BTC, STC, BTP, BTE, STP and STE groups. The external granular layer and external pyramidal layer of the cortex in the STP groups were severely affected as indicated by the presence of red neurons, whereas the deep layers of cortex were spared leaving only focal presence of red neurons.

Histomorphometry

Blunt and sharp trauma degenerated neuron cell counts

The degenerating cortical neurons in form of dark and red neurons were counted and presented in figures 4A and 4B. Neurons in the NTP, BTC, STC, BTP, BTE, STP and STE groups had increased number of these neurons per high power field.

Discussion

The elevation of MDA and reduction of GSH concentration in both blunt and sharp trauma groups in this experiment demonstrated oxidative stress which is implicated in accentuating other elements of secondary injury cascades in TBI [38]. However, the up-regulation of the activities of anti-oxidant enzymes like SOD, CAT and GPx in both blunt and sharp trauma is an evidence of adaptive response to mitigate the oxidative damage and thus protect the cerebral cortical neurons from further insult by the generated free radicals secondary to the inflicted trauma [39]. As reported by Macho *et al*. [40], reduced GSH and oxidative damage may lead to disruption of the mitochondrial transmembrane potential thus constituting early possible signalling events in apoptotic cell death. The elevation of GSH levels by progesterone in both BTP and STP trauma suggested a protective role for the cerebral neurons, while progesterone's ability in reducing the activity of SOD in the BTP and STP was consistent with the reports of Moorthy *et al.* [39].

In the open field test, the progeserone-treated rats exhibited signs of anxiety as shown by the reduction in the number of squares crossed, rearing and grooming, all of which may be attributed to the effect of the steroid despite the fact that the brain injury was not induced on the frontal lobe of the rats but 2.5mm posterior and 2.5 lateral to the bregma [41]. The significant increase in grip strength in the BT group suggests an increase in motor coordination and muscle tone in the blunt injury group [42]. Both BTP and BTE treatments elicited an increase in grooming and rearing suggesting an increase in anxiety status of the rats relative to the blunt trauma.

Although the NTC and NTE rats demonstrated normal cerebral cortical neurons, all other groups exhibited the presence of degenerated neurons in form of either red neurons (indicative of traumatized neurons in the state of degeneration), and dark neurons (deeply stained or pyknotic injured neurons which are already dead). In particular, progesterone induced neuronal death in all layers of the cortex of the rat's brain predominantly at external granular and external pyramidal layers and ganglionic layers of the cortex which is contrary to the work of Jing and Guo-min [7] who reported that progesterone possesses pleiotropic effects that may markedly attenuate the injury cascade associated with TBI. In the BT group, haemorrhage was present in the subarachnoid space, suggestive of the impact of the trauma to the head of the rat, this is consistent with reports [43, 44] who reported that (micro) haemorrhages may be present around contusions after TBI. In the ST group, there was the presence of widely spread red neurons observed in the cortex in agreement with the previous report of Andrew *et al.* [43]. The BTP group showed that the upper layers of the cortex had large numbers of red neurons which were focally distributed in addition to neuropil vacoulation in agreement with the report of Jing and Guo-min [7] that progesterone possesses pleiotropic effects which might attenuate the injury cascade associated with TBI. The observed contusion injury with subarachnoid haemorrhage in the STE group was consistent with the report of Andrew *et al.* [43]. Also, most areas of the cortex in the STE group were spared (absence of red neurons) consistent with earlier reports [45] stating that vitamin E supplementation may protect the brain-derived neurotrophic factor (BDNF) system from the deleterious effects of oxidative stress after TBI [45]. It might be that our higher dosage of 16 mg/kg dose for progesterone in this experiment accounted for differences in our findings compared with those workers who used 8 mg/kg dosage.

Histomorphometric study showed an increase in the red neuron count of BT group which was reduced in the BTP and BTE thus suggesting an ameliorative effect of progesterone and vitamin E in agreement with reports that steroids like

progesterone and vitamin E can exert protective effects on neurons after brain injury [20, 15, 45]. Similarly, STE also provided a reduction in the count of the red neurons thus supporting the report of Vaynman *et al*. [46] that vitamin E protects from the deleterious effects of oxidative stress after TBI. In contrast, STP did not show protection for sharp brain injury for reasons that are not clear.

Conclusion

This research demonstrated that both progesterone (at 16 mg/kg body weight) and TBI elicited injury of the cerebral cortical neurons as shown histologically with evidence of biochemical alteration in the markers of oxidative damage and oxidative enzymes. The partial neuro-protective effect of progesterone as shown in this study relates to the focal distribution of red neurons and sparing of the deep layers of the cerebral cortex. Vitamin E demonstrated better neuro-protective effect with focal presence of red neurons and a larger area of the cortex spared from the degenerative impact of the trauma to the cerebral cortex. In conclusion, administration of progesterone (16 mg/kg body weight) was not a viable neuro-protective agent in sharp brain injury, whereas vitamin E demonstrated better neuro-protective ability relative to progesterone.

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A three-year serial cross-sectional study of the prevalence of proteinuria and glycosuria in Oyo State using simple urinalysis

OI Omotosho and G Onoriede
Department of Chemical Pathology, College of Medicine, University of Ibadan, Nigeria

Abstract

Background: Urinalysis is one of the basic investigations used to detect presence of biochemical changes in urine. Amongst the commonest indicators in urinalysis are proteinuria and glycosuria which may be early biochemical markers for kidney disease and carbohydrate metabolic dysfunction. This 3-year cross-sectional study was conducted to find out the prevalence of proteinuria and glycosuria among apparently healthy volunteers in Oyo State

*Method***:** Fresh mid-stream urine samples were collected randomly over a period of 3 years (2013-2015) from 2779 apparently healthy adult volunteers (1555 males and 1224 females) aged 20 to 60 years from the thirty-three local councils in Oyo State. The samples were screened using dipstick method for the presence of glucose and protein.

*Results***:** In 2013, 1,238 subjects (731 males and 507 females) were screened and 4.9% (60 participants), 7.5% (93 participants), and 0.3% (4 participants) had proteinuria, glycosuria and 35combined PG respectively. In 2014, 718 subjects (398 males and 320 females) were recruited; 4.5% (32 participants) had proteinuria, 5.3% (38 participants) had glycosuria while 0.8% (6 participants) had combined proteinuria and glycosuria. In 2015, 823 subjects (426 males and 397 females) participated in the study. Proteinuria was observed in 4.5% (37 participants), glycosuria was found in 3.5% (29 participants) and the prevalence of combined proteinuria and glycosuria (PG) was 0.6% (5 participants). Although this 3year consecutive survey showed that glycosuria was more prevalent than proteinuria or their combined PG (G=5.8%, P=4.6%, PG=0.5%), the difference was not significant ($p>0.05$). Proteinuria was higher in females (4.8%) than in males (4.5%), glycosuria was more prevalent in males (6.2%) than in females (5.2%) while PG was almost similar (0.6% and 0.5%) in females and males respectively; the differences were not significant ($p>0.05$)

Conclusion: The **p**revalence of combined proteinuria and glycosuria was lower than either glycosuria or proteinuria existing singly over the 3-year period. This work affirms the usefulness of simple urinalysis as a screening method for glycosuria and proteinuria and by inference possible application of this simple method as a screening tool for the prevalence of diseases.

Keywords: *Prevalence, Urinalysis, Proteinuria, Glycosuria, Oyo state*

Résumé

*Contexte :*L'analyse d'urine est l'une des études de base utilisées pour détecter la présence de modifications biochimiques de l'urine. Parmi les indicateurs les plus courants en analyse d'urine sont la protéinurie et la glycosurie, qui peuvent être des marqueurs biochimiques précoces de l'insuffisance rénale et un dysfonctionnement métabolique des glucides. Cette étude transversale de trois ans a été menée pour déterminer la prévalence de protéinurie et de glycosurie chez des volontaires apparemment en bonne santé dans l'État d'Oyo.

Méthode **:** Des échantillons frais d'urine mi courant ont été aléatoirementprélevés sur une période de 3 ans (2013-2015) auprès de 2779 volontaires adultes apparemment en bonne santé (1555 hommes et 1244 femmes) âgés de 20 à 60 ans dans les trente-trois mairies de l'État d'Oyo. Les échantillons ont été criblés en utilisant la méthode 'dipstick' pour la présence de glucose et de protéine.

Résultats **:** En 2013, 1238 sujets (731 hommes et 507 femmes) ont été dépistés et 4,9% (60 participants), 7,5% (93 participants) et 0,3% (4 participants) avaient respectivement la protéinurie, la glycosurie et 35PG combinés. En 2014, 718 sujets (398 hommes et 320 femmes) ont été recrutés ; 4,5% (32 participants) avaient la protéinurie, 5,3% (38 participants) la glycosurie tandis que 0,8% (6 participants) une combinaison de protéinurie et de glycosurie. En 2015, 823 sujets (426 hommes et 397 femmes) ont participé à l'étude. Une protéinurie a été observée chez 4,5% (37 participants), une glycosurie chez 3,5% (29 participants) et la prévalence combinée de la protéinurie et de la glycosurie (PG) était de 0,6% (5 participants). Bien que cette enquête consécutive de trois ans ait montré que la glycosurie était plus prévalant que la protéinurie ou leur PG combinée (G = 5,8%, P = 4,6%, PG = 0,5%), la différence n'était pas

Correspondence: Dr. I.O. Omotosho, Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: iomotosho2014@gmail.com.

significative (p> 0,05). La protéinurie était plus élevée chez les femmes (4,8%) que chez les hommes (4,5%), la glycosurie était plus prévalant chez les hommes (6,2%) que chez les femmes (5,2%) tandis que la PG combinée était presque similaire (0,6% et 0,5%) chez les femmes et les hommes respectivement ; les différences n'étaient pas significatives (p> 0,05) *Conclusion:* La prévalence de protéinurie et de glycosurie combinée était plus faible que soit la glycosurie ou la protéinurie existants séparément sur la période de 3 ans. Ce travail affirme l'utilité de l'analyse simple d'urine comme une méthode de dépistage de la glycosurie et de la protéinurie et, par déduction, l'application possible de cette méthode simple comme outil de dépistage de la prévalence des maladies.

Mots-clés: *Prévalence, Analyse d'urine, Protéinurie, Glycosurie, État d'Oyo*

Introduction

Urinalysis is an array of tests performed on urine, it is one of the most common basic methods of medical diagnosis [1]. It is the physical, chemical, and microscopic examination of urine. Since urine formation is one of the major functions of the kidney, urinalysis is often used to detect covert kidney dysfunction which may manifest as proteinuria and glycosuria. Incidences of glycosuria and proteinuria are commonly used to prognose urinary tract or kidney infection, evaluate causes of kidney failure and screen for progression of some chronic conditions such as diabetes mellitus, glomerulonephritis and chronic urinary tract infections [2].

Glycosuria presents when glucose is excreted into the urine. Nearly all glucose filtered by the glomeruli is reabsorbed in the proximal tubules and only undetectable amounts appear in urine in healthy individuals. Glycosuria occurs when the filtered load of glucose exceeds the ability of the renal tubule to reabsorb it (i.e. plasma level is above the clinical threshold value of 180 to 200 mg per dl) [3]. Rarely, glycosuria may be due to an intrinsic problem with glucose reabsorption within the kidneys themselves, a condition termed renal glycosuria [4]. However, in those with renal glycosuria, glucose is abnormally eliminated in the urine due to improper functioning of the renal tubules. . To detect glycosuria, most tests rely upon reaction of glucose with glucose oxidase on dipstick to form hydrogen peroxide. The reductive reaction of this leads to liberation of oxygen which causes colour change.

Proteinuria is defined as urinary protein excretion of more than 150 mg per day (10 to 20 mg per dl) and is the hallmark of renal disease. Normally, no protein passes into the urine when the blood is filtered, because protein in the blood is too large to pass through the tiny holes in the kidney filters (glomerulus). However, the filter can be damaged in kidney diseases (glomerulonephritis), so that protein can pass into the urine resulting in nephrotic syndrome. Normal urinary proteins include serum globulins, albumin, and proteins secreted by the nephron. Detectable proteinuria may be first sign of renovascular, glomerular or tubulo-interstitial renal disease. Healthy adults normally excrete 80-50mg protein in urine daily. Alternatively, it may be caused by overflow of abnormal proteins in diseases such as multiple myeloma. Persistent significant proteinuria detected by dipstick requires further assessments such as with 24-hour urinary protein excretion, urinary protein/creatinine ratio, and microscopic examination of the urinary sediment, urinary protein electrophoresis, and assessment of renal function [5]. Proteinuria may result from a number of diseases like urinary tract infections, glomerulonephritis, nephritic syndrome, eclampsia, urinary schistosomiasis, hypertension and severe febrile illness [6].

Proteinuria is also an important predictor of progressive kidney damage and a potent independent cardiovascular risk marker and predictor [7,8]. Proteinuria can be detected by a variety of methods [9] including reagent-strip tests (e.g. Albustix®), which can be used in a point-of-care testing environment, and chemical tests available in the laboratory. Urinalysis for proteinuria is recommended as part of the initial assessment of patients with hypertension [10-12]. Proteinuria is a well-known marker of renal disease, and reduction of proteinuria is often associated with disease remission [13, 14]. Reports have indicated the possibility of a direct damage caused by the high protein levels present in the tubular fluid of patients with glomerular diseases. This situation imposes a high work load on tubular cells for the reabsorption of protein, with the consequent production of excess reactive oxygen species that further impair normal cell function such as glucose reabsorption [15-17] .

This argument is based on the finding of a higher protein excretion rate in patients with glycosuria [18]. However, the pathophysiology of tubular lesion proteinuria which often causes interstitial inflammation and fibrosis is still not clear [19, 20] On the other hand, several authors have suggested that increased ammoniagenesis by tubular cells subjected to heavy proteinuria may be noxious

to the interstitium [21]. Thus, the ammonia generated is thought to activate the third component of complement which then leads to the activation of the complement cascade [21].

Previous research found proteinuria to be a more potent predictor of End Stage Renal Disease (ESRD) than was haematuria in both men and women [22].

Unfortunately, most adults do not go for routine urinalysis to ascertain the functional status of their kidneys. This may result in late presentation of kidney disorders thus most cases of kidney diseases may not be diagnosed until the chronic stage when dialysis therapy becomes inevitable. Therefore, screening for proteinuria and glycosuria could help to identify individuals who are at high risk for cardiovascular and renal diseases

Methods

Oyo state is one of the 36 states of Nigeria. It is one of the three States Oyo, Ogun and Ondo carved out of the former Western State of Nigeria on 3rd February, 1976 by the Generals Murtala Mohammed/ Obasanjo led Military Government. Geographically, it covers approximately an area of 28,454 square kilometers and is ranked 14th by size spanning 3 geopolitical zones of Ibadan/Ibarapa, Oyo/Oke-Ogun and Ogbomoso all constituting 33 local councils of the state [23]. This study was a cross sectional study carried out on randomly selected adults from the 33 local councils of Oyo State from 2013 to 2015. A total of 2779 participants which included 1555 males and 1224 females were recruited for the study after ethical approval from Oyo State Ministry of Health Ethical Committee.

Pregnant women, participants on antihypertensive and/or hypoglycaemic drugs, steroids were excluded from the study. The age range of participants was 20- 60 years.

Informed consent of all participants was obtained after adequate counselling before enrolment into the study. The study was carried out as a field work whereby samples were collected from the headquarters of each of the 3 geopolitical divisions of the state (stated above) after sensitization through their council offices.

Fresh mid-stream urine specimen was collected randomly into a clean and dry universal urine bottle from consented participants. The urinalysis reagent strip (DIALAB® by Wiener Neudorf, Austria) [24] and urine specimen were allowed to reach room temperature (15-30^{o}C) prior to testing. The pH, presence of glucose and protein in the urine samples were determined using the urinalysis reagent strip above immediately after collection at the venue using improvised laboratory setting.

Briefly, the urine specimens were well-mixed, the reagent areas of the strip were completely immersed into the urine and immediately removed to avoid dissolving the reagents. The reagent areas were compared to the corresponding colour charts for p^{H}, glucose and protein on the canister label at mid-day to determine proteinuria and glycosuria as stated in the reagent strip bronchure [24].

The result of the colour comparison were scored on the grades of negative, trace, +1 to +4 corresponding to approximately 0, 15-30, 30mg,100mg, 300mg and 1000mg protein per 100ml for proteinuria and a similar scale for glycosuria according to Sheets and Lyman [25]. Basic standard laboratory procedures appropriate for field work like ensuring temperature equalization, contaminant free containers and others enjoined in the test strip protocol were ensured.

All data were presented statistically using tables and bar charts for comparative analysis. Data were analyzed using the Statistical Package for Social Sciences (SPSS) software computer program version 15.0 (SPSS, Chicago, IL). Chi square was used in comparing the values. Significant differences in prevalence was reported at $p \geq 0.05$

Results

Table 1 shows the overall data for the three years. Glycosuria was more prevalent (7.5%) than proteinuria (4.9%) while the incidence of proteinuria and glycosuria combined was 0.3% . The prevalence

Table 1: Prevalence of proteinuria and glycosuria among apparently healthy adults in Oyo State (2013 – 2015)

Year	Number	Proteinuria (%)	Glycosuria (%)	Proteinuria-Glycosuria (%)
2013	1238	60 (4.9)	93 (7.5)	4 (0.3)
2014	718	32 (4.5)	38 (5.3)	6 (0.8)
2015	823	37 (4.5)	29 (3.5)	5 (0.6)
Total	2779	129 (4.6)	160 (5.8)	15 (0.5)

of glycosuria in males (6.2%) was higher than that of females (4.5%) while prevalence of proteinuria in females (5.2%) was more than in males (4.8%). However, the difference in prevalence was not significant [p =>0.05].

The result obtained in 2013 shows that the prevalence of glycosuria (7.5%) was higher than that of proteinuria (4.9%). Also, the prevalence of glycosuria in males (8.3%) was higher than in females (6.3%) in this year; while proteinuria was higher in females (5.7%) than in males (4.2%). However, the combined prevalence (proteinuria and glycosuria) (PG) was 0.3% (Table 1).

The sex distribution of proteinuria and glycosuria among the volunteers was assessed and presented in figures 1 – 4. There was no statistically significant difference between male and female except in 2015 when more female (5.0%; 20/397) had glycosuria than male (2.1%; 9/426) participants (p = 0.023] (Figure 4).

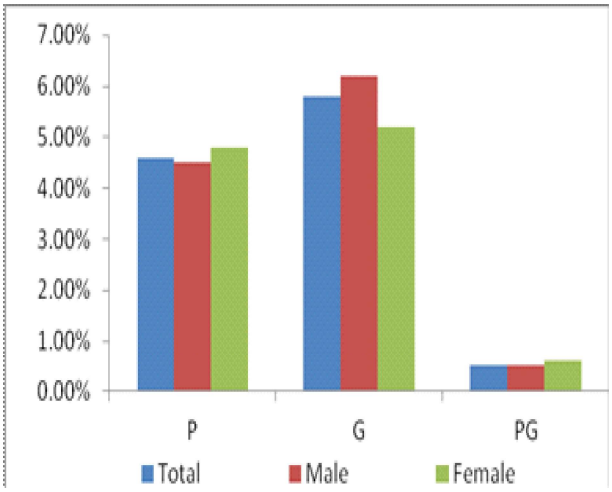

Fig.1: Shows the overall (2013-2015) prevalence of proteinuria (P), glycosuria (G), proteinuria and glycosuria (PG)

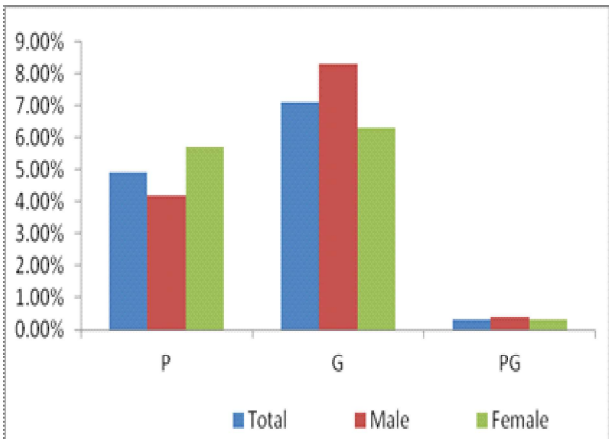

Fig.2: Shows the prevalence of proteinuria (P), glycosuria (G), proteinuria and glycosuria (PG) in 2013

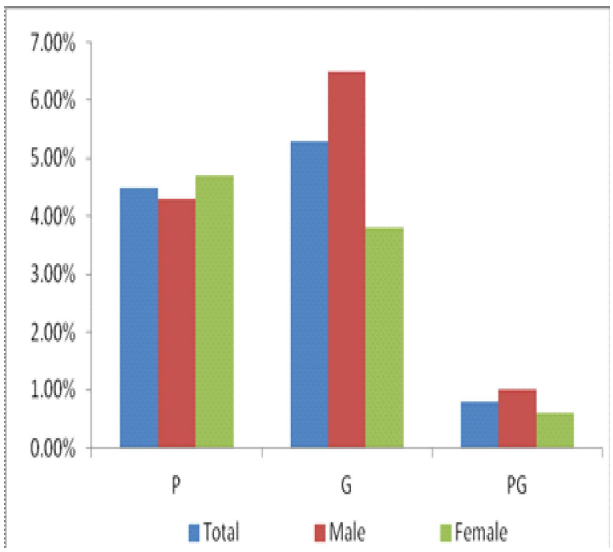

Fig.3: Shows the prevalence of proteinuria (P), glycosuria (G), proteinuria and glycosuria (PG) in 2014

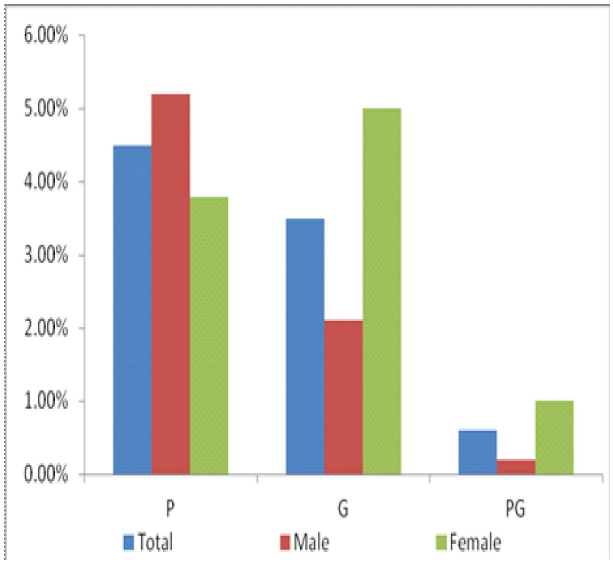

Fig.4: Shows the prevalence of proteinuria (P), glycosuria (G), proteinuria and glycosuria (PG) in 2015

Discussion

Urine analysis is a group of manual and/or automated qualitative and semi-quantitative tests performed on a urine sample [26]. Urine testing has been a part of medicine for many centuries. Hippocrates wrote about urine examination as early as 400 BC [27]. The dipstick analysis is cost-effective and the most common form of urine analysis method. Several epidemiological studies have applied basic urine biochemistry as tools for generating data that have helped in shaping public health policies [28, 29]. Glycosuria and proteinuria are some of the conditions that urinalysis has demonstrated significant benefits. Proteinuria is usually prognostic of renal diseases while glycosuria often indicates abnormality in carbohydrate metabolism.

Early detection and treatment of urine abnormalities (glycosuria, proteinuria, e.t.c.) often prevent serious diseases from getting worse [26].

Variation in the prevalence figures for glycosuria observed in this study for each year may be due to study population though on the average over 5% of the population had covert glycosuria. The glycosuria observed in this study may be due to high plasma glucose, resulting in a glucose load in the filtrate that exceeds the proximal tubule's ability to reabsorb glucose or reflect a defect in the proximal tubular cells' ability to reabsorb normal filtered glucose load. However, plasma glucose level was not determined to ascertain this since it was essentially meant as a field study and estimation of plasma glucose level was not part of the design.

The prevalence rate of >5% for glycosuria observed in Oyo state reported in this study is similar to previous studies; Venkatachalam *et al.,* [2] also observed a prevalence of 8.3% for glycosuria using dipstick as a screening test whereas in a survey published in Britain, it was stated that out of 5,562 people covered by the house-to-house survey 148 (2.7%) were found to have glycosuria [30, 31]. The high prevalence obtained in this study may be due to the randomness of participants selection since other diseases like diabetes and hypertension which were not excluded from the selection criteria might have added to the prevalence. Also, the low level of public health education and awareness in this environment might have also aided the higher prevalence by the general lack of adequate medical attention and late presentation of cases in hospitals among the citizens.

Although the average age of subjects in this study was not recorded, the average age of participants in this study (from the questionnaire >40years) suggested that glycosuria observed in this study may be an index of tubular dysfunction which may be an indicator of glomerular diseases in these participants since glycosuria in the elderly is an indication of late on-set of glucose metabolic dysfunction [32].

The observed proteinuria in this study may be a sign of glomerular or tubulo-interstitial renal disease which may be secondary to urinary tract infections, glomerulonephritis, urinary schistosomiasis and hypertension. Although persistent significant proteinuria detected by dipstick requires further assessment with 24-hour urinary protein excretion, this can be further clarified by urinary protein/creatinine ratio, microscopic examination of the urinary sediment and urinary protein electrophoresis for proper assessment of renal function [5]. In a similar study in Nigeria [33], they reported proteinuria in 4.7% adolescents during a routine urinalysis of asymptomatic adolescents. However in a study of urinalysis in primary health care centres in Saudi Arabia, proteinuria was present in 11.7% of the patients and glycosuria in 4.7% patients [34]. In addition to this, a study by Venkatachalam *et al.,* [2] observed prevalence of proteinuria to be 12.3%, using albumin specific dipstick as a screening test with mean age of 50.28 ± 15 years. In another study, 11.7% of the individuals screened were found positive for protein using dipstick test with a mean age of 50.94 ± 11.2 yr [35] while a prevalence as high as 30% was reported by Gujarat using presence of microalbuminuria as the index [36]. In another relevant case, Ashok *et al.,* studied different urine abnormalities in 1000 participants and observed proteinuria in 2.6% (26 participants) and glycosuria in 2% (20 participants) in the age range from 20 to 55 years [26].

The higher prevalence of proteinuria observed in females (4.8%) than in males (4.5%) despite the higher population of males (1555) to females (1224) in this study in 2013 and 2014 may be due to female being more predisposed to urinary tract infection than male as a result of the anatomical structure of the female genitalia.

The observation that glycosuria and proteinuria co-existed in a relatively similar proportion of participants in this study over the period may be an indication of the overall health status of participants indicating similar health education awareness and the possibility of other health challenges among the population. This may also underscore the prognostic value of urinalysis especially as screening tool to establish covert chronic diseases among the populace.

Limitations: It is pertinent to mention some of the limitations of this method and urinalysis in particular as screening tool for detecting covert diseases. The principle of methods adapted to be used on urinary reagent strips is based on "dry chemistry" techniques most of which are dependent on temperature, humidity and other physical characteristics. Ensuring these conditions using urinalysis especially directly on the field using improvised laboratory setting may bring variations in results. Also, since spot urine samples were randomly collected, interferences from other variables including diet, degree of hydration of the body and other factors might introduce interferences that might have affected the results. Aside from

above, different cohorts studied each year will make longitudinal inference or calculation of incidence difficult.

Conclusion

Application of simple urinalysis has revealed a rather significant prevalence rate of proteinuria and glycosuria in the 33 local council of Oyo state. The simplicity and cost effectiveness of this method in prevalence studies may be further explored in screening for other non-communicable diseases. The need to use this and similar health analysis data in health planning for the citizen of the state is also imperative. Although the results may not be confirmatory without further tests, it helps in early detection of diseases that could lead to death. Early treatment and follow up would reduce all complications related to glycosuria and proteinuria and reduce mortality rate.

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Histological alteration and oxidative variables in Wistar rats with induced-sepsis: the protective effect of tomato pomace powder

O Owoeye and AA Gbadamosi
Department of Anatomy, College of Medicine,
University of Ibadan, Ibadan, Nigeria

Abstract
Background: Sepsis is a systemic inflammatory response to infection causing morbidity and mortality and has oxidative damage as one of the mechanisms. We induced sepsis in rats by caecal ligation and perforation (CLP) and then investigated the possible protective effect of tomato pomace powder (TPP) on the sepsis-induced neuropathy using vitamin E (VIT E) as a standard antioxidant.
Methods: Thirty-nine male Wistar rats were randomized into six groups: Control (Cont) (N=5) received food and water; TPP (N=5) received TPP (50 mg/kg); VIT E (N=5) received VIT E (500 mg/kg); CLP (N=8) had CLP; TPP+CLP (N=8) received TPP (50 mg/kg) plus CLP; VIT E+CLP (N=8) received VIT E (500 mg/kg) plus CLP. The CLP was done on first day while all other administration lasted 21days after which, neurobehavioural tests were done, animals sacrificed and tissues processed for haematological, biochemical and histological tests.
Results: The CLP group had significant ($p<0.05$) increase in lipid peroxidation (LPO) level, a reduction of the glutathione (GSH) level and an increase in the activity of catalase enzyme activity when compared with the control, all of which were reversed to near control in the co-treated groups ($p < 0.05$). Total white cell and neutrophil counts were significantly ($p < 0.05$) higher in the CLP group compared with the control group. Histological alterations induced by sepsis included degeneration of Purkinje, granule and pyramidal neurons which were ameliorated by TPP and VIT E.
Conclusion: Our results indicated that TPP and VIT E demonstrated protective effects from brain damage caused by CLP-induced sepsis via maintenance of the anti-oxidant status.

Keywords: *Caecal Ligation and Perforation, Lycopersicon esculentum, Cerebellum, Hippocampal formation and Sepsis.*

Résumé
*Contexte :*L'état septique est une réponse inflammatoire systémique à une infection entraînant une morbidité et une mortalité et a undommage oxydatifcomme l'un des mécanismes. Nous avons induitl'état septique chez le rat par la ligature et perforationcaecale (CLP) et ensuite étudié l'effet de protection possible de la purée en poudre de tomates (TPP) sur la neuropathie induite par l'état septique à l'aide de la vitamine E (VIT E) comme un antioxydant standard.
Méthodes : Trente-neuf rats Wistar mâles ont été randomisés en six groupes :contrôle (cont) (N = 5) reçu la nourriture et l'eau ; TPP (N = 5) reçu TPP (50 mg / kg); VIT E (N = 5) reçu VIT E (500 mg / kg); CLP (N = 8) avait CLP; TPP + CLP (N = 8) reçu TPP (50 mg / kg) en plus de CLP; VIT E + CLP (N = 8) a reçu VIT E (500 mg / kg) plus de CLP.CLP a été réalisée le premier jour alors que toutes les autres administrations ont duré 21 jours, au terme desquels des tests neurocomportementaux ont été effectués, les animaux sacrifiés et les tissus traités pour des tests hématologiques, biochimiques et histologiques.
Résultats: Le groupe CLP présentait une augmentation significative ($p <0,05$) du taux de peroxydation lipidique (LPO), une réduction du taux de glutathion (GSH) et une augmentation dans l'activité de l'activité de l'enzyme catalase par rapport au contrôle, qui étaient tous inversé à proche du contrôle dans les groupes co-traités ($p <0,05$). Le nombre total de globules blancs et de neutrophiles était significativement plus élevé ($p <0,05$) dans le groupe CLP par rapport au groupe témoin. Les altérations histologiques induites par l'état septique comprenaient la dégénérescence de neurones de Purkinje, de granules et pyramidaux qui étaient améliorés par TPP et VIT E.
Conclusion: Nos résultats indiquent que TPP et VIT E ont démontré des effets protecteurs contre les dommages au cerveau causés par un état septique induit par CLP à travers le maintien du statut antioxydant.

Mots clés : *Ligature et perforation caecale, Lycopersicon esculentum, cervelet, formation hippocampique et état septique.*

Introduction

Sepsis is a systemic inflammatory response to infection and a major cause of morbidity and mortality worldwide [1]. The aetiology of sepsis among others is faecal peritonitis and might experimentally result in neuronal degeneration, peri-

Correspondence: Dr. O. Owoeye, Department of Anatomy, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: oowoeye2001@yahoo.com

microvessel oedema, and disruption of astrocyte processes [2]. However, secondary bacterial peritonitis in human as in acute intestinal perforation is an important cause of sepsis and death in surgical practice due to an intra-abdominal infectious focus. Sepsis leads to the production of reactive oxygen species which have been reported to play a role in the induction of many pro-inflammatory cytokines and mediators important in producing the acute inflammatory responses associated with sepsis [1].

Oxidative stress occurs when the body's antioxidant system is overwhelmed by excess reactive oxygen species [3]. Hence the need to protect the body from the deleterious effects of oxidative stress. The protective effect of phytochemicals in mitigating damage from oxidative stress appears promising. *Lycopersicon esculentum* (tomato), family Solanaceae, are rich sources of numerous beneficial nutrients and anti-oxidants which include lycopene, choline, alpha-lipolic acid, beta-carotene, lutein, vitamins A and C, folic acid, small amounts of magnesium and potassium [4]. Lycopene an open chain highly unsaturated carotenoid responsible for 80% anti-oxidant property of tomato reportedly inhibited iron catalysed lipid peroxidation and nitric oxide production in rat brain homogenates exposed to ischaemic brain injury [5]. Similarly, *Lycopersicon esculentum* demonstrated neuroprotection against cisplatin-induced alteration of microanatomy of rat cerebellum, dentate gyrus and Cornu Ammonis3 (CA3) of rat brain [6]. Vitamin E (α-tocopherol) is a fat-soluble vitamin found in many foods, fats, and oils. The main function of Vitamin E in humans appears to be that of an antioxidant to neutralize free radicals formed primarily in the body during normal metabolism and also upon exposure to environmental factors, such as cigarette smoke or pollutants [7]. Aside from maintaining the integrity of cell membranes throughout the body, α-tocopherol also protects the fats in low-density lipoproteins (LDLs) from oxidation.

Although the cerebellum accounts only for approximately 10% of the brain's volume, it contains over 50% of the total number of neurons in the brain [8]. The cerebellar cortex is divisible into three functional areas [9] namely: spinocerebellum; vestibulocerebellum, cerebrocerebellum whereas its medulla contains the four masses of cerebellar nuclei namely: dentate, emboliformis, globose, and fastigial all of which are composed of large, multipolar neurons with simple branching dendrites and from which the cerebellar efferents arise. The major functions of the cerebellum include: maintenance of balance, posture and muscle tone; motor coordination of voluntary movements; maintenance of learning and cognitive functions; regulation of saccadic and smooth eye movements [10, 11] and making movements more adaptive and accurate by modifying motor commands of the descending pathways [8]. The hippocampal formation is among others involved in long term spatial and episodic memory storage [12]. Alteration of the structural integrity of either the cerebellum or the hippocampal formation by sepsis may have untoward effect on their functions.

Previous studies using CLP have demonstrated oxidative parameter changes [1, 13, 14] and brain structural alterations [2]; however, no study has so far reported on the effect of *Lycopersicon esculentum* on this technique. In the present work, we aimed to test the beneficial effects of *Lycopersicon esculentum* as Tomato Pomace Powder (TPP) and vitamin E on the brain of adult male Wister rats. To that end, we induced sepsis by Caecal Ligation and Perforation (CLP) technique to study oxidative parameters, haematology and behavioural alterations and brain structural responses by light microscopy. We hypothesized that TPP could prevent CLP-induced brain tissue injury by inhibiting the ROS generation triggered by sepsis and thus answer the question of whether TPP can protect rat brain from induced sepsis. The findings (if protective) could stimulate further research in harnessing tomato's potential as an adjunct in sepsis management.

Materials and methods

Experimental animals

Male Wistar rats weighing 90–180 g were obtained from the College of Medicine animal house, University of Ibadan, Nigeria. They were housed in plastic cages with dimensions 29 cm x 27 cm x 30 cm, with wood shavings in a fly-proof, freely ventilated and naturally illuminated animal rooms at room temperature with a 12 hr light/dark cycle. The animals were acclimatized for two weeks and then divided into experimental and control groups by random sampling techniques, fed with commercial mouse cubes (Ladokun Feeds Nig. Ltd, Ibadan, Nigeria) and drinking water *ad libitum.* All procedures on animal handling were in accordance with ethical use of animals in research [15].

Processing and administration of tomato pomace powder (TPP)

Fresh tomatoes were purchased from Bodija market, Ibadan, Nigeria. The tomatoes were washed, sliced and squeezed to reduce the water content, the squeezed remains were dried in an oven at 50^{o} Celsius for two hours after which it

was grounded into powder which was stored as tomato pomace powder (TPP) in an air tight container as described by Owoeye and Onwuka [6]. The TPP was administered at 50 mg/kg using propylene glycol as the vehicle.

Preparation and administration of α-tocopherol (Vitamin E)

Each soft gelatine capsule containing 100 mg of DL-α-tocopheryl acetate as 100 mg vitamin E acetate was punctured and withdrawn with a new size 21 G needle attached to a new 1 mL insulin syringe. The syringe was attached to an intra-gastric tube for gavage to administer 500 mg/kg body weight daily for 21days.

Research Design

The thirty-nine rats were randomized into six groups and treated as follows:

Group 1 (Cont) (N=5) animals received water and food, served as control.

Group 2 (TPP) (N=5) animals treated with 50 mg/kg of tomato pomace powder (TPP).

Group 3 (VIT E) (N=5) animals treated with 500 mg/kg of vitamin E (VIT E).

Group 4 (CLP) (N=8) animals subjected to caecal ligation and perforation (CLP).

Group 5 (TPP+CLP) (N=8) animals treated with 50 mg/kg of TPP and subjected to CLP.

Group 6 (VIT E+CLP) (N=8) animals treated with 50 mg/kg of VIT E and subjected to CLP.

The doses used in the present study were selected based on previously published data: VIT E [16, 17]. The CLP was performed on first day of experiment while other treatments were given orally by gavage and lasted 21 days.

Induction of sepsis by Caecal Ligation and Perforation (CLP) technique

Rats in groups 4, 5 and 6 were subjected to sepsis by caecal ligation and perforation (CLP) method as previously described [13] on first day of the experiment. Briefly, they were anaesthetized with ketamine (80 mg/kg body weight, i.m.). Under aseptic conditions, a 3 cm midline laparotomy was performed to expose the caecum and adjoining intestine. The caecum was tightly ligated with a 3.0 silk suture at its base, below the ileocaecal valve, and was perforated once with 14-gauge needle. The caecum was then squeezed gently to extrude about (0.5 cm^3) of faecal matter through the perforation site and was then returned to the peritoneal cavity, and the laparotomy was closed with 4.0 silk sutures.

Post operation management

After CLP each animal was allowed to recover from anaesthesia. Operated animals were given a single dose of antibiotics i.m. (ceftriaxone at 50 mg/kg and gentamycin 25 mg/kg) and then returned to their cages to recover from anaesthesia. The rats were observed after CLP for the presence of signs of infection (piloerection, lethargy, tachypnea, and weight loss). On regaining consciousness, the animals were allowed access to feeds and water *ad libitium.*

Behavioural tests

Behavioural tests were performed on all the groups of animals both experimental and control on day 21 to evaluate motor function and equilibrium. Parameters assessed included: exploratory tests, motor function tests and equilibrium tests.

Line crossing and rearing

The apparatus used was a slight modification of published method [18]. It consisted of a square arena (56 cm × 56 cm × 20 cm) made of white wood and its floor divided by lines into 16 squares that allowed the definition of central and peripheral parts. At the beginning of the session, each rat was individually placed in the centre of the arena and its activity was recorded for 5 min. The number of squares crossed with all paws (crossing) and standing on hind legs (rearing) were evaluated during 5 minute sessions. The crossing numbers were indicators of locomotor while the rearing numbers indicated vertical and exploratory activities. At the end of each session, rats were removed from the open field and the experimental chamber was thoroughly cleaned with 70% ethanol and dried before introducing a fresh rat so as to eliminate olfactory bias [19].

Negative Geotaxis

This was used to assess motor coordination of animals when challenged on a sloped surface. The testing apparatus consists of sloped platform of 45 degrees from horizontal to the desktop; the rat was placed on the highest point facing downwards. The latency to turn and orient themselves to face up the slope was recorded. The duration of attempt for each animal was 2 minutes and the mean of two trials was recorded [20].

Haematological analysis

Blood for haematological parameters was obtained from the retro-ocular plexus of the animals using heparinized capillary tubes on day 21 after the behavioural tests into Ethylene Di-amine Tetra Acetic

(EDTA) acid treated sample bottles for the determination of full blood count which included: Red Blood Cell count, Haemoglobin count, Packed Cell Volume Count (PCV), White Blood Cell count and differential cell count (Lymphocytes, Monocytes, Neutrophils, Eosinophils). Analysis was done in the haematology laboratory of the Department of Veterinary Medicine, University of Ibadan

Sacrifice and sample collection

After the last administration on day 21 of the experiment, animals were weighed, blood samples collected, and were then euthanized with ketamine (80 mg/kg body weight) after which cervical dislocation was gently performed. The rat's brains were quickly dissected out, rinsed, mopped and weighed and then divided into two with the right half used for histology and the left half preserved for biochemical assays based on the method of Owoeye and Ojora [20]. The tissues meant for histological analysis were fixed in 10% formalin and later processed for histology by paraffin wax embedment method while those for biochemical analysis were kept in freshly prepared cold phosphate buffer solution at pH 7.4. The biochemical samples were later homogenized in phosphate buffer (pH 7.4) and the resulting homogenate was centrifuged at 10,000 x g for 15 min at minus 4^0C, the supernatant obtained was thereafter used for the biochemical estimations.

Assessment of Oxidative Stress and Antioxidant indices in the rat's whole brain

The left hemisphere of the brain preserved for biochemical assays as described above was used for biochemical assays. The level of reduced Glutathione (GSH) was estimated based on the method of Beutler *et al* [21] and expressed in µg/ml/mg. Malondialdehyde (MDA) level was determined by measuring the formation of thiobarbituric acid reactive substances (TBARS) present in the test sample according to the method of Varshney and Kale [22]. The activity of Superoxide dismutase (SOD) was determined according to the method of Del-Maestro *et al* [23], Catalase (CAT) activity was also determined according to method of Sinha [24]. All the biochemical tests were conducted in the Drug Metabolism & Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, Nigeria.

Statistical analysis

Descriptive data were expressed as the mean ± standard deviation (SD). Statistical analysis was performed using GraphPad software version 5.04, San Diego, CA, USA. and post-hoc test using Dunnet's test. Groups were compared by Student's t-test and one-way analysis of variance (ANOVA). Differences were considered statistically significant at $p<0.05$.

Results

General observations

Animals in the Control (Cont), tomato pomace powder (TPP) and vitamin E (VIT E) were generally active and fed well. There was no mortality in the groups without surgical interventions but there was 12.5% mortality in CLP exposed rats (2 animals in CLP group and 1 animal in TPP+CLP group). The first week post-op, rats that underwent CLP showed clinical symptoms of sepsis by exhibiting the following features: lethargy, reduced activity, reduced feeding and drinking, piloerection and alopecia.

Table 1: Effect of treatments on body weight differences and mean brain weight.

Groups	Cont	TPP	VIT E	CLP	TPP+CLP	VIT E+CLP
Body wt. diff. (g)	36.00±16.70	36.00±16.70	32.00±11.51	29.71±2.00*	13.04±3.00**	8.54±1.25**
Mean brain wt. (g)	1.64±0.23	1.50±0.14	1.46±0.09	1.60±0.10	1.60±0.19	1.66±0.15

Data are presented as Mean ± S.D. Control, Cont; Tomato pomace powder, TPP; Vitamin E, VIT E; Caecal ligation and perforation, CLP; Weight, wt.; Difference, diff. *P<0.05 versus Control. **P<0.05 versus CLP.

Body and brain weight changes

As shown in the table 1, the weight difference was lower in all the CLP groups when compared with the control group while there was a significant reduction of body weight in the TPP+CLP and VIT E+CLP groups relative to the CLP group ($p<0.05$). However, the body weight differences did not appear to affect the brain weight as shown in table 1.

Biochemical analysis

As shown in figure 1, sepsis (CLP) elicited oxidative stress as indicated by a significant ($p<0.05$) increase

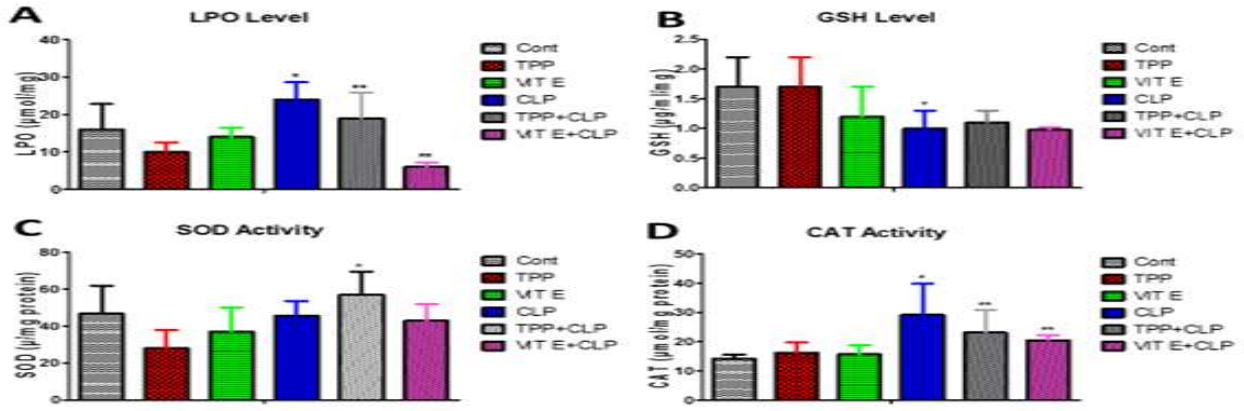

Fig. 1: *Effect of treatment on Superoxide Dismutase (SOD), reduced glutathione (GSH), Catalase (CAT), and Lipid peroxidation (LPO) in rat whole brain. Data are presented as Mean ± S.D. Control, Cont; Tomato pomace powder, TPP; Vitamin E, VIT E; Caecal ligation and perforation, CLP. *P<0.05 versus Control. **P<0.05 versus CLP.*

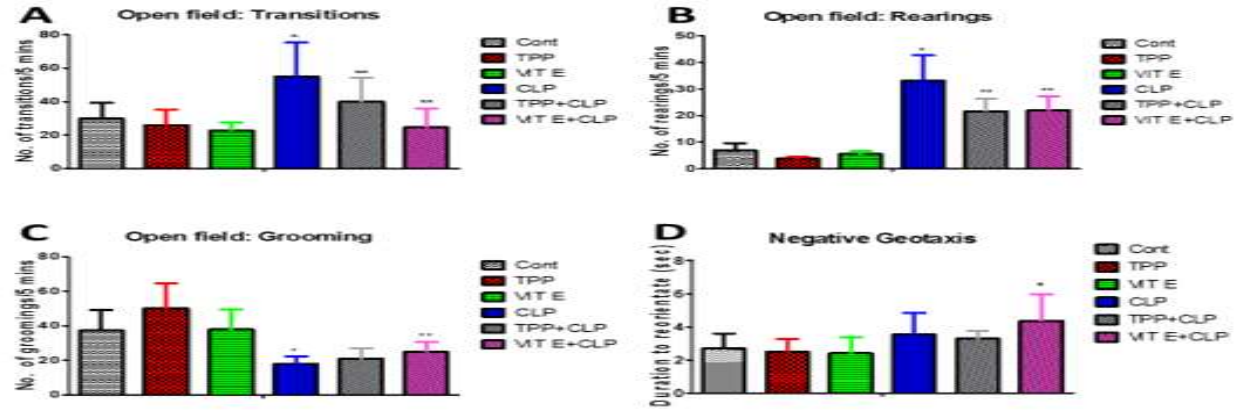

Fig. 2: *Histogram of behavioural tests in the control and treated groups. A: Transitions or horizontal movements measured as number of open field transitions, B: Vertical movements measured as number of open field rearings, C: Grooming measured as the number of grooms, D: Negative geotaxis, measured as time taken for rats to re-orient in a head-up direction. Values are expressed as mean ± S.D. Control, Cont; Tomato pomace powder, TPP; Vitamin E, VIT E; Caecal ligation and perforation, CLP. *P<0.05 versus Control. **P<0.05 versus CLP.*

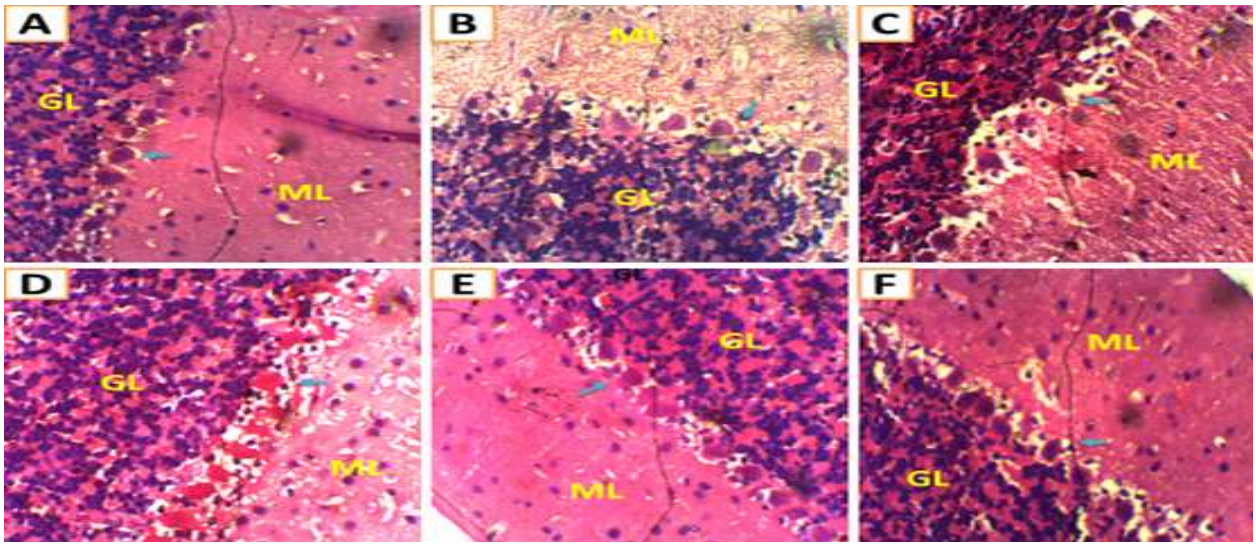

Fig. 3: *Representative Photomicrographs of Cerebellar Cortex of Rats. A- Cont group; B- TPP; C- VIT E; D, CLP; E, TPP+CLP; F, VIT E+CLP. Control, Cont; Tomato pomace powder; Vitamin E, VIT E; Tomato pomace powder, TPP; Caecal ligation and perforation, CLP. ML, Molecular layer; PL, Purkinje cell layer; GL-Granular cell layer; blue arrows show Purkinje neurons. Group D Purkinje neurons show eosinophilic nuclei. H&E-stained sections. Final magnifications: 400x*

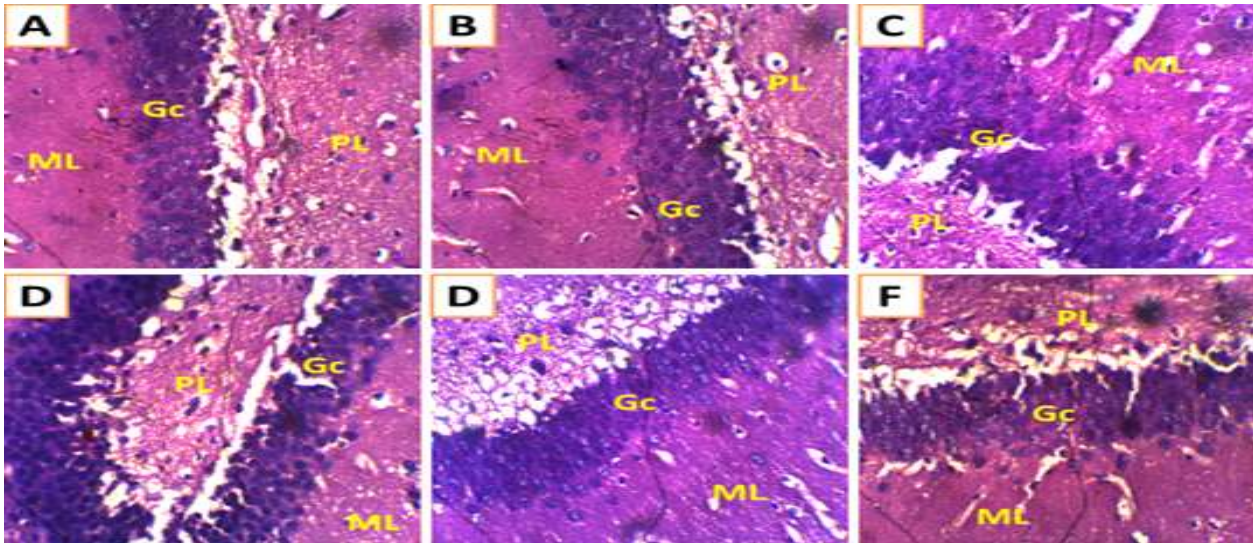

Fig. 4: *Representative Photomicrographs of Dentate Gyrus of Rats. A- Cont group; B- TPP; C- VIT E; D, CLP; E, TPP+CLP; F, VIT E+CLP. Control, Cont; Tomato pomace powder; Vitamin E, VIT E; Tomato pomace powder, TPP; Caecal ligation and perforation, CLP; Molecular layer, ML; Polymorphic layer, PL; Granular cell layer, GCL. H&E-stained sections. Final magnifications: 400x*

in the level of lipid peroxidation and a reduction in the level of GSH when compared with control group. Similarly, sepsis elicited a significant ($p<0.05$) increase in the activity of CAT relative to control. However, co-treatment of TPP and VIT E with CLP significantly reduced the level of LPO and the activity of CAT when compared with the sepsis (CLA) group as demonstrated in figure 1.

increases in the number of transitions and rearings when compared with the control. The number of grooming was significantly reduced in the CLP when compared with the control. However, co-treatment of CLP with TPP and VIT E both ameliorated these parameters. Negative geotaxis measured by the duration rats needed to re-orientate from the sloping position was prolonged in the CLP-treated groups when compared with the control as shown in figure 2.

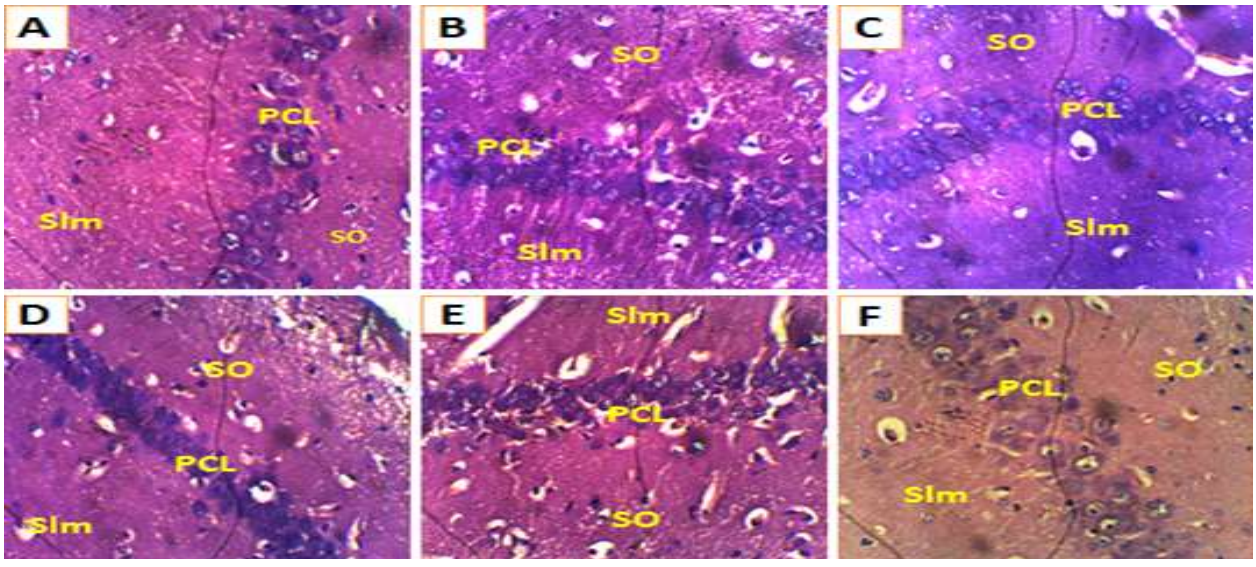

Fig. 5: *Representative Photomicrographs of Cornu Ammonis3 (Ca3) Field of Hippocampus of Rats. A- Cont group; B- TPP; C- VIT E; D, CLP; E, TPP+CLP; F, VIT E+CLP. Control, Cont; Tomato pomace powder; Vitamin E, VIT E; Tomato pomace powder, TPP; Caecal ligation and perforation, CLP; stratum oriens, SO; pyramidalis cell layer, PCL; stratum lacunosum moleculare, Slm. H&E-stained sections. Final magnifications: 400x.*

Behavioural tests

The data presented in figure 2A and 2B show that rats subjected to CLP were hyperactive at the end of the experiment as shown by the significant ($p<0.05$)

Haematology parameters

There was no significant differences between the means of red blood cell parameters and were therefore not displayed. However, CLP induced the

white blood parameters alterations shown in table 2, evidenced by the significant reduction of the lymphocytes but increased the total white cell count (TWCC) and neutrophils when compared with the control. The significant elevation ($p<0.05$) of the TWCC by 86% and neutrophils by 58% by CLP relative to control was reduced by the TPP+CLP treatment to 11% (TWCC) and 5% (neutrophils). Similarly, VIT E+CLP treatment reduced the effect of CLP to 31% and 16% for the TWCC and neutrophils respectively.

and pyramidal neurons of cornu ammonis3 of hippocampus. However, concurrent treatment with TPP and VIT E significantly reversed some of these alterations.

The mortality rate of 12.5% CLP groups recorded in our experiment fared better than the 33% mortality recorded in the experiments of [26]. This might be due to the prophylactic parenteral intramuscular injection of antibiotics (ceftriaxone and gentamycin) we administered to the rats

Table 2: Effect of treatments on the total white cell count and differential white cell count values.

Groups	TWCC ($x10^3/\mu L$)	Neutrophils ($x10^3/\mu L$)	Lymphocytes ($x10^3/\mu L$)	Eosinophils ($x10^3/\mu L$)
Cont	5.93±0,30	2.67±0.31	7.03±0.32	1.67±0.58
TPP	6.33±0.41	2.63±0.59	6.97±0.45	1.67 ± 1.16
VIT E	5.80±0.36	2.33±0.15	6.90±0.36	2.00 ±1.00
CLP	11.00±0.45*	4.23 ±0.25*	5.33 ±0.36*	3.00±0.00
TPP+CLP	9.77± 0.15**	2.90±0.30**	6.63±0.25	2.33±0.58
VIT E+CLP	10.50± 0.71	3.55±0.21	6.00±0.14	3.00±0.00

Data are presented as Mean ± S.D. Total white cell count, TWCC; Control, Cont; Tomato pomace powder, TPP; Vitamin E, VIT E; Caecal ligation and perforation, CLP. *P<0.05 versus Control. **P<0.05 versus CLP.

Histological evaluation of the cerebellar cortex, dentate gyrus and cornu ammonis3 (CA3) of hippocampal formation

The histology of the cerebellar cortex showed the normal three cellular layers in the Control, TPP and VIT E groups in addition to the normal large Purkinje neurons with basophilic-staining nuclei. The Purkinje cells of the CLP group (Figure 3D) showed eosinophilic nuclei indicating nuclear karyolysis when compared with the control group as shown in figure 3A. The Purkinje neurons of the TPP+CLP and VIT E+CLP groups are comparable with the Control cerebellum.

Granule neurons of dentate gyrus of CLP group (Figure 4D) and pyramidal neurons of the CA3 of CLP group (Figure 5D) are pyknotic or dark, whereas the neurons of control and other experimental groups exhibit open chromatin.

Discussion

This study investigated the effects of TPP and VIT E on CLP-induced sepsis. The results showed that CLP treatment caused mortality and reduction in the body weight of rats, induced oxidative stress, elicited leukocytosis, altered behavioural parameters and caused degenerative changes in the Purkinje neurons of the cerebellum, granule neurons of dentate gyrus

immediately after CLP induction to control possible surgery-associated infection, whereas they did not administer antibiotics to the operated animals which might explain our report of lower mortality. Our results also compares favourably with the reports of similarly low mortality rate of 15% reported by [13] who administered both antibiotics and fluid resuscitation after CLP. This suggests the importance of antibiotics as prophylaxis in potential septic cases. The observation of clinical features of sepsis in the CLP rats was supported by similar reports of [26]. Although changes in organ weight and weight coefficients induced by chemical substances have been shown to be a reliable and cheap marker of toxicity [27], the body weight reductions in all the CLP groups in this experiment had no effect on the brain weight of the animals suggesting that the toxicity was not quantifiable by brain weight changes.

The sepsis-induced increase in LPO and reduction of glutathione (GSH) levels in our study indicated a state of oxidative stress which was in consonance with earlier reports [1, 14]. Subsequent to activation, infiltrating neutrophils are reported to produce abundant oxygen radicals resulting in lipid and protein oxidation which might contribute to the increased LPO [28]. The observation that SOD enzyme activity was unchanged in this experiment

contradicted published reports [1, 14] who reported significant elevation of SOD enzyme. However, the sepsis significantly increased the activity of the enzyme CAT which breaks down the generated (H_2O_2), in agreement with previous findings [14]. The GSH reduction imposes an oxidative stress that can impair other cellular functions, in particular those regulated by the redox mechanism [29] hence the suggestion that decrease in GSH concentration is one of the most significant alteration in the antioxidant defense [30]. It was however observed that animals concurrently treated with TPP, VIT E and CLP had reductions in LPO level, increased level of GSH and increased SOD and CAT activities. Of note is the elevation of GSH which is important as a constituent of intracellular protective mechanisms against oxidative stress [1], as this might help in improving the oxidant status of the animals.

The host response towards invading pathogens from the introduced sepsis is usually characterized by systemic pro–inflammatory response that is primarily mediated by cytokines, plasma coagulation and complement cascades, and acute phase proteins release, and a cellular component involving leukocytes, especially neutrophils and vascular endothelium [28]. In this experiment, the significant elevation of the total white cell count by eighty-six percent and neutrophils by fifty-eight percent by CLP treatment accentuated the neutrophil response as the main effector cells in acute inflammation in the induced sepsis. This is similar to responses obtained in faecal perforation of peritonitis. Following activation, margination and trans-endothelial emigration from microvessels, infiltrating neutrophils are reported to produce abundant oxygen radicals resulting in lipid and protein oxidation and mitochondrial impairment which might cause further damage to tissues and can induce cell death [28]. However, the observation that co-treatment of TPP and VIT E lowered the total white cell count by eleven and five percent respectively relative to CLP suggested that both items demonstrated the capacity to reduce the toxicity induced by the sepsis.

The histological effect of sepsis demonstrated in the CLP group on the cerebella of the rats include the eosinophilic degeneration of Purkinje cell while the granule cells of the dentate gyrus (DG) and pyramidal neurons of the stratum pyramidalis of the cornu ammonis3 of the hippocampus exhibited pyknotic or dark neurons, evidences of the toxicity of sepsis. Activated neutrophils, which were elevated in this study, are known to generate increased oxygen radicals which might have resulted in oxidative damage. This is because toxicity associated with excessive free radical generation resulting in lipid peroxidation and oxidative damage could induce damages in the membranes of the cell and mitochondria, which might eventually lead to cell apoptosis and necrosis [1, 28, 31, 32]. The prolonged time taken for all CLP rats to re-orientate in the head-up direction suggested a possible vestibular or cerebellar injury which was demonstrated histologically in this experiment. However, the amelioration of the neuronal alterations observed in the TPP+CLP and VIT E+CLP brains demonstrated the capacity of both TPP and VIT E to mitigate the damaging oxidative effects of sepsis. Tomato pomace had earlier been reported to have ameliorated rat cerebellar and hippocampal neuronal damage by other toxicants like cisplatin, mercuric chloride, lead acetate and gamma radiation [6, 17, 20, 33] by reduction of the oxidative damage induced by these substances. In like manner, TPP and VIT E have demonstrated protective effects against CLP in this experiment by attenuating the brain tissue damage and also by decreasing oxidative stress, as confirmed by the histological study and biochemical results.

The consequence of the injury to the Purkinje cells, granule neurons and pyramidal neurons are possible in coordination of skeletal movements secondary to cerebellar injury, disruption of the memory recording (episodic, semantic and spatial), resulting from damage to the trisynaptic pathway of the perforant path which the hippocampal formation mediates [34]. The amelioration by TPP and VIT E of these possible effects of sepsis would prevent these important neurons from injury hence enabling them to perform their functions optimally. The limitation of this study included the lack of immunohistochemical studies to explain the neuro-inflammation and the pattern of neutrophilic reaction that accompanied the sepsis.

Conclusion

The results of this study showed that tomato pomace powder (TPP) and vitamin E demonstrated protective effects in reducing the brain damage caused by CLP-induced sepsis via maintenance of the anti-oxidant status. The gap in knowledge concerning the effects of TPP on sepsis-exposed subjects which our study aimed for has thus been filled and has answered the research question of whether TPP can protect rat brain from induced sepsis. The findings may stimulate further research to harness tomato's potential as a possible adjunct in sepsis management.

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Calcified dorsal wrist ganglion: a case report

AB Oladiran, SO Ogunlade and AB Omololu
Department of Surgery, College of Medicine,
University of Ibadan, Ibadan, Nigeria

Abstract
Introduction: A ganglion cyst around the wrist is a swelling which is a common cause of presentation on account of the cosmetic appearance, pain and features of nerve compression. Most wrist ganglions are dorsal. They are usually multiloculated cystic masses. Ossification is a rare finding of which the clinician needs to be aware.
Case Report: A 56 year male presented with a 3 month history of a painless, progressive swelling on the dorsal aspect of the left wrist. Examination revealed a firm, non-tender swelling on the dorsum of the left wrist which was attached to the underlying tendons. Plain radiography revealed a pedunculated radio-opaque mass on the dorsum of the wrist at the lunatotriquetral junction without cortical or medullary continuity with the carpal bones. He had surgical excision and the histopathology revealed features in keeping with a ganglion cyst with degenerative changes of the wall.
Conclusion: Ossified ganglion cysts can be treated without complications. Complete excision of the mass, stalk and a cuff of joint capsule is the most reliable form of treatment and gives a satisfactory outcome. This is especially true of calcified ganglion cyst as the presence of calcification makes other methods inappropriate.

Keyword: *Wrist ganglion, wrist swelling, calcified ganglion.*

Résumé
Introduction : Un kyste ganglion autour du poignet est un gonflement qui est une cause fréquente de présentation en raison de l'aspect esthétique, de la douleur et des caractéristiques de la compression nerveuse. La plupart des ganglions du poignet sont dorsaux. Ceux-ci sont généralement des masses kystiques multi-loculées. L'ossification est une découverte rare dont le clinicien doit être conscient.
Rapport de cas : Un homme de 56 ans s'est présenté avec une histoire de 3 mois de gonflement progressif et indolore sur la face dorsale du poignet gauche. L'examen a révélé un gonflement ferme et non douloureux dela face dorsale du poignet gauche qui était attaché aux tendons sous-jacents. La radiographie standard a révélé une masse radio-opaque pédonculée dela face dorsale du poignet, à la jonction lunatotriquetrale, sans continuité corticale ou médullaire avec les os du carpe. Il a eu une excision chirurgicale et l'histopathologie a révélé des caractéristiques correspondant à un kyste ganglionnaire avec des modifications dégénératives de la paroi.
Conclusion : Les kystes ganglionnaires ossifiés peuvent être traités sans complications. L'excision complète de la masse, du pédoncule et du manchon de la capsule articulaire est la forme de traitement la plus fiable et donne un résultat satisfaisant. Cela est particulièrement vrai pour les kystes ganglionnaires calcifiés, car la présence de calcification rend les autres méthodes inappropriées.

Mot-clé : *Ganglion du poignet, gonflement du poignet, ganglion calcifié*

Correspondence: Dr. A.B. Oladiran, Orthopaedic and Trauma Surgery, Department of Surgery, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: ajibola.oladiran@yahoo.com

Introduction

The wrist joint is composed of the proximal row of carpal bones and the distal end of the radius and ulna. It is involved in our day to day interaction with our environment and with other individuals in functional as well as aesthetic roles. Pathologies and deformities affecting the wrist therefore have a major impact on the individual. A ganglion is a common swelling in the wrist with cosmesis being the major complaint. Pain, limitation of motion and features of pressure on the surrounding nerves are other associated complaints. Ossification of ganglion cysts is uncommon and can often be linked to trauma [1]. In-spite of various treatment methods, complete surgical excision is the most consistent method of treatment. Our aim for this publication is to describe this rare.

We present a case of a male patient who presented to us with a calcified ganglion on the dorsum of the wrist.

Case report

S. A. is a 56 year old, right handed, man who presented with a 3 month history of a painless, slowly progressive swelling on the dorsal aspect of the left wrist. There was trauma following a fall 5 months prior to the onset of the swelling. There was pain

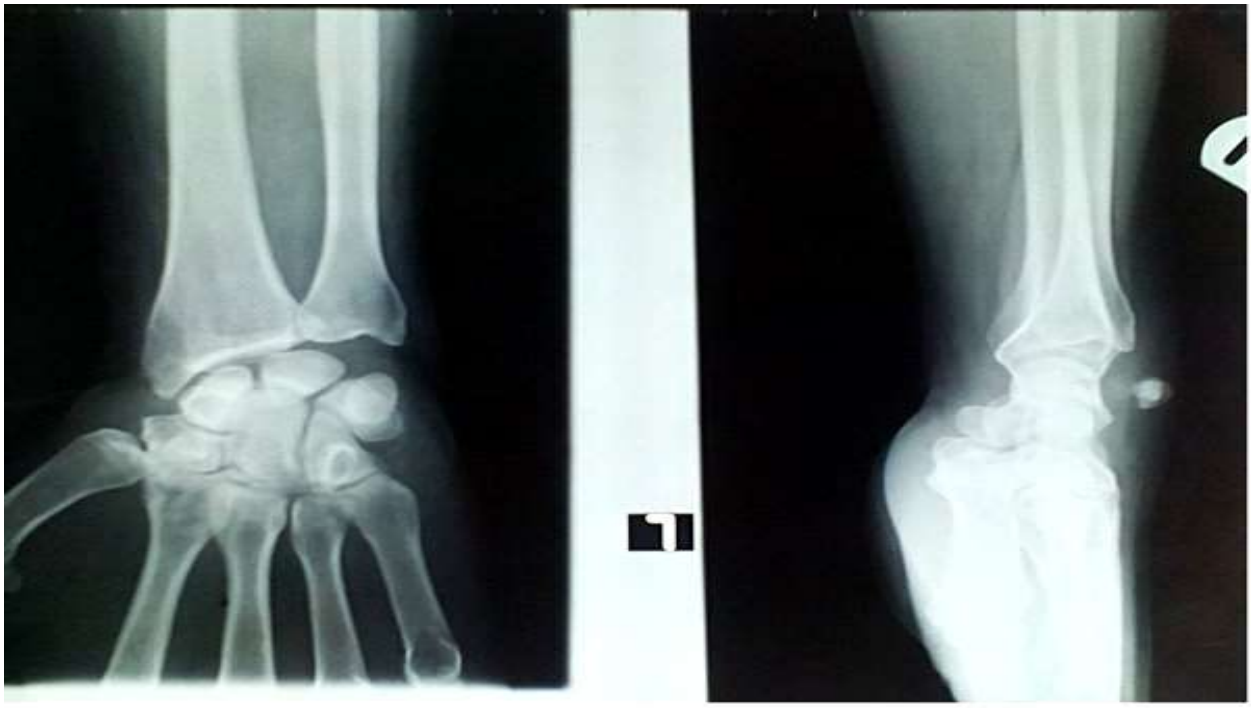

Fig. I: Pre-operative plain radiograph showing the calcified mass on the dorsal aspect of the wrist (arrow)

over the site immediately after the fall which subsided over a few weeks. There was no subsequent loss of function or limitation of movement in the wrist. At the time of presentation, he had no symptoms other than the appearance of the swelling. He had no comorbid conditions.

Examination revealed a firm swelling on the dorsum of the left wrist which was non tender, had no attachment to overlying skin but was attached to the underlying tendons. There was no neurovascular deficit or any sign of nerve compression. Plain radiographs (Figure I) revealed a pedunculated radio-opaque mass on the dorsum of the wrist at the lunatotriquetral junction (indicated by the arrow) without cortical or medullary continuity with the carpal bones. There were no associated fractures, dislocations or bony erosion.

He had surgical excision of the swelling via a transverse incision under Bier's Block. The operative findings were of a multiloculated cystic mass with fibrous walls containing gelatinous fluid with areas of calcification within it. The mass had a solitary stalk which was excised along with a small 1cm cuff of underlying joint capsule. Histopathology revealed a mass consisting of grayish white tissue weighing about 10 grammes. The microscopy revealed a cystic lesion lined by flattened cells and supported by dense fibrocartilagenous tissue stroma with a focal area of calcified degeneration of the wall. Features were in keeping with a ganglion cyst with degenerative changes of the wall. The post-operative period was uneventful and he was discharged home after recovery from anaesthesia. He had no complications and follow-up in the out-patient clinic showed no features of instability in the wrist.

Discussion

Ganglion cysts are one of the most frequently occurring masses of the wrist, often causing pain and interfering with daily activity [2]. Majority of ganglion cysts are found in the dorsal aspect of the wrist, with literature reporting values from 60-87% as being located on the dorsal surface. Ganglion cysts may affect any age group, however they are commoner in the third to fifth decades of life [3,4]. Trauma has been linked to the aetiology of wrist ganglion cyst. A study on volar wrist ganglion cysts associated with carpal tunnel syndrome found a history of direct trauma, usually wrist hyperextension, in half of their cases [5].

Various theories exist on the origin of dorsal wrist ganglion cysts. Joint stress leading to a rent in the capsule, thus allowing leakage of synovial fluid into the surrounding tissue leads to creation of the gelatinous cystic fluid within the wall. Joint pathologies like periscaphoid ligamentous injury as well as joint abnormalities leading to alteration in biomechanics are all thought to be pathways of causation of ganglion cyst. Joint stress may also cause mucinoid degeneration of adjacent connective

tissue with fluid accumulation leading to cyst formation. Mesenchymal cells may also be stimulated to secrete mucin by joint stress. All these have in common joint stress or injury and coalescence of small microcysts of mucin to form the eventual large cyst [3].

The clinical presentation of ganglion cysts consists of the cosmetic appearance of the lump, sometimes with aching in the wrist, pain on activity, especially repetitive wrist movements and sometimes features of nerve compression, particularly median nerve compression or carpal tunnel syndrome in volar ganglion cysts. Pain in dorsal ganglion cysts is thought to arise from compression of the terminal branches of the posterior interosseous nerve [6]. However pain is a variable symptom as one study found that 89% reported pain but only 19% felt that it interfered with activities of daily living [7]. The microscopic anatomy of the wall of the ganglion cyst consists of randomly oriented sheets of collagen arranged in loose layers without synovial lining [8,9].

Calcification of wrist ganglion is rare. Nakamichi and Tachibana reported "occult calcified mass" in 2 out of 128 patients investigated for an association between carpal tunnel syndrome and space occupying lesions around the wrist [10]. It is unclear whether the calcification seen in this index case was secondary to trauma and subsequent haematoma formation which later organised and calcified or whether it was spontaneous calcification of the degenerative tissue.

Conclusion

Ossification of ganglion cysts is a rare presentation. It is important for the clinician to bear this in mind to avoid misdiagnosis. Complete excision of the mass, stalk and a cuff of joint capsule is the most reliable form of treatment of ganglion cysts and gives a satisfactory outcome. This is especially true of calcified ganglion cyst as the presence of calcification makes other methods inappropriate.

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Efficacy of supervised work-place exercise over an unsupervised exercise-on-prescription in prediabetes: a randomized control trial among administrative staff of a Tertiary Health Centre, South-Western Nigeria

SO Martins, OF Folasire and AE Irabor
Department of Family Medicine, University College Hospital, Ibadan, Nigeria

Abstract
Introduction: Offering supervised work-place exercise to employees with prediabetes in a closed work group may be an efficient lifestyle intervention strategy to reverse prediabetes among them. This study compared the efficacy of supervised work-place exercise over unsupervised prescription exercise in prediabetic hospital administrative staff of a tertiary health centre in South-western Nigeria.
Method: A randomized control trial study design with a 3-month follow-up was employed. The study recruited 67 administrative staff of the University College Hospital, Ibadan with prediabetes following an initial screening exercise that involved 300 administrative staff. Participants were randomized into the intervention group (that received supervised work-place exercise; n= 33) and the control group (that received unsupervised exercise-on-prescription; n= 34). Anthropometry and blood glucose estimates were assessed at baseline and end of the study period. The change in these outcomes were compared between and within groups using the repeated measures analysis of covariance. The level of statistical significance was set at $p < 0.05$.
Results: At the end of this study, both groups had significant body weight and blood glucose reductions at 3-month follow-up as compared to the baseline period. However, the intervention group had significantly higher reductions in the mean body weight (×2.1± 0.4 kg vs -0.9 ± 0.2kg), fasting plasma glucose (×1.9 ± 0.3mmol/L vs ×1.1 ± 0.7mmol/L) and oral glucose tolerance test (×2.7 ± 0.9 mmol/L vs ×1.7 ± 0.4mmol/L) than the control group.
Conclusion: The supervised work-place exercise had higher efficacy over unsupervised exercise-on-prescription among hospital employees with prediabetes. The long-term impact of supervised work-place exercise on diabetes prevention and the sustainability of work-place exercise programs warrant further investigation.

Correspondence: Dr. S.O. Martins, Department of Family Medicine, University College Hospital, Ibadan, Nigeria. E-mail: segunmartinez@yahoo.com

Keywords: *Prediabetes, supervised exercise, exercise-on-prescription, work-place, administrative staff, University College Hospital*.

Résumé
Introduction : Proposer des exercices supervisés sur le lieu de travail aux employés atteints de pré-diabète dans un groupe de travail fermé peut constituer une stratégie d'intervention efficace du mode de vie pour inverser la tendance du pré-diabète parmi eux. Cette étude a comparé l'efficacité d'un exercice supervisé sur le lieu de travail par rapport à un exercice de prescription sans supervision chez le pré-diabétique personnel administratif hospitalier d'un centre de santé tertiaire situé dans le sud-ouest du Nigéria.
Méthodes : Un protocole d'étude randomisée avec un suivi de trois mois a été utilisé. L'étude a recruté 67 membres du personnel administratif du Collège Hospitalier Universitaire d'Ibadan atteints de pré-diabète à la suite d'un exercice de sélection préliminaire impliquant 300 membres du personnel administratif. Les participants ont été randomisés en groupe d'intervention (qui a bénéficié d'exercices supervisés sur le lieu de travail ; n = 33) en groupe témoin (qui a bénéficié d'exercices-sur-ordonnance non supervisés ; n = 34). Les estimations anthropométriques et glycémiques ont été évaluées au début et à la fin de la période d'étude. Les changements dans ces résultats ont été comparés entre les groupes et au sein des groupes en utilisant l'analyse à mesures répétées de la covariance. Le niveau de signification statistique a été fixé à $p <0,05$.
Résultats: À la fin de cette étude, les deux groupes présentaient une réduction significative du poids corporel et de la glycémie au suivi de trois mois par rapport à la période initiale. Cependant, le groupe d'intervention présentait des réductions significativement plus importantes du poids corporel moyen (-2.1 ± 0.4 kg par rapport à -0.9 ± 0.2 kg), de la glycémie à jeun (-1.9 ± 0.3mmol / L par rapport à -1.1 ± 0.7mmol / L) et du test de tolérance à la voie orale du glucose (-2,7 ± 0,9mmol / L vs -1,7 ± 0,4mmol / L) par rapport au groupe témoin.
Conclusion : Les exercices supervisés sur le lieu de travail ont une efficacité supérieure à celle des

exercices non supervisés sur ordonnance chez les employés d'hôpital atteints de pré-diabète. L'impact à long terme des exercices sur le lieu de travail supervisés sur la prévention du diabète et la durabilité des programmes d'exercices sur le lieu de travail justifient des recherches supplémentaires.

Mots-clés: *Pré-diabète, exercice supervisé, exercice sur ordonnance, lieu de travail, personnel administratif, Collège Hospitalier Universitaire*.

Introduction

Prediabetes is a condition in which individuals have blood glucose levels higher than normal but not high enough to be classified as diabetes mellitus [1,2].Prediabetes is largely asymptomatic and usually identified incidentally when patients are screened for type 2 diabetes mellitus [2]. Studies have supported the necessity of early screening and interventions for prediabetes to delay or reverse its progression into overt diabetes mellitus [1-3]. As the prevalence of diabetes mellitus increases worldwide, so is the prevalence of prediabetes increasing. In 2011, the International Diabetes Federation (IDF) global estimates showed that about 280 million people had prediabetes and estimated that by 2030, this number is expected to rise to nearly 400 million [4]. The number of people with prediabetes is increasing due to population growth, aging, urbanization, increasing prevalence of obesity and physical inactivity [2,3].

Inadequate moderate-intensity physical activity, amidst other risk factors, is a well-documented risk factor for prediabetes [5-7]. The World Health Organization (WHO) had recommended that adults aged 18–64 years should do at least 150 minutes of moderate-intensity physical activity throughout the week [8]. Uninterrupted sitting at workplaces for lengthy hours has been linked with high postprandial glucose and insulin levels which may lead to prediabetes [9]. Arguably, hospital administrative staff can be particularly vulnerable to chronic medical conditions like diabetes mellitus because of the greater number of hours spent in a sedentary position during administrative duties.Also, making out time for exercises might be extremely difficult for administrative staff with busy schedules.

Often, physical activity does not fit into a full-time employee's busy schedule and one possible solution to this challenge is to make physical activity a part of the work day. Supervision of work-place exercise is a feasible intervention that had been advocated for employees in a closed work group to improve physical activities, especially during work hours [10].Supervised exercise is an exercise carried out under supervision of a qualified fitness instructor while an exercise-on-prescription is an exercise that is carried out following a set of prescribed guidelines without supervision. Poor rates of adherence to exercise-on-prescription instructions present a potential barrier to the goal of increasing physical activity in individuals and as such, supervised exercise poses an advantage over exercise-on-prescription [9,10]. Supervised exercise has a predominant advantage of the ability of having a qualified fitness instructor to monitor, motivate and support an individual to get appropriate intensity and duration of physical activity [10].Two studies namely, the Study on Lifestyle-intervention and Impaired Glucose Tolerance Maastricht (SLIM) study [2] and the BeweegKuur programme [11] had proven the efficacy of supervised exercise over exercise-on-prescription on achieving significantly higher reductions in plasma glucose among their participants. Likewise, a 16-week group-based lifestyle interventional study done in a closed work group at a university worksite in Ohio between 2012-2014 showed the efficacy of supervised work-place exercise over an unsupervised prescription exercise on plasma glucose reductions among employees with prediabetes [12].

Since hospital administrative staff spend most of their workday at their desks, offering supervised work-place exercise to hospital administrative staff with prediabetes may be an efficient lifestyle intervention strategy to reverse prediabetes among them. A huge knowledge gap exists as there is no local study on the efficacy of supervised work-place exercise over an unsupervised prescription exercise in prediabetes among any group of workers in Nigeria. Therefore, this study was carried out to compare the efficacy of supervised work-place exercise regimen over unsupervised prescription exercise in prediabetes among hospital administrative staff of a tertiary health centre, south-western Nigeria.

Materials and methods

Study design

The study was carried out at the University College Hospital (UCH), Ibadan, South-western Nigeria. A randomized control trial design with a 3-month follow-up from February to April, 2015 was employed.

Recruitment of study participants

The study participants were 67 administrative staff of the University College Hospital, Ibadan who had

prediabetes following an initial screening exercise that involved 300 administrative staff. The sample size of 300 administrative staff for the initial screening exercise was determined from a total sample frame of 2,065 administrative staff (total number of the administrative members of staff in UCH, Ibadan) using the Leslie Kish formula ($N= Z^2pq/d^2$) for prevalence studies [13].Where N = Desired sample size and Z= The standard normal deviate set at 1.96 which correspond to 95% confidence level. An estimated sample size of 300 participants was determined based on a precision of 0.05 and a prevalence of 20.2% from a study of prevalence of prediabetes and its associated risk factors in eastern Uganda [14].A systematic sampling of one in seven staff was used to recruit participants from the sample frame (list of the 2,065 administrative members of staff UCH Ibadan) until estimated sample size of 300 participants was reached.

Study procedure

The 300-administrative staff underwent a screening exercise using fasting blood glucose and oral glucose tolerance test (OGTT) to detect prediabetes as defined by the America Diabetes Association (ADA) criteria [8]. Following the initial screening exercise, 67 administrative staff were found to have prediabetes and they were recruited for this study (Figure 1). The inclusion criteria for the study were: (i) participants with blood glucose in prediabetes range (ii) age of participant of 40 and above (iii) individuals that are not previously diagnosed with diabetes mellitus or not currently on medications for diabetes mellitus. Exclusion criteria for the study were: (i) non-consenting staff (ii) individuals with pre-morbid medical condition that prevented or limited participation in moderate-intensity physical activity e.g. osteoarthritis or heart problems (iii) pregnant women.

Study intervention

The 67 study participants that were found to have prediabetes were randomized by an independent observer into the intervention group (that received a supervised work-place exercise; n= 33) and control group (that received an unsupervised exercise-on-prescription; n= 34) using random numbers with double blinding of the investigator and study participants to eliminate bias (Figure 1). The 33 study participants in the intervention group performed aerobic exercise at moderate-intensity (running on a treadmill and riding on a stationary bicycle) 50 minutes-a-day for three days in a week under the supervision of a fitness instructor in the gymnasium of Physiotherapy department of UCH Ibadan for a 3-month period. The 34 study participants in the control group were given exercise-on-prescription for the same aerobic exercise at moderate-intensity and they were asked to carry out their exercise for 50 minutes-a-day for three days in a week on their own volition and choice venue throughout the 3-month period. The study participants in both groups received telephone calls designed to show concern and encouragement to continue compliance with the recommended exercise once every week during the 3-month period by the researcher.

Data collection

The demographic characteristics of the respondents were collected at the baseline of the study period using a semi-structured questionnaire. The duration and intensity of exercises done by participants was assessed with the Global Physical Activity Questionnaire (GPAQ) instrument developed by the WHO [15]. The GPAQ has previously been used in a survey to assess the profile of physical activity among Lagos State senior civil servants [16] and other population studies have also employed the GPAQ to describe physical activity levels [17-19]. The anthropometric (weight, height, BMI, waist-to-hip ratio) and blood glucose (FPG and OGTT) measurements of the respondents were evaluated at baseline and endline of the study period. The OGTT was performed as described by Akande *et al* [5] in their study. An initial fasting plasma glucose was determined after an overnight fast of 8 – 10 hours by collection of 2mls of venous blood sample following which participants were given a glucose drink containing 75g of anhydrous glucose. Then, another 2mls of venous blood sample was taken for an OGTT estimation after two hours of ingestion of the glucose drink. Estimation of plasma glucose was done by glucose oxidase method [5] and prediabetes was defined using the ADA criteria [8]. Height was measured in metres using a stadiometre, with the participant standing upright and without footwear. Body weight was measured in kilograms using a calibrated Seca® weighing scale, with the participant lightly clothed. Body Mass Index (BMI) was then calculated as body weight divided by the square of height. Using an inelastic measuring tape, waist circumference was measured in centimeters at the level midway between the lowest rib margin and the iliac crest while the hip circumference was measured in centimetres at the widest level over the greater trochanters. The waist-to-hip ratio (WHR) was calculated as waist circumference divided by hip circumference.

Outcome measures

In this study, the primary outcome measure was the change in blood glucose concentrations (FPG and OGTT) from baseline to endline of the 3-month period. Secondary outcome measures were changes in anthropometric measurements (weight, BMI, waist-hip ratio) from baseline to endline of the 3-month period. The study tested the null hypothesis, H_o, which states that there was no difference between the effect of supervised work-place exercise and unsupervised exercise-on-prescription on these outcome measures between intervention group and control group of the study participants.

Statistical analysis

All analyses were completed using SPSS (version 17). The analysis was conducted using an intent-to-treat approach and therefore included all randomized participants. Categorical variables were presented as frequency and percentages while continuous variables were presented as mean ± standard deviation. Between-group differences in baseline blood glucose and anthropometric measurements were assessed using a two-sample t-test. The changes in the primary and secondary outcomes were compared between and within groups using the repeated measures analysis of covariance (ANCOVA) test. The level of statistical significance was set at $p < 0.05$.

Ethical consideration

This study protocol was part of a larger study that was approved by the UI/UCH Institutional Review Committee with number UI/EC/14/0177. Each of the study participants also gave their written informed consent before the start of the study.

Results

From February to April, 2015, we randomly assigned 67 study participants to one of the two groups (33 to intervention and 34 to control). As shown in figure 1, the dropout rate was higher in the control group (three participants) as compared to the intervention group (one participant). The three participants in the control group dropped out due to loss of interest and voluntary withdrawal from the study while the only participant that dropped out in the intervention group did so due to lack of time to perform the exercise. Table 1 shows the characteristics of the 67 study participants at baseline. There were no statistical differences in baseline characteristics between the intervention and control groups.

Table 2 shows the between-group changes as noted in study respondents' characteristics from baseline to endline for intervention and control group. Reduction in body weight after three months was significantly higher in the intervention group (×2.1 ± 0.4kg) as compared to the control group (-0.9 ± 0.2kg). Also, a significantly higher decrease in BMI was seen in the intervention group (-0.9 ± 0.2kg/m^2) as compared to the control group (-0.3 ± 0.1kg/m^2). The intervention group showed a higher decrease in waist circumference and hip circumference as compared to the control group. However, these changes and the WHRs were not statistically significant. The intervention group showed a significantly higher decrease in FPG as compared to the control group (×1.9 ± 0.3mmol/L vs ×1.1 ± 0.7mmol/L respectively). Likewise, the intervention group had a significantly higher decrease in OGTT as compared to control group (×2.7 ± 0.9mmol/L vs ×1.7 ± 0.4mmol/L respectively).

Table 1: Baseline characteristics of study participants (N= 67)

Variable	Group		t	p-value
	Intervention (n= 33) M ± SD	Control (n= 34) M ± SD		
Age (Years)	51.2 ± 5.3	52.4 ± 3.8	3.141	0.711
Weight (Kg)	85.6 ± 3.9	84.1 ± 4.7	2.910	0.305
Height (m)	1.69 ± 1.3	1.71 ± 1.1	4.192	0.061
BMI (Kg/m^2)	29.7 ± 0.7	30.1 ± 0.9	1.822	0.093
Waist circumference (cm)	99.6 ± 3.0	101.2 ± 1.7	2.911	0.104
Hip circumference (cm)	103 ± 1.4	105.4 ± 0.6	1.693	0.071
WHR	0.92 ± 0.9	0.93 ± 1.2	7.014	0.082
FPG (mmol/L)	109.2 ± 4.1	107.6 ± 3.7	4.210	0.091
OGTT (mmol/L)	171.4 ± 3.9	176.1 ± 2.8	9.113	0.141

M ± SE: Mean ± Standard deviation; WHR: Waist-to-hip ratio; FPG: Fasting plasma glucose; OGTT: Oral glucose tolerance test

Table 2: Changes in study participants' characteristics from baseline to endline

Variable	Change Intervention (n= 33) M ± SD	Control (n= 34) M ±SD	F	p-value
Weight (Kg)	×2.1 ± 0.4	-0.9 ± 0.2	7.399	0.005*
BMI (Kg/m^2)	-0.9 ± 0.2	-0.3 ± 0.1	5.042	0.041*
Waist circumference (cm)	-3.6 ± 0.5	-1.2 ± 0.7	1.944	0.391
Hip circumference (cm)	-2.3 ± 0.4	-0.5 ± 0.1	8.711	0.719
WHR	-0.05 ± 0.01	-0.02 ± 0.00	2.006	0.201
FPG (mmol/L)	-1.9 ± 0.3	-1.1 ± 0.7	4.733	0.001*
OGTT (mmol/L)	-2.7 ± 0.9	-1.7 ± 0.4	1.309	0.001*

*M ± SE: Mean ± Standard deviation; WHR: Waist-to-hip ratio; FPG: Fasting plasma glucose; OGTT: Oral glucose tolerance test; *Statistically significant (p< 0.05)*

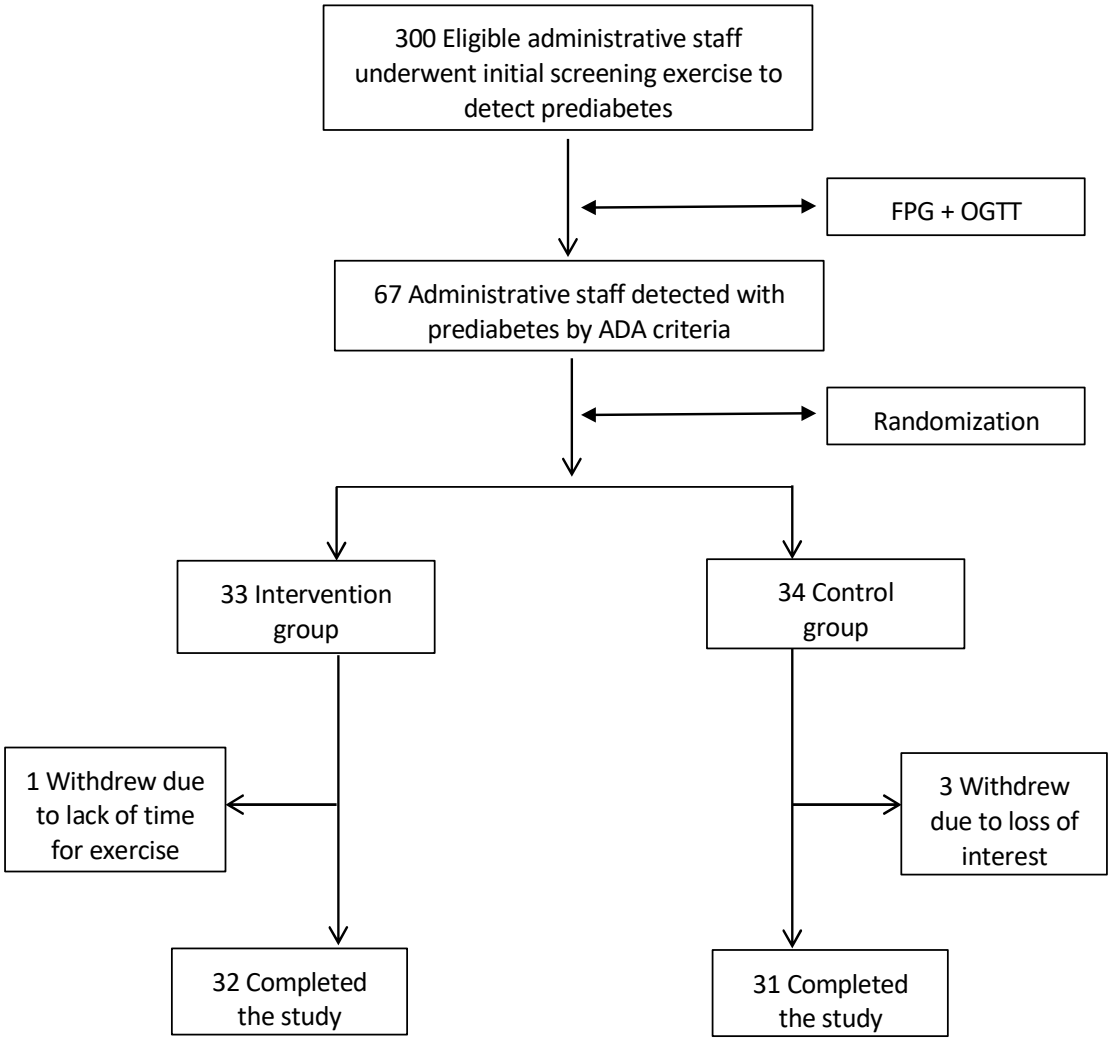

Fig. 1: Study profile

Discussion

The three-month supervised exercise intervention delivered at UCH Ibadan facilitated significant reductions in body weight and blood glucose among administrative members of staff with prediabetes. These results support the efficacy of supervised work-place exercise over an unsupervised exercise-on-prescription for promoting risk reduction from prediabetes. In a similar fashion to what was observed in our study, the 16-week supervised exercise delivered at a university worksite in Ohio between 2012-2014 found a significantly higher reduction in body weight in the intervention group versus control group from baseline to post-intervention (0.6 kg intervention versus 0.5 kg control) [12]. This significantly higher reduction led to a higher risk reduction in the development of diabetes mellitus among employees in the intervention group in that study.

The participants in the intervention group of our study also had higher reductions in the other anthropometric measures as compared to the participants in the control group however, these findings were not significant. A reason might be the short-term duration of the exercise program administered to the study participants whereby the desired significant effect size on the waist and hip circumference were not seen. Other intervention studies that had shown significant differences in these anthropometric measures include the long-term intervention studies such as the Da Qing study [20] the Finnish Diabetes Prevention Study [1] and the SHAPE3 Study[3]. Consequently, the respondents from our study pledged to adhere to recommended exercises beyond the completion of this study and it is expected that their adherence would further achieve significant reductions in their anthropometric measures as noticed in other long-term intervention studies.

Undoubtedly, having a sedentary lifestyle increases the individual's susceptibility to being overweight or obese; both of which could cause insulin resistance and the development of prediabetes. Administrative healthcare workers are susceptible to having a sedentary lifestyle due to their lengthy hours of uninterrupted sitting at workplace. A meta-analysis of workplace physical activity interventions by Conn *et al* [21] documented that workplace physical activity interventions can improve both health and important worksite outcomes.

The work-place exercise offered to the participants in the intervention group of our study achieved significantly higher reductions on OGTT and FPG as compared to participants in the control group. These findings among the study participants rejected the null hypothesis (H_o) stated at inception of this study that there would be no difference between the effect of supervised workplace exercise and unsupervised exercise-on-prescription on anthropometric and blood glucose measurements between the intervention group and control group. Our finding was similar to the findings of the SLIM study where the intervention group had higher reduction of OGTT and FPG (-0.8 ± 0.3 mmol/L and -0.1 ± 0.1 mmol/L respectively) as compared to the control group (0.2 ± 0.3 and 0.1 ± 0.1 mmol/L respectively) [2].

Limitations of the study

1. The likely presence of other chronic medical conditions and comorbidities like hypertension, dyslipidemia, obesity etc. among participants in this study was not an exclusion criterion and this could be a confounder which might have had an influence on the findings of this study.
2. The exercise intervention was carried out over a short duration of three months and this might affect the assertion that supervised exercise has more efficacy than unsupervised exercise in the prevention of type 2 diabetes mellitus.

Recommendations from the study

The long-term impact of supervised work-place exercise on diabetes prevention and the sustainability of work-place exercise programs warrant further investigation. Also, it is recommended that work places should have a dedicated fitness instructor for employees in a closed work group to offer supervised work-place exercises to at-risk members of staff.

Conclusion

Prediabetes is of public health importance especially the risk of its progression into type 2 diabetes mellitus. Achieving adherence to a physical activity program is challenging especially for hospital administrative workers who are known to have busy work schedules and less spare time for exercising. This study found that type 2 diabetes can be prevented by offering supervised work-place exercise to those individuals at high risk for the disease in a closed work group.

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First phase insulin response in students of the University of Ibadan with family history of diabetes mellitus

FM Abbiyesuku[1], OO Sonuga[1] and AA Sonuga[2]

Department of Chemical Pathology[1], College of Medicine, University of Ibadan, Ibadan and Department of SLT[2] (Biochemistry Option,), Ekiti State University, Ekiti, Nigeria

Abstract

Background: Impairment of the first phase of glucose-induced insulin secretion has long and repeatedly been recognized as an earliest detectable defect of β-cell function in individuals destined to develop type 2 diabetes mellitus. This study investigated the effect of positive family history of diabetes mellitus on the first phase insulin response in young adults.

Methodology: A cross-sectional study conducted among aged-matched 60 apparently healthy individuals, 30 with family history of diabetes among their 1st and or 2nd degree relatives (subjects) and 30 without family history of diabetes (controls). Glucose-oxidase method was used to assay serum glucose while serum insulin was assayed using Enzyme Linked Immunosorbent Assay. The insulin resistance index, insulin sensitivity index and *B*- cell function index was calculated using University of Oxford HOMA calculator, version 2.2 software. Statistical analysis was performed using SPSS version 17. Descriptive statistics, student's t-test, Mann-Whitney U- test and Odds ratio were done.

Results: Results are expressed as mean (SD). Young adults with family history of diabetes mellitus had significantly higher first phase insulin concentration, fasting glucose concentration, fasting insulin concentration, insulin resistance index and β-cell function index than those without family history [p=0.006, 0.014, 0.004, 0.000 and 0.031 respectively]. The insulin sensitivity index was significantly lower in offspring of diabetics than in those of non-diabetics [p=0.001].

Conclusions: Young adults with family history of diabetes among relatives have higher risk of developing the disease than their counterpart without family history.

Keywords: *First phase insulin response, family history, type 2 diabetes mellitus, young adult*

Correspondence: Dr. F.M. Abbiyesuku, Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: fmabbiyesuku@yahoo.com

Résumé

Contexte : La déficience de la première phase de la sécrétion d'insuline induite par le glucose a longtemps été reconnue comme l'un des premiers défauts détectables de la fonction des cellules βchez des individus destinés à développer un diabète sucré de type 2. Cette étude a examiné l'effet des antécédents familiaux positifs de diabète sucré sur la réponse insulinique de première phase chez les jeunes adultes.

Méthodologie : Une étude transversale réalisée parmi 60 personnesd'âge-appariés apparemment en bonne santé, 30 avec des antécédents familiaux de diabète parmi leurs relatifs de 1er et ou 2èmedegré (sujets) et 30 sans antécédents familiaux de diabète (contrôles). La méthode glucose-oxydase a été utilisée pour doser le glucose sérique, tandis que l'insuline sérique a été analysée à l'aide du dosage immunoadsorbant lié à l'enzyme. L'indice de résistance à l'insuline, l'indice de sensibilité à l'insuline et l'indice de fonction des cellules βont été calculés à l'aide de la calculatrice HOMA de l'Université d'Oxford, version logiciel 2.2. L'analyse statistique a été réalisée à l'aide de SPSS version 17. Des statistiques descriptives, le test t de l'étudiant, le test U de Mann-Whitney et lerapport decotes ont été effectués.

Résultats : Les résultats sont exprimés en moyenne (DS). Les jeunes adultes ayant des antécédents familiaux de diabète sucré ont une concentration en insuline, une glycémie à jeun, une concentration en insuline à jeun, un indice de résistance à l'insuline et un indice de fonction des cellules βnettement supérieurs en première phase que ceux sans antécédents familiaux [p = 0,006, 0,014, 0,004, 0,000 et 0,031 respectivement]. L'indice de sensibilité à l'insuline était significativement plus faible parmi les enfants des diabétiques que de ceux non-diabétiques [p = 0,001].

Conclusions : Les jeunes adultes ayant des antécédents familiaux de diabète parmi les membres de leur famille ont un risque plus élevé de développer la maladie que leurs homologues sans antécédents familiaux.

Mots-clés: *réponse insulinique de première phase, antécédents familiaux, diabète sucré de type 2, jeune adulte*

Introduction

Diabetes is increasing in children [1]. Both obesity and family history of diabetes are associated with increased risk of diabetes in youth, irrespective of the ethnic background [2]. Impairment of the first phase of glucose-induced insulin secretion has long and repeatedly been recognized as an early sign of β-cell dysfunction in type 2 diabetic patients [3]. Recent studies have also shown that minimal elevations in fasting plasma glucose, within the conventionally considered normal range, are accompanied by a diminution of first-phase insulin secretion [4].

A strong negative relationship has been demonstrated between the first-phase insulin release and the initial glucose increment after starting a glucose infusion. This finding suggested that an early surge of insulin secretion could limit the rise in blood glucose concentration. Researchers think that similar finding occur in response to carbohydrate that is ingested.

Pre absorptive insulin release, also known as cephalic phase insulin release (PIR), or first phase insulin release is one such anticipatory response to eating [5, 6]. Though it is a relatively minor component of total insulin secretion, it is an extremely important determinant of overall glucose tolerance [6]. Studies in both laboratory animals and humans have demonstrated that loss or impairment of this response leads to impaired glucose tolerance and diabetes [7, 8]. For example, intravenous administration of glucose in rats, which bypasses the oral cavity, leads to delayed insulin release and much higher blood glucose concentrations than when the same amount of glucose is orally ingested.

Progression to diabetes can be viewed as having definable stages characterized by changes in various metabolic parameters and β-cell function. Gordon *et al* [9] in 2004 proposed that there are 5 stages in the progression of diabetes, each of which is marked by important changes in β-cell mass, phenotype, and function. Stage 1 is best described as compensation: insulin secretion increases to maintain normal glucose levels in the face of insulin resistance resulting from obesity, physical inactivity, and genetic predisposition. Stage 2 occurs when glucose levels rise to levels of <5.0–6.5 mmol/l (89–116 mg/dl)—a stable state of β-cell adaptation. Stage 3 is an unstable period of early decompensation in which glucose levels rise relatively rapidly to stage 4, which is characterized as stable decompensation. Finally, there is the severe decompensation of stage 5 that represents profound β-cell failure with progression to ketosis as seen in diabetic patients [9].

It is widely thought that diminution of first-phase insulin release is the earliest detectable defect of β-cell function in individuals destined to develop type 2 diabetes and that this defect largely represents β-cell exhaustion after years of compensation for antecedent insulin resistance [3]. It is therefore important to investigate first phase insulin release in offspring of diabetic patients to detect early, if there is diminution in their first phase insulin response, as means of establishing a risk of developing overt diabetes in future.

Materials and methods

This is a cross-sectional study carried out among age-matched students of University of Ibadan, within a period of 10 months. A non-random sampling technique was used to select the study participants. 60 apparently healthy participants with age ranges from 18-25 years were recruited for this study; 30 subjects, with family history of diabetes mellitus among their first and or second degree relatives; 30 controls, without family history of diabetes mellitus. Ethical approval was obtained from the University of Ibadan/ University College Hospital Ibadan Health Research Ethics Committee (assigned number: UI/EC/13/0189).

Data collection

Data was collected by using pre-tested semi-structured interviewer administered questionnaire and informed consent form was obtained from all participants after educating them on the benefits and relevance of the study. Clinical measurements which include weight (Kg), height (meters) and body mass index (Kg/m^2) were measured with participants in light clothing without shoe. Blood pressure (mmHg) was measured with a standard digital sphygmomanometer on the left arm after at least 10 minutes of rest; pulse rate (beats per minute) was also counted at the wrist (radial artery) for exactly 60 seconds. Students that were pregnant, lactating, with chronic illness or diabetes mellitus, on steroid medication, obese (BMI $\geq$30Kg/m^2) and smokers were excluded from the study.

Specimen collection and storage

The procedure was done at the Metabolic Research Ward; University College Hospital Ibadan, and venous blood specimen was collected via an antecubital intravenous cannula in situ. After an overnight fast of at least eight (8) hours by each participant, fasting blood specimen [i.e. the baseline or minus five (-5) minute sample] was obtained from each participant. Then collection of the second blood specimen [i.e. the zero (0) minute sample] and administration of commercially prepared 75g oral

glucose solution to each participants, were done concurrently. Subsequently blood specimen was taken at 3rd, 9th and 15th minute post the administration of oral glucose solution from each participant. At each time of specimen collection, four (4) mls of venous blood was withdrawn via the antecubital intravenous cannula from each participant. Specimen bottles were then transported in ice packs to the laboratory immediately post collection. Each specimen bottle was allowed for full clot retraction before centrifuging at 3000g for 15 minutes. Then the serum was decanted into their respective labelled plain bottles and stored at -20°C for not more than a month, until analyzed for insulin and glucose concentration.

Assay methods

Serum glucose was determined by Glucose Oxidase method manually, serum insulin was determined by Enzyme Linked Immunosorbent Assay (ELISA) manually, while the insulin resistance index (HOMA IR), insulin sensitivity index (HOMA S) and *B*-cell function index (HOMA B) were calculated by using the University of Oxford HOMA calculator, version 2.2 software [10]. HOMA IR = [fasting glucose (mmol/L) × fasting insulin (μIU/mL)] ÷ 22.5. HOMA B = [20 × fasting insulin (μIU/mL)] ÷ [fasting glucose (mmol/L) - 3.5]. HOMA S = reciprocal of HOMA IR.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 17.0. Results are expressed as means (SD). Student's t-test for unpaired data was used to assess for significant differences between means of the demographic and clinical data, the serum insulin levels, the first phase insulin concentration, the insulin resistance index, the *B*-cell function index and the insulin sensitivity index of the subjects and controls. Due to the influence of obesity (BMI $\geq$30Kg/m^2) on insulin resistance, the data were corrected for BMI, by excluding outliers in both groups making them BMI-matched. Mann-Whitney U-test was used to assess for significant differences between means of the first phase insulin concentration of the subjects and controls. Odds ratio was used to give an estimate of risk of developing diabetes. The level of significance was taken to be $p < 0.05$.

Results

Demographic and clinical data

A total of 60 apparently healthy students participated in this study, 30 subjects and 30 controls. Of the subjects 76.7% have history of diabetes in their first degree relatives and the remaining 23.3% in their second degree relatives. The positive family history of diabetes, among 1st and 2nd degree relatives was predictive of the development of diabetes with odds ratios of 0.52 and 1.92 respectively. The age range of the participants was from 18 to 25 years with a mean age of 22.12(2.14) years. The means age of the two groups was similar with no significant difference ($p = 0.368$).

The mean of the pulse rate, blood pressure and height between the two groups were not significantly different. The means of the weight and the body mass index (BMI) were significantly higher in the subjects than in the controls ($p=0.000$ and 0.001 respectively). Though, the mean BMI in both groups are within normal (18.5-24.9 Kg/m^2). The mean fasting (at -5 minute)

Table 1: Demographic and clinical data of subjects and controls.

Parameters	Subject(n=30) Mean (SD)	Control(n=30) Mean (SD)	t	p
Pulse (beats/min)	82(13.50)	76 (15.68)	1.535	0.130
SBP (mm/Hg)	120(12.85)	120(11.80)	-0.147	0.884
DBP (mm/Hg)	75(8.87)	76(7.48)	-0.330	0.742
Weight (kg)	64.1(7.81)	55.5 (7.93)	4.232	0.000*
Height (m)	1.66 (0.08)	1.64 (0.06)	1.563	0.124
BMI (Kg/m^2)	23.3 (3.26)	20.7 (2.49)	3.421	0.001*
FSGC (mg/dl)	99 (10.80)	92 (8.57)	2.543	0.014*
FSIC (μIU/mL)	22.19 (22.01)	10.14 (3.66)	2.957	0.004*

** p is significant at < 0.05 values*

Abbreviation: ***SBP****- Systolic blood pressure,* ***DBP****- Diastolic blood pressure and* ***FSGC****- Fasting serum glucose concentration,* ***FSIC****-Fasting serum insulin concentration.*

serum glucose concentration and mean fasting (at -5 minute) serum insulin concentration were significantly higher in the subjects compared to the controls (p=0.014 and 0.004 respectively). The demographic and clinical data are summarized in table I.

First phase insulin concentrations

The first-phase insulin concentration was calculated as the average of the sum total of the four serum insulin determinations between the zero and fifteen minute's period of the test. This means that the sum total of serum insulin concentrations at 0^{th}, 3^{rd}, 9^{th} and 15^{th} minute divided by four as described by Arslanian *et al* [11] The first phase insulin concentration was significantly higher in the subjects than in the controls (p=0.006). This is presented in table 2.

Table 2: The first phase insulin concentration of subjects and controls.

Parameters (μIU/ml)	Subject(n=30) Mean (SD)	Control(n=30) Mean (SD)	t	p
First Phase Insulin Concentration (FPIC)	40.12 (21.83)	26.81 (12.91)	2.875	0.006*

** p is significant at < 0.05 values*

Insulin resistance index, Insulin sensitivity index and B-cell function index

The mean insulin resistance index and the mean *B*-cell function index were significantly higher in subject compare to the control (p=0.000 and 0.031 respectively). The mean insulin sensitivity index was significantly lower in subject compare to control (p=0.001). This is shown in table 3.

Table 3: Mean insulin resistance index (HOMA IR), mean *B*- cell function index (HOMA B) and mean insulin sensitivity index (HOMA S) of the subjects and controls.

Parameters	Subject(n=30) Mean (SD)	Control(n=30) Mean (SD)	t	p
HOMA IR	2.14 (0.82)	1.31 (0.47)	4.781	0.000*
HOMA B	139.56 (67.87)	109.31(30.74)	2.211	0.031*
HOMA S	56.55 (32.06)	84.01 (28.00)	-3.479	0.001*

** p is significant at < 0.05 values*

HOMA IR- Insulin Resistance index; HOMA B- B-cell function index; HOMA S- Insulin Sensitivity index.

Parameters following BMI-matching in the two groups

BMI is a measure of generalized obesity, and increasing adiposity is associated with insulin resistance. In order to remove the effect of higher adiposity (BMI) of subjects compared to controls, the two groups were made BMI-matched by excluding outliers in both groups. After making the two groups BMI-matched, the mean fasting serum glucose concentration was no longer statistically different, but it was still higher in the subjects compared to the controls. The mean fasting serum insulin concentration, mean insulin resistance index, mean *B*-cell function index and mean first phase insulin concentration remained significantly higher in the subjects than in the controls while, the mean insulin sensitivity index also remained significantly lower in the subjects compared to controls. The results are presented in table 4.

Discussion

Diabetes mellitus is a worldwide health challenge and having a positive family history markedly increases the risk of developing the disease, particularly in the first degree relatives [12-14]. The present study looked at first phase insulin response in young Nigerian students with (SFH+) and without (SFH-) family history of diabetes; as means of establishing a risk of developing overt diabetes in future.

The first phase insulin response occurs within the first few minutes following glucose intake or administration and subsides about 10-15 minutes after [6]. It involves the release of insulin already stored within the beta cells of pancreas in response

Table 4: Insulin resistance indices following BMI-matching in subjects and controls.

Parameters	Subject (n=26) Mean (SD)	Control (n=26) Mean (SD)	t	p
BMI	22.2 (1.47)	21.3 (2.17)	1.861	0.069
FSGC (mg/dl)	98 (11.02)	92 (8.39)	1.941	0.058
FSIC(μIU/ml)	22.59 (23.50)	10.22 (3.73)	2.651	0.011*
HOMA IR	2.09 (0.76)	1.32 (0.48)	4.286	0.000*
HOMA B	141.40 (70.64)	109.62 (30.48)	2.094	0.042*
HOMA S	58.54 (33.66)	83.15 (27.37)	-2.846	0.006*
FPIC (μIU/ml)	41.01 (22.96)	27.12 (13.76)	2.646	0.011*

** p is significant at < 0.05 values*

*Abbreviation: **BMI**- Body Mass Index; **FSGC**- Fasting Serum Glucose Concentration; **FSIC**- Fasting Serum Insulin Concentration; **HOMA IR**- Insulin Resistance index; **HOMA B**- B-cell function index; **HOMA S**- Insulin Sensitivity index and FPIC- First Phase Insulin Concentration.*

to the abrupt rise in the blood glucose level. This is to reduce the initial glucose load in the circulation, before the slow and sustained second phase insulin release takes over glucose homeostasis [6].

The first phase insulin concentration (FPIC) was calculated as the average of the four mean insulin determinations at zero (0), three (3), nine (9) and fifteen (15) minutes of the OGTT. This is similar to how FPIC was calculated in a study by Arslanian *et al* [11] in 2005, in which the FPIC was calculated as the mean of five insulin determinations at 2.5, 5.0, 7.5, 10.0, and 12.5 minutes of the hyperglycaemic clamp. In this study the FPIC was noted to be significantly higher in SFH+ than in SFH- which was at variance with the report by Arslanian *et al* [11] who reported no significant difference in the children (11-12 years) they studied. It was also observed that the total insulin released (TIR) during the test period was significantly higher in SFH+ [160.47 (87.30) μIU/ml] than in SFH- [107.24 (51.63) μIU/ml]; p=0.006; this is in keeping with the earlier report by DeFronzo [15].

It has been well documented that there is a dynamic interaction between insulin secretion, insulin resistance, insulin sensitivity and *B*-cell function [15]. This relationship is such that a low insulin sensitivity i.e. insulin resistance, stimulates an initial increase in β-cell function, resulting in increased insulin secretion in proportion to the severity of the insulin resistance, in order to maintain normal glucose tolerance [15].

Therefore in this study the β-cell function index, insulin sensitivity index and insulin resistance index were determined. It was found that the insulin resistance index (HOMA-IR) and the β-cell function index (HOMA-β) were significantly higher in the SFH+ compare to the SFH-, this is similar to the findings of Jin-Ook *et al* [16] in 2012. The insulin sensitivity index (HOMA-S) was significantly lower in the SFH+ compare to the SFH-; Arslanian *et al* [11] also reported similar findings where they concluded that family history of type 2 diabetes is associated with decreased insulin sensitivity and clearance; and that some of the determinants of glucose disposition index are genetic or heritable. This present study therefore supports the reports by DeFronzo [15] and Kasuga [17], which found that as insulin resistance increases, β-cells compensate by increasing insulin secretion, resulting in compensatory hyperinsulinaemia and the maintenance of normal glucose tolerance.

The findings of significantly higher fasting serum insulin concentration in SFH+ is similar to the report by Weyer *et al* [18] where it was concluded that fasting hyperinsulinaemia itself has a primary role in the pathogenesis of diabetes and whether amelioration of basal insulin hypersecretion will prevent diabetes remains to be elucidated. It was noted in this present study that both SFH+ and SFH- have normal mean fasting serum glucose concentration despite the significantly lower insulin sensitivity in SFH+. This could explain the higher insulin secretion in SFH+ to compensate for the low insulin sensitivity to maintain normoglyceamia as documented by DeFronzo [15] and Kasuga [17].

In concordance with previous studies by Rahim *et al* [19], Zafar *et al* [20] Adeleye *et al* [21], and Arslanian *et al* [11], the SFH+ have significantly higher BMI than the SFH-, though BMI in both groups are within the normal range. It was reported in the study by Adeleye *et al* [21] in 2002 that SFH+ had a significantly higher BMI compared to SFH-

and they concluded that a parental history of type 2 diabetes mellitus influences body fat and its distribution resulting in greater degrees of generalized and central/abdominal fat, implying a greater risk of developing type 2 diabetes mellitus in view of the relationship between body fat distribution and insulin resistance.

BMI is a measure of generalized obesity, and research has shown that there is association between adiposity and insulin resistance in adults and children [22, 23]. Due to the significant difference in the BMI of SFH+ compared to SFH- observed in this study and the known influence of adiposity on insulin resistance; the effect of relative higher adiposity in the SFH+ on measured parameters was adjusted for by matching the BMI in the two groups. After BMI matching in the two groups, the mean fasting serum glucose between SFH+ and SFH- was no longer statistically different, though it was still higher in SFH+. The fasting serum insulin concentration, first phase insulin concentration, insulin resistance value, insulin sensitivity index and *B*-cell function index remained significantly higher in SFH+ than in SFH-. These findings suggest that family history of diabetes mellitus (i.e. genetics) has a stronger influence on glucose metabolism than body mass index.

This study also showed that positive family history of diabetes mellitus among 1st and 2nd degree relatives were predictive of the development of diabetes mellitus with odds ratios of 0.52 and 1.92 respectively. This suggests that having a family history of diabetes among 2nd degree relative poses a greater risk of developing diabetes than having a 1st degree relative with the disease.

Conclusion

Therefore, from this study it can be concluded that young adults with family history of diabetes mellitus have significantly higher first phase insulin secretion to compensate for their state of insulin resistance and insulin insensitivity in order to maintain normal glucose tolerance. This is shown from the observation of the normal fasting serum glucose concentration reported in them, despite their significantly lower insulin sensitivity, when compared to those without family history of diabetes mellitus.

Recommendations

1. Further study is necessary to follow up offspring of diabetics in the nearest future to ascertain their glycaemic status and *B*-cell function; if there will be any progression to impaired glucose tolerance state.
2. Individual with family history of diabetes mellitus should be encouraged to go for regular medical check and to commence dietary and therapeutic life-style modification early.

Study limitations

1. The effects of counter regulatory hormones on insulin sensitivity were not determined in this study.
2. Age and BMI were matched in this study; gender-matching was not done, which could be a confounding factor in interpreting the results.

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Perception, experience and care of episiotomy among post natal women attending selected health facilities in Ibadan, Nigeria

CM Ndikom[1], GI Ajijolaiya-Adeniyi[2] and GB Ogbeye[3]
Department of Nursing[1], College of Medicine, University of Ibadan,
Department of Clinical Nursing[2], University College Hospital, Ibadan and
Directorate of Health Services[3], Federal University of Technology, Akure, Nigeria

Abstract
*Background***:** Episiotomy is a deliberate cut given on the perineum to widen the vaginal opening for the delivery of an infant but it is sometimes misused. The study aimed at determining the perception, experience and care of episiotomy among postnatal women.
Methods: This descriptive study was carried out in one selected tertiary, secondary and primary health care facility respectively in Ibadan. Purposive sampling techniques was used to select 219 participants. Data was collected using a self-structured questionnaire with reliability of 0.81 after obtaining ethical approval and informed consent. Two hundred (200) questionnaires were suitable for data analysis. Data were analysed using descriptive statistics and hypotheses were tested using chi-square at $p<0.05$.
Results: One hundred and seventeen (58.5%) of the respondents were between ages 28-37 years with a mean age of 29.7 years. A total of 108(54.0%) of the respondents had experienced episiotomy. Informed consents were not obtained from most of the respondents before episiotomies were performed on them. Also, 78(72.2%) affirmed that they experienced pain and discomfort from episiotomy with 31 (28.7%) admitting that the pain affected their ability to care for their babies while 16 (14.8%) affirmed that the experience also resulted in discomfort during sexual intercourse. Furthermore, 92(85.2%) out of the 108 claimed that they were given information on the care of episiotomy after the procedure and thus, were able to use the various methods of episiotomy care effectively without any complications.
Conclusion: Episiotomy rate in this study was higher than the recommended evidenced-based rate for optimum care. Therefore, efforts should be made to reduce the rate at which episiotomies are performed by health workers on parturient mothers. In addition, women should be given appropriate information on episiotomy.

Keywords: *Episiotomy care, experience, perception, postnatal women*

Correspondence: Mrs Chizoma M. Ndikom, Department of Nursing, College of Medicine, University of Ibadan, Ibadan. Nigeria. E-mail: cmndikom@yahoo.com

Résumé
Contexte **:** L'épisiotomie est une coupure délibérée sur le périnée destiné à élargir l'ouverture vaginale lors de l'accouchement, mais elle est parfois mal utilisée. L'étude visait à déterminer la perception, l'expérience et les soins de l'épisiotomie chez les femmes postnatales.
Méthodes : Cette étude descriptive a été réalisée dans un établissement de soins de santé tertiaire, secondaire et primaire sélectionné à Ibadan, respectivement. Des techniques d'échantillonnage par choix ont été utilisées pour sélectionner 219 participantes. Les données ont été collectées à l'aide d'un questionnaire auto-structuré avec une fiabilité de 0,81 après avoir obtenu l'approbation éthique et le consentement éclairé. Deux cents (200) questionnaires étaient appropriés pour l'analyse des données. Les données ont été analysées à l'aide de statistiques descriptives et les hypothèses testées à l'aide du chi-carré à $p <0,05$.
Résultats : Cent dix-sept (58,5%) des répondantes étaient âgés de 28 à 37 ans et avaient un âge moyen de 29,7 ans. Un total de 108 (54,0%) des répondantes avaient eu une épisiotomie. Les consentements éclairés n'ont pas été obtenus de la plupart des répondants avant l'épisiotomie. De plus, 78 (72,2%) ont déclaré souffrir de douleur et déconfort à cause de l'épisiotomie et 31 (28,7%) ont admis que la douleur affectait leur capacité à prendre soin de leur bébé, tandis que 16 (14,8%) ont affirmé que l'expérience avait également provoqué une gêne pendant les rapports sexuels. En outre, 92 (85,2%) des 108 ont déclaré avoir reçu des informations sur les soins de l'épisiotomie après la procédure et pouvaient ainsi utiliser efficacement les différentes méthodes de traitement de l'épisiotomie sans complications.
*Conclusion :*Le taux d'épisiotomie dans cette étude était supérieur au taux recommandé basé sur la preuve pour des soins optimaux. Par conséquent, des efforts devraient être faits pour réduire le taux d'épisiotomies par les agents de santé sur les mères parturientes. De plus, les femmes devraient recevoir des informations appropriées sur l'épisiotomie.

Mots-clés: *Episiotomie, expérience, perception, femmes postnatales*

Introduction

The use of episiotomy at vaginal birth has long been part of the traditional procedure of midwives and obstetricians as introduced by Joseph DeLee in 18th century [1]. However, recent evidences shows that routine episiotomy did not improve maternal and neonatal outcomes, rather, it is a perineal trauma associated with short and long term morbidity for women with vaginal delivery which impact her quality of life and make her birth experience more traumatic [2].

Episiotomy is a surgical incision of the perineum performed to widen the vaginal opening for the delivery of an infant [3]. It is also described as a surgical incision through the perineal tissue that is designed to enlarge the vulva outlet during delivery and to minimize the risk of severe spontaneous, maternal trauma as well as expedite the birth when there is evidence of foetal compromise [4]. Although episiotomy has become one of the most commonly performed surgical procedures in the world, it was introduced without strong scientific evidence for its effectiveness [5, 6] and had since be adopted as a standard practice worldwide. However, over the last several decades, there has been a growing body of evidence that episiotomy does not provide these purported benefits, rather, it is associated with pain and discomfort which often interferes with basic daily activities for the woman such as walking, sitting and passing urine and also negatively impacts on motherhood experiences [7] and may contribute to more severe perineal lacerations and future pelvic floor dysfunction [3, 8].

The incidence of the procedure varies greatly throughout the world, in different hospitals and around the country, but in overall, about 70% to 80% undergo episiotomy during first vaginal delivery [9, 10]. Approximately 70% of women who have a vaginal birth will experience some degree of damage to the perineum, due to a tear or cut (episiotomy), and will need stitches [11]. This damage may result in perineal pain during the first few weeks after the birth, and some women experience long-term pain and discomfort during sexual intercourse. However, the prevalence of episiotomy is not the same in different countries; Asian race are presumed to have smaller and tighter perineum, so the routine episiotomy may reduce the risk of perineal tearing during delivery [12]. Episiotomy was performed in approximately 63% of all deliveries in the USA, with higher rates among women experiencing their first childbirth [13]. The incidence of episiotomies has been on the decline, from nearly 2 out of 3 vaginal births in 1979 to less than 1 in 5 in 2004 [14].

Despite this decline, obstetricians and midwives continue to over use this procedure ten times more often than is called for [3,15], and the practice of routine or selective episiotomy is still rampant in some countries and mostly in developing nations such as Nigeria [9].

Studies have shown that episiotomies were more common among women who had delivery for the first time than women who have delivered twice or more before (55% vs 12%) [14, 15]. Two types of episiotomy have been described, median and mediolateral. The mediolateral episiotomies are rarely associated with anal-sphincter lacerations. Therefore, it is more commonly practiced in the developing parts of the world [16].

The practice of routine episiotomy during hospital deliveries has been shown to be the principal risk factors for severe tearing during delivery, infection, loss of sexual pleasure and incontinence, all of which can be prevented [17]. In addition, women who had been subjected to episiotomies have pain experience and wound healing problems which was approximately two times higher than those who do not receive episiotomy [18, 19].

In recent times, there has been a great opposition to the routine use of episiotomy and it has become unacceptable in modern obstetric or midwifery practice [3, 20]. Even the World Health Organization has taken a stand against routine episiotomy especially among primiparae. In addition, the idea that episiotomy prevents third and fourth degree tears of the perineum or protects the pelvic floor has been repeatedly disapproved [21].

Although, episiotomy reduces duration of the second stage of labour which may be important for maternal reasons (e.g., hypertensive state) or foetal reasons (e.g., persistent foetal bradycardia), but the pain and discomfort associated with its use can interfere with mother-infant interactions and the reestablishment of parental sexual intercourse.

The risks associated with episiotomy have been identified. They are: increased maternal blood loss, increased postpartum pain and increased dyspareunia and opined that most women do not understand the indication for the relevance of episiotomy and even how to care for the incision during the postpartum period. Although, it is vital to give episiotomy in some situations, most women are not well informed and prepared for the procedure; hence, they may be generally dissatisfied with the birth experience. It is important to ensure that, before

any surgical procedure is performed, the client must be duly informed about the reason for the intervention and her informed consent gained. This study sought to determine the perception, experience and care of episiotomy among post-natal women attending selected health facilities in Ibadan.

Materials and methods

The study adopted a cross-sectional descriptive design to determine the perception, experience and care of episiotomy among postnatal women. The study was conducted across the three levels of health care system, namely: University College Hospital (UCH), Adeoyo Maternity Teaching Hospital and Primary Health Centre, Ojoo. One facility was chosen at each level of health care based on client flow. Respondents were selected also using purposive sampling, thus, only mothers who had previous delivery and were attending the postnatal/ infant welfare clinic were recruited to participate in the study. The total of 219 respondents were recruited for the study while the exclusion criteria are women who never had a vaginal delivery.

A 50-item validated structured questionnaire was used for data collection. The instrument has four sections: Section A elicited data on socio demographic characteristics of the respondents. Section B contained items on their obstetric history. Section C was made up of items on perception of episiotomy, while section D sought information about the experience and care of episiotomy among the women. The validity of the questionnaire was established through face and content validity criteria. Test-retest reliability was used to determine the reliability of the instrument. The instrument was administered on 10 mothers at State Hospital, Ring road, Ibadan Oyo State twice within 3 weeks interval.

The result was correlated using Spearman rho correlations with coefficient of 0.81. Ethical clearance for the study was obtained from UI/UCH Ethical Review Committee with assigned number UI/ EC/13/0286. The study complied with the ethical requirements of the various institutions used. Only mothers who consented to participate in the study were recruited. Participation was made voluntary and the right of any participant to withdraw from the study at any stage without any adverse consequences on the care they receive in the clinic was stressed to them. A total of 200 questionnaires were retrieved out of 219 distributed, giving a response rate of 92.2%.

Data generated were analyzed using descriptive and inferential statistics. Descriptive statistics include frequency tables, percentages and charts.

Results

Socio-demographic characteristic

Out of the 200 respondents that were studied, 117 (58.5%) were between 28 and 37years while 18 (9.0%) are 37years and above. Majority of the participants are married 197 (98.5%). A total of 163 (81.5%) of the respondents were from Yoruba ethnic group, while 76 (38.0%) of the respondents had Polytechnic education. Seventy (35.0%) were self-employed while 62 (31.0%) were unemployed.

The obstetric history reveals that 90 (45.0%) of the respondents have just had a child. Up to 64 (32.0%) had two children, 31 (15.5%) had 3 children, while just 15 (7.5%) had four or more children. The mode of first delivery for 164 (82.0%) of the respondents was spontaneous vaginal delivery.

Table 1: Socio-Demographic Characteristics of Respondents

Variables age in years	Frequency (n= 200)	Percentage (100%)
18-27	65	32.5%
28-37	117	58.5%
>37	18	9.0%
Marital Status		
Married	197	98.5%
Single	3	1.5%
Occupation		
Civil Servants	68	34.0%
Self Employed	70	35.0%
Unemployed	62	31.0%
Ethnic Groups		
Yoruba	163	81.5%
Ibo	29	14.5%
Hausa	8	4.0%
Educational Status		
No formal education	3	1.50%
Primary Education	9	4.50%
Secondary Education	56	28.00%
Polytechnic Education	76	38.00%
University Education	56	28.00%
Number of child/children		
1	90	45.0
2	64	32.0
3	31	15.5
>4	15	7.5
Mode of first delivery		
Spontaneous vaginal	164	82.0
Assisted	11	5.5
Caesarean section	19	9.5
No response	6	3.0

Perception of respondents about episiotomy

The perceptions of respondents concerning episiotomy as stated in table 2 show that 109 (54.5%)

of the respondents agreed that not all episiotomies given to a woman during delivery are necessary. Similarly, 170 (85.0%) affirmed that most women would have had safe delivery even without episiotomy. Feelings of pains and discomforts after episiotomy affect women's activities of daily living as claimed by 125 (62.5%). Up to 186 (93.0%) of respondents attested that self-perineal care instruction should be given to women by midwives during antenatal visits. Up to 190 (95.0%) respondents stated that if proper perineal care is done, it will aid effective healing and decision to perform episiotomy during child birth should be based only on attending midwives' discretion 141 (70.5%).

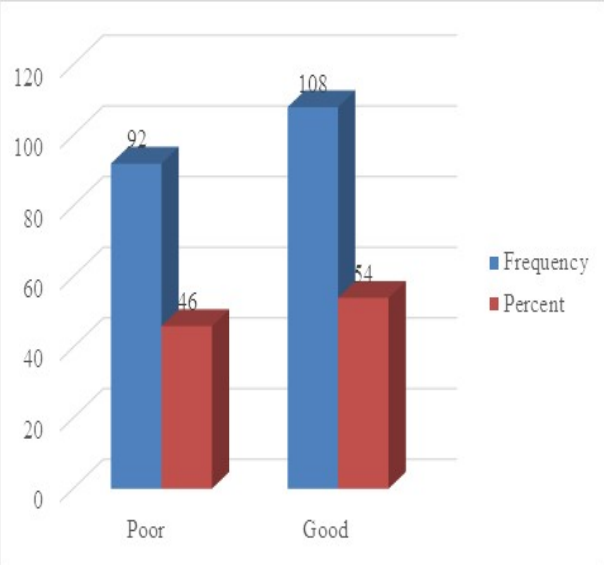

Fig. 1: Respondents' Level of Perception

Figure 1 shows that 108 (54.0%) of the respondents had a good perception of episiotomy whereas 92 (46.0%) had a poor perception towards episiotomy.

Respondents' episiotomy experience

Table 3 reveals respondents episiotomy experience. Out of the 200 respondents studied, 108(54.0%) had experienced episiotomy, while 92 (46.0%) had never experienced the procedure. Of those who had experienced episiotomy, 50 (46.3%) indicated that the reason for their experience of episiotomy was due to big nature of their babies. Other reasons mentioned were risk of perineal tear/rigid perineum 37(34.3%) among others. Fifty-nine (54.6%) of the respondents said informed consent was not obtained from them before they were subjecting them to episiotomy procedure but 47(43.5%) said their consent was sought.

Furthermore, table 4 shows that 78 (72.2%) of the respondents positively affirmed that they experienced pain and discomfort related to episiotomies they undergone. In the same vein, 69 (63.9%) of the respondents did not agree that their experience of pain and discomfort from episiotomy interfered with caring for their babies. Similarly, 63.9% also disagreed that the pain and discomfort from episiotomy interfered with sexual pleasure during intercourse.

Care of Episiotomy by Respondents

Episiotomy care methods utilized by respondents presented on table 5 shows that most 92 (85.2%) of

Table 2: Perception of respondents regarding episiotomy

Perception	Agree (%)	Disagree (%)	Undecided (%)
Episiotomy is sometimes given to a woman when it is not needed	109(54.5)	60(30.0)	31(15.5)
Many women would have had a safe delivery without episiotomy	170(85.0)	11(5.5)	19(9.5)
Episiotomy is very necessary for first time mothers	58(29.0)	123(61.5)	19 (9.5)
If a woman is to be given episiotomy she should be duly informed	110(55.0)	76 (38.0)	14(7)
Episiotomy distorts a woman's self esteem	84(42.0)	86(43.0)	30(15.0)
Feelings of pains and discomforts from episiotomy affects a woman's activities of daily living	125(62.5)	53(26.5)	22(11)
Most women do not enjoy sex after episiotomy	41(20.5)	106(53.0)	53(20.5)
It is better to have a natural tear than episiotomy	53(26.5)	110(55.0)	37(18.5)
Episiotomy doesn't heal on time compared to natural tear	35(17.5)	101(50.5)	64(32.0)
Self-perineal care instructions should be given to women by midwives	186(93.0)	4(2.0)	10(5)
If proper care is done, it will aid effective healing	190(95.0)	5(2.5)	5(2.5)
Pain relief measures should be given to women after episiotomy	185(92.5)	8(4.0)	7(3.5)
Decision to perform episiotomy during child birth should be based only on attending midwives discretion	141(70.5)	41(20.5)	18(9)

Table 3: Respondents' respondents' experience of episiotomy and reasons for episiotomy

Experience of episiotomy	Frequency N=200	Percentage (%)
Ever had episiotomy		
Yes	108	54.0
No	92	46.0
Reasons for Episiotomy	*Frequency N=108*	*Percentage (%)*
Big baby	50	46.3
Fetal distress	7	6.5
Assisted/instrumental baby	10	9.3
Risk of perineal tear/Rigid Perineum	37	34.3
Breech delivery/Face Presentation	3	2.7
Maternal exhaustion	1	0.9

Table 4: Episiotomy and Childbirth Experience

Episiotomy experience	Frequency	Percent (%)
Episiotomy made child birth experience	*n=108*	
Better	66	61.1
Worse	8	7.4
Not pleasurable	25	23.1
Faster	1	0.9
Had epidural	1	0.9
No response	7	6.6
Ways in which episiotomy made childbirth worse/unpleasant	*n=33*	
Sitting	16	48.5
Walking	3	9.1
Defecating	4	12.1
Urinating	9	27.3
No response	1	3.0
Experienced pain and discomfort from episiotomy	*n=108*	
Yes	78	72.2
No	25	23.1
Don't know	5	4.7
Pain and discomfort interfered with caring for baby	*n=108*	
Yes	31	28.7
No	69	63.9
Don't know	8	7.4
Pain and discomfort interfered with sexual intercourse with partner	*n=108*	
Yes	16	14.8
No	69	63.9
Don't know	23	21.3
Was informed and consent taken before episiotomy was performed	*n=108*	
Yes	47	43.5
No	59	54.6
Don't know	2	1.9

respondents were informed about episiotomy care by health workers. Up to 98 (58.3%) of those that received information used sitz bath while 62 (36.9%) practiced regular changing of pad and keeping vagina clean and dry. Eighty two (89.1%) out of the 96 that received information said the measures were effective in the care of episiotomy.

Test of Hypotheses

Ho1: There is no significant association between respondents' age and their experience of episiotomy X^2=0.167 p= 0.920, therefore, the null hypothesis is not rejected at p >0.05

Ho2: There is no significant association between respondents' perception and their experience of

Table 5: Respondents' care of episiotomy

Care of episiotomy	Frequency	Percentage
Received information on episiotomy care	*n=108*	
Yes	92	85.2
No	16	14.8
*Methods used for episiotomy care**		
Sitz bath	98	58.3
Regular changing of pad and keeping of vagina clean	62	36.9
Drugs	2	1.2
No Response	6	3.6
The method was effective		
Yes	82	89.1
No	3	3.3
Don't know	1	1.1
No response	6	6.5

*Note: * indicates multiple responses*

Table 6: Association between Variables

Ho1: Association between respondents' age and their experience of episiotomy

	Experience of episiotomy			
Age	Yes	No	X^2	p-Value
18-27	36(18.0)	29(31.5)	0.167	0.920
28-37	63(58.3)	54(58.7)		
>37	9(8.3)	9(9.8)		

Ho2: Association between respondents' perception and their experience of episiotomy

	Experience episiotomy			
Perception	Yes	No	X^2	p-value
Poor (<7)	46(42.6)	46(50.0)	1.097	0.295
Good (≥7)	62(57.4)	46(50.0)		

episiotomy $\mathbf{X^2}$= 1.097, p=0.295. Therefore, the null hypothesis is not rejected at p >0.05

Table 6 on test of Hypotheses showed no significant association between age and episiotomy experience X2 0.167 p=0.920, also there is no significant association between perception and experience of episiotomy. Both hypotheses were not rejected.

Discussion of findings

This study showed that the mode of delivery of the respondents was through spontaneous vaginal delivery and the duration of labour for their first vaginal delivery is between 6-15 hours which is acceptable in midwifery practice though it varies in individuals and subsequent babies [22]. Over 50% of the women in this study had episiotomy which is still higher than 10% recommended by World Health Organization which calls for continuous retraining of labour ward staff especially the midwives and other health professionals who usually conduct most of the deliveries [8]. The major reasons adduced for the procedure were big babies, risk of perineal tear and assisted/instrumental delivery. Other reasons mentioned were fetal distress, first vaginal birth/rigid perineum and abnormal presentations. All these reasons highlighted by participants corroborate with the indications stated for episiotomy in literatures reviewed.

It is noteworthy to say that the affirmation by Thacker and Banta [13] that most women do not understand the indication nor the relevance of episiotomy is negated by the results of these findings as majority of the respondents are aware of the indications of episiotomy performed on them during childbirth as stated above.

Although the methods of episiotomy care used by respondents' were effective, a greater proportion positively affirmed that they experienced

pain and discomfort from episiotomy, though the pain did not interfere with the care of their baby for most of them. Only a few agreed that the pain affected their ability to care for their baby, a few others said the pain affected their sexual pleasure. This is in line with the views of Kettle *et al* [11] that some women experienced long-term pain and discomfort during sexual intercourse as a result of episiotomy.

In general, the ways in which episiotomy made childbirth experience unpleasant as mentioned by respondents include sitting, walking, defecating and urinating. This is in conformity with Inyang-Etoh & Umioiyoh's [7] view that pains from episiotomy often interfere with basic daily activities of the women such as walking, sitting and passing urine and also negatively impacts on motherhood experiences.

According to the findings, 108 (54.0%) a little above average of respondents claimed they have had the intervention performed on them showing that the rate of the procedure in our environment is still higher than expected. This does not correspond with the report that the incidence of episiotomies is on the decline, from nearly 2 out of 3 vaginal births in 1979 to less than 1 in 5 in 2004 [14]. However, there is some agreement between these findings and the statement by American College of Obstetricians-Gynaecologists [10] which states that approximately 70% of women who have a vaginal birth will experience some degree of damage to the perineum, due to a tear or cut (episiotomy).

Among the respondents that had episiotomy, (92.0%) indicated that it was during their first vaginal delivery as compared to (7.1%) women who had delivered before. This finding is in congruence with that of Sule and Shittu, Sari *et al* [15,23] in their study titled Need for and consequences of episiotomy in vaginal birth which revealed that episiotomies were more common among women who are having delivery for the first time than women who has delivered before (55% vs 12%). The experience of episiotomy was not associated significantly with the women's age.

Conclusion

The findings revealed that the number of respondents that had episiotomy in this study is one hundred and eight (54.0%) which is still far higher than 10% recommended by World Health Organization as episiotomy procedure is becoming obsolete. Hence, skilled birth attendants should be abreast of the current management of second stage of labour especially for women having first childbirth vaginal delivery and reduced the routine use of episiotomy in order to avert the unpleasant consequences.

To achieve evidence-based recommendations for optimal care, trainings and retraining should be organized for midwives and other health professionals that are directly concerned with deliveries. Expectant mothers should be well educated during antenatal visits on measures to avoid need of episiotomy.

Recommendations

In light of the study findings, it is recommended that self-perineal care instruction can be introduced to the women during antenatal and then it can be used postnatal.

- Midwives should be knowledgeable about when to give episiotomy to further reduce its routine use and risks associated with the procedure
- Midwives should obtain informed consent before giving episiotomy so that the women can have a sense of self-esteem.
- Local anaesthesia should be administered before the procedure and analgesics given after delivery to alleviate the feelings of pain and discomforts
- The importance of relieving episiotomy pain and enhancing wound healing in postnatal mothers must be emphasized in all birth centres to promote satisfactory birth experience among childbearing age women.

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Comparing optical and ultrasound methods of axial length measurement for ocular biometry in a tertiary institution in Southwest, Nigeria.

AS Alabi[1], OT Aribaba[1], AO Alabi[2], A Rotimi-Samuel[1], AO Onakoya[1] and FB Akinsola[1]

Departments of Ophthalmology[1], Guinness Eye Centre and Radiotherapy[2], LUTH, Idi-Araba, Lagos, Nigeria.

Abstract

Introduction: Cataract extraction and artificial intraocular lens implantation is one of the most frequent and successful ophthalmic surgical procedures done today. One major challenge associated with cataract surgery is the accuracy of the intraocular lens power calculation necessary for attaining the desired post-operative refraction and this depends on accurate determination of pre-operative biometric data especially axial length.

Aim: The aim of the study was to compare the ultrasound and optical measurement of axial lengths (AXL) among Pre-operative Cataract Patients in the Department of Ophthalmology, Lagos University Teaching Hospital (LUTH), Lagos.

Methods: The study was a comparative cross-sectional study carried out among pre-operative cataract patients aged 40 years and above. All participating patients had axial length measurement with IOL Master, immersion ultrasound technique and contact ultrasound technique. Equipment used were SW-2100 Ophthalmic A/B Scan (Tianjin Suowei Electronic Technology Co., Ltd, China), Immersion Scleral Shell and IOL Master (Carl Zeiss Meditec AG, Jena, Germany).

Results: One hundred and thirteen eyes of 67 patients were included in the study and the mean age was 61.15 years (SD= 10.78 years). Axial lengths values with IOL Master were the highest with mean values of 23.72+/-1.13mm, followed by the immersion ultrasound technique with mean values of 23.31+/-0.91mm. The axial length by the contact ultrasound technique was the least with mean values of 23.28+/-1.04mm.

Conclusion: The difference in axial length measurements between the optical biometry and the two ultrasound techniques was significant.

Keywords*: Axial length, ultrasound biometry, optical biometry, contact technique, immersion technique, IOL Master.*

Correspondence: Dr. A.S. Alabi, Me Cure Eye Centre, Oshodi, Lagos State, Nigeria. E-mail: alabisundade@yahoo.com.

Résumé

Introduction : L'extraction de la cataracte et l'implantation des lentilles intraoculaires artificielles sont l'une des interventions chirurgicales ophtalmiques les plus fréquentes et les plus réussies à ce jour. Un défi majeur associé à la chirurgie de la cataracte est la précision du calcul de la puissance de la lentille intraoculaire nécessaire pour atteindre la réfraction postopératoire souhaitée, ce qui dépend de la détermination précise des données biométriques préopératoires, en particulier de la longueur axiale.

Objectif : Le but de l'étude était de comparer les mesures ultrasonores et optiques des longueurs axiales (AXL) chez les patients préopératoires de la cataracte au département d'ophtalmologie à l'hôpital d'enseignement universitaire de Lagos (LUTH) à Lagos.

Méthodes : L'étude était une étude transversale comparative menée auprès de patients atteints de cataracte préopératoire âgés de 40 ans et plus. Tous les patients participants ont eu une mesure de longueur axiale avec IOL Master, une technique par ultrasons par immersion et une technique par ultrasons par contact. Les matériels utilisésétaient le scanner SW-2100 ophtalmique A/B (Tianjin SuoweiTechnologie Electronique Co., Ltd, Chine), Immersion Scléral Shell et IOL Master (Carl Zeiss Meditec AG, Jena, Allemagne).

Résultats : Cent treize yeux de 67 patients ont été inclus dans l'étude et l'âge moyen était de 61,15 ans (écart-type = 10,78 ans). Les valeurs de longueur axiale avec IOL Master étaient les plus élevées avec des valeurs moyennes de 23,72 ± 1,13 mm, suivies par la technique àultrasons par immersion avec des valeurs moyennes de 23,31 ± 0,91 mm. La longueur axiale par la technique à ultrasons de contact était la plus faible avec des valeurs moyennes de 23,28 ± 1,04 mm.

Conclusion : La différence de longueur axiale entre la biométrie optique et les deux techniques ultrasonores était significative.

Mots - clés *: Longueur axiale, biométrie à ultrasons, biométrie optique, technique de contact, technique d'immersion, IOL Master.*

Introduction

Cataract is the most common cause of blindness and severe visual impairment in Nigeria responsible for 43% and 45.3% respectively [1]. Cataract extraction and artificial intraocular lens implantation is one of the most frequent and successful ophthalmic surgical procedures done today [2,3]. One major challenge associated with cataract surgery is the accuracy of the intraocular lens power calculation necessary for attaining the desired post-operative refraction and this depends on accurate determination of pre-operative biometric data [4,5]. The accurate estimation of the appropriate power of intraocular lens is key to the success of contemporary day cataract surgery and the aim of accurate power calculation is to provide an intraocular lens (IOL) that fits the specific needs and desires of the individual patient, and not the routine of the surgeon [6].

Biometry is a vital pre-operative step in modern cataract surgery as the surgical removal of the crystalline lens deducts approximately 20 Dioptres from the refractive power of the human eye [7]. Therefore eyes without lenses are grossly hypermetropic, but today's cataract surgery alleviates this challenge through the implantation of intraocular lens ideally in the same location as the crystalline lens [7]. The curvature of the anterior corneal surface (keratometry), expressed in dioptres or millimeters of curvature, the anterior chamber depth expressed in millimeters and the anteroposterior dimension of the eye (axial length), expressed in millimeters are the key parameters required for lens power calculation which is a well-established field of ocular biometry [8-10]. The accurate determination of desired post cataract surgery refraction depends on minimization of errors associated with the measurement of these parameters [4,11,12].

The axial length can be determined using either the ultrasound method or the optical method [4,5,13]. The ultrasound method can either be by the applanation technique, where the ultrasound probe is in direct contact with the cornea which is commonly used, or by the immersion technique, where the ultrasound probe does not come in direct contact with the cornea which is considered to give a more accurate result [4,14].

Ultrasound biometry performed using the contact technique causes compression of the cornea; this reduces the anterior chamber depth and influences the axial length. The applanation distorts the measuring process and the calculation of the final dioptric power of the intraocular lens [14]. The immersion technique where the probe tip does not come in contact with the cornea, but coupled to the eye through a fluid in a shell placed on the cornea is preferred over the contact (applanation) technique, as there is no corneal compression [4,14].

The optical method of axial length measurement is based on the principle of partial coherence interferometry (PCI) and reached its application maturity with the innovation of the IOL master [12]. The optical biometry does not require contact with the globe so corneal compression artefacts are eliminated [12,13].

The purpose of this study was to compare axial lengths measured by IOL Master with those measured by the contact ultrasound and immersion ultrasound techniques. The paucity of local studies and the limited availability of optical biometry, despite increasing number of cataract surgeries with intraocular lens implant and the increasing demand for optimal visual outcome after cataract surgery make this study relevant at this time.

Materials and methods

Study design

The study was a cross sectional comparative study conducted on all consenting consecutive patients, aged 40 years and above scheduled for cataract extraction at the Department of Ophthalmology, Lagos University Teaching Hospital (LUTH) after ethical clearance was obtained from the ethical board of the same institution. The study compared optical technique, ultrasound immersion technique and ultrasound contact technique of axial length measurement. Equipment used were SW-2100 Ophthalmic A/B Scan (Tianjin Suowei Electronic Technology Co., Ltd, China), Immersion Scleral Shell and IOL Master (Carl Zeiss Meditec AG, Jena, Germany). The axial length measurements using the three methods were performed by the same experienced observer to eliminate inter-observer error.

The optical determination of their axial length was with the IOL Master. Ten acceptable measurements were taken for the axial length. The average of these measurements automatically calculated by the machine was taken as the measured value. In addition readings obtained with the signal-to-noise ratio (SNR) value two (2) or greater as recorded by the IOL Master Machine were taken.

The ultrasonic axial length determination (immersion technique) used the A-scan probe (transducer) placed perpendicularly/ vertically and made to touch the normal saline in the central portion of the scleral immersion shell without touching/ depressing the cornea. The probe was a 10MHz solid probe, with built-in fixation light, with a depth

detection range of 15mm to 35mm for the axial length. The measurement gain was set at 70decibels. An automated sequence of ten (10) readings was taken. Unreliable readings were discarded with standard deviation of the final set < 0.12.The axial length was recorded in millimetres and in two decimal places. The ultrasonic axial length determination (contact technique) was similar to the immersion technique but without immersion shell with the probe placed directly on the cornea.

All patients were assessed and individuals with axial length 20mm to 29mm were included in the study. While those with axial length less than 20mm, greater than 29mm, corneal pathologies, previous corneal surgeries and allergy to topical anaesthetics were excluded.

Informed consent was duly obtained from each study participant. A pilot study was conducted with ten patients not selected for the actual study. This was used for the calibration of the IOL Master and SW2100 A scan machines. Information collected includes age, sex, eye measured, optical axial length, ultrasonic immersion axial length, and ultrasonic contact axial length.

The potential source of bias in this study was the measuring techniques used for the three methods of axial length determination. This was minimized as the parameters were measured by one experienced observer and the steps for measurement as stated in the methodology were painstakingly followed by the observer.

Data were analysed with Statistical Package for Social Sciences (SPSS) version 20. Statistical significance of any observed difference between the findings of two techniques were determined using paired 't' test. Agreements among the findings of the techniques were determined using Pearson correlation test. Statistical significance for all comparisons was given as p value < 0.05.

Results

One hundred and thirteen (113) eyes of 67 patients had measurement of their axial length determined. The mean age was 61.15 years +/- 10.78. Table 1 showed the age and sex distribution of the patients. There were more female participants than male participants as depicted in table 1, with M: F ratio of 1:1.5. Furthermore, more left eyes (63) than right eyes (50) were measured during the study.

Table 1: Age And Sex Distribution of the Patients

Age group (In years)	Male N=27	Female N=40	Frequency	Percentage (%)
40 – 49	4	5	9	13.4
50 – 59	10	11	21	31.3
60 - 69	3	13	16	23.9
≥70	10	11	21	31.3

Mean Age 61.15 ± 10.78

Table 2, shows the descriptive statistics of axial length by the three methods. The values of the axial length measurements of the 113 eyes by the IOL Master were the highest, followed by the immersion method and least with the contact ultrasound method.

Table 3, compared the axial length measurements by ultrasound immersion technique with the axial length measurements by ultrasound contact technique, showing that the mean measurement of the 113 eyes by immersion technique (23.31+/- 0.91) was longer than that by the contact technique(23.28+/- 1.04) with a mean difference of 0.03mm.

Table 2: Descriptive statistics of axial lengths by the three methods

Measurements Axial Lengths (n=113)	Mean ± SD (mm)	Range (mm)
Contact USS AXL	23.28 ± 1.04	20.24 - 25.63
Immersion USS AXL	23.31 ± 0.91	21.13 - 25.61
IOL Master AXL	23.72 ± 1.13	21.12 – 28.27

A paired-samples t-test was conducted to evaluate the difference between the AXL measured by contact and immersion techniques. The axial lengths of the 113 eyes measured by the Immersion method were not significantly longer than those measured by ultrasound Contact technique, (t (113) = -0.45, p=0.65).

Table 5, compared the axial length measurements by ultrasound immersion technique with the axial length measurements by the IOL Master, showing that the mean measurement of the 113 eyes by the IOL Master (23.72+/- 1.13) was longer than that by the ultrasound immersion technique (23.31+/- 0.91) with a mean difference of 0.41mm.

A paired-samples t-test was conducted to evaluate the relationship between the AXL measured by ultrasound Immersion method and IOL Master. The axial lengths measured by the IOL master were significantly longer than those measured by ultrasound Immersion technique,(t (113) = -4.69, p <0.0005).

Table 6, there was positive correlation between the axial lengths measured by the three

Table 3: Comparison between Ultrasound Immersion AXL and Ultrasound Contact AXL

Paired Variable	Mean (mm)	Mean Difference (mm)	t	Df	P
Contact USS Immersion USS	23.28 ± 1.04 23.31 ± 0.91	-0.03	-0.45	112	0.65

Table 4: Comparison between Ultrasound Contact AXL and IOL Master AXL

Paired Variable	Mean (mm)	Mean Difference(mm)	t	Df	P
Contact USS	23.28 ± 1.04	-0.44	-4.47	112	< 0.000
IOL Master	23.72 ± 1.13				

Table 5: Comparison between Ultrasound Immersion AXL and IOL Master AXL

Paired Variable	Mean (mm)	Mean Difference (mm)	t	Df	P
Immersion USS IOL Master	23.31 ± 0.91 23.72 ± 1.13	-0.41	-4.69	112	< 0.0005

Table 6: Pearson Correlation between Immersion, Contact and IOL Master AXL

	Contact AXL (n=113)	Immersion AXL (n=113)	IOL Master AXL (n=113)
Contact AXL	1	0.749**	0.540**
Immersion AXL	0.749**	1	0.604**
IOL Master AXL	0.540**	0.604**	1

*** Correlation statistically significant at 0.001*

methods and these relationships were statistically significant. Correlation between axial length measured by immersion and axial length by contact method was positive and significant at r = 0.749. Similarly, correlation between axial length measured by contact ultrasonic and IOL Master was positive and significant at r = 0.540. Correlation between axial length measured by immersion ultrasonic and IOL Master was also positive and significant at r = 0.604.

Discussion

This study was a hospital based comparative cross-sectional study conducted among patients, who visited the investigation room of the Department of Ophthalmology, LUTH for pre-operative biometry. One hundred and thirteen eyes of 67 patients out of the 120 eyes recruited eventually had their measurements analysed in the study, with a record of 94.17% participation among the recruited eyes. The reasons for the drop out were incomplete data, missed data and wide variation in data.

The mean age of the patients was 61.15 years (SD=10.78) with 71.64% of them being 55 years or older. The mean age of this study is similar to several other studies [15-17]. This is relevant bearing in mind that age-related cataract is the leading cause of blindness and low vision globally, accounting for nearly 51% of all world blindness, with an estimated 20 million people blind from the disease [18,19]. Globally, cataracts cause moderate to severe visual impairment in 53.8 million, 52.2 million of whom are in low and middle income countries [19].

The study recorded a male-to-female ratio of 1:1.5, showing that more females (59.7%) visited the investigation room of the Department of Ophthalmology, LUTH for biometry. Some similar studies also recorded more female than male [16,20-22]. Observations often have shown that more females than males have cataract and undergo cataract surgery. This may be explained by the longer life span of women and therefore their over-representation in the age groups where cataract is most common.

This study elucidated that the IOL Master (optical technique) gave the longest measurements of axial length, with a mean value of 23.73mm (SD=1.13), followed by the immersion ultrasonography with a mean value of 23.31mm (SD=0.91) and the contact ultrasonography gave the shortest measurements of axial length with a mean value of 23.28mm (SD=1.04). This pattern is similar to study by Sanchis-Gimeno and co-worker [21], where the axial length measurement with the IOL Master and the immersion ultrasonography were longer, with a mean value of 23.70 mm and the axial length measurements with contact ultrasound was shorter, with mean value of 23.60mm. However in contrast to our study, Sanchis-Gimeno and colleagues [21] found that the difference in measurements was not statistically significant. This may be due to the small sample size of 30 used in their study.

The axial length measurements by the IOL Master were significantly longer than the axial length measurements by either the contact or the immersion ultrasonic method; however the values obtained by the three methods were closely correlated. This study agrees with Several Studies [20,22,23] that compared optical axial length measurements versus contact ultrasonic axial length measurements and reported statistically significant difference, in which the optical values were longer. Nemeth and colleagues [23] in their study that reported a significantly high correlation co-efficient (r= 0.985) between optically measured axial length values and contact ultrasonic values, in which the optical values were significantly higher, similar to the finding of this study.

Furthermore, the significantly high correlation co-efficients recorded in this study for the axial length measurements of the three methods show similarity to some other studies [20,21].

The explanation for the difference in axial length (AXL) measurements may be a consequence of the different measuring points between the optical (IOL Master) and the ultrasonography (contact and immersion techniques) methods. The optical method measures the axial length along the visual axis, whereas the ultrasonic methods measure the axial length along the optical axis. Moreover, the optical method measures from the tear film to the Retinal Pigment Epithelium (RPE), while the ultrasound wave is reflected at the Internal Limiting Membrane (ILM). This results in a difference that is equivalent to the retinal thickness of the fovea, which is about 130microns [24].

In addition, an important reason for this difference may be the pressure exerted on the globe by the ultrasound probe during contact ultrasonic measurement, which can result in corneal indentation and shortening of the axial length. However, immersion ultrasonic method helps to minimize the indentation of the cornea, thereby making immersion axial length measurement closer to those of the IOL Master.

All patients that participated in this study preferred the IOL Master to the ultrasonic techniques for the reason that it is non-contact and thus, the

most convenient and comfortable of the three methods. Similar observation was reported by Eletheriadis [20] in his study.

Conclusion

This study demonstrated that axial length measurements were highest with the IOL Master optical biometry and least with the contact technique ultrasonic biometry. The difference in measurements between the optical biometry and the two ultrasonic techniques was significant, however, with Pearson's correlation. The IOL Master optical biometry should be made the gold standard in axial length determination. Centres not equipped with IOL Master should use immersion technique ultrasound biometry instead of contact technique ultrasound biometry, as axial lengths measured with immersion technique are closer and correlate more to the axial lengths measured with IOL Master optical biometry.

Further scientific research to fully elucidate the effect on IOL power determination is required.

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Knowledge of glaucoma management among glaucoma patients on medical therapy in a tertiary hospital

A Aina[1], O Olawoye[2], T Oluleye[2], I Uyanne[1] and I Aina[3]
Ophthalmology Unit, Department of Surgery[1], Bowen University Teaching Hospital Ogbomoso, Departments of Ophthalmology[2] and Radiology[3], University College Hospital, Ibadan Oyo-State.

Abstract
Aim: To determine the level of knowledge of glaucoma management among glaucoma patients on medical therapy attending Bowen University Teaching Hospital Ogbomoso.
*Method***:** The study was a descriptive hospital-based cross-sectional study which was conducted between January and October 2016 at the eye clinic of Bowen University Teaching Hospital Ogbomoso Oyo-State. Patients with primary open angle glaucoma (POAG) aged 40 years and above were recruited into in the study. Semi-structured questionnaire was used to obtain socio-demographic data, medical history and patient's knowledge about glaucoma management. Data was analyzed using IBM SPSS software version 21. Level of statistical significance was set at p-value <0.05.
*Result***:** A total of 180 patients participated in this study. Mean age of the patients was 67.9 ± 10.5years (range 40-85 years). Only 18(10%) of the patients had a good knowledge of the purpose of glaucoma treatment. Less than half (48.3%) of the participants could recall the names of their anti-glaucoma medications. Younger age, having no formal education and unskilled employment were associated with poor knowledge of glaucoma.
Conclusion: Patient's knowledge about glaucoma management was very poor in this study. We recommend that ophthalmologists should put up strategies for better patient education about glaucoma and its management. Glaucoma support groups should be established to improve dissemination of information about glaucoma.

Keywords: *Glaucoma, ophthalmologists, management, semi-structured.*

Résumé
Objectif : Pour déterminer le niveau de connaissancede la gestion du glaucome chez les patients atteints du glaucome visitant l'Hôpital d'Enseignement Universitaire de Bowen, Ogbomosho pour la thérapie médicale.
Méthode **:** L'étude était une étude transversale descriptive réalisée dans un hôpital, qui était mené entre janvier et octobre 2016 à la clinique ophtalmologique de l'Hôpital d'Enseignement Universitaire de Bowen, Ogbomosho Oyo-State. Les patients atteints de glaucome à angle ouvert primaire (GPAO) âgés de 40 ans et plus ont été recrutés dans l'étude. Un questionnaire semi-structuré a été utilisé pour obtenir des données sociodémographiques, les antécédents médicaux et les connaissances des patients sur la gestion du glaucome. Les données ont été analysées à l'aide du logiciel IBM SPSS version 21. Le niveau de signification statistique a été fixé à une valeur p <0,05.
Résultat **:** 180 patients au total ont participé à cette étude. L'âge moyen des patients était de 67,9 ± 10,5 ans (rangeant de 40 à 85 ans). Seulement 18 (10%) des patients connaissaient bien le but du traitement du glaucome. Moins de la moitié (48,3%) des participants pouvaient se rappeler les noms de leurs médicaments anti-glaucome. Le jeuneâge, l'absence d'éducation formelle et un emploi non qualifié étaient associés à une faible connaissance du glaucome.
Conclusion : Les connaissances des patients sur la gestion du glaucome étaient très faibles dans cette étude. Nous recommandons aux ophtalmologistes de mettre en place des stratégies pour une meilleure éducation des patients sur le glaucome et son traitement. Des groupes de soutien du glaucome devraient être mis en place pour améliorer la diffusion des informations sur le glaucome.

Mots clés : *Glaucome, ophtalmologistes, gestion, semi-structuré*

Introduction

Glaucoma is the leading cause of irreversible blindness and the second leading cause of blindness globally [1, 2]. In the year 2013, the global prevalence of glaucoma was reported to be 3.54% (approximately 64 million people) for the population aged 40–80 years [1]. This was estimated to increase to 76million in year 2020 and 111.8 million in year 2040 [1]. This major increase is expected from Asia and Africa and is

Correspondence: Dr. Akinsola S. Aina, Ophthalmology Unit, Department of Surgery, Bowen University Teachng Hospital, Ogbomoso, Nigeria. E-mail: solarhema2013@yahoo.com

attributable to the expected change in the number of older persons (increased life expectancy) in these regions. The prevalence of glaucoma from a study done in Ghana was 8.4% for the population aged 30years and above [3] while 6.9% was reported for a population based study in south-western Nigeria [4].

Glaucoma is one of the major causes of blindness in Africa and is reported to blind 147,000 people in the Nigerian population aged over 40 years [5,6] The Nigerian National Blindness and Visual Impairment Survey showed that glaucoma accounted for 0.7% of the prevalence of blindness [5]. Primary Open Angle Glaucoma (POAG) is a painless condition therefore patients often present with advanced disease, sight loss and massive optic nerve damage [7]. As a result of this, there is the need to adopt strategies that will improve the awareness among the population at risk and effectively manage the identified cases thereby preventing glaucoma blindness. Good knowledge of glaucoma is very important, as the disease has been shown to reduce quality of life even in the early stages and this worsens with increased severity [8].

Glaucoma management is mainly based on intraocular pressure (IOP) reduction. This IOP reduction can be achieved in two broad ways; namely, medical and surgical (including laser). Medical management is not just administering drugs to patients, it involves educating the patient about the use of the drugs, its effect in altering glaucoma disease course, its side effects and other alternatives available to patients in managing this lifelong disease.

One of the factors that improve level of compliance in glaucoma patients is health education which is aimed at improving their knowledge about glaucoma management [9]. Educating the patient, simplifying treatment regimens, involving care-providers and customization to the patient's lifestyle had been shown to improve compliance [10]. A study done in an urban tertiary care hospital of North India on knowledge of glaucoma patients concerning medications concluded that there was a need to better educate patients by providing them detailed information [11]. This would help to reduce patients' frustration, improve compliance, and increase the efficacy of anti-glaucoma therapy [11]. In order to make health education achieve its desired objective, it should be aimed at filling up the gaps that exists in knowledge among the targeted population. This may improve compliance with medications in the patients, delay glaucoma progression and ultimately prevent avoidable blindness which is one of the aims of vision 2020 (The Right to Sight).

The aim of this study was to determine the level of knowledge of glaucoma management among glaucoma patients on medical therapy attending Bowen University Teaching Hospital Ogbomoso in order to guide the development of appropriate teaching materials that will be relevant for providing health education to glaucoma patients.

Methods

This study was a descriptive hospital-based cross-sectional study which was conducted between January and October 2016 among patients with POAG on medical therapy attending the eye clinic of Bowen University Teaching Hospital (BUTH), Ogbomoso Oyo state Nigeria. Inclusion criteria were patients with POAG aged $\geq$ 40 years who had been on medical management for glaucoma for a minimum of 6 months prior to the study. Glaucoma patients who have had glaucoma surgery done on any of the eyes and those with other ocular co-morbidity causing poor vision were excluded from the study. Total sampling of consecutive patients that met the inclusion criteria during the study period (January and October 2016) was done. History of medical illnesses such as hypertension, diabetes mellitus and chronic obstructive pulmonary airway disease in the participants was obtained.

Semi-structured questionnaire was used to obtain the socio-demographic data, medical history and their knowledge about glaucoma management. The definitional criteria of International Society of Geographical and Epidemiological Ophthalmology (ISGEO) [12]for glaucoma was used in making the diagnosis and to reaffirm the diagnosis in those earlier diagnosed. ISGEO criterion 2 was used to make diagnosis in patients that could not satisfactorily complete the visual field test. Respondents who provided correct answers to at least 75% of the questions on glaucoma symptoms, risk factors, investigations and purpose of treatment were categorised as having good knowledge. The questionnaire was pretested and appropriate corrections made to standardize it.

The data obtained was entered into the computer and analyzed using IBM SPSS software version 21. The age distribution, gender and socio-demographic characteristics, medical history and knowledge of glaucoma management were presented using frequency tables and charts. Chi-square test was performed to determine the effect of socio-demographic characteristics on the knowledge of

glaucoma management. The level of statistical significance was set at p-value <0.05.

Table 1: Socio-demographic characteristics of respondents

Parameters	Frequency N= 180	Percentage (%)
Age (years)		
40-49	11	6.1
50-59	17	9.4
60-69	66	36.7
70-79	64	35.6
≥ 80	22	12.2
Sex		
Male	98	54.4
Female	82	45.6
Marital status		
Married	146	81.1
Widowed	34	18.9
Type of family		
Monogamous	144	80.0
Polygamous	36	20.0
Tribe		
Yoruba	168	93.4
Igbo	6	3.3
Others	6	3.3
Educational level		
No formal education	40	22.2
Primary education	76	42.2
Secondary education	47	26.1
Tertiary education	17	9.5
Others		
Occupation		
Unemployed	6	3.3
Farmer	6	3.3
Artisan/labourer	41	22.8
Trader	92	51.2
Retired	29	16.1
Other professional	6	3.3
Average monthly income to household(1$ = ¦ 480)		
<$37.5	53	29.5
$37.5 -$75	52	28.9
>$75 -$175	58	32.2
>$175 -$300	11	6.1
>$300	6	3.3
Religion		
Christianity	152	84.4
Islam	28	15.6
Total	180	100.0

Approval for this study was obtained from the Bowen University Teaching Hospital institutional ethical committee. Informed consent was obtained from each participant. The study conformed to the principles and tenets of the declaration of Helsinki for studies on human subjects.

Results

One hundred and eighty glaucoma patients participated in this study. The mean age of the patients was 67.9 ± 10.5 years. The median age was 69years (range 40 to 85years). About two-fifth (40%) of the patients were between the ages of 60 – 69 years (Table 1). There were 98 (54.4%) males and 82 (45.6%) females with male to female ratio of 1.2: 1. Other sociodemographic characteristics are presented in table 1.

Duration of glaucoma diagnosis and treatment.

All the patients commenced anti-glaucoma medication at the time of first diagnosis. A significant proportion of the patients 70 (38.9%) had been on anti-glaucoma medication for more than five years as shown in figure 1.

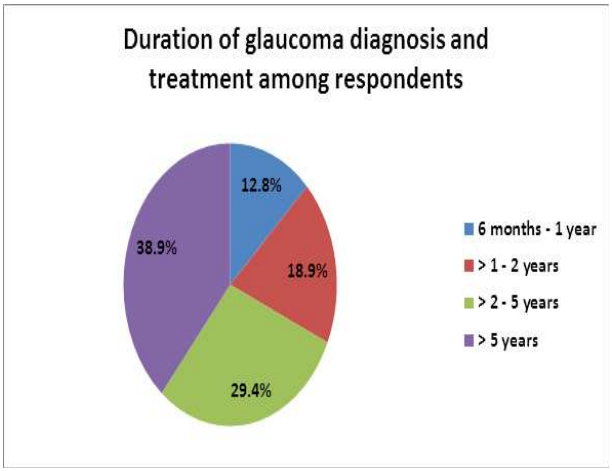

Fig.1. Duration of glaucoma diagnosis and treatment among respondents

Other medical co-morbidities.

Systemic hypertension was the most common medical disease among the patients occurring in 104 (57.8%) of the patients while COPD only occurred in 5 (2.8%) patients as shown in table 2.

Knowledge of glaucoma management

Only 18 (10%) patients knew the purpose of glaucoma treatment as shown in figure 2. Good knowledge about the symptoms and risk factors was demonstrated in 108(60%) of patients and 103 (57.2%) patients had good knowledge of investigations for glaucoma. Less than half 87 (48.3%) of the patients were able to recall the names of the anti-glaucoma medications they were presently using. The attending doctor was the source of knowledge about glaucoma management in 174(96.7%) of the patients.

Table 2: Medical history of patients.

Medical Condition	Frequency (N=180)	Percentage (%)
Diabetes Mellitus		
Yes	39	21.7
No	141	78.3
Total	180	100.0
Hypertension		
Yes	104	57.8
No	76	42.2
Total	180	100.0
*COPD**		
Yes	5	2.8
No	175	97.2
Total	180	100.0
Other medical diseases		
Yes	12	6.7
No	168	93.3
Total	180	100.0

**Chronic Obstructive Pulmonary Disease*

Discussion

Our study shows that most of the patients had poor knowledge of the purpose of glaucoma management. This was similar to the finding from a study [13] in northern Nigeria where only 17% of the respondents had good knowledge of glaucoma. Several other studies found out that patients' knowledge of glaucoma is low and there is the need to improve it since it directly affects treatment success [11,14-17]. Glaucoma also being a painless slowly progressive disease may make many patients pay poor attention to its management. Our study noted that younger individuals, widow hood, having no formal education and being an unskilled worker were associated with poor knowledge of glaucoma among patients. This was similar to findings of a study which reported low educational level and low socioeconomic status as factors associated with poor knowledge among glaucoma patients [13]. Despite the fact that there was poor knowledge concerning the purpose of glaucoma management in this study, more than half of the patients still had good knowledge of symptoms, risk factors of glaucoma and knowledge of the investigations that had been carried out on them. Many of the patients who presented to the hospital already had symptoms because they were presenting at a late stage of the disease.

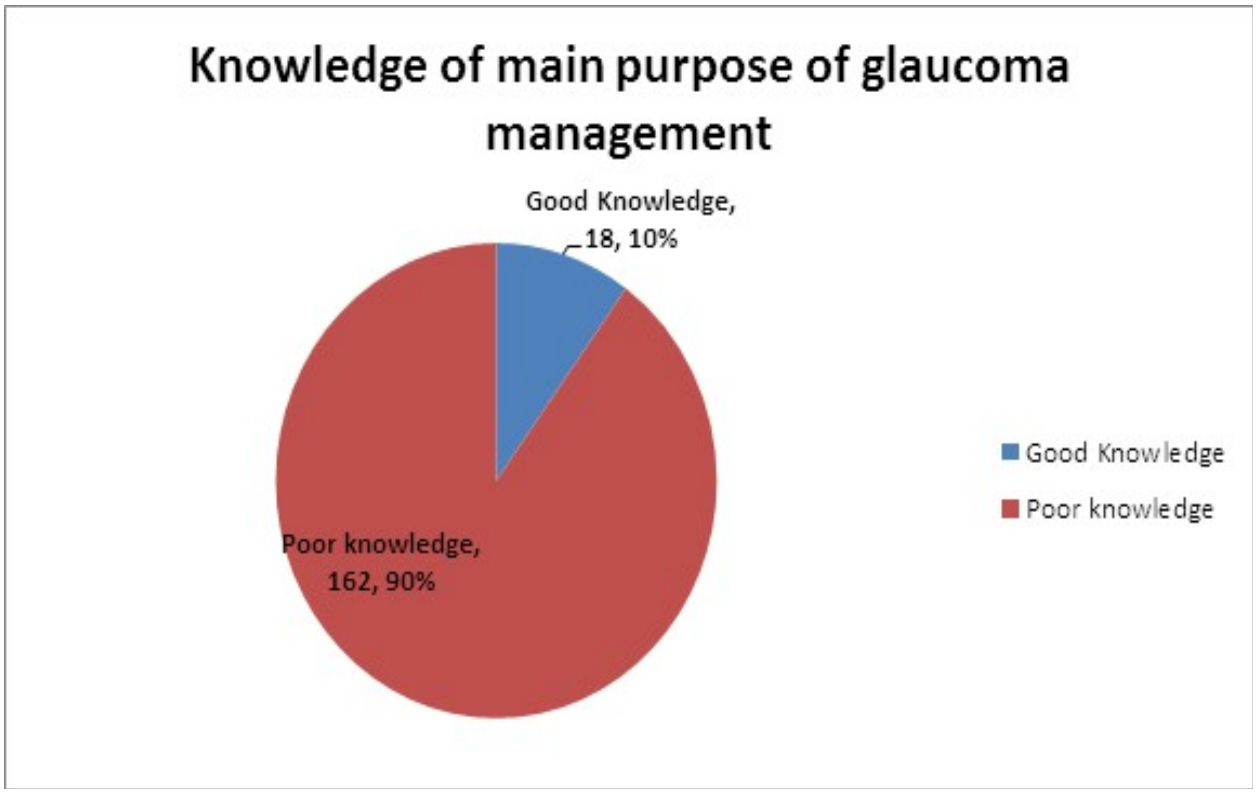

Fig. 2

Effect of sociodemographic characteristics on knowledge of the purpose of glaucoma management. Age, marital status, educational level and occupation of respondents were significantly associated with knowledge of the purpose of glaucoma management as shown in table 3.

Table 3. Effect of socio-demographic characteristics on knowledge of the purpose of glaucoma management.

Variables	Knowledge of Glaucoma			Pearson Chi-Square(χ^2)	p-value
	Good. (%)	Poor. n(%)	Total. n(%)		
***Age (years)*				11.034	0.000*
40-65	0(0.0)	64(100.0)	64(100.0)		
>65	18(15.5)	98(84.5)	116(100.0)		
Sex				3.594	0.058
Male	6(6.1)	92(93.9)	98(100.0)		
Female	12(14.6)	70(85.4)	82(100.0)		
***Marital Status*				4.658	0.027*
Married	18(12.3)	128(87.7)	146(100.0)		
Widowed	0(0.0)	34(100.0)	34(100.0)		
****Tribe*				1.429	0.613
Yoruba	18(10.7)	150(89.3)	168(100.0)		
Non Yoruba	0(0.0)	12(100.0)	12(100.0)		
***Educational level*				5.714	0.014*
No formal education	0(0.0)	40(100.0)	40(100.0)		
Formal education	18(12.9)	122(87.1)	140(100.0)		
Occupation				4.899	0.027*
Skilled	12(15.8)	64(84.2)	76(100.0)		
Unskilled	6(5.8)	98(94.2)	104(100.0)		
Average monthly income **to household (1**$ = N480**)**				0.571	0.450
Below**$**75	12(11.4)	93(88.6)	105(100.0)		
Above**$**75	6(8.0)	69(92.0)	75(100.0)		
Number of dependents				2.860	0.091
None	6(6.4)	88(93.6)	94(100.0)		
Dependents	12(14.0)	74(86.0)	86(100.0)		
Religion				4.812	0.028*
Christianity	12(7.9)	140(92.1)	152(100.0)		
Islam	6(21.4)	22(78.6)	28(100.0)		
***Duration of glaucoma treatment*				2.930	0.134
≤ 1year	0(0.0)	23(100.0)	23(100.0)		
Above 1 year	18(11.5)	139(88.5)	157(100.0)		
Family history of glaucoma				1.100	0.294
Yes	6(7.4)	75(92.6)	81(100.0)		
No	12(12.1)	87(87.9)	99(100.0)		

N = 180, *p value < 0.05 (i.e significant) ** p value was obtained from Fisher's exact test

Increasing age is one of the risk factors for glaucoma which was similar to the findings of other studies [4,16,18,19] on glaucoma. Prevalence of glaucoma increases with age in all populations. The Yorubas were the dominant ethnic group in this study. These findings were also in keeping with findings of similar studies in the southwestern region of Nigeria [4,18]. The proportion of the patients with diabetes in this study was similar to the findings of a study done in Rivers state, Nigeria where the proportion of patients with diabetes was 20% [20]. However the proportion with systemic hypertension was slightly higher (57.8%) in this study compared to the proportion (33.3%) reported in Rivers state. Increasing age is a risk factor for these chronic medical diseases hence these diseases frequently coexist with glaucoma [21].

Less than half of the patients (48.3%) could recall the name of the anti-glaucoma medications they were using. This was higher than the findings of a study done by Osman *et al* in Saudi Arabia where only 16.1% of the respondents were able to recognize their anti-glaucoma medications [19]. This might be related to the literacy level of patients or the

importance attached to their anti-glaucoma medications. This study showed that many of our patients (96.7%) got their knowledge about glaucoma from the attending ophthalmologist nevertheless the patients' knowledge about their disease is still inadequate. Although it is important for ophthalmologists to discuss with their patients, they may not be able to provide all the information required for adequate patient knowledge in a busy glaucoma clinic. Therefore we recommend that a counselling unit is incorporated in the glaucoma clinic where properly trained counsellors can help to further enhance patients' knowledge about their disease. We also recommend that locally relevant and targeted health education materials be developed by ophthalmologists to further enhance glaucoma patients' understanding of their treatment.

Conclusion

This study found out that there was poor knowledge about glaucoma management among glaucoma patients on medical therapy attending Bowen university teaching hospital Ogbomoso, Oyo State. Young individuals, widows, individuals with no formal education and unskilled workers were more likely to have low level of glaucoma knowledge in this study. Ophthalmologists should put together series of health education programmes targeted at ensuring that glaucoma patients have good understanding of the purpose of their disease management. This is likely to be a motivation factor in achieving good compliance in them. Glaucoma counselling unit should be established in Bowen University Teaching Hospital Ogbomoso Oyo State, Nigeria.

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Refractory oedema treated with modified peritoneo-venous shunt in Nephrotic Syndrome Patients

MO Hassan[1], FA Arogundade[1], KA Adelusola[2], AA Sanusi[1], OO Okunola[1], BA Omotoso[1], SO Oguntola[1] and A Akinsola[1].

Renal unit, Departments of Medicine[1] and Morbid Anatomy[2], Obafemi Awolowo University Teaching Hospital Complex, P.M.B 5538, Ile-Ife, Osun State, Nigeria

Abstract

Background: Refractory oedema remains a challenge in nephrotic syndrome patients. Repeated paracentesis sometimes results in hypotension and invariably acute kidney injury. Intravenous re-infusion of ascitic fluid, a modified form of peritoneo-venous shunt (MPVS) is an alternative treatment modality targeted at preventing haemodynamic instability and correction of hypoproteinemia. We assessed the usefulness and safety of MPVS among nephrotic syndrome patients with refractory oedema.

*Methods***:** Twenty six consecutive patients with refractory oedema were recruited. A total of 165 sessions of MPVS were performed using peripheral vein. Evaluation of treatment was done by assessment of weight, abdominal girth, urine volume, urinary protein and serum protein. Renal biopsy was performed to determine histological diagnosis. Data were analyzed using statistical package for social sciences (SPSS) version 16.

*Results***:** Compared to baseline parameters, the median weight (58.5 versus 85.5 kg, p<0.001); abdominal girth (89.3 versus 110.0 cm, p<0.001); and urinary protein excretion (1.7 versus 5.2 g/24hrs, p<0.001) at 8 weeks follow up were significantly lower while the serum albumin (28.0 versus 19.7 g/L, p<0.001) and urinary output (3050.0 versus 785.0 mls, p<0.001) at 8 weeks follow up were significantly higher. The mean percentage reduction in weight, abdominal girth, urinary protein excretion, percentage increase in urinary output as well as increase in serum albumin levels at the end of the same period were 28.2%, 16.6%, 43.3%, 251.5% and 34.4%, respectively. None of the patients bled from drainage site or developed intra-abdominal haemorrhage. No mortality was recorded.

Conclusion: Modified peritoneo-venous shunt using a peripheral vein is a novel, effective and safe technique for treating refractory oedema in nephrotic syndrome.

Keywords*: Abdominal paracentesis, Intravenous re-infusion of ascites, Nephrotic syndrome, Peritoneo-venous shunt, refractory oedema*

Correspondence: Prof. F.A. Arogundade, Renal Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Nigeria. E-mail: fatiu3@yahoo.com. fatiuaro@oauife.edu.ng

Résumé

Contexte : L'œdème réfractaire reste problématique chez les patients atteints du syndrome néphrotique. Une paracentèse répétée entraîne parfois une hypotension et des lésions rénales invariablement aiguës. La ré-infusion intraveineuse de liquide ascitique, une forme modifiée de shunt péritonéo-veineux (MPVS), est une alternative de traitement visant à prévenir l'instabilité hémodynamique et à corriger l'hypo-protéinémie. Nous avons évalué l'utilité et l'innocuité du MPVS chez les patients atteints du syndrome néphrotique présentant un œdème réfractaire.

Méthodes **:** Vingt-six patients consécutifs présentant un œdème réfractaire ont été recrutés. Un total de 165 sessions de MPVS a été réalisées en utilisant la veine périphérique. L'évaluation du traitement a été effectuée en fonction du poids, de la circonférence abdominale, du volume des urines, des protéines urinaires et des protéines sériques. Une biopsie rénale a été réalisée pour déterminer le diagnostic histologique. Les données ont été analysées à l'aide du logiciel statistique pour les sciences sociales (SPSS) version 16.

Résultats **:** Comparé aux paramètres de base, le poids médian (58,5 kg contre 85,5 kg, p <0,001) ; circonférence abdominale (89,3 versus 110,0 cm, p <0,001) ; et l'excrétion urinaire de protéines (1,7 versus 5,2 g / 24h, p <0,001) à 8 semaines de suivi étaient significativement plus faibles alors que l'albumine sérique (28,0 versus 19,7 g / L, p <0,001) et le débit urinaire (3050,0 versus 785,0 ml, p <0,001) à 8 semaines de suivi étaient significativement plus élevés. Le pourcentage moyen de réduction du poids, du tour de taille abdominal, de l'excrétion des protéines urinaires, de l'augmentation du pourcentage du débit urinaire ainsi que de l'augmentation des taux d'albumine sérique à la fin de la même période était de 28,2%, 16,6%, 43,3%, 251,5% et 34,4%, respectivement. Aucun des patients n'a saigné du site de drainage ni développé d'hémorragie intraabdominale. Aucune mortalité n'a été enregistrée.

Conclusion : Le shunt péritonéo-veineux modifié utilisant une veine périphérique est une nouvelle technique efficace et sûre pour traiter l'œdème réfractaire dans le syndrome néphrotique.

Mots-clés : *Paracentèse abdominale, Ré-infusion intraveineuse d'ascite, Syndrome néphrotique*, *Dérivation péritonéo- veineuse, œdème réfractaire.*

Introduction

Mobilization of oedema remains a challenge in the management of refractory nephrotic syndrome with associated anasarca. Quite often, patients develop abdominal discomfort with associated respiratory distress [1]. Modalities of treating refractory oedema which include strict bed rest, salt and water restriction, diuretics, intravenous administration of salt-poor albumin as well as repeated paracentesis are often inadequate and sometimes, repeated paracentesis results in hypotension which may precipitate acute kidney injury [2, 3]. Even though intravenous infusion of albumin after paracentesis may prevent these serious complications, the cost implications of commercially-prepared albumin and possible untoward side effects limit its availability. Intravenous re-infusion of ascitic fluid is a better and useful alternative technique for ascitic fluid removal and simultaneous replacement of serum protein with little adverse effect on systemic circulation [4-9].

The original peritoneo-venous shunt was designed by LeVeen and colleagues in 1974. The shunt included a surgically placed permanent catheter which transmits ascitic fluid from the peritoneal cavity into the central venous circulation (external or internal jugular veins) via a one-way valve that prevents backflow of venous blood [10]. Movement of ascitic fluid through the shunt is controlled by a positive pressure gradient between the fluid-filled peritoneal cavity and the central venous vessels.

In this study, we describe a novel method, modified peritoneo-venous shunt (MPVS) for treatment of nephrotic syndrome patients with refractory oedema. In contrast to the original peritoneovenous shunt, our method involves intermittent drainage of ascitic fluid from the peritoneal cavity (paracentesis) into a single blood collection bag and re-infusion of ascitic fluid into the circulation via a blood giving set, which permits active flow into the peripheral vein (Figure 1). The blood collection bag is used as a drainage system while one-way ascites flow is guaranteed by the blood giving set.

In the past, several different modalities have been employed for ascitic fluid removal and re-infusion; however, fever, anaphylactic reactions, gastrointestinal bleeding and disseminated intravascular coagulopathy have been reported as common complications particularly in cirrhotic patients [11, 12]. However, it remains to be seen whether intravenous re-infusion of ascitic fluid will be effective and safe for the treatment of refractory oedema in selected cohorts of nephrotic syndrome patients with a normal coagulation profile. This report describes modified peritoneo-venous shunt technique using a peripheral vein in our nephrotic syndrome patients with refractory oedema; and assessed the efficacy and safety of the procedure.

Materials and methods

Twenty six consecutive patients with refractory oedema were recruited. Criteria for inclusion were failure of oedema to resolve after strict best rest, salt and water restriction; and maximal dose of diuretics which included a thiazide diuretic for three weeks. Exclusion criteria included abnormal clotting profile, clinical, laboratory or ultrasonographic data suggesting malignancy and spontaneous bacterial peritonitis. The study was done in accordance with the Helsinki Declaration of 1975, as revised in 2000 and written consent was obtained from all patients. Socio-demographic profile, duration of ascites, creatinine clearance, 24-hr protein excretion, serum albumin, complete blood count, erythrocyte sedimentation rate, clotting profile, lipid profile and number of sessions of MPVS performed were documented. Estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI Creatinine 2009 Equation software (National Kidney Foundation™).

MPVS was performed after excluding malignancy and infection by ascitic fluid cytology and culture. Intermittent abdominal paracentesis was done with the aid of a 16G needle and 2L of ascitic fluid collected by gravity into a single plastic citrate-phosphate-dextrose-adenine (CPDA) blood bag using sterile technique (Figure 1A). The ascitic fluid was then re-infused through a peripheral intravenous line using a blood giving set with in-built filter (Figure 1B) over six hours under intravenous Augmentin coverage (600 mg twice daily for 5 days). On the average, each patient received 7 sessions of MPVS while the interval between two successive MPVS session was 48 hrs. All patients were continued on standard of care treatments including frusemide, thiazide diuretics, angiotensin converting enzyme inhibitors and statins. Evaluation of treatment was done by assessment of weight, abdominal girth, urine volume, urinary protein and serum protein before the procedure and at 2, 4, 6 and 8 weeks after treatment. Treatment failure was

defined as an increase in weight (>50% of weight loss after paracentesis) [5].

Renal Biopsy

Percutaneous renal biopsy was performed after oedema had resolved. Automated spring-loaded biopsy needle (size 16) was used. Three renal biopsy samples were taken from each patient, which were processed for light microscopy. Sections were made from formalin fixed paraffin embedded tissue and stained Haematoxylin-Eosin, Periodic-acid Schiff (PAS), Masson's trichrome and Jones Silver Stains. Histological diagnosis was then determined by a Nephropathologist.

Data analysis

Data obtained was analyzed using statistical package for social sciences (SPSS) version 16. Continuous data were expressed as mean (±SD) and median (IQR). Categorical data was summarized using frequencies and percentages. A spearman's correlation was used to determine relationship between variables. A p-value <0.05 was regarded as statistically significant.

Results

One hundred and sixty five sessions of MPVS were performed on the patients with a median of 7 sessions (IQR, 6.0-8.0). The demographic and clinical characteristics of the studied patients are stated in table 1. There was male preponderance; with 19 males and 7 females (M: F; 2.7:1). The mean age was 26.1 ± 3.8 years. The clinical and laboratory parameters of the studied patients during and after treatment are shown in table 2. When measurements at 4 weeks follow up were compared to the baseline measurements, the median weight (71.0 versus 85.5 kg, p<0.001); abdominal girth (101.0 versus 110.0 cm, p<0.001); urinary protein excretion (4.1 versus 5.2 g/24hrs, p<0.001) were significantly lower than the baseline parameters while the serum albumin (23.0 versus 19.7 g/L, p<0.001) and urinary output (1310.0 versus 785.0 ml/day, p<0.001) were significantly higher than the baseline parameters. Similarly, when compared to baseline parameters, the median weight (58.5 versus 85.5 kg, p<0.001); abdominal girth (89.3 versus 110.0 cm, p<0.001); and urinary protein excretion (1.7 versus 5.2 g/24hrs, p<0.001) at 8 weeks follow up were significantly lower while the serum albumin (28.0 versus 19.7 g/L, p<0.001) and urinary output (3050.0 versus 785.0 ml/day, p<0.001) at 8 weeks follow up were significantly higher. The median reduction in weight, abdominal girth, urinary protein excretion, increase in urinary output and increase in serum albumin levels at the end of 4 weeks of follow up were 12.5 (8.0-19.1) kg, 9.0 (6.0-11.0) cm, 2.1 (0.2-2.1) g/24hrs, 540.0 (362.5-757.5) ml/day and 2.0 (1.0-3.0) g/L,

Table 1: Demographics and baseline clinical parameters of studied patients

Number of patients	26
Sex (M:F)	2.7:1
Age (years; Mean ± SD)	26.1 ± 3.8
Duration of Oedema (wks)	12.0 (10.0-14.0)
Weight (kg)	85.5 (81.5-89.1)
Abdominal girth (cm)	110.0 (108.0-112.3)
Urinary output (ml/day)	785.0 (718.0-890.0)
Creatinine clearance (ml/min)	103.0 (83.5-111.3)
eGFR (ml/min/1.73m^2)	99.0 (78.3-113.8)
Total cholesterol (mmol/L)	7.4 (7.0-8.4)
International normalised ratio	1.08 (1.03-1.13)
Erythrocyte sedimentation rate(mm/hr)	101.0 (87.8-118.5)
Packed cell volume (%)	32.0 (30.0-33.0)
Platelet (mm^3)	186.5 (166.5-223.5) x10^3
24-hr protein excretion (g/24hr)	5.2 (4.1-8.2)
Serum Albumin (g/L)	19.7 (17.0-22.0)
Number of session of MPVS	7.0 (5.8-8.0)
Histology (light microscopy)	
Focal segmental glomerulosclerosis	21 (80.8%)
Minimal change disease	2 (7.7%)
Membranous nephropathy	2 (7.7%)
Diffuse proliferative lupus glomerulonephritis	1 (3.8%)

+eGFR, estimated glomerular filtration rate; MPVS, modified peritoneo-venous shunt

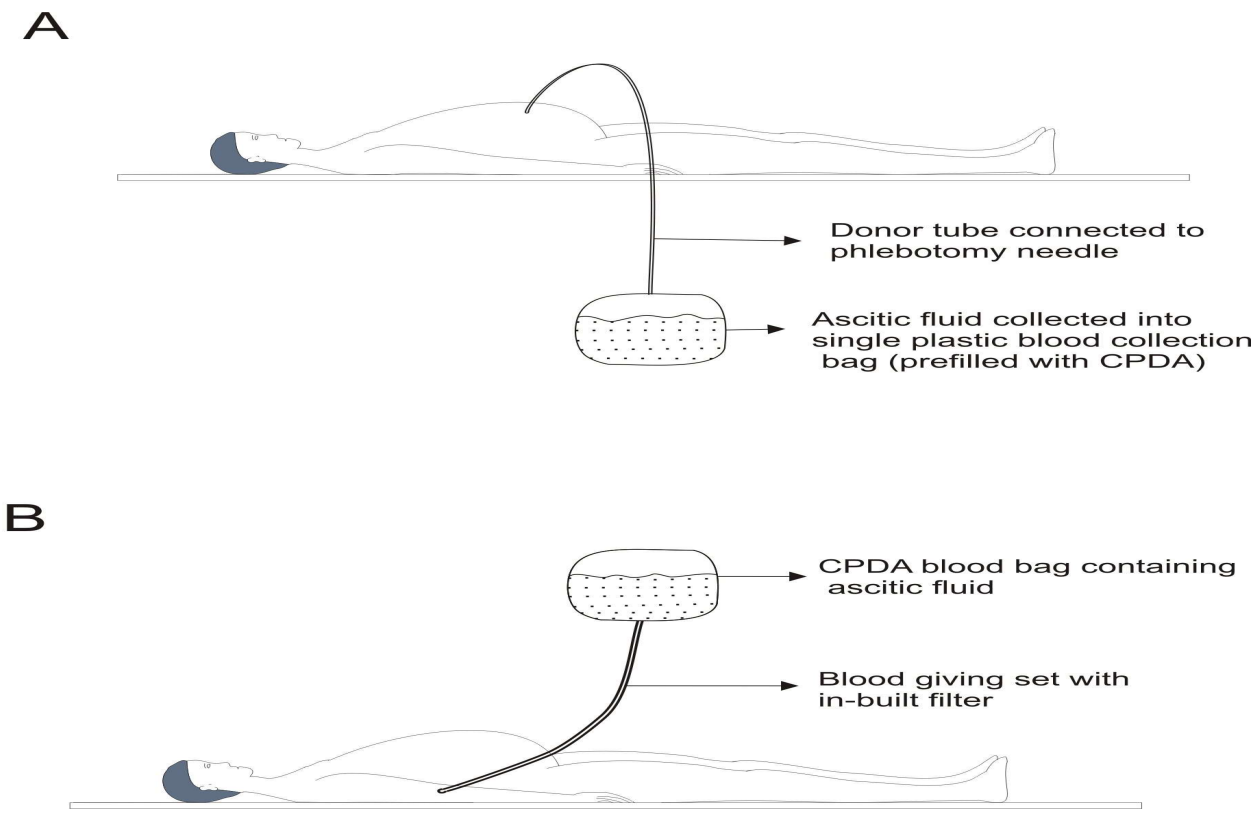

***Fig.1**: Procedure for paracentesis and reinfusion of ascitic fluid (modified peritoneo-venous shunt). Ascitic fluid is drained into a single plastic citrate-phosphate-dextrose-adenine (CPDA) prefilled blood bag using sterile technique. The ascitic fluid was reinfused into the circulation through a peripheral intravenous line using a blood giving set with in-built filter*

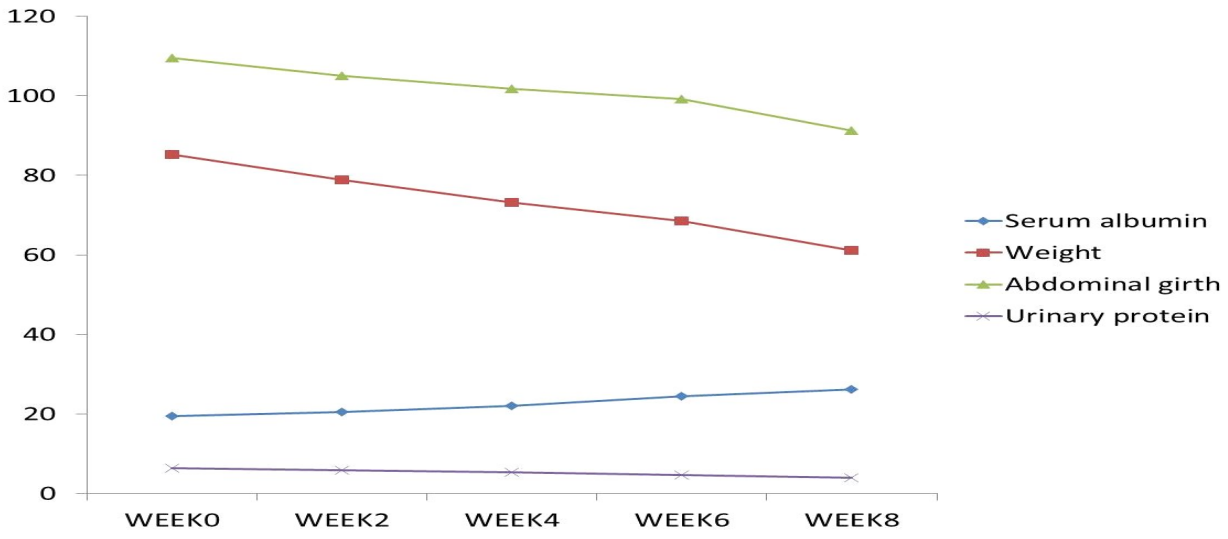

Fig. 2: Comparison of changes in mean urinary protein, mean serum albumin, mean weight and mean abdominal girth of studied patients over 8 weeks.

respectively while at 8 weeks of follow up, the median reduction in weight, abdominal girth, urinary protein excretion, increase in urinary output and increase in serum albumin levels were 29.5 (21.1-32.0) kg, 21.3 (15.8-25.6) cm, 3.2 (0.6-4.3) g/24hrs, 2220.0 (1672.5-2607.5) ml/day and 7.0 (5.8-9.3) g/L, respectively. The variations in weight, abdominal girth, serum albumin levels and urinary protein over the follow up period are shown in figure 2. On further analysis, the mean percentage reduction in weight, abdominal girth, urinary protein excretion, percentage increase in urinary output as well as

Table 2: Clinical and Laboratory parameters during treatment

Parameter	Baseline Median (IQR)	After 4 weeks Median (IQR)	After 8 weeks Median (IQR)	*P value
Clinical				
Weight (kg)	85.5 (81.5-89.1)	71.0 (64.8-76.9)	58.5 (53.8-62.1)	<0.001
Abdominal girth (cm)	110.0 (108.0-112.3)	101.0 (100.0-102.0)	89.3 (85.9-92.0)	<0.001
Urinary output (ml/day)	785.0 (718.0-890.0)	1310.0 (1175.0-1662.5)	3050 (2480.0-3435)	<0.001
Laboratory				
Packed cell volume (%)	32.0 (30.0-33.0)	32.0 (30.0-32.0)	31.0 (31.0-32.0)	0.906
Platelet (mm^3)	186.5 (166.5–223.5) x 10^3	189.6 (166.6-234.1) x 10^3	189.5 (165.3-223.7) x 10^3	0.292
Erythrocyte sedimentation rate (mm/hr)	101.0 (87.8-118.5)	80.0 (65.0-95.3)	58.5 (44.8-73.8)	<0.001
Serum albumin (g/L)	19.7 (17.0-22.0)	23.0 (20.-24.0)	28.0 (26.0-29.0)	<0.001
Creatinine (µmol/L)	98.0 (90.0-112.5)	94.0 (88.0-104.0)	88.5 (84.0-98.8)	<0.001
eGFR (ml/min/1.73m^2)	99.0 (78.3-113.8)	106.0 (85.8-120.0)	116.0 (91.8-127.0)	<0.001
Urea (mmol/L)	5.5 (4.5-7.4)	5.0 (4.1-7.3)	4.5 (4.0-5.5)	<0.001
Sodium (mmol/L)	130.0 (123.0-132.0)	131.5 (126.0-133.0)	134.5 (130.0-136.3)	<0.001
Potassium (mmol/L)	3.7 (3.5-3.8)	3.4 (3.2-3.7)	3.5 (3.2-3.6)	0.011
Bicarbonate (mmol/L)	22.0 (20.8-22.3)	22.0 (22.0-24.0)	24.0 (22.0-25.3)	0.010
Cholesterol (mmol/L)	7.4 (7.0-8.4)	6.4 (6.0-7.4)	5.5 (5.2-6.3)	<0.001
24-hr protein excretion (g/24hr)	5.2 (4.1-8.2)	4.1 (2.1-7.7)	1.7 (1.2-4.3)	<0.001

*p-values were calculated by comparing values after 8 weeks on treatment with baseline values using Mann-Whitney test

Table 3: Comparison between treatment responder and non-responder patients after treatment

Parameter	Responders (N=22)	Non-Responders (N=4)	*P value
Clinical			
Number of sessions of MPVS	6.5 (5.0-7.0)	8.0 (6.5-8.0)	0.081
Weight (kg)	55.0 (52.8-60.0)	89.5 (81.3-94.8)	<0.001
Abdominal girth (cm)	88.3(85.4-91.0)	108.5(100.8-117.8)	<0.001
Urinary output (ml/day)	3200 (2875-3605)	780 (675-1005)	<0.001
Laboratory			
Packed cell volume (%)	31.0 (31.0-32.0)	31.5 (29.5-32.8)	0.864
Platelet (mm^3)	186.5 (166.0-211.5) x 10^3	232.2 (178.0-232.2) x 10^3	0.172
Erythrocyte sedimentation rate (mm/hr)	52.5 (44.0-71.3)	83.0 (73.8-89.3)	0.004
Serum albumin (g/L)	28.0 (27.0-29.0)	16.0 (15.0-16.0)	<0.001
Creatinine (µmol/L)	87.5 (83.8-91.0)	140.0 (126.5-158.0)	<0.001
eGFR (ml/min/1.73m^2)	119.5 (101.5-128.0)	58.0 (46.5-59.8)	<0.001
Urea (mmol/L)	4.4 (4.0-4.8)	13.7 (12.2-14.5)	<0.001
Sodium (mmol/L)	134.5 (130.0-136.3)	133.0 (127.0-137.5)	0.706
Potassium (mmol/L)	3.5 (3.4-3.6)	3.4 (3.1-3.6)	0.389
Bicarbonate (mmol/L)	24.0 (22.0-26.0)	20.5 (20.0-21.8)	0.007
Cholesterol (mmol/L)	5.5 (5.2-6.1)	6.9 (5.5-8.0)	0.096
24-hr protein excretion (g/24hr)	1.4 (1.2-3.7)	12.0 (10.4-13.0)	<0.001

MPVS, modified peritoneo-venous shunt; eGFR, estimated glomerular filtration rate.*p-values were calculated by comparing values between responders and non-responders using Mann-Whitney test

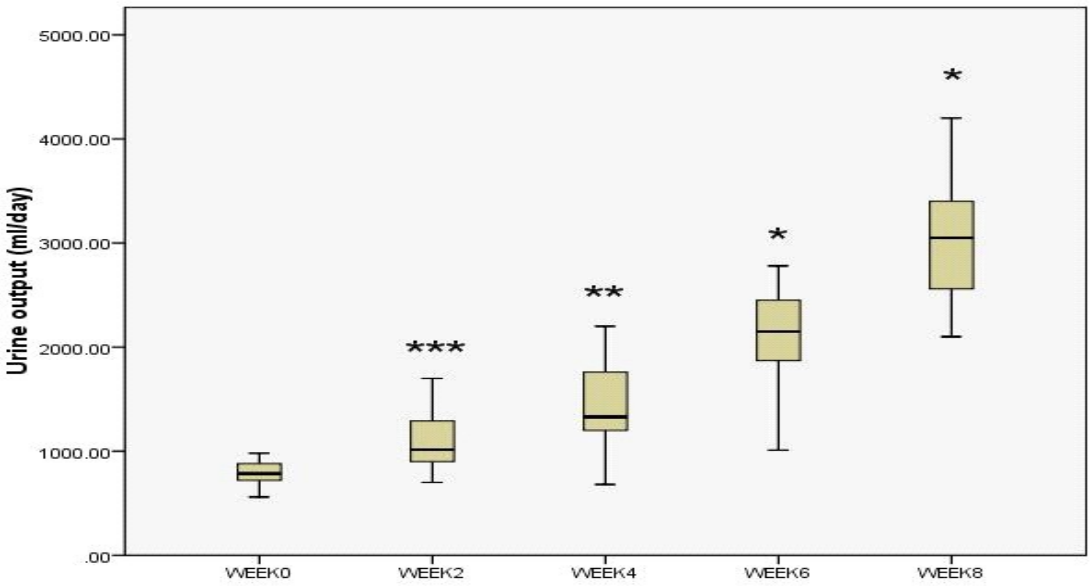

Fig. 3: Changes in urine output (in mls) over 8weeks. The box-plot represents lower and upper quartiles, the whiskers represent sample minimum and maximum. *p<0.001, **p = 0.001, ***p = 0.295 compared to WEEK0 using Kruskal Wallis test.

increase in serum albumin levels at the end of 4 weeks were 14.3%, 7.1%, 18.2%, 68.4% and 13.0%, respectively while the mean percentage reduction in weight, abdominal girth, urinary protein excretion, percentage increase in urinary output as well as increase in serum albumin levels at the end of 8 weeks were 28.2%, 16.6%, 43.3%, 251.5% and 34.4%, respectively.

Figure 3 shows progressive increase in urinary volume. Urinary volume was strongly associated with eGFR ($r = 0.672$, $p<0.001$) and serum albumin levels ($r = 0.793$, $p<0.001$) while it showed an inverse correlation with urinary protein excretion ($r = -0.807$, $p<0.001$), weight ($r = -0.693$, $p<0.001$) and abdominal girth ($r = -0.777$, $p<0.001$). There was inverse relationship between serum albumin levels and total cholesterol ($r = -0.679$, $p<0.001$).

Four patients did not respond to MPVS treatment. As shown in table 3, measured variables were compared between treatment responders and those that did not respond to MPVS therapy. Compared with treatment responders, patients who had treatment failure had severe kidney disease, severe oedema, severe dyslipidaemia and significantly reduced serum albumin levels. Two patients developed self-limiting mild and transient fever, which did not require treatment. Ascitic fluid leakage which resolved spontaneously was observed in 5 patients. One patient developed peritonitis which was treated successfully with antibiotics. None of the patients bled from puncture wound site or developed intra-abdominal haemorrhage. Four (15.4%) patients developed deep vein thrombosis while on admission. No mortality was recorded. Focal segmental glomerulosclerosis (FSGS) was diagnosed on histology in 21 (80.8%) patients including the four that had treatment failure.

Discussion

Oedema is one of the major clinical manifestations of nephrotic syndrome which may vary from mild periorbital puffiness to anasarca [13]. Patients generally respond to the combination of dietary sodium restriction and diuretic therapy, usually with a loop diuretic. However, some are resistant to this regimen leading to development of refractory oedema. Oedema is considered refractory if therapy with bed rest, salt and water restriction, and diuretics (which must include a thiazide) at maximum doses fails to result in diuresis. At times, administration of intravenous diuretics with albumin infusion does not usually give the desired effect and even paracentesis with intravenous infusion of albumin may lead to untoward effects [2, 3]. Modified peritoneo-venous shunt, a simple technique that allows removal of large volume ascitic fluid and re-infusion of filtered protein-rich ascitic fluid is targeted at preventing haemodynamic instability while correcting the

hypoproteinemia. It is therefore hypothesized that MPVS may be a useful technique for the treatment of refractory oedema especially in the settings where there is limited access to commercially-prepared albumin.

Our study demonstrated that MPVS using peripheral vein is effective in the mobilization of oedema. There was significant symptomatic relief of ascites and peripheral oedema in our patients comparable to the finding of earlier studies that used original peritoneo-venous shunt technique [14-18]. We also observed sustained and progressive reduction of weight and abdominal girth as well as diuresis in majority of our patients which is also similar to the findings from previous reports [19, 20]. There was also significant increase in serum albumin from baseline prior to MPVS and this may be due to infusion of protein-rich ascitic fluid into the systemic circulation, thus restoring intravascular volume via increased intravascular oncotic pressure [21, 22].

Our study showed that patients who had treatment failure had advanced renal disease, severe hypoalbuminaemia and severe fluid retention when compared with patients that responded to MPVS therapy. In addition, urine volume was strongly correlated with eGFR, serum albumin levels, urinary protein excretion and degree of fluid retention. Because of its association with fluid retention, urinary output tends to be greater in patients with relatively normal GFR and renal function. Taken together, this may explain the reason why the patients who had significantly reduced eGFR, severe hypoalbuminaemia and severe proteinuria did not respond to the treatment. We also demonstrated a strong association between low serum albumin levels and elevated serum cholesterol levels. Besides triggering refractory oedema, hypoalbuminaemia stimulates increased hepatic synthesis of circulating lipids ultimately resulting in nephrotic dyslipidaemia.

In contrast to previous reports that suggested that ascitic fluid leakage is a common complication following paracentesis [23, 24], only a few of our patients developed self-limiting ascitic fluid leakage. Likewise, infection was not a major limitation in this study. Only one of our patients developed peritonitis which resolved with antibiotic treatment. This is not in support of previous study that documented infection as a major risk factor for mortality in cirrhotic patients that undergone reinfusion of ascitic fluid [25]. It is plausible that ascitic fluid cell count and culture that were carried out before performing MPVS could have contributed to very low incidence of infection/peritonitis recorded in this study. In addition, the procedure was done intermittently and no cannula or needle was left in-situ for more than 3-6 hrs. Our findings therefore suggest that ascitic fluid cell count and culture should be done before MPVS is performed on nephrotic syndrome patients with refractory oedema, in order to reduce the risk of infusing infected ascitic fluid or disseminating occult malignancy. Also, intravenous cannulas should be removed as early as possible to remove potential source of infection.

Although enhanced fibrinolytic activity of ascitic fluid as a result of deficiency of plasminogen activator inhibitor and enhance basal tissue plasminogen activator have been documented [26-29], we did not observe any anaphylactic reaction, gastrointestinal bleeding or disseminated intravascular coagulation in this study. Therefore, clotting profile must be checked before performing the procedure, and if there are clotting abnormalities, the procedure should be considered hazardous and deferred until such is corrected.

It was not surprising that majority of our patients had focal segmental glomerulosclerosis (FSGS) as refractory oedema is common in idiopathic FSGS patients. They typically present with difficult to manage oedema with associated severe hypoalbuminaemia and proteinuria that is refractory to corticosteroid and other immunosuppressives [30]. Proteinuria leads to hypoalbuminaemia and low plasma oncotic pressure, thus modifying starling forces which regulate the distribution of fluid between plasma and interstitium, resulting in increased interstitial fluid and worsening of oedema.

This study is a short term observational study and the data generated from this study can only be regarded as baseline. The study design did not afford us the opportunity to assess the efficacy and safety of long-term use of MPVS in nephrotic syndrome patients with relapsing nephrotic syndrome. Further study is therefore needed to confirm the efficacy of MPVS in treating relapsing nephrotic syndrome. Another possible limitation of this study might be inability to perform immunofluorescence/ immunoperoxidase as well as electron microscopy tests on the renal biopsy samples. Nevertheless, all the histological diagnoses were confirmed by a Nephropathologist.

In conclusion, MPVS using a peripheral vein is a useful novel technique to remove ascitic fluid and supply protein simultaneously; with little influence on the systemic circulation. It is effective, safe and cheap for treating refractory oedema in

selected nephrotic syndrome patients with normal clotting profile particularly in resource-poor setting where there is limited access to commercially-prepared albumin.

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Diabetic retinopathy in Ilorin: a hospital-based study

LB Olokoba[1], AO Mahmud[1], FG Adepoju[1], AB Olokoba[2] and A Joseph[3]

Departments of Ophthalmology[1] and Medicine[2], University of Ilorin Teaching Hospital, lorin, and Department of Microbiology[3], Bowen University Teaching Hospital, Iwo, Nigeria

Abstract

*Background***:** Diabetic retinopathy is the main cause of blindness associated with diabetes mellitus. Due to the increasing burden of diabetes mellitus in Nigeria, there is a need to determine the prevalence of diabetic retinopathy in diabetic patients. This study aims to determine the prevalence of diabetic retinopathy among diabetic patients.

Methodology: This was a hospital-based cross-sectional study, carried out at the Diabetic, and Ophthalmology clinics of University of Ilorin Teaching Hospital, Ilorin from November 2011 to July 2012. A total of 365 patients had validated, semi-structured, and interviewer-administered questionnaires administered to obtain information on socio-demographic characteristics, and clinical information on Diabetes mellitus. General physical and ocular examination were done. Dilated funduscopy with indirect slit lamp bio-microscopy using +90Diopter Volk lens and binocular indirect ophthalmoscopy using +20Diopter lens were also done for retina and macular examination.

Results: A total of 365 patients were enrolled, with age ranging from 19 and 90 years, and a mean age of 45.8 ±16.3 years. The male to female ratio was 1: 2.2. Out of the 365 patients enrolled, 44(12.1%) had features of diabetic retinopathy in one or both eyes. Out of those with diabetic retinopathy, 24 (6.6%) had diabetic macular oedema with and without other features of diabetic retinopathy. Mild, moderate, and severe non-proliferative diabetic retinopathy was seen in 20(5.5%), 11(3.0%), and 1(0.3%) patient respectively while 5(1.4%) had proliferative diabetic retinopathy.

Conclusion: The prevalence of diabetic retinopathy in our study is lower than previously reported, and it is highest in patients with DM less than 10 years. There is therefore a need to start screening for DR early.

Keywords*: Prevalence, macular oedema, diabetic retinopathy, diabetes mellitus*

Correspondence: Dr. Lateefat B. Olokoba, Department of Ophthalmology, University of Ilorin Teaching Hospital, Ilorin,Nigeria. E-mail: drlbolokoba@gmail.com

Résumé

Contexte **:** La rétinopathie diabétique (RD) est la principale cause de cécité associée au diabète sucré. En raison de la charge croissante du diabète sucré au Nigéria, il est nécessaire de déterminer la prévalence de la rétinopathie diabétique chez les patients diabétiques. Cette étude vise à déterminer la prévalence de la rétinopathie diabétique chez les patients diabétiques.

Méthodologie : Il s'agissait d'une étude transversale réalisée à l'hôpital dans les cliniques de diabétologie et d'ophtalmologie de l'Hôpital d'Enseignement Universitaire d'Ilorin, Ilorin de novembre 2011 à juillet 2012. Un total de 365 les patients avait reçu des questionnaires validés, semi-structurés et administrés par un intervieweur afin d'obtenir des informations sur les caractéristiques socio-démographiques et des informations cliniques sur le diabète sucré. Un examen physique et oculaire général a été effectué. Une fundus-copie diluée avec une biomicroscopie à fentelampée indirecte utilisant une lentille + 90Diopter Volk et une ophtalmoscopie indirecte binoculaire à l'aide d'une lentille + 20Diopter ont également été réalisées pour l'examen de la rétine et du maculaire.

Résultats : Au total, 365 patients ont été inclus, avec un âge compris entre 19 et 90 ans et un âge moyen de 45,8 ± 16,3 ans. Le ratio hommes : femmes était de 1: 2,2. Parmi les 365 patients inclus, 44 (12,1%) présentaient des signes de rétinopathie diabétique dans un œil ou les deux.Parmi les personnes atteintes de rétinopathie diabétique, 24 (6,6%) présentaient un œdème maculaire diabétique avec et sans autres caractéristiques de la rétinopathie diabétique. Une rétinopathie diabétique non-proliférative légère, modérée et grave a été observée chez 20 (5,5%), 11 (3,0%) et 1 (0,3%) patients respectivement, tandis que 5 (1,4%) avaient une rétinopathie diabétique proliférative.

Conclusion : La prévalence de la rétinopathie diabétique dans notre étude est inférieure à celle rapportée précédemment et elle est la plus élevée chez les patients atteints de diabète de moins de 10 ans. Il est donc nécessaire de commencer le dépistage précoce de la RD.

Mots - clés *: prévalence, œdème maculaire, rétinopathie diabétique, diabète sucré*

Introduction

Diabetes Mellitus (DM) arises from defects in insulin secretion, insulin action or both [1]. It is broadly classified into type 1 DM, type 2 DM, gestational DM and other specific types of DM (1). DM is one of the most common non communicable diseases with an increasing incidence worldwide [2]. The increasing incidence is as a result of inherited risk and changes in lifestyle (sedentary lifestyle, abnormal eating habits), as well as an increase in life span (DM occurs more in older people) [2]. The World Health Organization (WHO) estimated 171million people globally lived with DM in the year 2000, and this number is projected to increase to 366 million by the year 2030, with the most significant increase occurring in developing countries [2]. While most individuals affected with DM in the developed countries are elderly, majority of subjects in developing countries are younger (46-64years), which intensifies the consequences of DM in these societies [3]. There is substantial evidence that DM is an epidemic. And low and middle income countries face the greatest burden of DM [4].

In Nigeria, the national prevalence of DM is 2.2% meaning about 3.3 million have DM [5]. As the prevalence of DM increases, so will the risk of developing diabetic retinopathy (DR) [6]. In 2002, the global average risk of blindness from DR amongst people with DM was calculated as 0.75% i.e. one person out of every 133 people with DM will go blind [6]. However, the average risk of blindness from DR tends to be higher in resource poor regions. An important reason for this is that the infrastructure and resources required to effectively address DR are either inadequate or absent [7]. WHO estimated that DR is responsible for 4.8% of the 37.0million cases of blindness throughout the world [6].

In the recently concluded Nigerian Blindness Survey, DR accounted for 0.02% of the total blindness in adults 40years and above [8]. Fortunately, DR has a ten to twenty year delay before onset allowing a small window of opportunity for early detection through regular and routine screening and treatment [7]. In our institution, University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria with the availability of Laser equipment and the human resources to deliver Laser photocoagulation, the goal is to reduce blindness from DR by providing prompt treatment (laser photocoagulation). This study was designed to determine the prevalence of DR with a view to developing a protocol for screening of DM patients in order to achieve this goal.

Materials and methodology.

Study design and duration

This was a hospital-based, cross-sectional study, carried out at the Diabetic and Ophthalmology clinics of UITH, Nigeria from November 2011 to July 2012.

Study site

The UITH is a 700-bedded urban teaching hospital, with a specialist DM clinic and a well-supported Eye department. This provides an ideal set-up for DM patients to get regular eye examinations and treatment when necessary.

Subject selection

On each clinic day, an average of 60 DM patients were seen. The list and case notes of all patients booked to be seen at the clinic were retrieved from the medical records department a day before the clinic. Using a systematic random sampling technique, 20 DM patients were selected and screened on each clinic day. The case notes of the selected patients were marked to prevent them from being recruited again at their next clinic visit. The first patient to be recruited each clinic day was chosen by balloting in a simple random fashion. Thereafter, with a sampling interval of 3, every third patient was selected using a systematic random sampling technique. Patients with confirmed diagnosis of DM (based on a fasting blood glucose $\geq$7mmol/L or oral glucose tolerance test $\geq$11.1mmol/L), and those already on treatment for DM were included in the study while patients with significant opacity in the cornea or crystalline lens (cataract) dense enough to preclude the adequate visualization of the anterior and or posterior segments of the eye; and eligible patients who declined consent were excluded.

Approval for the study was obtained from the Ethics and Research committee of the UITH. Verbal and informed consent was also obtained from all the participants. The patients were given an identification tally to bring to eye clinic that same day where they had both general and ocular examinations. Ocular examination was carried out at the Eye clinic. Distant visual acuity was carried out with an illuminated wall-mounted Snellen's chart at six meters.

Anterior segment examination was carried out with a slit lamp (Haag streit, Bern, Switzerland). Particular attention was paid to anterior chamber depth, presence or absence of significant corneal and/or lens opacity and rubeosis irides.

Intra-ocular pressure (IOP) was measured with Perkins hand held tonometer. The patients thereafter had their pupils dilated with 1% Tropicamide (Mydriacyl^{R}) and 2.5% phenylephrine. For those with elevated BP, their pupils were dilated with only Mydriacyl.^{R} Those with elevated IOP had deferred examination until IOP was controlled, while those with features of shallow anterior chamber were excluded from examination to avoid the risk of triggering an acute angle closure glaucoma.

A direct ophthalmoscopy was carried out, then a dilated funduscopy with indirect slit lamp bio-microscopy using non contact +90Diopter Volk lens was also carried out for retina and macular examination. Further retina examination was also carried out with a binocular indirect ophthalmoscope using +20D lens for a wider view of the retina.

A diagnosis of DR was made when a patient had a minimum of one micro-aneurysm in any field, as well as exhibiting haemorrhages (dot, blot, or flame shaped) and or hard exudates, or presence of macular oedema. Proliferative DR was diagnosed when there was neo-vascularisation, (on the disc or elsewhere) or pre-retinal haemorrhage or vitreous haemorrhage.

The patients were graded based on the more severely affected eye using the international clinical diabetic retinopathy disease severity scale [11]. The instrument (Tonometer) was calibrated at the beginning of each day of study according to the manufacturer's instructions.

Statistical analysis

Data collation and editing were done manually to detect omission and ensure uniform coding. The data was entered into a computer and statistical analysis was carried out with Epi-info version 6.1 statistical software. Frequency tables were generated for all the variables. Quantitative variables were expressed as mean and standard deviation.

Results

A total of 365 patients were enrolled, with age ranging from 19 and 90 years, a mean age of 45.8 ±16.3 years. Majority of the patients were in their sixth and seventh decades i.e. 51-70years. (table 1) Majority of the respondents were females - 250(68.5%). Type 2 DM was the main type of DM as 352 (96.4%) had type 2 DM. The mean duration of DM was 14.1 ±13.09 years. Majority of the patients 203 (55.6%) had DM for 1-10years, 66 patients (18.1%) had DM for 11-20 years. (table 2) Out of the 365 respondents, 44(12.1%) patients had features of DR in one or both eyes while 321 subjects (87.9%) did not. The prevalence of DR among the DM patients was 12.1%.

Out of those with features of DR, 24 (6.6%) respondents had diabetic macular oedema with and without other features of DR. Mild, moderate, and severe non-proliferative DR was seen in 20(5.5%), 11(3.0%), and 1(0.3%) patient respectively while 5(1.3%) had proliferative diabetic retinopathy.

Table 1: Age distribution of respondents

Age distribution	Frequency	Percentage (%)
≤ 20	2	(0.5)
21-30	7	(1.9)
31-40	20	(5.5)
41-50	50	(13.7)
51-60	108	(29.6)
61-70	119	(32.6)
71-80	49	(13.4)
81-90	10	(2.7)
Total	365	(100.0)

Mean±SD = 45.83±16.28

Table 2: Clinical parameters among respondents

Findings	Frequency	Percentage(%)
Gender		
Male	115	31.5
Female	250	68.5
Types of DM		
Type 1	12	3.3
Type 2	352	96.4
Gestational DM	1	0.3
Duration of DM		
1-10 years	203	55.6
11-20 years	66	18.1
21-30 years	49	13.4
> 30 years	47	12.9

Discussion

This study took a cross-sectional look at attendees of the DM clinic of UITH, and determined the prevalence of DR amongst them. The mean age in our study population was lower than other Nigerian studies. Ashaye *et al* [13] and Omolase *et al* [14] in south west, Nigeria found the mean age of their DM patients to be 57.5 and 57.6 years respectively. Lawan and Mohammed [15] in Kano, northwest, Nigeria found the mean age of their DM patients to be 54.0years. Nwosu [16] in Nnewi, south east, Nigeria found a mean age of 57.2years. In our study, majority of the patients were in their sixth and seventh decades of life. This is different from that

of Lawan and Mohammed [15] who found that majority of their DM patients were in their sixth decade (50-59years). It is also different from that of Osuntokun in Ibadan, south west Nigeria who found that majority of their DM patients were in their fifth decade [17]. The age difference between our study and other Nigerian studies may be due to differences in sample sizes, the study settings, study populations, inclusion and exclusion criteria. Furthermore, geographical and cultural differences, and the differences in the period of time the studies were carried out may also have influenced differences in the mean age of the study population. The higher mean age of DM patients may translate to a longer duration of DM, which in turn may influence the onset of complications of the disease, and DR. Several studies have identified longer duration of DM as a risk factor for DR [13,14,16].

In this study, most of the patients were females compared to males. This is similar to the findings of Erasmus *et al* [10] in Ilorin, north central, Nigeria of nearly three decades earlier, and Onakpoya *et al* [18] in Ile-Ife, south west, Nigeria. Similarly, Lawan and Mohammed [15] and Mumba *et al* [19] in Tanzania found more females than males in their studies respectively. However, other authors in other regions of Nigeria (Ashaye *et al,* Omolase *et al,* and Nwosu) reported more males than females in their studies [13,14,16]. The higher number of female patients is probably because the health seeking behaviour of females tend to be better than males [20], and this may explain the larger population of females in this study. The prevalence of DR in this study was 12.1%. This is lower than the 15.1% that was reported by Erasmus *et al* in the same institution nearly three decades earlier [10].

The prevalence of 12.1% is similar to the findings of Bella *et al* [21] in Ibadan, south west Nigeria and Magulike *et al* [22] in Enugu, south east Nigeria who found prevalence rates of DR of 12.1% and 12.75% respectively. The prevalence reported in this study is however lower than that reported by Omolase *et al* [14] (15.0%).

Furthermore, Rotimi *et al* in the analysis of a cohort of West African type 2 DM patients and their unaffected spouse reported a prevalence of 17.9% [23]. Githeko *et al* reported a prevalence of 18.3% in a study among DM patients attending a rural health institution in central Kenya [24]. The Chennai Urban Rural Epidemiological Study (CURES) carried out in south India found an overall prevalence of DR of 17.6% [25]. Similarly, in the Pakistan survey of Sindh province, the overall prevalence of DR reported was 15.3% [26]. Khandekar *et al* reported a prevalence of DR of 14.4% among registered DM patients in Oman [27]. The Australian Diabetes, Obesity and Lifestyle study (AusDiab) found an overall prevalence of DR of 15.3% in their population aged 25 years and above with DM [28].

There are possible explanations for the apparent decline in the prevalence of DR reported in this study compared to what was reported by Erasmus *et al* [10] in the same institution nearly three decades earlier. Firstly, it is possible that improvements in the clinical management of DM (e.g better glycaemic and blood pressure control) might have led to a gradual decline in DR frequency. There is an increase in knowledge and newer pharmacologic agents available for better management of DM compared to what obtains about three decades ago. Thus better glycaemic and blood pressure control may delay the onset of DR.

Secondly, differences in the DR classification system used. The study of Erasmus *et al* used the Jackson, Goldin and Marine classification while our study used the Early Treatment Diabetic Retinopathy Study (ETDRS) classification. Thirdly, a large proportion of the DR patients in the study of Erasmus *et al* had concomitant systemic hypertension which may have influenced the prevalence of DR in them.

Fourthly, the differences in the period of time the studies were carried out may also have influenced the prevalence of DR. Fifthly, the differences in the method of identifying DR in the studies. Erasmus *et al* used direct fundoscopy while our study used slit lamp biomicroscopy and binocular indirect ophthalmoscopy even though the later method was expected to identify more cases of DR.

A high prevalence of DR in DM patients was reported by Ashaye *et al,* and Nwosu who reported prevalence rates of 42.1% and 33% respectively. The high prevalence rates reported in their studies may be due to the relatively fewer number of patients studied. Ashaye *et al* [13] studied 76 type 2 DM patients while Nwosu [16] studied 100 patients as against the 365 patients in our study. The differences in the prevalence rates of DR in other Nigerian studies may also be due to differences in the duration of DM in the sample populations, study setting, methodologies and classification methods for identifying and classifying DR, sub-types of DM, the degree of blood glucose control, associated co-morbid conditions such as systemic hypertension etc. Studies have shown that the degree of glycaemic control, and associated co-morbid conditions such as systemic hypertension etc influence the prevalence of DR [13,30].

In Europe and America, studies have reported a high prevalence of DR. Klein *et al* reported a prevalence of 35.1% in the Beaver Dam Eye Study (BDES) in Wisconsin [29]. A high level of DR (50.3%) was also found in the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) in DM patients diagnosed at age 30 or more years [30]. The reason for the high prevalence of DR reported in the aforementioned studies may be due to the fact that funduscopy in these studies were carried out with standard seven field stereoscopic fundus camera through dilated pupils. This has more sensitivity over slit-lamp biomicroscopy used in our study for the detection of features of DR. Furthermore, differences in the duration of DM in the sample populations, sub-types of DM, the degree of blood glucose control, associated co-morbid conditions such as systemic hypertension or dyslipidaemia etc may have played a role.

Majority of the patients with DR had non-proliferative DR. Proliferative DR was present in 5(1.4%) patients. This is similar to the 1.2% reported by Onakpoya *et al* [18] in a study of type 2 DM patients, and the 2.0% reported by Omolase *et al* [14]. One of the patients with proliferative DR had tractional retinal detachment, and was promptly referred to another centre for vitrectomy as she could not benefit from laser treatment only. The other four patients with proliferative DR were treated with pan-retinal photocoagulation. The detection of patients with un-treated vision-threatening retinopathy (defined by the presence of proliferative DR) is of concern as these patients would have gone blind from a potentially treatable cause.

A major limitation in this study was the exclusion of patients with significant cataract from the analysis which may have missed out some patients as DM is a cause of cataract independent of DR. Selection bias is also a strong possibility.

In conclusion, the prevalence of DR in our study is lower than previously reported, and it is highest in patients with DM less than 10 years. There is therefore a need to start screening for DR early.

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Amplified pain perception in patients with diabetic neuropathy is associated with altered serum calcitonin gene related peptide (CGRP)

OO Akintoye[1], AA Oniyide[2] and BV Owoyele[3]

Department of Physiology[1], Ekiti State University, Ado Ekiti, Department of physiology[2], Afe Babalola University, Ado Ekiti and Department of Physiology[3], University of Ilorin, Ilorin, Nigeria.

Abstract

Introduction: Diabetic polyneuropathy (DPN) is the most common complication of diabetes mellitus, affecting up to 50% of patients whose first symptom is usually a painful sensation. The DPN among the other micro-vascular complications of diabetes mellitus is the major cause of death in these patients. Diabetes mellitus is associated with cardiovascular diseases with risk factors like dyslipidaemia, endothelial dysfunction, inflammation, vascular wall abnormalities and oxidative stress leading to vasoconstriction, been one of the hypothetical cause of DPN. Calcitonin gene-related peptide (CGRP) is the most potent micro-vascular vasodilator currently known. This study evaluates the relationship between serum level of CGRP in DPN patients and their level of pain perception.

*Materials and method***:** Sixty volunteers were recruited for the study and divided into groups A and B. Group A consisted of 30 healthy volunteers who were randomly selected in the community. Group B was made up of 30 volunteer patients who presented with DPN having minimum of two symptoms (pain plus any other) and diagnosed (using Biothesiometer) at the diabetic clinic in Ekiti-State University Teaching Hospital, Ado-Ekiti, Ekiti-State. All subjects were trained and informed consents were obtained. They all underwent the sub-maximal effort tourniquet test, blood sample were taken and serum separated for the analysis of CGRP. Independent-Sample t-test was used to analyse the results and significance level was at $p \leq 0.05$.

*Result***:** The time of pain tolerance was significantly lower in DPN (42.68±1.91 seconds) compared to control group (61.80±3.21 seconds). Serum level of CGRP (97.89±1.84) in DPN patients was significantly lower compared to control group (146.07±5.63).

Conclusion: This study has shown that patients with DPN are more susceptible to pain, which may be associated with lower levels of Calcitonin Gene Related Peptide. Thus there is an inverse relationship between diabetic peripheral neuropathic pain and CGRP

Correspondence: Dr. B.V. Owoyele, Department of Physiology, University of Ilorin, Ilorin, Nigeria. E-mail: deleyele@yahoo.com

Keywords: *Diabetic polyneuropathy, dyslipidaemia, endothelial dysfunction, inflammation*

Résumé

Introduction : La polyneuropathie diabétique (DPN) est la complication la plus courante du diabète sucré affectant jusqu'à 50% des patients dont le premier symptôme est généralement une sensation douloureuse. Le DPN parmi les autres complications micro-vasculaires du diabète sucré est la principale cause de décès chez ces patients. Le diabète sucré est associé à des maladies cardiovasculaires présentant des facteurs de risque tels que la dyslipidémie, le dysfonctionnement endothélial, l'inflammation, les anomalies de la paroi vasculaire et le stress oxydatif conduisant à unevasoconstriction, constituant l'une des causes hypothétiques de la DPN. Le peptide associé au gène de la calcitonine (CGRP) est le vasodilatateur micro-vasculaire le plus puissant actuellement connu. Cette étude évalue la relation entre le taux sérique de CGRP chez les patients atteints de DPN et leur niveau de perception de la douleur.

Matériel et méthode **:** Soixante volontaires ont été recrutés pour l'étude et répartis en groupes A et B. Le groupe A était constitué de 30 volontaires en bonne santé choisis au hasard dans la communauté. Le groupe B était composé de 30 patients volontaires présentant une DPN d'au moins deux symptômes (douleur et tout autre) et diagnostiqués (à l'aide d'un bio-thésiomètre) à la clinique diabétique de l'Hôpital d'Enseignement Universitaire de l'Etat d'Ekiti, Ado-Ekiti, l'Etat d'Ekiti. Tous les sujets ont été formés et des consentements éclairés ont été obtenus. Ils ont tous subi le test de garrot sous-maximal, des échantillons de sang ont été prélevés et le sérum séparé pour l'analyse du CGRP. Le test t pour échantillon indépendant a été utilisé pour analyser les résultats et le niveau de signification était à p dd 0,05.

Résultat **:** Le temps de tolérance à la douleur était significativement plus bas dans le DPN (42,68 ± 1,91 seconde) que chez le groupe témoin (61,80 ± 3,21 secondes). Le taux sérique de CGRP (97,89 ± 1,84)

chez les patients atteints de DPN était significativement inférieur par rapport au groupe témoin (146,07 ± 5,63).
Conclusion: Cette étude a montré que les patients atteints de DPN sont plus sensibles à la douleur, ce qui peut être associée à des taux plus faibles de peptide lié au gène de la calcitonine. Il existe donc une relation inverse entre douleur neuropathique périphérique diabétique et CGRP.

Mots clés: *Polyneuropathie diabétique, dyslipidémie, dysfonctionnement endothélial, inflammation*

Introduction

Chronic pain is recognized as pain that extends beyond the period of healing, with levels of identified pathology that in most cases are low and insufficient to explain the presence and/or extent of the pain [1]. Chronic pain, also defined as a persistent pain that "disrupts sleep and normal living which ceases to serve a protective function, but instead degrades health and functional capability "[2].

Diabetic mellitus (DM) is a known global metabolic disorder, with higher prevalence noted recently in the developing nations around the globe [3]. It is a group of metabolic diseases characterized by high blood sugar levels over a prolonged period [4]. The fasting blood glucose level is usually $\geq$ 7.0 mmol/l and this value is obtainable on two separate occasions. Moreover, plasma glucose $\geq$ 11.1 mmol/l detected two hours after a 75 g oral glucose load or glycated haemoglobin (HbA1C) level $\geq$ 48 mmol/mol" [4] is characteristic of DM.

In 2013, the World Health Organization estimated that about 422 million (8.5%) adults globally were living with DM, out of which about 50% have diabetes polyneuropathy (DPN) [5]. Diabetes mellitus is associated with wide range of cardiovascular complications, affecting the cardiovascular system directly by its effect on atherosclerosis of the large arteries (macrovascular complications e.g. ischaemic heart disease, stroke) and small arteries (microvascular complications e.g. neuropathy, nephropathy and retinopathy) [6], indirectly by enabling risk factors leading to vasoconstriction, such as endothelial dysfunction, dyslipidaemia, inflammation, and vascular wall abnormalities [7]. All these point to the fact that these patients have relative vasoconstriction and poor capillary response in their vascular bed which results in constant relative ischaemic insult to nerves [8].

Diabetes polyneuropathy is the most common microvascular complication of diabetes mellitus [9]. This condition may either be silent or go undetected for many years while causing its damage on the nerve cells [10] or present with classical clinical symptoms which are usually insidious at onset [11]. Statistically, DPN is the most common cause of non-traumatic nerve damage in the world [12]. Approximately twelve percent (12%) of DPN patients present with neuropathic pain [13]. Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system [14]. The DPN patients usually present with one or more of these symptoms; tingling, shooting, numbness as well as burning pain sensation especially in the limbs, and more frequently in the lower limbs [11].

Diabetic polyneuropathy affects all peripheral nerves including somatosensory neurons (pain fibres), motor neurons and the autonomic nervous system. It is the main initiating factor for foot ulceration, Charcot neuroarthropathy, and lower-extremity amputation [15]. The pathogenesis and progression of DPN is complicated, but the recent hypothesis suggests that neuroimmune interactions [16] and glial cells [17] actively contribute to the pathogenesis and the progression of the associated pain.

Nerve Growth Factor (NGF) was the first neurotrophin identified as having a key role in the survival and function of sensory and sympathetic neurons in the peripheral nervous system (PNS), as well as basal forebrain cholinergic neurons in the CNS [18,19]. Two to three decades ago, there were multiple reports of reduced levels of NGF and its regulated neuropeptides (CGRP and SP) in dorsal root ganglion (DRG) of sensory neurons and spinal dorsal horn in rodent models of painful diabetic neuropathy and chemotherapy induced peripheral neuropathy (CIPN), that are peripheral neuropathic pain models [20,21].

Calcitonin Gene-Related Peptide (CGRP) belongs in the calcitonin gene peptide superfamily [22]. It is a 37-amino acid neuropeptide derived from the gene encoding calcitonin [23,24]. CGRP is found in almost every system in the body [25], occurring in two isoforms, alpha (α) and beta (β) CGRP [26,27]. Alpha CGRP is the predominant form in the peripheral nervous system, while the β isoform is mainly present in the enteric nervous system [28]. Immunohistochemistry demonstrated that CGRP is mainly produced in the cell bodies of both ventral and dorsal root neurons [29], which is primarily localized to C and A sensory fibres [30] and these fibres display a wide innervation throughout the body with extensive perivascular localization, and serve a dual role in sensory (nociceptive) and efferent (effector) functions [31,32]. After synthesis, CGRP is stored in large, dense-core vesicles within the

sensory nerve terminal [33]. It may act locally as a paracrine molecule or at more distant site leading to measurable quantities in the systemic circulation exhibiting a range of biological effects on various tissues of the body systems, including those associated with gastrointestinal, endocrine and central nervous systems (CNS) (34,35). The peptide micro-vascular vasodilatory potency is 10-fold more effective than the most potent prostaglandins and 10–100 times more potent than other vasodilators such as Acetylcholine (Ach) and Substance P (SP) which makes CGRP debatably the most potent endogenous micro-vascular vasodilator known [36, 37].

There is increasing evidence that there is a deficiency of nerve growth factor (NGF), and its dependent neuropeptides, substance P and CGRP, in diabetes mellitus [38]. Though, the scope of this work does not permit direct assay of NGF, the study was carried out to determine the association between serum CGRP and pain perception in DPN patients'.

Methods

Human subjects

Sixty (60) volunteers were recruited for the study based on the recommendation of Voorhis and Morgan [39]. Thirty (30) healthy volunteers were randomly selected in the community to serve as control and 30 volunteer patients with type II diabetes with DPN complication according to the criteria established by American Diabetes Association [40], were selected from diabetic clinic in Ekiti State University Teaching Hospital.

Protocol

These individuals were older than 20 years, with the mean age of the control group at 51.7±1.72 years and that of DPN at 58.17±1.6 years. The known diagnosed diabetic neuropathic patients selected are the ones who presented with minimum of two symptoms, pain plus any other symptom (tingling, shooting, numbness mostly in the limbs). Their Vibration Perception Threshold (VPT) was also measured, using a biothesiometer, to define the presence of diabetic neuropathy with a cut off VPT of more than 25 volts for the diagnosis of loss of protective sensation which was carried out at diabetic clinic in Ekiti-State University Teaching Hospital, Ado-Ekiti.

They were recruited, trained on what they should expect during the study and informed consent was obtained. All subjects underwent the following procedures: history taking, physical examination, Blood Pressure (BP) measurement, Quantitative sensory test (sub-maximal effort tourniquet test) and biochemical analysis. All procedures were done in the morning after an overnight fast. Subjects were excluded if they had; another neurological or painful disorder, on-going infection, immunosuppression, smoking, psychiatric illness, myocardial infarction, blood diseases that affect neutrophil and lymphocyte counts (e.g. leukaemia) or inability to give written informed consent. Approval (Protocol number: EKSUTH/A67/2016/12/005) was obtained from the Research and Ethical Review Committee of the Ekiti State University Teaching Hospital, Ado Ekiti, Ekiti State, Nigeria

Sub-maximal effort tourniquet test

The ischaemic pain testing (sub-maximal effort tourniquet test) was based on the method described by Plesan *et al*. [41]. A blood pressure cuff was placed around the non-dominant arm of the subject. The cuff pressure was increased to 20mmHg above the subject's systolic pressure. With the pressure maintained, subject performed a hand grip exercise on an elastic ball. The subject closes his/her eyes for the entire procedure to minimize distraction and time cues. Subjects were then asked to indicate when they first detected the pain and when they could no longer tolerate the pain (to a maximum of 5 minutes). Once pain tolerance was reached, the pressure curve was immediately deflated and end-points were measured in seconds with the process performed 3 times and average of the readings documented [41].

Pain tolerance assessment

The pain tolerance was defined as the point subject could no longer withstand the pain and the time taken for this to occur was recorded in seconds. The process was performed 3 times and the average wass documented.

Biochemical analysis

Determination of Fasting Blood Sugar (FBS)

Blood samples were collected at the cubital vein while the fasting blood sugar analysis was done immediately using digital glucometer (On Call Plus II, ACON Laboratories, Inc., San Diego, USA). The remaining blood sample was collected in a plain bottle, allowed to clot and centrifuged at 3000 rpm for 10 minutes. Serum was separated into another plain bottle and stored at -70^{0}C in the refrigerator until the analysis of CGRP.

Determination of serum calcitonin gene related peptide

Measurement of CGRP was done using enzyme immunoassay technique (ELISA) kit (Elabscience

Biotechnology Co. Ltd, China). This assay employs the competitive inhibition enzyme immunoassay technique. A monoclonal antibody specific to Calcitonin Gene Related Peptide (CGRP) has been pre-coated onto a microplate and a competitive inhibition reaction was launched between biotin labeled CGRP and unlabelled CGRP (Standards or samples) with the pre-coated antibody specific to CGRP. After incubation we washed off the unbound conjugate. Then, we added avidin conjugated to Horseradish Peroxidase (HRP) to each microplate well and incubated. The amount of bound HRP conjugate was inversely proportional to the concentration of CGRP in the sample. After addition of the substrate solution, the intensity of colour developed was inversely proportional to the concentration of CGRP in the sample. [42]

Statistical analysis

All data were expressed as the Mean ± SEM. The effects of the varied intervention of each of group were tested for homogeneity using Independent-Samples *t* test using SPSS version 20 software with the level of significance set at $p \leq 0.05$.

Results

Effect of diabetic polyneuropathy on fasting blood sugar (FBS)

The FBS among the control group and patients with DPN are shown in figure 1. There is a significantly higher FBS in DPN (8.09±0.81 mmol/l) compared with the control group (4.38±0.09 mmol/l) with the $p< 0.01$.

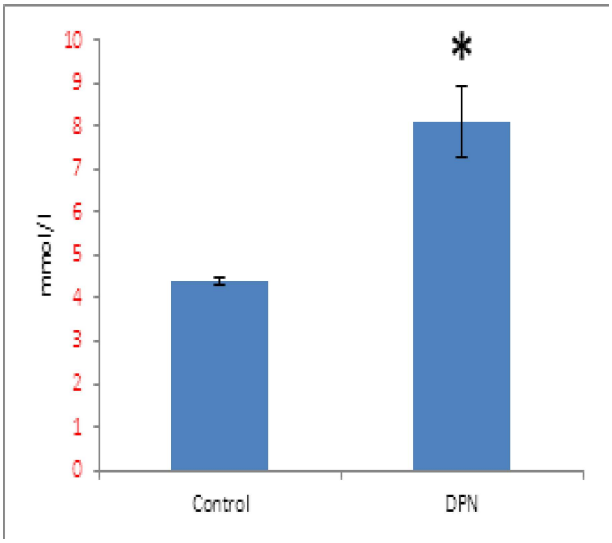

Fig. 1: Fasting Blood Sugar (FBS) level among the Control and Diabetic Neuropathy Patients. Values are expressed in mean± SEM. There is a significantly higher FBS level in DPN (8.09±0.81 mmol/l) compared to the control (4.38±0.09 mmol/l) with p value at 0.00

Effect of diabetic polyneuropathy on pain tolerance

Figure 2 shows the pain tolerance among the control and patients with DPN. There is a significantly lower pain tolerance in DPN (42.68±1.91 seconds) compared to the control group (61.80±3.21 seconds) with the $p<0.03$.

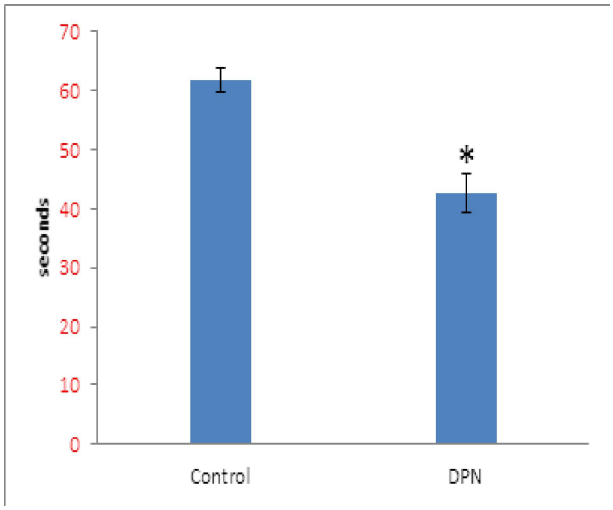

Fig. 2: Pain tolerance in the Control and Diabetic Neuropathy Patients using sub-maximal effort tourniquet test. Values are expressed in mean± SEM. There is a significantly lower pain tolerance in DPN (42.68±1.91 seconds) compared to the control (61.80±3.21 seconds) with $p < 0.03$

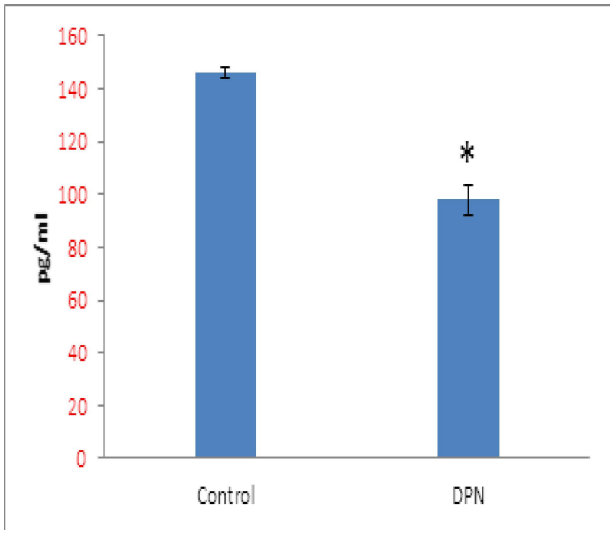

Fig. 3: Serum level of Calcitonin Gene Related Peptide (CGRP) in the Control and Diabetic Neuropathy Patients . Values are expressed in mean± SEM. There is a significantly lower serum level of CGRP in DPN (97.89±1.84) compared to the control (146.07±5.63) with $p < 0.01$.

Effect of diabetic polyneuropathy on serum calcitonin gene related peptide (CGRP)

Serum level of CGRP among the control group and diabetic neuropathy patients are shown in figure 3. The level of serum CGRP (97.89±1.84 pg/ml) in patients with DPN is significantly lower compared to the control group (146.07±5.63 pg/ml) with the $p<0.01$.

Discussion

This study investigated the significant association between systemic CGRP and pain perception of DPN patients.

The results showed that, there was a significantly higher FBS in DPN group compared to the control group. This finding reaffirms the basic underlying hyperglycaemic status of these patients which has been traced to the root of all the micro-vascular and macro-vascular complications of diabetes mellitus [43]. There was also a significantly lowered pain tolerance in DPN group compared to the control group. Farmer *et al.* described the pain associated with diabetes as hyperalgesia, allodynia, paresthesia and spontaneous pain [44]. In a relative hyperglycaemic condition, the affinity of aldose reductase for glucose is high, leading to the conversion of the extra glucose to more sorbitol. Sorbitol does not cross cell membranes and accumulates intracellularly in the nervous tissue, thus generating osmotic stress. Osmotic stress increases the intracellular fluid molarity as well as water influx, Schwann cell damage and nerve fibre degeneration [45]. These changes result with increases in wall thickness with the hyalinization of the vessel walls and the basal lamina of arterioles and capillaries, leading to nerve ischaemia [46], which eventually leads to nerve damage and abnormal pain sensation noticed in the patients.

The results of this study showed a significantly lowered serum level of CGRP in DPN group compared to the control group. This corroborates the findings of Wang *et al.* who reported that the circulating CGRP levels are decreased in diabetes mellitus patient [47]. CGRP as a micro-vascular vasodilator has a potency that is 10-fold higher than the most potent prostaglandins and 10–100 times greater than other vasodilators such as Ach and SP [37]. This makes CGRP arguably the most potent endogenous micro-vascular vasodilator currently known [36]. This action is via the CGRP-induced increase in cAMP led to activation of protein kinase A and, in some cases, the opening of ATP-sensitive Potassium (k) channels, which is now considered an important pathway leading to vasodilatation [48].

It is obvious from above literature, that CGRP plays a crucial role in the response of the perivascular vessels to pain stimuli. The results of this study however suggest a positive correlation between relative vasoconstriction of these vessels and poor vascular response, which would result in lower pain tolerance observed in DPN patients when compared to the control group.

Calcitonin Gene Related Peptide gene transfer selectively upgrades Th2 and downgrade Th1 cytokines synthesis, playing a vital role in the body's innate anti-inflammatory process. However, our result shows that DPN patients have lower level of CGRP, which further explains their lower pain tolerance when compared to the control group.

Bennett *et al.*[49] and Tomlinson *et al.*[50] reported that diabetes mellitus is associated with down-regulation of NGF, and as a consequence, a loss of CGRP-containing sensory neurons, main while, one of the current hypothesis of DPN suggests the active role of neuroimmune interactions in the onset and progression of DPN [16]. This then may raise the question that maybe there is an auto-antibody targeted at the NGF and CGRP production in DPN, even though the scope of this work does not address NGF assay and isolation of such antibodies if they were, but the result of our serum CGRP in DPN is suggestive.

Overall, there is need to further investigate the therapeutic roles of CGRP in the management of DPN.

Conclusion

This study has shown that patients with DPN are more susceptible to pain, which may be associated with lower levels of Calcitonin Gene Regulating Peptide

Ethical clearance

Approval was obtained from the Research and Ethical Review Committee of the Ekiti State University Teaching Hospital, Ado Ekiti, Ekiti State, Nigeria.

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Knowledge, attitude and practices regarding Buruli ulcer among rural inhabitants in Ogun State, Nigeria

PI Otuh[1,2], OK Adeyemo[1], EE Nwezza[3], OJ Daniel[4] and FO Soyinka[5]

Department of Veterinary Public Health and Preventive Medicine[1] and Veterinary Teaching Hospital[2], University of Ibadan, Ibadan, Department of Mathematics/ Computer Science/Statistics and informatics[3], Federal University Ndufu Alike Ikwo, Ebonyi State, Department of Community Medicine and Primary Care[4], Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State and Ogun State Tuberculosis, Leprosy and Buruli Ulcer Control Programme[5], Ministry of Health, Abeokuta, Ogun State, Nigeria

Abstract

*Background***:** *Mycobacterium ulcerans* disease referred to as Buruli ulcer (BU) is a health burden in West African sub-region. The mysterious nature of BU is ascribed to peculiarities surrounding its mode of transmission and pathology. Buruli ulcer is predominantly found in rural communities with difficulty in assessing the true prevalence because of poor understanding of the disease as well as disinclination towards quality health-seeking behaviors which leads to underreporting of the disease. This study was designed to ascertain the extent of knowledge of BU, the attitudinal disposition of inhabitants in the susceptible communities and predisposing practices which might increase their risk to the disease.

*Methods***:** A descriptive cross-sectional Knowledge, Attitude and Practices (KAP) survey was conducted in eight randomly selected Local Government Areas in Ogun State from May 2014 to July 2015. Purposive (respondents with cases of BU) and simple random sampling were employed for this study. Structured pre-tested questionnaire was administered to consenting respondents from selected communities. Data generated were analyzed using Pearson's Chi-square and logistic regression.

*Results***:** Respondents showed (69.7%, 7.2%, 46.7%) good knowledge, attitude and practices towards BU, respectively. Majority (62%) believed BU to be an affliction of spiritual or ancestral origin. There was significant association between BU knowledge and occupation (÷2 = 9.952, df =4, p-value=0.041); attitude and education (÷2 = 20.058, df=3, p-value=0.000) and predisposing practices with age, education and occupation (÷2 = 13.788, df=3, p-value=0.003, ÷2 = 8.295, df=3, p-value=0.04, ÷2 = 40.544, df=4, p-value=0.000), respectively.

Conclusion: Despite the relatively good knowledge, there was generalized reluctance of associating with BU patients shown by the marked poor attitude recorded in this study. It is obvious that the populations under study were ignorant, hence susceptible to increased exposure to the risks of BU. Buruli ulcer enlightenment programs should be initiated in the affected communities in Ogun State.

Keywords: *Buruli ulcer, mycobacterium ulcerans KAP survey, rural populace.*

Résumé

Contexte **:** La maladie *Mycobacterium ulcerans* dénommée ulcère de Buruli (UB) est un fardeau pour la santé dans la sous-région de l'Afrique de l'Ouest. La nature mystérieuse de l'UB est attribuée aux particularités de son mode de transmission et de sa pathologie. L'ulcère de Buruli se rencontre principalement dans les communautés rurales avec des difficultés à évaluer la prévalence réelle en raison d'une mauvaise compréhension de la maladie et d'un manque de volonté d'adopter des comportements de qualité qui favorisent la santé ce qui conduit à une sous-déclaration de la maladie. Cette étude visait à déterminer l'étendue des connaissances sur l'UB, la disposition attitudinale des habitants des communautés vulnérables et les pratiques prédisposant susceptibles d'accroître leur risque de contracter la maladie.

Méthodes **:** Une enquête descriptive transversale sur les connaissances, les attitudes et les pratiques (CAP) a été menée dans huit communes sélectionnées de manière aléatoire dans l'État d'Ogun, de mai 2014 à juillet 2015. Un échantillonnage au choix (les répondants avec cas d'UB) et un échantillonnage aléatoire simple ont été utilisés pour cette étude. Un questionnaire pré testé structuré a été administré aux répondants consentants des communautés sélectionnées. Les données générées ont été analysées à l'aide de la régression logistique et du chi carré de Pearson.

Résultats **:** Les répondants ont montré (69,7%, 7,2%, 46,7%) de bonnes connaissances, attitudes et

Correspondence: Dr. Patricia I. Otuh, Veterinary Teaching Hospital, University of Ibadan, Ibadan, Nigeria. E-mail: ifunanyachukwu.ihuaku@gmail.com

pratiques vis-à-vis de l'UB, respectivement. La majorité (62%) pensait que l'UB était une affliction d'origine spirituelle ou ancestrale. Il existait une association significative entre la connaissance de l'UB et la profession ($\chi2$= 9,952, df = 4, valeur p = 0,041); attitude et éducation ($\chi2$ = 20.058, df = 3, p-value = 0,000) et pratiques prédisposant avec l'âge, l'éducation et la profession ($\chi2$ = 13,788 df = 3, p-value = 0,003 ; $\chi2$ = 8,295, df = 3, valeur p = 0,04 ; $\chi2$ = 40,544, df = 4, p-value = 0,000), respectivement.

Conclusion : En dépit de connaissances relativement bonnes, il existait une réticence généralisée à s'associer aux patients atteints d'UB révélée par l'attitude nettement médiocre enregistrée dans cette étude. Il est évident que la population étudiée était ignorante et donc susceptible d'être davantage exposée aux risques de l'UB. Des programmes de sensibilisation à l'ulcère de Buruli devraient être lancés dans les communautés touchées de l'Étatd'Ogun.

Mots clés : *Mycobacterium ulcerans*, *au hasard, questionnaire, prédisposant, ulcère de Buruli*

Introduction

Neglected Tropical Diseases (NTDs) are abundant in under-developed or developing countries causing outcomes of devastating magnitudes [1]. Buruli ulcer (BU) is one of the leading neglected tropical disease in West Africa with outcome of untold misery among rural people who are ignorant about the disease [2–4]. There is peculiar obvious difficulty of proper BU disease reporting system and data documentation in most endemic regions [5,6]. Increasing prevalence of BU in sub-Saharan Africa especially in West Africa is reported as not being solely due to outbreak of totally new infections but as a result of all-embracing focus on dynamic inputs of individual endemic countries on BU targeted surveillance [4].

In Nigeria, BU is not on the list of notifiable diseases captured with the current disease surveillance system and therefore has limited awareness among healthcare workers as well as the populace unlike other West African countries [4,7]. Only few cases of BU have been documented in Nigeria with previous reports focusing on clinical cases recorded either at hospital presentation or as a result of active case searches despite the fact that the country is within the BU belt that spans across neighboring countries in West Africa [8–11]. Up till now, the exact mode of transmission is yet unknown which hampers efforts to prevent and control the disease [12–14]. Therefore in order to achieve prevention and control, there is need to understand the knowledge, attitude and practices of the people living in areas where the disease is endemic. [15]. Quite a number of West African countries have adequately established National BU control programme saddled with the responsibilities of carrying out organized BU national active case search periodically, integrating grass-root awareness and free rural healthcare outreach where information on BU are disseminated and myths surrounding the disease demystified [4,7,16,17].

Ogun State is closely bordered with Benin Republic which is described as a BU epicenter and information on the epidemiology of BU in Ogun State is scarce. Establishment of information regarding BU among the most predisposed rural populace is very vital in achieving meaningful goals of finding out its prevalence which is uncertain in most endemic countries, encouraging affected people to report early and receive prompt treatment so as to forestall extensive devastating effects of BU [14,18,19]. Gathering information on BU in Ogun State is an essential step in assessing the status of this disease in the state. This targeted approach will thus ensure that BU level is delineated and consequently measured in the state and if absent also evaluated. Therefore, the aim of this study was to conduct a comprehensive descriptive observational study on Buruli ulcer in Ogun State using KAP survey to evaluate the disposition of the rural populace to the disease.

Materials and methods

Study locations

This study was conducted in Ogun State, south west Nigeria sharing close proximity with Benin Republic to the west. Ogun State is historically divided into three regions; Ijebu region (Ogun East), Egba region (Ogun Central), Yewa region (Ogun West) comprising of 20 Local Government Areas (LGAs) and has an estimated population of 3.8 million people [20]. Eight LGAs were randomly selected across the three regions of the state. From Ijebu region comprising nine LGAs; Ogun waterside, Ijebu North, Remo North and Sagamu LGAs were selected while Abeokuta North and Odeda LGAs were selected from Egba region consisting of five LGAs. Finally, Yewa region with six LGAs had Yewa North and Yewa South LGAs selected. This was done to ensure evenly distributed geographical spread representation (Figure 1).

Study design

Descriptive Observational study adopting Knowledge, Attitude and Practices (KAP) survey on rural inhabitants residing within the three regions of Ogun state was employed. Pre-visit was made to all

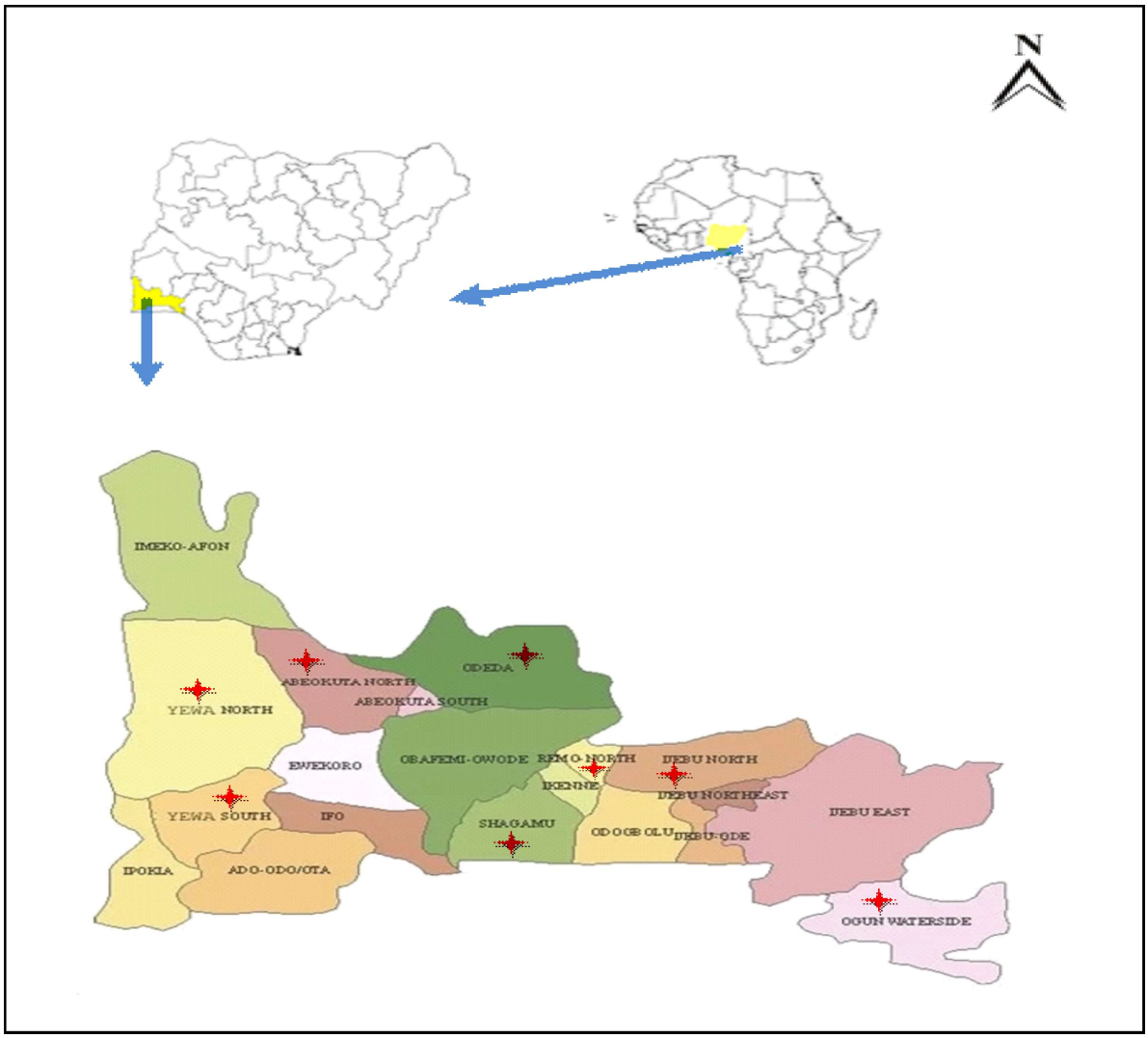

Fig 1: Map of Ogun State showing study locations
(Inserts: Maps of Africa and Nigeria)

the regions and contacts established with local government health units of the eight randomly selected LGAs.

Data collection

Altogether, the randomly selected eight LGAs were surveyed between May 2014 and July 2015 using cross-sectional method. Well structured questionnaire containing demographic information of respondent and questions on what respondent knew in relation to BU, beliefs as regards BU patients together with what is actually done concerning seeking healthcare and taking other actions relating to BU was used. The questionnaire utilized in this study was pre-tested for consistency, reliability and validity in Ajibode community, Akinyele LGA, Oyo state (locations were at the exterior of the main study area for this survey). The conclusions and experiences from the pre-testing of the questionnaire served as means to refine and clarify questions as well as filling instructions prior to starting actual data anthology. The sample size of participants (respondents) as to the number of questionnaire to be used in the survey was calculated taking into consideration of expected Prevalence of BU at 50% [21]. Thus:

$n = 1.96^2 P_{exp}(1-P_{exp})/ d^2$

Where,

n is minimum required sample size,

P_{exp} is expected prevalence (which is usually 50% in a case of an unknown prevalence of the disease under study) = 0.5 (50%),

d is desired absolute precision which is 0.05 for 95% confidence interval.

$1.96^2 0.5(1- 0.5)/ 0.05 = 3.8416 \times 0.25/0.0025 =$ 384 questionnaires.

The eight participating LGAs had a total of 86 communities of which through random selection

42 gave their approval to take part in the survey. Respondents were selected at each gathering from the community visits (10 willing adults interested in participating in the survey were randomly chosen). The well structured questionnaire was distributed across the 42 communities to the overall 420 consenting respondents [22]. In Yewa region (Ogun west), 60 questionnaire were distributed across six communities in Yewa south LGA; 60 questionnaire in six communities within Yewa North LGA while Egba region (Ogun Central) had 120 questionnaire distributed among seven and five communities in Odeda and Abeokuta LGA respectively. However four LGAs; Ijebu-North, Ogun waterside, Sagamu and Remo North had 180 questionnaires distributed across 18 communities.

Data analysis

STATA version 12 statistical software was used for statistical analysis. Demographic characteristics of respondents were presented by descriptive and exploratory analysis. The responses to the questionnaire were scored on a scale of 1-6; 1-3 as poor and 4-6 as on good. Pearson's chi-square was used for testing possible associations between categorical variables while multivariable adjusted logistic regression analysed the relationship between demographic (independent variables) and the level (good/poor) of the dependent variables; knowledge, attitude and practices. The statistical significance was measured at p-value $\leq \alpha_{0.05}$ level of significance.

Ethical consideration: Ethical approval (HREC REG. NUMBER: NHREC/8/10/2012) was obtained from the Ethical Research Committee of Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Ogun State. Consenting patients' confidentiality will be protected and beneficial outcome of this survey will be communicated to the respondents as contained and signed in the informed consent form.

Results

Demographic characteristics of KAP survey respondents

A total of 390 questionnaires were returned and analysed. The mean age of respondents was 38.4±9.9. More than one-quarter of the respondents; 109 (27.9%) were 30 years and below; 98 (25.0%) were between 32years and 39 years; 94 (24.2%) were between 40years and 46years while the remaining 89 (22.9%) were 47years old and above. Gender category revealed that 230 (58.9%) of males and 160 (41.1%) of females participated. About one-third of the respondents; 136 (34.9%) had primary education; 124 (31.8%) had secondary education; 23 (5.8%) had tertiary education while 107 (27.5%) had no education at all. Farmers (168) made up 43.0% of occupation category; 109 (28.0%) were businessmen/women, 7.4% students, 4.1% fishermen while 17.5% were government workers (Table 1).

The respondents showed 69.7% and 30.3% good and poor knowledge; 7.2% poor and 92.8% good attitude while 46.7% and 53.3% respondents had good and poor practices towards factors predisposing to BU, respectively (Table 2).

Table 1. Socio-demographic characteristics of respondents

Variable	Category	Frequency	Percentage
Gender	Male	230	58.9
	Female	160	41.1
Age	≤30	109	27.9
	32 – 39	98	25.0
	40 – 46	94	24.2
	≥47	98	22.9
Occupation	Farmers	168	43.0
	Traders	109	28.0
	Students	29	7.4
	Fishermen	16	4.1
	Civil servants	68	17.5
Education	No education	107	27.5
	Primary	136	34.9
	Secondary	124	31.8
	Tertiary	23	5.8

Table 2. Knowledge, attitude and practice status of respondents.

Variables	Category	Frequency	Percentage
Knowledge Status	Good	272	69.7
	Poor	118	30.3
Attitude Status	Good	28	7.2
	Poor	362	92.8
Practices Status	Good	182	46.7
	Poor	208	53.3

Respondent's knowledge of Buruli ulcer.

The knowledge category revealed that 307 (78.7%) of the respondents had heard about Buruli ulcer; of which 197 (50.5%) know the local name as *egbo ada ijina* (wound that can never heal), 98 (27.2%) call it *ofa* (evil arrow from the evil world) while 28 (7.2%) know BU as *aisan tioogbogun* (disease without remedy). The respondents proffered divergent perceived causes of BU ranging from germs (11%), money rituals (12%), curse from gods (26%) and spiritual attack (36%) as shown in Figure 2. A total of 380 (97.4%) respondents showed a high

level of ignorance on availability of free BU treatment opportunity.

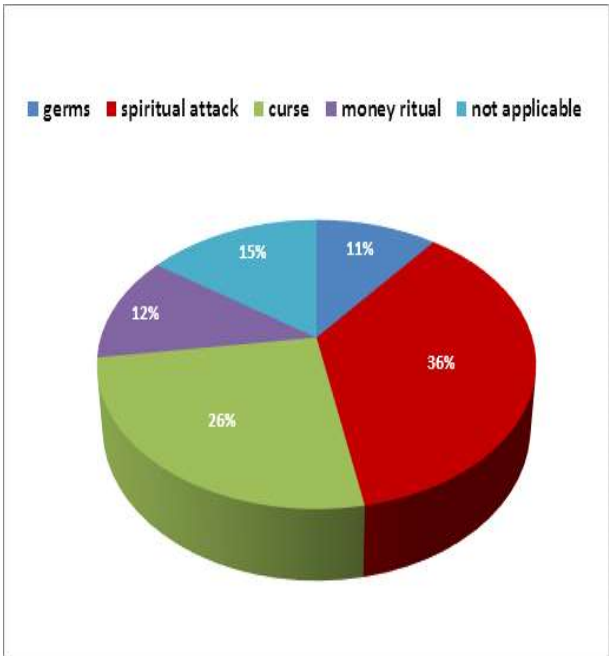

Fig 2: Respondents' distribution of perceived causes of Buruli ulcer.

There was significant difference between occupation and knowledge of respondents on Buruli ulcer (÷2 = 9.952, df =4, p-value=0.041). Traders showed less likelihood to be knowledgeable (OR=0.5; 95%CI: 0.3 – 0.8) while Civil servants (OR=1.4; 95%CI: 1.2 – 1.8) showed higher likelihood of being knowledgeable about the disease (Tables 3 and 4).

Respondents' attitude towards Buruli ulcer.

Only 43 (11%) of the respondents indicated that they can live with a BU patient, however 206 (52.8%) respondents believed that BU is contagious hence will isolate themselves from BU patients. Education was found to be significantly associated with attitude towards BU (÷2= 20.058, df=3, p-value=0.00). Females are about three times more likely to show good attitude (OR= 2.9; 95%CI: 1.3 – 6.7; p=0.01) while those in business have less likelihood to show good attitude (OR= 0.2; 95%CI: 0.0 – 0.7). As indicated in Tables 5 and 6.

Respondents' predisposing practices towards Buruli ulcer

Respondents' practices towards BU revealed that 352 (90.3%) engaged in farming activities, of which 133 (54.6%) do not use protective covering (booths, hand gloves) during farming. Majority of the respondents listed well water as their source of water for domestic nd commercial use nevertheless 142 (38%) of the

Table 3: Knowledge of Buruli ulcer with respect to gender, education, occupation and age.

Variables	Category	Poor knowledge n (%)	Good knowledge n (%)	Total	χ2	df	α-value
Gender	Male	50(12.8)	180(46.1)	230(58.9)	0.201	1	0.654
	Female	30(7.9)	130(33.2)	160(41.1)			
	Total	80(20.7)	310(79.3)	390(100.0)			
Education	No education	17(4.3)	91(23.2)	108(27.6)	3.005	3	0.391
	Primary education	29(7.4)	107(27.6)	137(34.9)			
	Secondary education	30(7.9)	94(24.0)	124(31.9)			
	Tertiary education	4(1.0)	18(4.6)	22(5.6)			
	Total	80(20.7)	310(79.3)	390(100.0)			
Occupation	Farmer	23(5.9)	145(37.2)	168(43.1)	9.952	4	0.041**
	Businessmen/women	30(7.9)	79(20.2)	110(28.1)			
	Student	7(1.8)	22(5.6)	29(7.4)			
	Fisherman	3(0.8)	13(3.3)	16(4.1)			
	Government	17(4.3)	51(13.0)	67(17.3)			
	Total	80(20.7)	310(79.3)	390(100)			
Age	≤30	19(4.8)	91(23.2)	110(28.1)	1.880	3	0.597
	32-39	22(5.9)	74(18.9)	97(24.7)			
	40-46	18(4.6)	77(19.6)	95(24.2)			
	≥47	21(5.4)	68(17.6)	90(23.0)			
	Total	80(20.7)	310(79.3)	390(100.0)			

** = *significant*

Table 4: Factors associated with knowledge of respondents on Buruli ulcer

Variable	Category	OR	95%CI	P-value
Gender	Male	1		
	Female	0.9	0.6 – 1.5	0.88
Occupation	Farmers	1		
	Business	0.5	0.3 – 0.8	0.02**
	Fishing	1.1	0.4 – 3.0	0.79
	Student	1.7	0.2 – 2.0	0.49
	Civil servant	1.4	1.2 – 1.8	0.02**

Table 5: Attitude of respondents with respect to age, gender, occupation and level of education

Variables		Poor attitude n(%)	Good attitude n(%)	Total	X^2	Df	α-value
Age	≤31	105(26.7)	5(1.3)	110(28.0)	6.165	3	0.105
	31-39	90(22.9)	7(2.0)	97(24.9)			
	40-46	84(21.6)	10(2.5)	94(21.2)			
	≥47	76(19.6)	13(3.3)	89(22.9)			
	Total	355(90.8)	35(9.6)	390(100.0)			
Gender	Male	216(55.2)	14(3.6)	230(58.8)	5.598	1	0.180
	Female	139(35.6)	21(5.6)	160(41.2)			
	Total	355(90.8)	35(9.2)	390(100.0)			
Education	No education	97(24.7)	11(2.8)	108(27.5)	20.058	3	0.000**
	Primary education	121(31.0)	14(3.8)	135(34.9)			
	Secondary education	121(31.0)	3(0.8)	124(31.8)			
	Tertiary education	16(4.1)	7(1.8)	23(5.9)			
	Total	355(90.8)	35(9.2)	390(100.0)			
Occupation	Farmer	149(38.2)	19(4.8)	168(43.0)	6.376	4	0.173
	Businessmen/women	106(27.0)	4 (1.0)	110(28.0)			
	Student	25(6.6)	3(0.8)	28(7.4)			
	Fisherman	15(3.8)	1(0.3)	16(4.1)			
	Government	59(15.3)	9(2.3)	68(17.6)			
	Total	355(90.8)	35(9.2)	390(100.0)			

***** = significant***

Table 6: Factors associated with attitude of respondents on Buruli ulcer

Variable	Category	OR	95%CI	α-value
Age	≤ 31	1		
	31-39	0.6	0.2 – 1.4	0.29
	40-46	1.4	0.1 – 25.3	0.80
	≥47	0.7	0.2 – 3.3	0.92
Gender	Male	1		
	Female	2.9	1.3 – 6.7	0.01**
Occupation	Farmers	1		
	Business	0.2	0.0 – 0.7	0.02**
	Fishing	1.1	0.1 – 9.5	0.94
	Student	—	———	——
	Civil servant	0.6	0.2 – 1.9	0.39

*** = significant*

Table 7: Practices of respondents with respect to age, gender, occupation and level of education

Variables	Category	Poor practice n (%)	Good practice n (%)	Total	X^2	df	α-value
Age	≤31	16(4.1)	92(23.7)	108(27.8)	13.788	3	0.003 **
	32-39	4(1.0)	94(24.2)	98(25.3)			
	40-47	11(2.8)	82(21.1)	93(24.0)			
	49+	2(0.5)	82(21.1)	89(22.9)			
	Total	33(8.5)	355(91.5)	388(100.0)			
Gender	Male	15(3.9)	214(55.1)	229(59.0)	2.166	1	0.141
	Female	18(4.7)	141(36.3)	159(41.0)			
	Total	33(8.6)	355(91.4)	388(100.0)			
Education	No education	3(0.8)	105(27.1)	108(27.8)	8.295	3	0.04**
	Primary education	12(3.1)	123(31.7)	135(34.8)			
	Secondary education	14(3.6)	108(27.8)	122(31.4)			
	Tertiary education	4(1.0)	19(4.9)	23(5.9)			
	Total	33(8.5)	355(91.5)	388(100.0)			
Occupation	Farmer	1(0.3)	166(42.8)	167(43.0)	40.544	4	0.00**
	Businessmen/women	17(4.4)	93(24.0)	110(28.4)			
	Student	9(2.3)	19(4.9)	28(7.2)			
	Fisherman	1(0.3)	15(3.9)	16(4.1)			
	Government	5(1.3)	62(16.00	67(17.3)			
	Total	33(8.5)	355(91.5)	388(100.0)			

** = *significant*

respondents still accessed rivers and streams for different purposes. There were significant differences between education (X^2 = 8.295, df =3, p-value =0.04), age (X^2=13.788, df =3, p-value=0.003), occupation (X^2 = 40.544, df =4, p-value=0.00) and predisposing practices towards Buruli ulcer (Table 7).

Discussion

This study provides an insight into the status of BU from the different regions(Ogun West, Ogun Central and Ogun East) of Ogun State, a finding which collaborated the focal distribution of BU in nature [23]. Demographic profile of respondents indicated that more males participated in the survey than females. However, analyses revealed that assessment of outcome variables of knowledge, attitude and practices when judged on the basis of "poor" or "good" indicated that more females were better than the males. This is in line with other studies which illustrated the commitment of females towards BU patients [5,6]. Notwithstanding overall assertion of good knowledge, respondents were unaware that BU was caused by germs. This disclosed the high level of ignorance leading to poor attitude towards BU patients portrayed by majority of the people. This similarly affected their disposition to the choice of treatment options an off shoot of the reason why many were not aware of the free treatment opportunity for BU patients [6,16,17,19]. Despite the generally poor attitude to BU by the respondents, females showed better attitude and practices towards BU in accordance with previous reports [5,6]. Women are usually more emotionally attached to their children, hence better attitude and practices shown by them [17]. This study equally exposed the fact that there is currently no specific name for BU as description across the communities in local languages is in relation to the chronic nature of the ulcer and not specifically to its etiology.

Association of knowledge of Buruli ulcer with occupation by the respondents may not be unconnected to the fact that majority of the farmers had either their children or themselves suffering from BU. Sudipendra and Avik, [24] discovered that farmers were more likely to be exposed to risks associated with BU than other occupations and therefore better knowledgeable about the disease. Agricultural activities in general was found to be more associated to BU than other sources of economic earnings by families with BU patients [25,26]. However several other studies revealed no association of occupation with knowledge of BU [27,28]. The association determined between knowledge of BU and occupation indicated that traders were less likely to be knowledgeable about

BU. Maybe because, traders are less likely to come in contact with the risks associated with BU although no previous literature exists to validate or disclaim this.

The findings from this study also showed attitude towards BU to be associated with the level of education of the respondents. This outcome is similar to that of Gyasi *et al*., [29] who associated factors like health seeking behaviors with attitude to BU. Practices towards BU was found to be associated with multiple variables (age, education and occupation) which might be attributed to the vulnerable younger people knowing more about BU and hence applying better practices more than the older ones with fewer BU patients in their category. More educated BU patients in a related study had better understanding and sought orthodox health service compared to the non-educated ones who preferred traditional remedies supporting this study which indicated that different levels of education significantly differed with their practices towards BU [30]. Gender and occupation were risks associated to attitude of respondents towards BU. The essential role of women in health giving responsibilities was highlighted in this study as they demonstrated about three times better attitude than males. Fishermen were more likely to have better practices than other livelihoods within the occupation variable as previously documented [5–7,31].

This study therefore highlighted the acuity into the level of Buruli ulcer's knowledge; the attitude as well as practices of the people in BU susceptible locations in Ogun State.

Conclusion

Population studies are very important in understanding peculiar diseases inherent in a population. Information on such diseases from the affected people offers very important direction mostly to researchers as well as for government intervention. Ascertaining in-depth information on peoples' knowledge, attitude and practices towards BU from this study has provided a vital insight to the disease which hitherto was lacking in Ogun State. Majority of the affected people did not believe that BU was treatable; many believed that witchcraft was the cause and many more did not know that treatment was free. It is quite obvious that from this study, education of both rural populace and healthcare providers are of urgent importance. This study has thrown more light on these imperative areas and will subsequently spur many to access medical help early to forestall extensive disfigurement. Government of Ogun state should strengthen public health department of the State Ministry of Health and all healthcare units of the LGAs to undertake epidemiological studies on BU in all LGAs of the state as this will help to establish annual BU prevalence in Ogun State. Several other disease conditions can present with a chronic ulcer which may not be BU as such intensive BU enlightenment campaign in these communities will be needed. The Federal Ministry of Health should equally have an extended plan of conducting a national Buruli ulcer survey across Nigeria.

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Frequency and determinants of postoperative fibrinous uveitis after paediatric cataract surgery at a tertiary hospital in southwest Nigeria

BA Olusanya and AM Baiyeroju

Paediatric Ophthalmology and Strabismus Unit, Department of Ophthalmology, College of Medicine, University of Ibadan, Ibadan, Nigeria.

Abstract

Aims: To determine the occurrence and risk factors of fibrinous uveitis following paediatric cataract surgery.

Methods: This was a retrospective interventional study of children aged less than 16 years who underwent cataract surgery at the University College Hospital, Ibadan, Nigeria between January 2008 and December 2012. Case records of eligible patients were reviewed and patients with missing or incomplete records were excluded. Information retrieved included age at presentation and at surgery, type of childhood cataract, morphology of the cataract, type of surgery performed, occurrence of fibrinous uveitis, and final visual outcome.

*Results***:** A total of 197 eyes of 137 children were studied. Eight-six (62.8%) were boys. The mean age at the time of surgery was 76.1 (±50.5) months. A total of 126 (64.0%) eyes underwent cataract surgery with implantation of polymethylmethacrylate intraocular lens. Seventy (35.5%) eyes had fibrinous uveitis; 15 (21.4%) of these eyes subsequently developed optic capture of intraocular lens. Older age at presentation, older age at surgery, uveitic cataracts, traumatic cataracts and intraocular lens implantation were associated with fibrinous uveitis in bivariate analyses. With logistic regression analysis, however, only intraocular lens implantation was found to be associated with fibrinous uveitis.

Conclusion: Fibrinous uveitis is a relatively common complication of paediatric cataract surgery in our setting. Implantation of polymethylmethacrylate intraocular lens is a significant risk factor for fibrinous uveitis after paediatric cataract surgery.

Keywords: *Paediatric cataract, surgery, fibrinous uveitis, Nigeria*

Résumé

Objectifs : Déterminer la présence et les facteurs de risque d'uvéite fibrineuse après une chirurgie de la cataracte pédiatrique.

Méthodes : Il s'agissait d'une étude rétrospective portant sur l'intervention d'enfants âgés de moins de 16 ans ayant subi une opération de la cataracte auCollège Hospitalier Universitaire d'Ibadan (Nigéria) entre janvier 2008 et décembre 2012. Les dossiers de patients éligibles ont été examinés et les patients, avec information manquante ou incomplète, exclus. Les informations récupérées comprenaient l'âge au moment de la présentation et à la chirurgie, le type de cataracte infantile, la morphologie de la cataracte, le type de chirurgie adoptée, la survenue d'une uvéite fibrineuse et le résultat visuel final.

Résultats **:** Au total, 197 yeux de 137 enfants ont été étudiés. Quatre-vingt-six (62,8%) étaient des garçons. L'âge moyen au moment de la chirurgie était de 76,1 (± 50,5) mois. Au total, 126 yeux (64,0%) ont subi une chirurgie de la cataracte avec implantation d'une lentille intraoculaire en polyméthylméthacrylate. Soixante-dix (35,5%) des yeux avaient une uvéite fibrineuse ; 15 (21,4%) de ces yeux ont par la suite développé une capture optique de la lentille intraoculaire. Un âge plus élevé au moment de la présentation, un âge plus avancé au moment de la chirurgie, la cataracteuvéitique, la cataracte traumatique et l'implantation de la lentille intraoculaire étaient associés à une uvéite fibrineuse lors des analyses bivariés. Avec l'analyse de régression logistique, cependant, seule l'implantation d'une lentille intraoculaire a été associée à une uvéite fibrineuse.

Conclusion: L'uvéite fibrineuse est une complication relativement fréquente de la chirurgie de la cataracte pédiatriquedans notre location. L'implantation d'une lentille intraoculaire en polyméthylméthacrylate est un facteur de risque important d'uvéite fibrineuse après une chirurgie de la cataracte pédiatrique.

Mots - clés : *cataracte pédiatrique, uvéite fibrineuse*, *chirurgie, Nigéria*

Introduction

Childhood cataract is becoming a major cause of childhood blindness in Sub-Saharan Africa [1]. This could be attributed to the success with the efforts at reducing childhood blindness caused by corneal opacities secondary to measles and vitamin A deficiency [2]. The significance of the burden of

Correspondence: Dr. B.A. Olusanya, Department of Ophthalmology, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: bolutife@yahoo.com; bolusanya@comui.edu.ng

blindness from childhood cataract is related to the concept of "blind person years"; and it has been postulated that vision restoring cataract surgery in one blind child has similar impact as restoring sight to 10 adults [3].

Optimising visual potential and prevention of permanent visual impairment from childhood cataract requires that the cataract is detected early and that effective treatment is instituted as soon as possible [4]. The treatment for childhood cataract involves surgical removal and optical rehabilitation to restore and improve vision. One of the common postoperative complications of cataract surgery in childhood is fibrinous uveitis [5,6]. This is a severe form of intraocular inflammation, which if not properly managed, can result in profound loss of vision despite removal of the cataract.

Fibrinous uveitis may be more common in children of African descent because of a higher degree of iris pigmentation [7]. Some other risk factors for postoperative fibrinous uveitis include uveitic cataract, traumatic cataract, retained soft lens material, instrument-related debris, and prolonged surgical manipulation [7-10]. Severe postoperative fibrinous uveitis may be associated with a variety of sequelae including optic capture of intraocular lens (IOL) within the pupil, occlusio pupillae and dense posterior capsule opacification. These complications increase the risk of subsequent poor visual outcome.

Poor visual outcome after cataract surgery in children militates against efforts at improving the quality of life of the affected children and significantly limits their productivity and contribution to the economy of the country. Therefore, it is important to understand the risk factors for the occurrence of postoperative fibrinous uveitis with a view towards developing preventive measures that may reduce the incidence of this complication and optimize the visual outcome of cataract surgery in children of African descent. The objective of this study was to determine the frequency and risk factors of fibrinous uveitis as a postoperative complication of paediatric cataract surgery.

Subjects and methods

The study was a retrospective interventional study conducted over a five-year period. Patients aged less than 16 years who underwent cataract surgery at the paediatric ophthalmology unit of the University College Hospital, Ibadan, Nigeria between January 2008 and December 2012 were studied. Case records of eligible patients were reviewed and patients with missing or incomplete records were excluded from the study.

Study data was obtained from the case records of the patients with the use of a proforma. Information retrieved included age at presentation, age at surgery, gender, presenting symptoms, onset of symptoms, history of trauma or redness of the eye(s), laterality of cataract, type of childhood cataract, morphology of the cataract, type of cataract surgery performed, occurrence of fibrinous uveitis, treatment given for fibrinous uveitis, sequelae of fibrinous uveitis and final visual outcome.

For the purpose of this study, fibrinous uveitis was defined as the occurrence of severe postoperative inflammatory response evidenced by presence of $\geq$ 3+ of cells in the anterior chamber and the formation of a fibrin membrane visible on slit-lamp examination of the anterior segment.

All patients underwent surgery under general anaesthesia. All surgeries were performed by consultant ophthalmologists. Surgical technique used was either extracapsular cataract extraction with or without posterior chamber intraocular lens (PCIOL) implant or manual small incision cataract surgery with PCIOL implant. Intraocular lenses were generally implanted in patients aged 2 years and above, while those aged below 3 years also underwent primary posterior capsulotomy and anterior vitrectomy routinely. All patients who received intraocular lens were implanted with rigid polymethylmethacrylate (PMMA) lenses with optic diameter of 6.0mm and overall diameter of 12.50mm. Postoperatively, all patients received a standardized regimen consisting of subconjunctival steroids and antibiotics given immediately after the surgery; a course of topical steroids, antibiotics and pupil dilating eye drops; as well as a course of oral steroids (Table 1).

For eyes that developed fibrinous uveitis, the frequency of the topical steroid eye drops was increased to every 30 minutes or hourly depending on severity and subconjunctival steroid injections were repeated as necessary. In addition, intensive pupillary dilatation using phenylephrine was performed three to four times a day.

Ethical approval was obtained from the Ethics Review Board of the hospital. The study adhered to the tenets of the Declaration of Helsinki and confidentiality of patients' information was strictly maintained throughout the study.

Data was analysed using IBM SPSS version 20.0 (IBM Corps., New York, USA). Bivariate analyses were carried out using Independent T-test and Chi-Square test. Multivariable analysis was conducted using binary logistic regression analysis.

Any p value less than 0.05 was adjudged to be statistically significant.

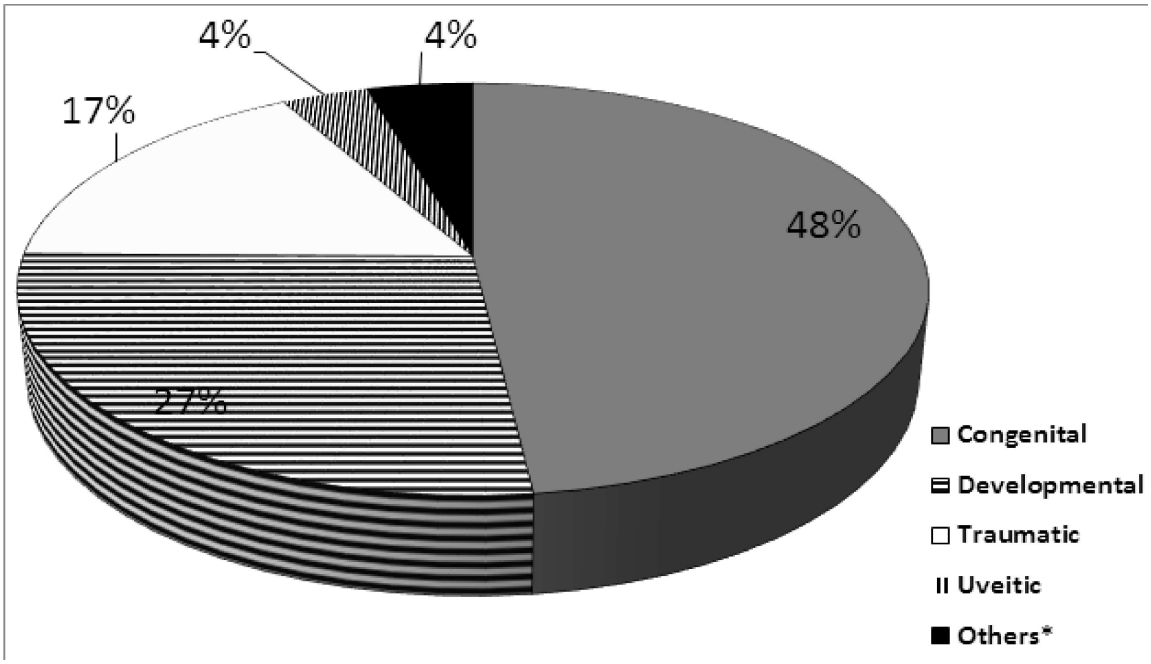

Fig. 1: Aetiological types of childhood cataracts in 137 children.
*Includes syndromic cataracts e.g. Marfan's syndrome and Down syndrome.

Results

Two hundred and thirty-one eyes of 162 children underwent cataract surgery during the study period. Of these, the records of 25 children were either missing or incomplete. Thus, a total of 197 eyes of 137 children were included in the study. Eight-six (62.8%) were boys. Mean age at presentation was 70.3 (±50.9) months while the mean age at the time of surgery was 76.1 (±50.5) months. Sixty-six (48.2%) of the patients had an onset of symptoms at birth or within the first year of life, while the remaining (51.8%) had onset of symptoms after the 1st year of life. Eighty-five (62.0%) children had bilateral cataracts but only 60 (43.8%) had surgery performed on both eyes during the period of the study. The frequency distribution of the aetiological type of childhood cataract is shown in Figure 1. Median postoperative follow up duration was 11 months with a range of 1 week to 62 months.

A total of 72 eyes (36.5%) had primary posterior capsulotomy and anterior vitrectomy; while 126 (64%) eyes were implanted with a PCIOL. The morphology of the cataracts was recorded at time of surgery. Seventy- five (38.1%) eyes had total

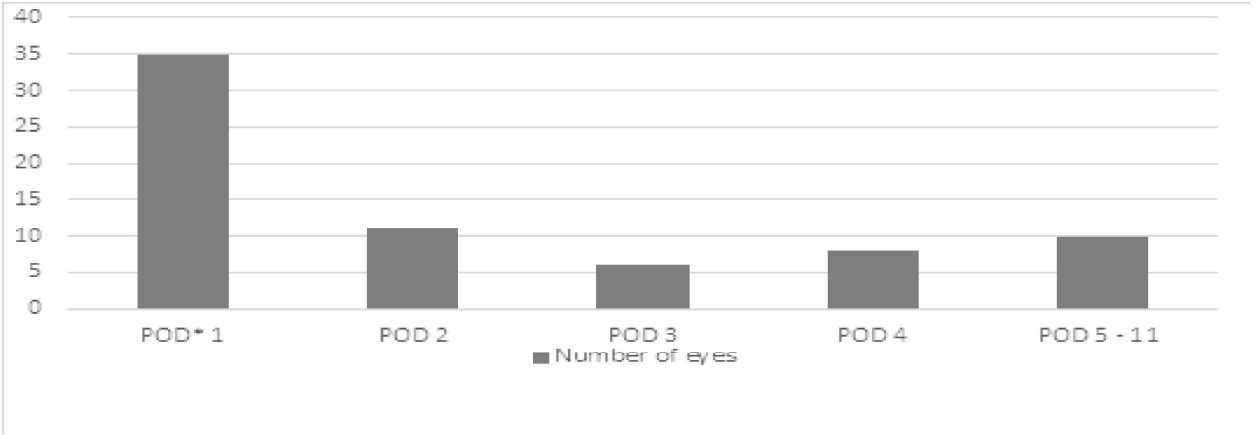

Fig. 2: Onset of Fibrinous uveitis in 70 eyes
*POD – Postoperative day

cataracts; 56 (28.4%) had lamellar cataracts; 23 (11.7%) had milky cataracts while membranous cataracts were noted in 16 (8.1%) eyes.

Table 1: Standard postoperative treatment regimen administered following paediatric cataract surgery at paediatric ophthalmology unit of the University College Hospital, Ibadan

Subconjunctival Injection (immediately after surgery)			
1	Dexamethasone sodium phosphate		2mg
2	Methylprednisolone acetate suspension		10mg
3	Gentamicin sulfate		20mg
Topical medications (starting on 1st Postoperative day)			
1	Dexamethasone (0.1%) eye drops		every 2 hours
2	Ciprofloxacin (0.3%) eye drops		every 4 hours
3	Tropicamide (1%) eye drops		three times a day
4	Dexamethasone ointment (combined with neomycin and polymyxin B)		at bed time
Oral medications (starting on 1st Postoperative day)			
1	Prednisolone tablets	1mg/ kg	every other day for 8 doses (i.e. 2 weeks)

Seventy (35.5%) eyes had fibrinous uveitis following cataract surgery. Sixty (85.7%) of these cases had manifested by the 4th day after surgery; and the onset of the fibrinous uveitis ranged between the 1st and the 11th day postoperatively (see Figure 2). In 39 (55.7%) eyes the fibrinous uveitis resolved within 7 days following intensive treatment described above (Table 2).

Among the eyes that had fibrinous uveitis, 32 (45.7%) subsequently had late postoperative complications involving the pupil. These complications included posterior synechiae (21 eyes); optic capture of the intraocular lens (15 eyes); and occlusio pupillae (11 eyes). Eight of the 11 eyes with pupil occlusion underwent pupilloplasty. The remaining three patients defaulted from follow up clinic visits.

Table 2: Frequency distribution of duration of fibrinous uveitis

Duration (days)	Number of eyes (%)
<3 days	11 (15.7%)
3 to 7days	28 (40.0%)
8 to 14 days	18 (25.7%)
>14 days	13 (18.6%)
Total	70 (100%)

Further analysis revealed that the mean age at surgery of the children who developed fibrinous uveitis was 80.7 months compared to 62.4 months in those who did not develop fibrinous uveitis (p = 0.008). In addition, the eyes of children who were older than 3 years at presentation or at surgery were more likely to develop fibrinous uveitis compared to those aged 3 years and below (Table 3). Moreover, eyes that had onset of symptoms in the first year of life were 2.6 times more likely to develop fibrinous uveitis compared to those with onset of symptoms after the first birthday (Table 3). Similarly, eyes with traumatic cataract were 2.7 times more likely to develop fibrinous uveitis compared to the eyes with other types of cataracts, while eyes with uveitic cataracts were 9.7 times more likely to develop fibrinous uveitis compared to other types of cataract. Likewise, eyes that received an PCIOL implant were 13 times more likely to develop fibrinous uveitis compared to those that did not receive an implant (Table 3).

There was no statistically significant difference between the eyes who had fibrinous uveitis and those who did not with respect to gender, laterality of the cataract, morphology of the cataract or the order of surgery i.e. whether it was the first or second eye to undergo surgery. With multivariable analysis using a logistic regression model, only PCIOL implantation was significantly associated with postoperative fibrinous uveitis.

Sixty (85.7%) of the 70 eyes with fibrinous uveitis had objective assessment of their visual acuity using a Snellen acuity chart. Thirty (50%) of these eyes had best corrected visual acuity (BCVA) between 6/5 and 6/18 as at the last follow up visit, and 18 (30%) eyes had BCVA worse than 6/60. On the other hand, 24 (34.8%) of the eyes that did not have fibrinous uveitis had BCVA between 6/5 and 6/18 while 30 (43.5%) eyes had BCVA worse than 6/60. This difference was not statistically significant (p=0.184).

Table 3: Effect of some clinical and surgical characteristics on the occurrence in of Fibrinous uveitis

Variable	Fibrinous uveitis Yes n (%)	No n (%)	Odds ratio (95% C.I.)	p value
Age at presentation				
0 – 36 months	19 (22.6%)	65 (77.4%)	0.4	
> 36 months	51 (45.1%)	62 (54.9%)	(0.2- 0.7)	0.001*
Age at Surgery				
0 – 36 months	11 (16.7%)	55 (83.3%)	0.2	
> 36 months	59 (45.0%)	72 (55.0%)	(0.1-0.5)	<0.001*
Gender				
Male	42 (34.1%)	81 (65.9%)	0.9	
Female	28 (37.8%)	46 (62.2%)	(0.5-1.6)	0.600
Onset of symptoms				
Within 1st year of life	28 (25.7%)	81 (74.3%)	2.6	
After the first birthday	42 (47.7%)	46 (52.3%)	(1.4- 4.8)	0.001*
Traumatic cataract				
Yes	13 (56.5%)	10 (43.5%)	2.7	
No	57 (32.8%)	117 (67.2%)	(1.1-6.4)	0.025*
Second eye to undergo surgery				
Yes	20 (33.3%)	40 (66.7%)		
No	50 (36.5%)	87 (63.5%)	0.9(0.5-1.7)	0.669
PCIOL implantation				
Yes	64 (50.8%)	62 (49.2%)	13.0	
No	5 (7.4%)	63 (92.6%)	(4.9-34.5)	<0.001*
Uveitic cataract				
Yes	5 (83.3%)	1 (16.7%)		
No	65 (34.0%)	126 (66.0%)	9.7(1.1-84.7)	0.022*

** p value < 0.05 (i.e. statistically significant)*
C.I. = Confidence Interval

Discussion

This study demonstrates that the occurrence of postoperative fibrinous uveitis is relatively common, occurring in about a third of our patients. This rate of occurrence is similar to some earlier reports in East African children [5,6], but is significantly higher than the 12% reported by Bowman *et al* [11], also in East Africa. One significant difference between our study and Bowman's study is the use of hydrophobic acrylic IOLs in 64% of their patients compared to PMMA IOLS in all of our patients.

In addition, the frequency of fibrinous uveitis in the present study is higher than the 13% stated in a previous report from our hospital [12]. The difference in proportions of eyes that were implanted with IOLs may be responsible for the lower frequency in the earlier study. About one third of the eyes in the earlier study had IOL implantation compared to approximately two-thirds in the current report.

Moreover, our results suggest that PCIOL implantation is the major determinant for the development of postoperative fibrinous uveitis among children undergoing cataract surgery in our facility. PMMA lenses have been shown to be associated with more postoperative inflammation [13]. Although, hydrophobic acrylic IOLs have been specifically recommended for use in children [14], we were constrained to use PMMA lenses in our patients on account of their lower cost and better availability.

The reason for the lack of association between uveitic cataracts and fibrinous uveitis when controlling for other variables in our study may be related to the small number of eyes with uveitic cataracts. Previous studies have demonstrated that

the risk of fibrinous uveitis is higher following surgery for uveitic cataracts in Caucasian patients [7,8]. To the best of our knowledge, no studies have reported on this association in African children. Further studies on larger cohorts of African patients with uveitic cataracts may shed more light on this.

Similarly, it is not immediately clear why we found no association between traumatic cataracts and fibrinous uveitis in this study. This may also be related to the relatively small numbers eyes that underwent surgery for traumatic cataract. Traumatic cataracts are known to be associated with an increased risk of fibrinous uveitis [15,16]. Hence, more studies are necessary to clarify the status of this association in our population.

A significant proportion of the eyes that developed fibrinous uveitis had late postoperative complications which may have contributed to poor visual outcome in some of them. This portrays the need for preventing the occurrence of postoperative fibrinous uveitis. Based on our findings, discouraging the use of PMMA IOLs in children undergoing cataract surgery may substantially reduce the occurrence of fibrinous uveitis. Therefore, there is an urgent need to make hydrophobic acrylic IOLs more affordable and readily available in our setting.

This study has a number of limitations. Firstly, the surgeries were not performed by the same surgeon and we did not collect information on duration of each surgery. In addition, information about the placement of the IOL in the bag or in the sulcus was not available for all patients. Thus, subtle differences in surgical technique or variations in duration of surgery may account for some of the differences in the occurrence of fibrinous uveitis in our patients.

Similarly, the postoperative evaluation of the patients was not performed by the same ophthalmologist and there might have been variations in the assessment of postoperative fibrinous uveitis. Actually, the use of a laser flare-cell photometer would have provided an objective assessment of the anterior chamber inflammation. But this was not available in our institution during the period of the study.

Furthermore, we did not collect information regarding the level of compliance with the regimen for postoperative medications. Oftentimes, children can be quite uncooperative for instillation of eye drops and strong motivation on the part of parents and caregivers is required to ensure good compliance. As a result, differences in the level of compliance may, in fact, be a source of confounding in this study's findings. Finally, the retrospective nature of the study limited the collection of data from all eligible patients because of missing records.

In conclusion, fibrinous uveitis is a common postoperative complication of paediatric cataract surgery and PMMA IOL implantation is a major risk factor for its occurrence. We implore donor agencies that are interested in reducing childhood blindness to strongly support the adoption of the use of hydrophobic acrylic IOLs in child eye health tertiary facilities (CEHTFs). Such support would enable the provision of optimal care to children requiring cataract surgery at affordable costs. Furthermore, manufacturers of hydrophobic acrylic lenses should be encouraged to supply their products at subsidized rates to paediatric ophthalmology units in resource-limited settings such as ours.

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The dimensions of the tibial condyles differ in Nigerians

RS Ajani[1], BA Abiola[2] and SO Ogunlade[3]

Departments of Anatomy[1], College of Medicine, Universityof Ibadan,
Department of Neurological Surgery[2], University College Hospital and
Department of Surgery[3], College of Medicine, University of Ibadan, Nigeria

Abstract

Objective: The tibia is the larger and medially positioned of the two bones of the leg and is involved in knee articulation. Its proximal part consists of the medial and lateral condyles whose superior surface is known as medial and lateral plateau respectively. The knee joint is commonly involved in chronic osteoarthritis which may invariably require knee replacement surgery. This surgical procedure entails excision and replacement of a portion of proximal tibial metaphysis with implants. The available tibial implants consist of excessive number of sizes that may be inappropriate for our population. Thus the need to generate proximal tibial dimensions that may assist in the manufacture of tibial implants appropriate for Nigerians becomes pertinent hence the rationale for the study.

Materials and method: One hundred and thirty one adult tibiae (right:44.3% and left:55.7%) obtained from macerated cadavers were used for the study. On the superior surface of each condyle, the anteroposterior length (APL), transverse length (TL) , intercondylar length (ICL) and mediolateral length (MLL)were measured.

Results: The mean APL of the right tibial medial condyle was significantly ($p< 0.05$) longer than that of its lateral condyle (44.27±4.10 vs 39.49±3.89 mm). For the left tibia, the mean APL of the medial condyle was also significantly longer (43.55±4.38 vs 39.23±4.02 mm). The mean TL for the right tibial medial and lateral condyle was 30.30±3.42 and 30.84±3.67 mm respectively. The mean TL for the left tibial medial and lateral condyle was 30.16±3.16 and 30.59±3.30 mm respectively. The mean ICL of right tibia was 13.03±1.81 and that of the left tibia was 12.85±1.47 mm. The mean MLL of right tibia was 74.17±6.68 while that of the left tibia was 73.60±6.01mm. The differences in the various parameters between the right and left tibia were insignificant.

Conclusion: There is asymmetry between the anteroposterior length of the medial and lateral condyles. When compared with similar studies, the dimensions of the tibial condyles in Nigerians were different from those of other nationals. Thus there exists racial variations in the dimensions of tibial condyles and this has to be considered in the manufacture of tibial implants for knee arthroplasty. Results of this study may thus serve as reference values for Nigerians.

Keywords: *Tibial condyle dimensions, tibial implants, Nigerians*

Abstrait

Objectif **:** Le tibia est la partie la plus grande et la plus médiane des deux os de la jambe et est impliqué dans l'articulation du genou. Sa partie proximale est constituée des condyles médial et latéral dont la surface supérieure est respectivement appelée plateau médial et latéral. L'articulation du genou est couramment impliquée dans l'arthrose chronique qui peut nécessiter invariablement une chirurgie de remplacement du genou. Cette intervention chirurgicale implique l'excision et le remplacement d'une partie de la métaphyse tibiale proximale par des implants. Les implants tibiauxdisponibles consistent en un nombre excessif de tailles qui peuvent être inappropriées pour notre population. Ainsi, la nécessité de générer des dimensions tibiales proximales pouvant aider à la fabrication d'implants tibiaux appropriés pour les Nigérians devient pertinente, d'où la raison d'être de l'étude.

Matériel et méthode : Cent trente et un tibias adultes (droit : 44,3 % et gauche: 55,7%) obtenus à partir de cadavres macérés ont été utilisés pour l'étude. Sur la surface supérieure de chaque condyle, la longueur antéropostérieure (APL), la longueur transversale (TL), la longueur inter-condylaire (ICL) et la longueur médio-latérale (MLL) ont été mesurées.

Résultats : La moyenne APL du condyle médial tibial droit était significativement plus longue ($p <0,05$) que celle de son condyle latéral (44,27 ± 4,10 vs 39,49 ± 3,89 mm). Pour le tibia gauche, la moyenne APL du condyle médial était également significativement plus longue (43,55 ± 4,38 vs39,23 ± 4,02 mm). Le TL moyen pour le condyle médial et latéral tibial droit était respectivement de 30,30 ± 3,42 et de 30,84 ± 3,67mm. Le TL moyen pour le condyle médial et latéral tibial gauche était respectivement de 30,16 ± 3,16 et de 30,59 ± 3,30mm. L'ICL moyenne du genou droit était de 13,03 ± 1,81 et celle du genou gauche de 12,85 ±

Correspondence: Dr. R.S. Ajani, Department of Anatomy, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: rsaajani@yahoo.co.uk.

1,47mm. Le MLL moyen du genou droit était de 74,17 ± 6,68 tandis que celui du genou gauche était de 73,60 ± 6,01mm. Les différences dans les divers paramètres entre le tibia droit et gauche étaient insignifiantes.

Conclusion **:** Il existe une asymétrie entre la longueur antéropostérieure des condyles médial et latéral. Quand comparés à des études similaires, les dimensions des condyles tibiaux chez les Nigérians étaient différentes de celles des autresres sortissantsnationaux. Il existe donc des variations raciales dans les dimensions des condyles tibiaux et il faut en tenir compte dans la fabrication d'implants tibiaux pour arthroplastie du genou . Les résultats de cette étude peuvent donc servir de valeurs de référence pour les Nigérians.

Mots clés :*dimensions tibiale de condyle, implants tibial, Nigérians*

Introduction

The tibia is the larger and the medially positioned of the two bones that constitute the skeletal framework of the leg, while the other being the fibula. It is a long bone consisting of two epiphyses (proximal and distal) and in between them is the diaphysis. It is formed both by intramembranous (the epiphyses) and endochondral (diaphysis) ossification. The proximal epiphysis is the growing end of the bone and consists of the medial and lateral condyles. Both condyles differ in shape and length with the medial being oval and longer while the lateral is circular [1].

The superior surface of each condyle is known as tibial plateau and the two plateaus are separated by the intercondylar eminence and the morphology of the plateaus differs [2]. The plateaus provide attachments for the respective meniscus and the lateral has a more extensive coverage for its meniscus than the medial plateau [3]. The medial meniscus occupies 50-60 % of the medial condyle [4] and is connected to the lateral meniscus by four ligaments [4,5]. The femoral condyles articulate with the respective tibial condyles in the knee joint articulation. The knee joint is the largest and most complex synovial articulation in the body. Its anterior, medial and lateral aspects are superficial; they are not overlaid by muscles but only with skin.

This, coupled with the fact that its stability largely depends on ligaments (which could get torn or ruptured) make it very prone to injury particularly in contact sports. Normally, the surfaces of the femoral and tibial condyles involved in the knee articulation are covered with hyaline cartilage, this with the synovial fluid maintain the integrity of the surfaces. Due to its large surface area and most of it being superficial, the knee joint is very prone to degenerative changes. These arthritic changes may be due to obesity, part of ageing process or trauma however, in most cases the cause is unknown. The initial management of osteoarthritis of the knee include analgesia and physiotherapy maneouvres, these measures only offer symptomatic relief and may not halt the progression of the pathology. When the disability i.e. knee joint movement becomes severely limited coupled with severe pain, the need for surgical intervention may become inevitable. Surgical options for knee joint osteoarthritis include joint replacement which may be either partial or total.

These procedures involve replacement of the proximal tibia and or distal femur with prostheses. The production of these knee implants are by very few manufacturers in very limited number of countries. Also the knee implants are available in very limited sizes and they are not one size-fit-all. The universal fitness of these implants is thus an important issue that requires appropriate consideration and resolution. Studies have shown that proximal tibial dimensions vary along racial and gender line [2,3,6-8]. Since osteoarthritis of the knee also afflicts Nigerians, it thus becomes pertinent to generate proximal tibial dimensions in adult Nigerians that may serve as reference data for the populace. This may assist the manufactures of knee implants to produce those that are appropriate for Nigerians and thus make knee replacement surgery less cumbersome. This was the rationale for this study.

Materials and method

One hundred and thirty one (131) bones with a right to left ratio of 58:73 were used for the study. These bones were products of macerated cadavers used for gross anatomy dissection by undergraduate students spanning several years. All the cadavers were unclaimed Nigerians (as the corpses of non-Nigerians would have been collected for burial). They were sourced from facilities located in south west Nigeria. The post –dissected cadavers were macerated serially and the bones obtained were warehoused in the Bone store of the Anatomy Department of the College of Medicine, University of Ibadan, Nigeria. Only bones with intact features and without any evidence of previous fractures, deformities or arthritic changes were recruited for the study. No documentation as to the age and gender of the tibae. Bones that had pathological features or erosion of the proximal end were excluded from the study.

By means of a digital caliper graduated in millimetres, the following measurements on the superior surface of each of the condyle were taken (i) anteroposterior length (APL) represented by

arrows 'a' and 'd' in figure 1, (ii) the transverse length (TL) at approximately midpoint along the transverse plane represented by the arrows 'b' and 'e' and (iii) the intercondylar length (ICL) arrow 'c'. The APL was measured from the most anterior end to the most posterior end of each condyle.

While the TL was measured from the respective tubercle of the intercondylar eminence to the corresponding medial or lateral plateau at the midpoint. Measurement of each tibia was done twice independently by the authors. Having noticed the closeness of the obtained values; the average value was accepted and recorded as the result for each parameter and for each of the tibiae. The summation of the transverse lengths of the condyles and the intercondylar length of each side constituted the mediolateral length (MLL) for the respective side (i.e. MLL = b+c + e). The obtained data was analyzed with SPSS version 21 and expressed as means plus standard deviation with level of significance set at $P < 0.05$.

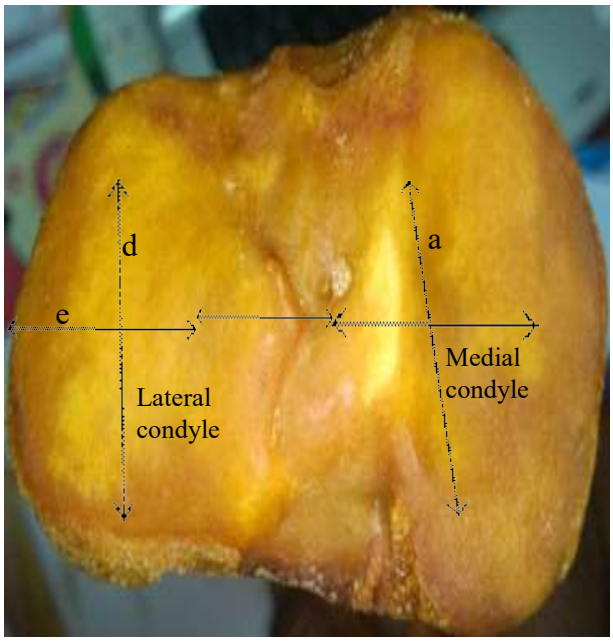

Fig. 1 : Left Tibia (superior surface) shhowing arrows: a-anteroposterior (AP) lenght of the medial condyle; b-transverse length (TL) of the medial condyle; c-inter-condylar distance (ICL); d- anteroposterior length of the lateral condyle and e-transverse length (TL) of the lateral condyle.

Results

A total of 131adult tibiae with the right constituting 44.3% (58) and the left being 55.7 % (73) were used for the study. The mean APL of the medial condyle of the right tibia (44.27±4.10 mm) was significantly longer than that of the lateral condyle (39.49±3.89 mm) (p= 0.01). However, there was no significant difference between the mean transverse lengths of both condyles of the right tibia (30.30±3.42 vs30.84±3.67 mm). The mean APL of the left tibial medial condyle was significantly longer than that of its lateral condyle (43.55±4.38 vs 39.23±4.02 mm; p= 0.01). The mean transverse lengths of both condyles of the left tibia were not significantly different (30.16±3.16 vs30.59±3.30 mm). The median APL of each of the condyle of both tibiae was closer to the respective maximum APL than the minimum APL (Table 1). For the transverse length, the median value was midway between the respective minimum and maximum values for all the four condyles (Table 1). The right tibia median ICL was midway between the minimum and maximum values (13.11 vs9.53; 17.98 mm). For the left tibia the median ICL was closer to the maximum value (13.06 vs 15.38; 9.24 mm). For all the measured parameters, their mean values were very close to the respective median value (Table 1).

Comparison between the right and left tibiae

The mean APL of the right tibial medial condyle was marginally and insignificantly higher than that of the left tibia (44.27±4.10 vs 43.55±4.38 mm). While the lateral condyles of both right and left tibiae had very similar mean APL (39.49±3.89vs39.23±4.02mm). The mean TL of the medial condyle of the right and left tibia respectively was almost same (30.30±3.42 vs30.16±3.16 mm). Similar results were obtained for the mean transverse length of the lateral condyle (30.84±3.67 vs30.59±3.30 mm) (Table 2).

Discussion

The results of this direct measurement study showed the existence of asymmetry between the anteroposterior length (APL) of the tibial condyles with the medial condyle being significantly longer. This significant asymmetry is in agreement with similar measurements amongst the Turkish population [6], Koreans [7], Japanese population [8], French [2] and South Indians [3]. The mean APL for the adult Turkish population was 50.1±4.1 mm for the medial condyle and 42.3±3.3 mm for the lateral condyle. Although these were higher than those of this study, the asymmetry was statistically significant.

The fact that the Turkish evaluation was a magnetic resonance imaging (MRI) study may not offer complete explanation for the higher values as there might be some degree of genetic input as a result of racial differences. In this Turkish study, it was observed that none of the available tibial implant design exhibited a perfect conformity to the proximal tibial morphology with regards to shape and size. Thus the need to have knee implants that meet the

Table 1: Values of the Parameters measured

Parameter (mm)	Right Tibia N=58		Left Tibia N=73	
	Medial condyle	Lateralcondyle	Medialcondyle	Lateralcondyle
Mean APL	44.27±4.10	39.49±3.89	43.55±4.38	39.23±4.02
Minimum APL	31.73	26.26	29.66	28.88
Maximum APL	52.93	47.15	54.16	47.02
Median APL	44.02	39.77	43.57	39.68
Mean TL	30.30±3.42	30.84±3.67	30.16±3.16	30.59±3.30
Minimum TL	22.99	20.91	21.53	22.68
Maximum TL	38.52	38.87	39.60	38.57
Median TL	30.74	31.40	30.52	30.73
Mean ICL	13.03±1.81		12.85±1.47	
Minimum ICL	9.53		9.24	
Maximum ICL	17.98		15.38	
Median ICL	13.11		13.06	
Mean MLL	74.17±6.68		73.60±6.01	
Minimum MLL	58.42		56.82	
Maximum MLL	86.69		87.16	

APL Anteroposterior length, TL transverse length, ICL Intercondylar length
MLL Mediolateral length.

Table 2 Comparison of mean values of the measured parameters between right and left tibia.

Parameter (mm)	Medialcondyle		P-value	Lateralcondyle		P-value
	Right	Left		Right	Left	
Mean APL	44.27±4.10	43.55±4.38	0.17	39.49±3.89	39.23±4.02	0.36
Mean TL	30.30±3.42	30.16±3.16	0.41	30.84±3.67	30.59±3.30	0.34
Mean ICL	13.03±1.81	(Right tibia)		12.85±1.47	(Left tibia)	0.26
Mean MLL	74.17±6.68	(Right tibia)		73.60±6.01	(Left tibia)	0.30

APL Anteroposterior length, TL transverse length, ICL Intercondylar length

Table 3: Comparison of the results with those of other studies

Study	Right					Left				
	TL		AP		MLL	TL		AP		MLL
	MC	LC	MC	LC		MC	LC	MC	LC	
Gupta *et al* [17] (N=50) (cm)	2.70 ±0.24	2.66 ±0.24	4.55 ±0.29	4.08 ±0.27	6.77 ± 0.31	2.76 ±0.27	2.92 ±0.32	4.36 ±0.47	4.06 ±0.40	6.88 ± 0.65
Ivan [18] (cm)			4.08 ±0.42	3.67 ±0.41	6.62 ± 0.51			4.13 ±0.42	3.54 ±0.39	6.66 ± 0.56
Srivastava *et al* [9] (N150)(cm)	2.97	2.92	3.86	3.64		2.75	2.97	3.99	3.69	
This Study (mm)	30.30 ±3.42	30.84 ±3.67	44.27 ±4.10	39.49 ±3.89	74.17 ±6.68	30.16 ±3.16	30.59 ±3.30	43.55 ±4.38	39.23 ±4.02	73.60 ±6.01

APL Anteroposterior length, TL transverse length, MML mediolateral length, MC medial condyle, LC lateral condyle

need of the Turks was suggested. The mean APL values for the adult Korean population were 48.5± 3.7 mm and 43.5 ± 2.9 mm respectively for the medial and lateral condyle. The Korean study entailed computerized tomographic scanning of the proximal tibiae in cadavers and it was observed that the results obtained were lower than the size of commercially available knee implants.

This observation according to the authors could lead to mediolateral overhang of the implant if used in knee arthroplasty. They therefore concluded that the results of the study could assist implant manufacturers in the design and production of knee implants that best suit the Korean populace. Results of another computerized tomographic study of adult French citizens who had unicompartmental knee arthroplasty (UKA) by Servien et al [2] put the mean APL of the medial and lateral plateau of the tibia at 50.8± 3.3 mm and 47.2 ± 3.3 mm respectively. This French study compared the tibial plateau dimensions with available UKA implants from nine different manufacturers and noted that none of these implants had an asymmetric tibial compartment. The implication of this observation according to them was that the available UKA implants would result either in mediolateral overhang or reduced anteroposterior coverage.

The reduced anteroposterior coverage may result in the load being transmitted to cancellous bone as opposed to cortical bone, this might lead to tibial implant collapse. Srivastava et al [9] measured parameters similar to those of our study in 150 cadaveric tibiae of north Indian extraction and reported the mean APL of the right medial condyle to be 38.63 mm and that of lateral condyle 36.47 mm. The respective mean APL values for the left were 39.94 and 36.94 mm . Similar cadaveric study of south Indian subjects reported a mean APL of 40.6 ± 3.9 mm for the right medial condyle and 34.8 ±3.7 mm for the right lateral condyle while the results for the left were 39.2 ±3.6 mm and 32.6 ±3.4 mm respectively. These results showed some degree of asymmetry between the right and the left tibia and the medial and lateral plateaus; with the pattern of asymmetry being similar to that of the present study. Our study and those of the Indians (north and south) have certain features in common namely cadaveric and being direct measurement; yet our results were higher than those of the Indians. This observation gives credence to the assertion that racial differences affect the morphology of the tibia as a bone and the condylar plateaus in particular. Cheng *et al* [10] noted that the smaller sized tibial implants being used for Chinese had under sized mediolateral length while the larger size implants were oversized.

Yang *et al* [11] also made similar observation that the smaller tibial implants exhibited mediolateral undersizing while the larger ones had overhang . Quite a number of studies have demonstrated that most of the available tibial component designs do not fit adequately with the anthropometric parameters of different ethnic groups [10-14].This has stimulated studies that tend to generate anthropometric parameters of the tibia that may serve as baseline data in the manufacture of tibial implants that meet the specifications of different ethnic groups.

Attached to the surface of each plateau is a fibrocartilaginous structure known as the meniscus. Each meniscus is peripherally situated and has two tips known as the anterior and posterior horn. The distance between the anterior and posterior horns may thus reflect the anteroposterior length of the respective condyle. In a study by Koyuncu *et al* [15], in which the distance between the anterior and posterior horn of each meniscus was measured in 105 cadaveric human fetuses grouped into first trimester, second trimester, third trimester and term. It was observed that the mean distance between the anterior and posterior horns of the medial meniscus was significantly greater than that of the lateral meniscus in all the four developmental periods and in fact the respective values for the medial meniscus were about twice that of the lateral meniscus. From the foregoing, it may thus be concluded that the longitudinal growth of the medial condyle occurs at a faster rate than that of the lateral condyle. This differential growth rate though about twice during the foetal period is sustained till adulthood with reduction in the gap as evidenced by the mean APL values of our study.

The above explains why the mean APL of the medial condyle was longer than that of the lateral condyle in all the cited studies including the present study. Unlike the APL, the mean TL values were very similar for both condyles and for both sides. This is in concordance with the results of similar studies (Table 3). However, the mean TL still varies along racial and ethnic lines.

Yue *et al* [16] reported the mean mediolateral length (MML) of the tibial condyle in Chinese male and female as 75.2 ±3.6 and 66.2±2.1 mm respectively. The same study reported 78.7 ±5.4 and 69.0±4.2 mm as the MLL for American male and female respectively. Our results are similar to those of the Chinese male but lower than that of the

American male. This may be due to the fact that the Americans on the average have greater body status than Nigerians. The mean MLL for the Turkish population was 71.9±4.4 mm which is similar to that of the present study.

None of the studies reviewed measured the intercondylar length (ICL). Our study showed that the mean ICL of the right tibia was marginally and insignificantly longer than that of the left tibia. Our study was thus the first to document the tibia intercondylar distance.

Comparing all the measured parameters of the right tibia with the respective tibial counterpart, we did not observe any significant difference rather they were similar (Table 2).

This observation was also noted in similar studies that were compared with the present one as stated in Table 3. This may be the basis why available tibial implants are not side specific. The results of this study thus further reinforces the non-side specific manufacture of the available tibial implants.

We also noted that the mean APLs were closer to their respective maximum values while for the transverse length, they were midway between their respective minimum and maximum values. For the mediolateral length, the mean value was also closer to the respective maximum value. For all the assessed parameters, the mean and respective median values were very similar. Thus from these two observed relationships between the mean and the range (minimum and maximum) on one hand and the mean and median on the other hand; it may thus be deduced that the obtained values were fairly representative of the study population. Thus the data generated by this study may be a template for the production of tibial implants that will be suitable for adult Nigerians scheduled for knee replacement surgeries.

Knee osteoarthritis is the commonest osteoarthritis of large joint [19], and as such a good knowledge of the tibial condylar measurement in our environment will be beneficial to both clinician and the industry involved in knee arthroplasty.

Conclusion

The tibia, and by extension the knee, has variable anatomy and geometry that is irrespective of gender and race. This should be strongly considered in the design and manufacture of the tibia implant for knee arthroplasty.

The clinical relevance of this study is that anatomic design of tibial implant that takes the proximal tibial parameters of Nigerians into consideration will allow for increased rotational alignment of the tibia and better coverage of the tibia. This will reduce soft tissue entrapment and collapse of the implant; both of these will increase postoperative restoration of function to the osteoarthritic knee. Data from this study may thus serve as a guideline in the design of tibial implant suitable for the Nigerian population. To the best of our knowledge, this is the first that will document the dimensions of the tibial condyles in Nigerians.

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