

Research Article

Factors Influencing Adherence to The Use of Inhalers for Control of Asthma in Adult Out-Patients in a Nigerian Teaching Hospital

*Azeez A.I.¹, Ige O.M.² and Ladipo M.M.A.³

¹State Hospital, PMB 7537 Secretariat Ibadan. Oyo State, Nigeria

²Department of Medicine, University College Hospital, Ibadan, Nigeria

³Department of Family Medicine, University College Hospital, Ibadan, Nigeria.

Received: February 2017; Accepted in final form: September 2016

Abstract

Asthma remains a poorly controlled disease despite the availability of new management guidelines and effective medications leading to increasing morbidity and mortality. The objective of this study was to determine the factors that influence adherence to the use of inhalers for the control of asthma in adult asthmatics. The study was a cross-sectional analytical conducted over a year from the first of June 2010 at the Medical Outpatient Clinic of University College Hospital Ibadan. The study population was composed of 355 randomly selected adults aged between 18 years and 55 years with an established diagnosis of asthma already on treatment and follow up. Chi-square test was used for bivariate analyses to test the significance of the association between categorical variables and asthma control and adherence to drugs. Logistic regression analysis was performed for the various factors to show the predictors of asthma control and adherence to treatment. There were 188 females (53%) and 167 males (47%). The mean age of the consenting patients was 39.04 years (SD± 11.335). Patients with correct inhaler technique had good asthma control (72.9%) compared to those with incorrect inhaler technique (61.9%), (p=0.085). Patients who used metered dose inhalers (MDI) and dry powder inhalers (DPI) had good asthma control (83.7%) compared to those who used MDI (62.9%) alone and DPI (57.7%) alone, (p=0.001). This study showed that a high proportion of patients on both MDI and DPI had better control of asthma than those on either DPI or MDI alone. And that the predictor of good asthma control was inhaler preference.

Key words: Adherence, Asthma control, Inhaler preference, Inhaler technique.

INTRODUCTION

Asthma remains a poorly controlled disease despite the availability of management guidelines and effective medications leading to increasing morbidity and mortality. The prevalence of asthma is rising throughout the world despite the implementation of both national and international guidelines and availability of pharmacological therapy. Asthma has therefore become a major public health problem, given the steady increase of its incidence during recent years and the resulting medical resource utilization (Janson *et al*, 2005; Onyedum *et al*, 2013).

Patients frequently do not adhere to their treatment regimen for a variety of reasons, including incorrect inhaler use and underestimation of disease severity. Historically, inhaled short-acting beta-adrenergic agonists (SABA) have been the mainstay of asthma management after which the long acting beta-adrenergic agonists (LABA) became available (Lynd *et al* 2003). The increased recognition that airway inflammation plays an integral role in asthma has resulted in a shift from the use of SABA and LABA to inhaled corticosteroid (ICS) agents as the mainstay of therapy in asthma management (Lynd *et al*, 2002; Pollart and Elward 2009; Bethesda 2009; Rachelefsky Mlunde, 2009).

Inhaler drugs in asthma management are grouped into metered dose inhalers (MDI) and dry powder inhalers (DPI) (Hess 2005; Papi *et al*, 2011). Salbutamol (ventoline) is a SABA available as metered dose inhalers MDI. They are aerosols driven by propellants, cheap and easily available but

some patients have difficulty coordinating actuation with inhalation. Dry powder inhalers are inhalation driven, easy to use, expensive and contain fluticasone or budesonide as the ICS and salmeterol or formoterol as the LABA.

To date advances in asthma management have been pharmacological rather than device driven. To achieve disease control, patients must adhere to the regimen (regimen adherence) and use inhaler effectively (device adherence). Most patients preferred to have some participation in management decision making but not necessarily to treat it. Most considered that they were not carried along in treatment decision making than they would have wanted (Caress *et al* 2005). To improve adherence to therapy and achieve better control, treatment decisions should be conducted in co-operation with the patients and should take into concern their lifestyle factors (Braido *et al*, 2016).

The increasing prevalence of asthma and failure of control are sources of concern in most parts of the world. Despite guidelines on the management of asthma there is increasing failure of control due to different factors and hence the need to examine the proper utilization of inhaled medications for the management of asthma. In a study conducted in United States of America (USA), it was found that ICS adherence was associated with higher income but not related to educational level, whereas excessive SABA use was associated with lower level of education (Susan *et al* 2008). The use of inhaled corticosteroids is the gold standard in asthma management because of their effectiveness in managing chronic inflammatory airway disease associated with asthma

*Address for correspondence: E-mail: rogbaayilola@yahoo.com

Tel: 08023635934, 08034428328;

(Spangler 2012). However, in a study conducted in Nigeria, it was found that physicians were not prescribing inhaled corticosteroids according to new guideline on asthma management. (Desalu *et al* 2013).

In Canada, it was reported that the prevalence of oropharyngeal symptoms in asthma patients using ICS and an ICS plus a LABA was high according to a research done and this may affect their use of inhalers (FitzGerald 2008). Underutilization of steroids may be due to advanced age and co-morbidities according to another study conducted in Ontario, Canada (Sin and Tu 2001). Putman reported in a study done in USA that health beliefs and attitude towards asthma can have important influence over adherence to asthma treatment regimen (Putman 2004). There was a positive relationship between adherence to medication and male gender, higher educational level, absence of health insurance, fewer comorbidities, longer duration of disease and satisfactory knowledge of medicines according to the findings of Odesanya and Oragwu. (Odesanya RU and Oragwu N 2015).

A review of literature showed that patients often understate their symptoms, were able to tolerate poor symptom control, lacked proper knowledge of correct inhaler usage, and showed poor adherence to therapy (Stephen *et al* 2006). Educating patients in inhaler techniques, successful communication between patients and health care workers and reinforcing understanding of asthma medications can improve outcome (Lexley *et al*, 2002; Moffat 2007; Gillissen 2007). This study was set out to establish the factors influencing adherence to the use of inhalers and the effects on asthma control in adult asthmatics.

MATERIAL AND METHOD

The study was a cross-sectional analytical conducted between 1st June 2010 and 31st of May 2011 at the Medical Outpatient Clinic of the University College Hospital (UCH), Ibadan, Oyo State in the South Western area of Nigeria. Three hundred and fifty five adult Nigerians between the ages of 18 and 55 years with an established diagnosis of asthma and on inhaler therapy and follow up were recruited for the study. A simple random sampling technique with computer generated random numbers was used for selection.

Data collection: A structured questionnaire was administered to consenting subjects. A preliminary (pilot) study was done on 40 patients that involved the entire research procedure to identify potential problems and amendments were done where necessary.

Inclusion criteria include consenting patients 18 to 55 years old, patients with established diagnosis of asthma and demonstrated 12-15% reversibility, history of the use of inhalers for more than 12 months. Exclusion criteria include patients with other lung diseases like tuberculosis and bronchiectasis and chronic obstructive airway disease. Patients with chronic illness that may affect their functional status (such as ischaemic heart disease or cardiac failure).

Adult Asthma Therapy and Control Assessment Questionnaire: This questionnaire which measures asthma therapy and control with the response options “yes”, “no” and “unsure” has been validated and used in previous studies (Markson *et al* 2001; Diette *et al* 2009). The Cronbach alpha is 0.85.

Asthma control was assessed on a scale of 3-23 by the use of the spirometer readings and asking the patients the following questions. "In the past four weeks, did you feel that your asthma was well controlled?", "In the past four weeks, did you miss any work, school or normal activity because of your asthma?" , "In the past four weeks did your asthma wake you up at night?", "In the past twelve months, did you miss any work, school or normal activity because of your asthma?", "In the past twelve months, did your asthma wake you up at night?,". "In the past four weeks, what was the highest number of puffs a day you took of this inhaler?", "In the past twelve months, on days you use an inhaler for quick relief, how many puffs a day do you usually take?"

FEV1% was used to classify patients into three asthma categories of severity. Patients with FEV1% greater than 80% was classified as having mild asthma, those with FEV1% between 60%-80% were classified as having moderate asthma while those with FEV1% less than 60% were classified as having severe asthma.

Patients with mild asthma (FEV1%>80%) were given a score of three, those with moderate (FEV1% 60%-80%) were given a score of two while those with severe asthma (FEV1%<60%) were given a score of one.

Patients using more than 12 puffs of inhaler per day scored one point, 9-12 puffs was scored two points, 5-8 puffs was scored three points, 1-4 puffs was scored four points and no puffs scored five points.

Scores were totaled and categorized into two groups. Statistical analysis showed the mean score to be 12 points. Patients with an asthma control score less than 12 points were categorized as having poor asthma control while those with an asthma score of 12 and above were categorized as having good asthma control.

Adherence was assessed on a scale of 1-13 by asking the following questions. "In the past twelve months, have you at any time taken medicine(s) for your asthma?", "Do you believe you are able to take your asthma medicine(s) as directed?", "Do you use an inhaler for quick relief from asthma symptoms?", "What best described how you take your controller medicine?" Individual scores were totaled and categorized into two groups. Statistical analysis showed the mean score to be seven points. Patients with an adherence score less than seven were categorized as having poor adherence while those with scores of seven and above were classified as having good adherence.

Measurement of lung function: Spirometry was performed with the handheld Spirobank II (MIR Medical International Research USA, Inc) after withholding short acting inhaled bronchodilator therapy for at least six hours before the study, the best of three efforts of forced expiratory volume in one second (FEV1) and FVC were recorded for each patient. The FEV1% was calculated for each patient and also entered into the records. The spirometry was done by a trained personnel and the equipment meets ATS standards for accuracy and reproducibility.

Data Analysis: The data was analyzed using SPSS (Statistical Package for Social Sciences) software version 15. Frequency tables and diagrams were used for relevant variables. Chi-square test was used for bivariate analyses to test the significance of the association between categorical variables and asthma control and adherence to drugs. Logistic

regression analysis was performed for the various factors to show the predictors of asthma control and adherence. A p-value < 0.05 was considered to indicate statistical significance.

Ethical Approval: The study was approved by the Ethical Review Committee of the University College Hospital, Ibadan, Nigeria.

RESULTS

Socio-demographic characteristics of respondents; Table 1 shows Socio-demographic characteristics of the respondents.

Table 1:
Socio-demographic characteristics of respondents

Variable	Frequency(n)	Percentage (%)
Age group (years)		
<30	89	25.1
30-39	66	18.6
40-49	102	28.7
50+	98	27.6
Sex		
Male	188	53.0
Female	167	47.0
Religion		
Christianity	190	53.5
Islam	163	45.9
Traditional	2	0.6
Ethnic group		
Yoruba	284	80.0
Igbo	36	10.1
Hausa	11	3.1
Others	24	6.8
Marital status		
Single	94	26.5
Married	244	68.7
Separated	4	1.1
Divorced	1	0.3
widowed	12	3.4
Family setting		
Monogamous	290	81.7
Polygamous	65	18.3
Total	355	100.0

Three hundred and fifty five Nigerians who met the criteria for recruitment were included in the study and interviewed. The mean age of the respondents was 39.04 (SD+ 11.335) years. Almost one third of the patients 102(28.7%) were between 40-49 years of age and 50 years and above were 98(27.6%). One quarter of the respondents 89(25.1%) were less than 30 years of age while the remaining 66(18.6%) were between 30-39 years of age. Male respondents constituted a little above half of the respondents 188(53.0%) while there were 167(47.0%) female respondents. Majority of the respondents 284(80.0%) were Yorubas . Others were Igbo 36(10.1%), Hausa 11(3.1%) and from other ethnic groups 24(6.8%).

Distribution of asthma severity based on lung function measurements; Over one third of the respondents had

moderate asthma 135(39.0%), severe asthma was documented in 131(37.9%) while 80(23.1%) of the respondents were mild cases.

Distribution of Inhaler techniques and drug adherence: Majority of the respondents 181(60.5%) had correct inhaler techniques while 118(39.5%) had incorrect inhaler technique. About half of the respondents had good drug adherence 181(51.0%) while 174(49.0%) had poor drug adherence.

Table 2:
Association of drug adherence with asthma treatment plan, inhaler technique and types of inhalers

Variable	Good n(%)	Poor n (%)	χ^2	p
Asthma treatment plan				
Yes	25 (62.5)	15 (37.5)	2.392	0.302
No	151 (49.5)	154 (50.5)		
Unsure	5 (50.0)	5 (50.0)		
Inhaler technique				
Correct	129 (71.3)	52 (28.7)	56.031	<0.001*
Incorrect	32 (27.1)	86 (72.9)		
Inhaler preference				
MDI**	73 (31.9)	156 (68.1)	110.633	<0.001*
DPI***	17 (65.4)	9 (34.6)		
MDI+DPI	84 (97.7)	2 (2.3)		
Types of inhaler Reliever				
Yes	174 (52.1)	160 (47.9)	2.783	0.095
No	7 (33.3)	14 (66.7)		
Controller				
Yes	181 (98.8)	2 (1.1)	324.022	<0.001*
No	0 (0)	149 (100)		

*Significant at 5% level of significance
DPI**= dry powder inhaler, MDI***=metered dose inhaler

Association of drug adherence with inhaler techniques and inhaler preferences: Table 2 shows association of drug adherence with inhaler techniques and inhaler preferences. Respondents with correct inhaler techniques had a higher proportion with good adherence (71.3%) compared to those with incorrect inhaler technique (27.1%). (p<0.001). Respondents who used both MDI+DPI had a greater proportion with good adherence (97.7%) compared to those who used DPI (65.4%) and MDI (31.9%). (p<0.001).

Association of asthma control with inhaler techniques and inhaler preferences of respondents: As shown in Table 3, a higher proportion of patients with correct inhaler technique had good asthma control (72.9%) compared to those with incorrect inhaler technique (61.9%), (p=0.044). A higher proportion of patients that used MDI+DPI had good asthma control (83.7%) compared to those who used MDI alone (62.9%) and those who used DPI alone (57.7%). (p=0.001).

A higher proportion of patients who used relievers (68.3%) had good asthma control compared to those who did not (28.6%), (p<0.001). Also, a higher proportion of patients who used preventers had good asthma control (69.9%) compared to those who did not (64.4%), (p=0.286).

Table 3:
Association between asthma control with inhaler preference of respondents

	Good n(%)	Poor (%)	n	χ^2	P-value
Inhaler technique					
Correct	132 (72.9)	49 (27.1)	4.057	0.044*	
Incorrect	73 (61.9)	45 (38.1)			
Inhaler preference					
MDI**	144 (62.9)	85 (37.1)			
DPI***	15 (57.7)	11 (42.3)	13.725	0.001*	
MDI+DPI	72 (83.7)	14 (16.3)			
Types of inhalers					
<i>Reliever</i>					
Yes	228 (68.3)	106 (31.7)	13.855	<0.001*	
No	6 (28.6)	15 (71.4)			
<i>Controller</i>					
Yes	128 (69.9)	55 (30.1)	1.138	0.286	
No	96 (64.4)	53 (35.6)			

*Significant at 5% level of significance

Metered dose inhalers; * Dry powder inhalers

Association of asthma control and drug adherence: Figure 1 shows the association between asthma control and adherence to the use of inhalers. A higher proportion of patients with good adherence had good asthma control (70.2%) compared to those with poor adherence to the use of inhalers (61.5%), ($\chi^2=2.969$, $p=0.085$).

Logistic regression analysis of good drug adherence on selected variables: Table 4 shows the logistic regression of good drug adherence on variables. After adjusting for other variables, the predictors of good adherence include inhaler techniques and inhaler preferences. Respondents with correct

inhaler technique were about five times more likely to have good adherence compared to those with incorrect inhaler technique (OR=5.061; 95%CI=2.637-9.710). Also, respondents who used MDI only were about sixty-six times less likely to have good adherence compared to those that used MDI+DPI (OR=0.015; 95%CI=0.003-0.065). Also those who used DPI only were about thirty-four times less likely to have good adherence compared to those who used MDI+DPI (OR=0.029; 95%CI=0.005-0.165).

Logistic regression analysis of good asthma control on selected variables: Table 5 shows the logistic regression output of asthma control on selected variables. After adjusting for other variables, the predictor of good asthma control was inhaler preference.

Patients with a monthly income of \leq N5, 700 were about one and half times less likely to have good asthma control compared to those with an income $>$ N5,700. (OR=0.657;95%CI=0.236-1.830). Patients who used MDI were about two times less likely to have good asthma control compared to those who used both MDI+DPI (OR=0.462; 95%CI=0.229-0.933) while patients who used DPI were about three times less likely to have good asthma control compared to those who used both MDI+DP, (OR=0.297; 95%CI=0.101-0.870)

Patients less than 30 years of age (OR=0.735; 95%CI=0.276-1.955) and 30-39 years of age (OR=0.914; 95%CI=0.398-2.101) were about two times less likely to have good asthma control compared to those 50 years and above. Those between 40-49 years of age were twice more likely to have good asthma control compared to those of 50 years and above (OR=1.166; 95%CI=0.541-2.509)

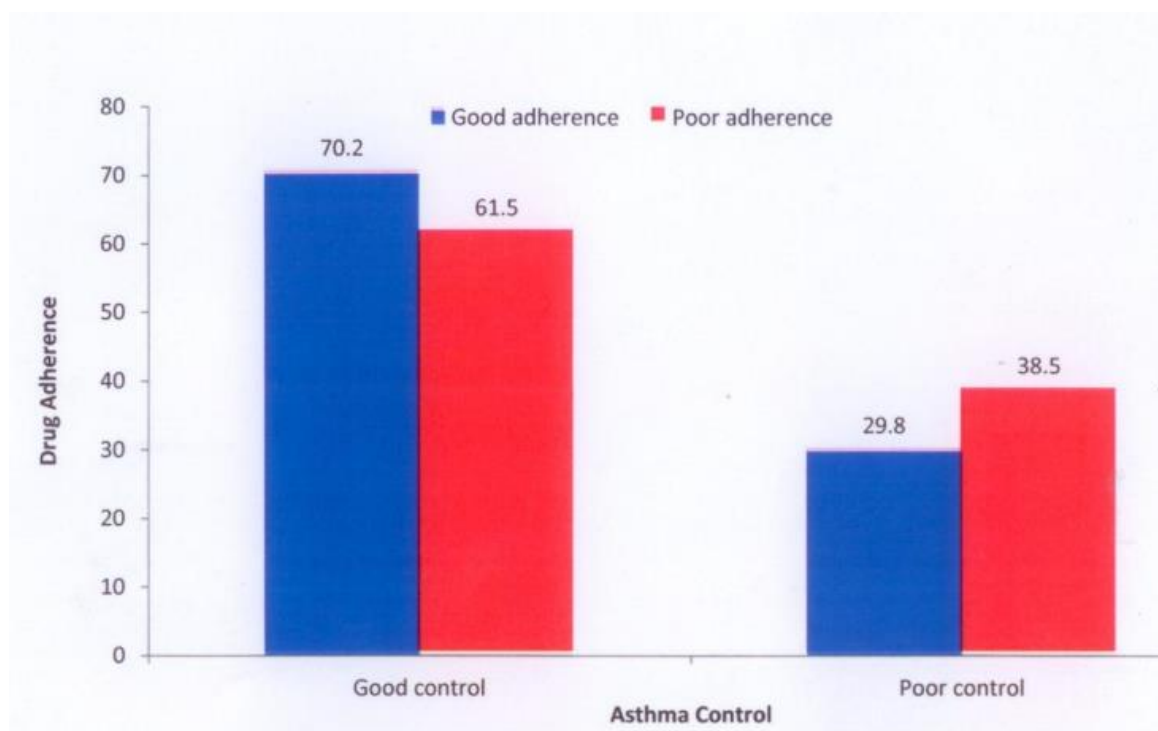


Figure 1
Association between asthma control and adherence to the use of inhalers

Table 4: Logistic regression analysis of good drug adherence on selected variables

Variable	Odds Ratio	95%Ci	P-Value
Age (years)			
Less than 30	0.515	0.150-1.767	0.291
30-39	1.072	0.400-2.873	0.890
40-49	0.907	0.380-2.167	0.826
50 and above	1		
Marital status			
Single	1.205	0.242-6.003	0.820
Married	0.433	0.130-1.446	0.173
Others	1		
Inhaler technique			
Correct	5.061	2.637-9.710	<0.001*
Incorrect	1		
Inhaler preference			
MDI**	0.015	0.003-0.065	<0.001*
DPI***;	0.029	0.005-0.165	<0.001*
MDI+DPI	1		

*Significant at 5% level of significance;

Metered dose inhalers; * Dry powder inhalers

Table 5:

Logistic regression analysis of good asthma control on selected variables

Variable	Odds Ratio	95%Ci	P-Value
Age (years)			
Less than 30	0.735	0.276-1.955	0.537
30-39	0.914	0.398-2.101	0.832
40-49	1.166	0.541-2.509	0.695
50 and above	1		
Marital status			
Married	1.246	0.584-2.659	0.569
Others	1		
Inhaler technique			
Correct	1.482	0.848-2.590	0.168
Incorrect	1		
Inhaler preference			
MDI**	0.462	0.229-0.933	0.031
DPI***	0.297	0.101-0.870	0.027
MDI+DPI	1		
Reliever			
No	1.995	0.542-0.734	0.299
Yes	1		

*Significant at 5% level of significance; **Metered dose inhalers;

*** Dry powder inhalers

DISCUSSION

The non-adherence to inhaled cortico-steroids which are DPI documented in low income groups could have been due to the fact that DPI drugs are very costly and not affordable. In this study, majority of the respondents used MDI whereas a minority used DPI while others used both DPI and MDI. This means that a low proportion of the respondents used DPIs which are inhaled cortico-steroids. The inhaler type preference among the respondents was possibly as a result of the high cost of DPIs. This was corroborated by a study conducted in Nigeria which reported that only 20% of their respondents used inhaled corticosteroids (Umoh *et al* 2013)

This study showed that a little above half of the respondents used their inhaler correctly and a third of the respondents used the inhaler wrongly. This was contrary to what was reported by Onyedun and others that majority of asthma patients studied used their inhalers inaccurately (Onyedun *et al* 2014). Patients' training in inhaler techniques by the physicians, pharmacists and nurses is very important in management of asthma and helping patients to maintain inhaler techniques once learned and stay motivated to continue regular therapy for asthma. Prescribing an appropriate inhaler device for asthma that the patient accepts and can handle correctly is very important in management of asthma as shown by a literature review (Anderson 2005). This allows for good adherence and acceptable level of asthma control.

Good adherence to the use of inhaler has a positive influence in the acceptable level of asthma control. This study showed that a high proportion of patients on both MDIs and DPIs had better control of asthma than those on either DPIs or MDIs alone. Majority of the respondents that had good adherence to the use of DPIs also had good control of their asthma since they contain the ICS and LABA as controller drugs which are important in the management of persistent asthma. This was similar to the findings in a previous study that budesonide and formoterol given as combination drugs in turbobhalers gave adequate control of asthma symptoms and maintenance of good lung function (Ige and Sogaolu 2004).

A review by Makela *et al* showed that non-adherence to inhaled medications for asthma and COPD is associated with poor control of symptom, higher healthcare utilization and reductions in health-related quality of life (Makela,2013). One of the objectives of this study was to find out the relationship between adherence to the use of inhalers and control of asthma. It was demonstrated that respondents with good adherence had better asthma control. The more a patient adhere to his therapy the better the control of asthma and so patients should be counseled to use their drugs effectively to achieve a better control of asthma. In a study conducted in Iran, it was found that patients did not take their drugs(lower adherence) especially the "preventers" when they were controlled because of inadequate knowledge of asthma (Tavasoli *et al* 2006).

Apart from when they are apparently well, forgetfulness, fear of addiction, social stigma and high costs are other factors reported to be associated with non-compliance with medication according to Waheed and others (Waheed *et al*, 2015). It was also shown in this study that the predictor of good asthma control was inhaler preference. This could be due to the fact that MDIs are cheaper and easier to use while DPIs though more efficacious than MDIS are costlier.

In conclusion, a higher proportion of patients with good adherence to the use of inhalers had good asthma control. This study showed that the predictors of good adherence to the use of inhalers include inhaler technique and inhaler preference and so also the predictor of good asthma control was inhaler preference.

REFERENCES

- Anderson P. (2005). Patient preference for and satisfaction with inhaler devices. *Euro Respir Review*. 14:109-16.
Bethesda. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.

- National Heart, Lung, and Blood Institute (NHLBI). National Asthma Education and Prevention Program. [Online] 2007 [cited 2009 Jul 21st]; Available from: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln>
- Caress A-L, Beaver K, Luker K, Campbell M and Woodcock A.(2005). Involvement in treatment decisions: what do adults with asthma want and what do they get? Results of a cross sectional survey. *Thorax*. 60: 199-205.
- Diette GB, Sajjan SG, Skinner EA, Weiss TW, Wu WA and Markson LE.(2009). Using the Paediatric Asthma therapy assessment Questionnaire to measure asthma control and healthcare utilization in children. *Patient*; 2(4): 233-241.
- FitzGerald JM, Charn CKN, Holroyde MC, and Boulet L-P. (2008). The CASE survey: Patient and physician perceptions regarding asthma medication use and associated oropharyngeal symptoms. *Can Respir J*. 15(1):27-32.
- Gillissen A.(2007).Patients' adherence in asthma. *J of physiology and Pharmacology*. 58(5):205-22
- Hess DR. (2005).Metered dose inhalers and dry powder inhalers in aerosol therapy. *Respiratory Care*. 50 : 1376-1383.
- Ige OM and Sogaolu OM. (2004). A single bilnded randomised trial to compare the efficacy of once daily budesonide(400) administered by turbuhaler with beclomethasone dipropionate(400) given twice daily through a metered-dose inhaler in patients with mild to moderate asthma. *Afr. J.med.Sci*; 33:155-60.
- Janson R, Accordini E, Almar M, Bugiani A, Carolei L. and Cazzoletti I. (2005). Changes in the use of anti-asthmatic medication in an international cohort. *Eur Respir J*. 26:1047-1055.
- Lexley M, Pinto P, Yuri C, Cecil KD, Duane M and Donald TS. (2002). Understanding and Use of Inhaler Medication by Asthmatics in Specialty Care in Trinidad. *Chest*. 121 (6):1833-40.
- Lynd LD, Daphne PH, Peter DP and Aslam HA.(2002). Patterns of inhaled asthma medication use: a 3-year longitudinal analysis of prescription claims data from British Columbia, Canada. *Chest*.122:1973-81.
- Markson LE, Vollmer WM, Fitterman L,Connor EO, Narayaman S and Berger M. (2001).Insight Into Patient Dissatisfaction with Asthma treatment. *Arch Intern Med*. 2001; 161: 379-84.
- Moffat M, Cleland J, van der Molen T and Price D. (2007).Poor communication may impair optimal asthma care: a qualitative study. *Family Practice*. 24(1):65-70.
- Onyedum C C, Ukwaja K N, Desalu O O and Ezeudo C.(2013). Challenges in the management of bronchial asthma among adults in Nigeria:A systematic review.*Ann Med Health Sci Res*.3:324-9.
- Papi A , Haughney J, Virchow JC, Roche N, Palkonen S and Price D.(2011). Inhaler devices for asthma: a call for action in a neglected field. *Eur Respir J*. 37 (5): 982-5.
- Pollart SM and Elward KS.(2009). Overview of changes to asthma guidelines: diagnosis and screening. *Am Fam Physician*. 79 (9):761-7.
- Putman H.(2004). Predictors of Asthma Treatment Adherence in Rural Appalachian Adults with Asthma. *Online Journal of Rural Nursing and Healthcare*. 4 (2):31-51.
- Rachelefsky G. (2009). Inhaled Corticosteroids and Asthma Control in Children: Assessing Impairment and Risk. *Pediatrics*. 123 (1): 353 -366.
- Sin DD and Tu JV. (2001).Under use of inhaled steroid therapy in elderly patients with asthma. *Chest*. 119:720 - 25.
- Spangler DL.(2012). The role of inhaled corticosteroids in asthma treatment: a health economic perspective. *Am J Manag Care*. 18(2): S35-9.
- Stephen T H, David P and Erkkka V. (2006). Asthma out of control? A structured review of recent patient surveys. *BMC Pulmonary Medicine*. 6(Suppl 1):S2.
- Susan LJ, Gillian E, Kelly PW and Paul DB. (2008).Predictors of Asthma Medication Nonadherence. *Heart Lung*. 37(3): 211-18.
- Tavasoli S, Heidarnazhad H and Kazemnejad A.(2006). Factors Affecting Patients'Compliance to Metered-Dose Inhaler Drugs in Two Asthma Clinics in Tehran, Iran. *Iran J Allergy Asthma Immunol*. 5(4):187-93