East African Medical Journal Vol. 96 No. 3 March 2019
MEDICATION USE AND LUNG FUNCTION AMONG ASTHMATICS SEEN IN AN OUTPATIENT CHEST CLINIC IN ADDIS ABABA, ETHIOPIA -A NEEDS ASSESSMENT
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MEDICATION USE AND LUNG FUNCTION AMONG ASTHMATICS SEEN IN AN OUTPATIENT CHEST CLINIC IN ADDIS ABABA, ETHIOPIA -A NEEDS ASSESSMENT

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ABSTRACT

Introduction: **Asthma is significant in Ethiopia and appropriate treatment has been inconsistent. We evaluated lung function and medication use among asthmatics seen in the outpatient chest clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.**

Methods: **A cross-sectional study was conducted from July 1 to December 30, 2015. Chart review was used to obtain clinical information and spirometric values on those with physician-diagnosed asthma. Airflow obstruction was defined as a FEV1/FVC < 70% and an FEV1< 80% predicted.**

Results: **96 study subjects were identified. The mean age was 53 ± 12 years; 64.6% (n=62) were female. Twenty-five percent (n=24) had normal spirometry and 75% (n=72) had airflow obstruction. In multivariate analysis, impaired lung function was associated with longer duration of asthma (adjusted OR 3.89, 95% CI 1.24–12.24) and an asthma exacerbation in the last 12 months (adjusted OR 3.38, 95% CI 1.11–10.30). Of those 72 asthmatics with impaired lung function, 94.4% (n=68) were using SABA but only 56% (n=40) were on ICS.**

Conclusion: **Most study asthmatics had impaired lung function and were not on appropriate asthma treatment. These findings suggest a need for more readily**

available and inexpensive asthma medications as well as qualified physicians to guide asthma management in Ethiopia.

INTRODUCTION

Asthma is a common chronic lung disease that affects more than 300 million people around the world (1). Approximately 2 million Ethiopians (2.3% of the population) are estimated to have asthma (2). Despite improved treatment options and the existence of asthma management guidelines, surveys conducted in America, Europe, Asia-Pacific, and Japan have shown that control of asthma is suboptimal for many patients (3). The level of asthma control is generally low in Ethiopia as in other African countries (4-5), in part, reflecting physician continued reliance on short-acting beta agonist (SABA) without adequate use of controller medications such as inhaled corticosteroids (ICS) (4, 6).

Inappropriate asthma management may also result in an accelerated decline in lung function. Previously identified risk factors for worsening lung function include young age, male gender, duration of disease, more prominent eosinophilic airway inflammation, asthma exacerbations, and cigarette smoking (7). Recent studies have also shown increased mortality associated with reduced lung function in asthmatics (8).

The objective of this study was to evaluate lung function and use of appropriate medication among a subset of asthmatics undergoing spirometry in the outpatient chest clinic of Tikur Anbessa Specialized Hospital (TASH), the largest public hospital in Addis Ababa, Ethiopia.

MATERIALS AND METHODS

This cross-sectional study was conducted from July 1 to December 30, 2015 at the chest clinic of TASH, which is the largest tertiary hospital in Ethiopia, offering diagnosis and treatment for approximately 370,000-400,000 patients per year. Chest clinic has over 500-visits/month; asthma patients account for nearly one-third of these monthly visits. Patients were referred from all over Ethiopia, but a majority of the asthmatic patients were from Addis Ababa and nearby Oromiaya, Amhara, and Southern Nations Nationalities and People regions. Thi s study setting was chosen because of the number of asthmatics seen and the availability of a well-organized longitudinal database.

We had previously identified 182 consecutive asthmatic subjects for a study of the level of asthma control and risk factors for poor asthma control among clinic patients seen at TASH located in Addis Ababa, Ethiopia (9). Subjects for the current study comprised a subset of 96 subjects who had undergone spirometry and also fulfilled inclusion criteria of adults ≥18 years of age with physician-diagnosed asthma on treatment for at least the previous six months and routine clinic follow-up care. Those with active lung infections, physician diagnosed bronchiectasis or chronic obstructive pulmonary disease (COPD), or incomplete data were excluded from the study. A pre-tested data collection form was utilized to obtain demographics, respiratory symptoms (i.e., cough, breathlessness, wheeze, and chest tightness), current medications, comorbidities, and spirometry from clinic records. Asthma exacerbation was defined as the self-report of worsening respiratory symptoms for greater than 48 hours in the past 12 months.

Asthma severity and control were assessed based on the GINA asthma symptom control assessment tool at the time of the clinic visit (1). This tool uses frequency of symptoms, night waking due to asthma, limitation of activity, and frequency of reliever medication use and has been previously correlated to other standardized asthma control scores (10). Accordingly, "well controlled" asthma was defined by the absence of daytime symptoms (no more than twice a week), the absence of nighttime symptoms, no limitations in activities, and limited need for rescue medication (not more than twice a week). "Partially controlled" asthma was present when daytime symptoms or rescue medication use was present more than twice per week, and night waking or activity limitation were present in any week, while "uncontrolled" asthma was defined as the presence of any three or more of these individual features within any week (1). For reporting in this study, patients were classified in two groups: uncontrolled asthma and controlled asthma (well and partially controlled).

Spirometry was measured using a Diagnostic EasyOne Plus model 2001 SN spirometer, which was calibrated according to the manufacturer's recommendations. Spirometric acceptability and reproducibility were determined using the published criteria of the European Respiratory Society and the American Thoracic Society (ATS) (11). The normal reference values for pulmonary function were based on data published by ERS/ECCS with adjustment for black Africans (12). Currently, there are no reference data for Ethiopians and racial differences may exist. Normal spirometry was defined as FEV1 $\geq$ 80% predicted and FEV1/FVC $\geq$ 70%; airflow obstruction was defined as FEV1 < 80% predicted and FEV1/FVC$\leq$ 70%. The degree of spirometry impairment was classified using ATS standards (11).

Statistical analysis was performed using IBM SPSS statistics Version 20 (Armonk, NY: IBM Corp). Categorical variables were summarized as frequencies and percentages while continuous data were described using mean, median, standard deviation, or interquartile range. The association between potential factors and impaired lung function was explored using bivariate logistic regression. All the factors that showed a $p \leq 0.20$ were assessed in a multivariate logistic regression model using a stepwise strategy to identify independent factors associated with poorly controlled asthma. Odds ratios (OR) and their 95% confidence intervals (CI) were determined. A $p < 0.05$ was regarded as statistically significant.

The Institutional Review Board of Addis Ababa University College of Health Sciences approved this study.

RESULTS

A total of 96 patients were recruited for this study from July to December 2015. Their mean age was 53 ± 12 years and 62 (64.6 %) were females. The average duration of asthma was 19.8 ±13.6 years (Table 1). Of the 96 asthmatics, 55.2% (n=53) had daytime symptoms (>twice a week), 62.5% (n=60) had nighttime symptoms and 42.7% (n=41) had activity limitations. By GINA criteria, 49% (n=47) of the group had well/partly controlled asthma and the remaining 51% (n=49) had uncontrolled asthma (Table 1).

The group spirometric means were: FEV1 1.59 ± 0.81 liter (54 ± 27 % predicted), FVC 2.53 ± 0.79 liters, (86.0 ± 26.9 % predicted), and FEV1/FVC 0.63 ± 0.16 %. Of the 96 asthmatics,

25% (n=24) had normal spirometry and 75% (n=72) had airflow obstruction. None of the subjects had restriction. For those 72 asthmatics with airflow obstruction, 13.9% (n=10) had mild, 15.3% (n=11) had moderate, 19.4% (n=14) had moderately severe, 30.6% (n=22) had severe, and 20.8% (n=15) had very severe impairment. Compared to those with normal spirometry, asthmatics with abnormal lung function were younger (52.5 ± 11.7 vs. 56 ± 12.6 years, p=0.034) and had a longer duration of asthma (21.6 ± 13.4 vs.14.4 ± 13.3 years, p=0.026).

Table 1

Baseline characteristics of physician-diagnosed asthmatics that had undergone spirometry seen in chest clinic at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia (n = 96)

Variable	Characteristic	Frequency	Percent (%)
Age (year): mean ± SD		53 ± 12	
Gender	Male	34	35.4
	Female	62	64.6
Duration of asthma, mean, years(SD)		19.8 ±13.6	
School education	≤ Primary level	21	21.9
	≥ Secondary level	75	78.1
Smoking status	Current smoker [a]	1	1.1
	Ex-smoker	5	5.2
	Nonsmoker	90	93.7
Use of biomass fuel for Cooking	Yes	37	38.5
	No	59	61.5
Body mass index [b]	Normal/under weight	31	57.4
	Overweight/ Obese	23	42.6
Exacerbation in the last 12 month	Yes	46	47.9
	No	50	52.1
Comorbidities [c]	Yes	45	46.9
	No	51	53.1
Incorrect inhaler Technique	Yes	34	35.4
	No	62	64.6
Inhaled corticosteroids	Yes	54	56.3
	No	42	43.7
SABA use	Yes	92	97.9
	No	4	2.1
FEV1	>= 80%	24	25.0
	< 80%	72	75.0
GINA symptom assessment	Well/ Partially controlled	47	49.0
	Uncontrolled	49	51.0

a Current smoker = person who was smoking during the time of study
b Normal BMI = 18–25 M2/kg
c Comorbidities include allergic rhinitis, GERD

In both Bivariate and Multivariable analysis, the unadjusted longer duration of asthma was found to be a significant risk factor for impaired lung function. Otherwise, those with normal versus impaired lung function were not significantly different in terms of GINA asthma control, respiratory symptoms, gender, or education level. Notably, smoking history, exposure to biomass fuel and having an asthma exacerbation in the past 12 months were not significantly associated with impaired pulmonary function (Table 2).

Of the 96 patients, 95.8% (n=92) were using short acting beta agonist (SABA) medication, and only 56.3% (n=54) were using inhaled corticosteroids (ICS) therapy. 91.7% (n=88) of the group used more than one canister of salbutamol per month; 19.8% (n=19) were taking oral steroids.

Most of those with impaired lung function were taking medications. Of the 72 patients with airflow obstruction, 94.4% (n=68) were using SABA medication, however only 56% (n=40) were using ICS therapy. A total of 8 study patients were using a combination of long acting beta agonist (LABA) and ICS, all were in the group with abnormal spirometry. 93.1% (n=67) of those with impaired lung function used more than one canister of albuterol per month; 18.1% (n=13) of this group was taking oral steroids.

Table 2

Bivariate and multivariable analysis of factors associated with lung function (N = 96)

	Character	**FEV1>=80%predicted**	**FEV1<80%predicted**	***P value**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Number of subjects		24	72			
Duration of asthma (Years)	=< 10 > 10	12(41.4%) 12(17.9%)	17(58.6%) 55(82.1%)	0.02	5.38(4.23-6.53)	3.89(1.24-12.24)
Age (Years)	=<35 > 35	3(50%) 21(23.3%)	3(50%) 69(76.7%)	0.16	3.29(0.62-17.51)	1.94(0.27-3.61)
Gender	Male Female	9(26.5%) 15(24.2%)	25(73.5%) 47(75.8%)	0.81	1.13(0.43-2.94)	0.06(0.00-0.12)
Formal Education	No Yes	21(28%) 3(14.3%)	54(72%) 18(85.7%)	0.21	2.33(0.62-8.75)	1.578(0.26-2.90)
Incorrect Inhaler Technique	No Yes	18(29%) 5(15.6%)	44(71%) 27(84.4%)	0.16	2.21(0.74-6.64)	1.99(0.89-3.09)
Inhaled corticosteroids use	No Yes	12(29.3%) 12(22.2%)	29(70.7%) 42(77.8%)	0.44	1.45(0.57-3.67)	0.61(0.31-1.53)

Short Acting Beta Agonist use	No Yes	0(0%) 24(26.1%)	4(100%) 68(73.9%)	0.99	0.00	0.00
Exacerbation in the last 12 months	No Yes	9(18%) 15(32.6%)	41(82%) 31(67.4%)	0.10	0.67(0.26-1.43)	0.45(0.18-1.17)
Asthma control (GINA assessment tool)	Well/ Partly controlled Uncontrolled	20(26.7%) 4(19%)	55(73.3%) 17(81%)	0.48	1.55 (0.46-5.15)	0.50(0.30-1.70)
Smoking	No Yes	0(0%) 22(24.7%)	1(100%) 67(75.3%)	1.00	0.000	0.000
Biomass fuel use for cooking	No Yes	14(24.6%) 10(27%)	43(75.4%) 27(73%)	0.79	0.88(0.34-2.26)	0.07(0.03-1.01)
BMI ($Kg/M^{2)}$	<25 >= 25	6(19.4%) 6(26.1%)	25(80.6%) 17(73.9%)	0.56	0.68(0.19-2.47)	0.34(0.08-1.00)
Comorbidities	No Yes	11(21.6%) 13(28.9%)	40(78.4%) 32(71.1%)	0.41	0.68(0.27-1.71)	0.679(0.21-1.15)

**P value represents the p value for the adjusted OR.*

DISCUSSION

In our cohort of asthmatics recruited from the chest clinic of a large public hospital in Addis Ababa, Ethiopia, a majority of patients had airflow obstruction and were using SABA but not ICS medications. A very small percent was using combination LABA/ICS therapy, which is not readily available in Ethiopia.

Our spirometry results are in agreement with other published studies. Lung function in asthmatics has been shown to be lower than predicted, reflecting an accelerated decline in lung function over time (13). Furthermore, as in our study, duration of disease has been previously identified as risk factors for accelerated decline in lung function in asthmatics (7).

A significant percent of our study asthmatics was not using ICS. This may in part explain the significant reduction in lung function found in our study. Inhaled corticosteroids (ICS) have been shown to reduce the chronic inflammation seen in asthmatic airways (14), and treatment with ICS may therefore reduce the accelerated rate of decline in ventilatory function seen in some asthmatic patients. In addition, several studies have shown beneficial effects on lung function both during the first few years of treatment and long-term (15). More aggressive treatment with ICS in our patient population may have led to less lung function impairment.

It is well known that reliever medications such as SABA suppress symptoms but have no effect on the underlying airway inflammation. Without concomitant anti-inflammatory therapy, poor asthma control with an increased risk of morbidity and mortality can result (8, 29). Several studies have also shown that high SABA use (i.e., greater than one canister per month), especially in those asthmatics with FEV1 < 60% predicted, is a known risk factor for

disease exacerbation, even in patients with few symptoms (16). In addition, multiple studies have demonstrated that a low ratio of controller to reliever medication is associated with adverse outcomes (17). The recognition of such increased risk has resulted in significant changes in guidelines and best practice recommendations in asthma management, such as the Global Initiative for Asthma (1). In our study, we found an underutilization of ICS and an over reliance on SABA therapy; most of our patients were using more than one SABA canister per month and many were not following GINA treatment guidelines.

These findings further support those of a recent study from Ethiopia which showed a high prevalence of inappropriate asthma therapy primarily attributed to limited accessibility of asthma medications (18). Insufficient prescribing of ICS may facilitate asthma exacerbations (19); in our cohort nearly half of the patients had exacerbations within the previous 12 months.

The results of our study can be used to change practice patterns in similar low resource settings. Physicians must be educated on the appropriate use of ICS in the management of asthmatics. This can be done through the dissemination of national guidelines modified for local practices. A greater availability of low cost asthma medications, especially LABA/ICS combination therapy, needs to occur. Pharmaceutical companies should follow similar policies previously developed for low cost, widely available HIV medications.

Finally, training of pulmonologists in low-resource countries is necessary. Until recently, there had been a complete lack of qualified pulmonary physicians at TASH. Currently, 9 Ethiopian physicians have been trained in pulmonary medicine through the East African Training Initiative (20). We believe that this added subspecialty training would greatly improve the care of asthmatic patients, especially those with severe disease.

This study has several limitations. Patients were recruited from the chest clinic of a large tertiary public hospital, possibly influencing generalizability of the findings. Treatment adherence was not regularly assessed, which could have contributed to the high percent of poor asthma control. These two factors may have resulted in more severe disease among study subjects but would not have invalidated our findings. Physician diagnosis was used to identify study participants, making misclassification possible. Bronchodilator responsiveness was not obtained and therefore some of the study patients may have had COPD rather than asthma. However, those physicians working in chest clinic are knowledgeable about differences in asthma and COPD, making misclassification less likely. The sample size was not large enough for more detailed analyses, supporting the need for further research.

CONCLUSION

Our study showed a lack of appropriate treatment for over one-third of study asthmatics with impaired lung function. We believe that more readily available and inexpensive asthma medications as well as qualified physicians to guide management of this common respiratory illness are needed both in Ethiopia and other similar low-resource countries.

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