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ORIGINAL ARTICLE

CHARACTERIZATION OF ASTHMA AND ITS DETERMINANTS IN ETHIOPIA: PART OF THE AFRICAN SEVERE ASTHMA PROJECT

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ABSTRACT

Introduction: *Asthma is a major public health problem globally affecting 339 million people with 300,000 annual death. African Severe Asthma Program was a multi-country prospective cohort study designed to characterize severe asthma in three African countries, Ethiopia, Uganda and Kenya. In this study, we describe the baseline characteristics and disease severity among asthmatics enrolled in the Ethiopia site of African Severe Asthma Program.*

Methods: *Asthmatics seen at Tikur Anbessa Specialized Hospital from August 2016 to May 2018 were studied. Asthma was diagnosed based on symptoms and spirometry. Baseline demographic and clinical data were collected using a structured questionnaire. Standardized research tools were used to assess asthma severity, asthma control and asthma quality of life.*

Results: *A total of 419 asthmatic patients were enrolled in the study; the mean age for the group was 52 ± 8 years and 58.2 % were female. The majority of the participants, 365 (87.2%), had a prior diagnosis of asthma with a median (IQR) age at first diagnosis of 29 (IQR: 22 - 36) years. A family history of asthma was present in 149 (35.6%) subjects. Current or previous cigarette smoking was reported in 8.6% of the participants. Overall, 93.8% of the participants reported uncontrolled asthma symptoms (ACQ >1.5). More than half of the patients, had severe persistent asthma and 35% presented with one or more comorbidities.*

Conclusions*: In Ethiopia, asthmatics presenting to a tertiary care hospital were characterized as predominantly female with late onset disease, poor control, and associated comorbidities.*

Key Words: *Asthma, Characteristics, determinants and Severe*

INTRODUCTION

Asthma is a common chronic disease that is estimated to affect as many as 339 million people worldwide and cause over 300,000 deaths each year(1). In addition, according to the 2015 Global Burden of Diseases Report on Asthma, 22 million disability-adjusted life years (DALYs) are annually lost to asthma (2). In Africa, the prevalence of asthma is approximately 119 million or 13.8% of the population. The rates are higher in urban compared to rural areas and are increasing over time (3), possibly reflecting greater exposure to environmental risk factors, increased cigarette smoking, and a more westernized affluent lifestyle (4-8)

Globally, 5-10% of patients have severe disease (9-11). However, control of asthma (usually defined as minimal or no symptoms, normal activities and sleep, and optimal pulmonary function) may be achieved in the majority of patients (12-14).

Lack of asthma control may be due to a number of factors including an incorrect diagnosis, under treatment, ongoing exposure to sensitizing agents, and an unresponsive underlying inflammatory process (15-18).

Finally, various comorbid conditions are increasingly recognized as frequent contributors to uncontrolled asthma. The identification of comorbidities is now recognized as an integral part of the core management of asthma (15, 16).

In Ethiopia, 2.5 million adults and children (2.3% of the population) have asthma (19) and an increasing prevalence of disease has resulted in significant public health challenges (20-22). Little is still known about the characteristics of these asthmatics and the control and severity of their asthma, which is information important to lessen the country's burden of disease.

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This study was undertaken to describe the baseline characteristics, disease control, and severity among asthmatics enrolled in the Ethiopian site of the African Severe Asthma Program (ASAP), a multi-country prospective cohort study designed to characterize severe asthma in three African countries, Ethiopia, Uganda and Kenya.

METHODS

Study design and setting: This study was a prospective observational cohort study designed to investigate the prevalence, determinants, and impact of severe asthma in Ethiopia as part of ASAP (23). All enrolled asthmatics were recruited from chest clinic of Tikur Anbessa Specialized Hospital (TASH), the largest public tertiary medical center in Ethiopia.

Study participants:
Asthmatics were required to have at least one of the following: 1) more than one characteristic respiratory symptom, 2) physician diagnosed asthma, 3) use of asthma medications with improvement in symptoms, 4) history of wheezing in the past 12 months, and 5) pre-bronchodilator Forced Expiratory Volume in One second (FEV_1) ratio <0.70% and bronchodilator reversibility ≥12% and ≥200 mL (3). The diagnosis of asthma was confirmed by an expert pulmonologist. All asthmatics presenting to TASH over the age of 12 years were recruited. Subjects were excluded for the following reasons: 1).

contra-indications to spirometry testing, 2) a known diagnosis of an alternative lung disease (e.g. chronic obstructive pulmonary disease (COPD), bronchiectasis, pulmonary fibrosis and tuberculosis (TB), 3) age over 70 years, 4) pregnancy determined by self-reported last menstrual period, and fixed airflow obstruction on spirometry as defined as post-bronchodilator FEV_1/FVC ratio <0.70. Eligible patients were consecutively enrolled until the sample size was attained. Subjects were seen monthly for the first six months and then at 9 and 12 months. GINA based stepwise therapy was utilized to adjust treatment; all asthma medications were provided by the project. The study enrolled participants from August 2016 to May 2018.

Questionnaires: All eligible patients who provided written informed consent underwent a respiratory focused clinical evaluation using a pre-developed case report form (CRF) to collect data on socio-demographics, respiratory symptoms, vital signs, respiratory system signs, exposures to indoor and outdoor pollutants, known asthma triggers, tobacco smoking, psychosocial issues, and comorbidities (allergies, GERD). Asthma control was assessed using the Asthma Control Questionnaire (ACQ) (24), while the National Heart, Lung and Blood Institute (NHLBI) Expert Panel Report (EPR3) guidelines (25), were used for asthma severity grading.

Depression was assessed and graded using the Patient Health Questinnaire-9 PHQ-9) (26) and quality of life was assessed using the Asthma Quality of Life Questionnaire (AQoL) (27). We also assessed work and activity impairment with the Work Productivity and Activity Impairment Due to Asthma tool (WPAI: asthma) (28).

Spirometry: Spirometry was performed according to American Thoracic Society/European Respiratory Society(ATS/ERS)guidelines (29) using a Pneumotrac® spirometer with Spirotrac® V software (Vitalograph Ltd., Buckingham, United Kingdom). To achieve uniformity, we used the National Health and Nutrition Examination Survey (NHANES) references values for %predicted FEV_1 and %predicted FVC as there are no appropriate African reference values to date (30). Pre- and post-bronchodilator spirometry was performed for only those with FEV_1 ratio <0.70. We used 4 doses of inhaled salbutamol (400mcg) separated by one minute and repeated spirometry after 15 minutes.

Skin prick test (SPT): SPT was performed by trained nurse and interpreted according to published international guidelines (31). Common aero- and food allergens were preselected based on their published occurrence in African settings and included; house dust mite mix, soy bean, Blomia Tropicalis, Bermuda Grass(Cynodon Dactylon), Mold Mix IV, Aspergillus Fumigatus, dog epithelia (Canis Fam), cat epithelia (Felis Domesticus), German cockroach (Blat Germ), egg white, cow milk, and peanut (Arachys Hypogaea)(32).

Definitions
Uncontrolled asthma was defined as an ACQ score of ≥1.5 (24). Asthma exacerbation was defined according to the ATS/ERS definition as "events characterized by a change from the patient's previous status" (33). We considered only exacerbations that required a patient to either visit a health facility or to be hospitalized (i.e. moderate to severe exacerbations) as recommended by the ATS/ERS guidelines (33,34). Allergic sensitization was defined as having at least one positive allergen on the ASAP allergen panel of 12 allergens as previously defined in other studies (35) Depression was graded by the PHQ-9 Questionnaire as follows: 0-4 none, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe (26). Moderate to severe depression included everyone with scores ≥10.

Statistical analysis
Descriptive statistics were used to summarize enrolled patients' characteristics. For categorical variables, we present frequencies and percentages. For continuous variables, median and the interquartile ranges are presented. All analyses were done using STATA version 14 software

Ethical considerations

Ethics approval was obtained from College of Health Sciences Institutional review board (IRB) at Addis Ababa University, Ethiopia. All patients provided a written informed consent. Patients below 18 years provided assent while their parents/legal guardians gave written consent.

RESULTS

There were a total of 419 asthmatics enrolled in the study. Socio-demographic characteristics are shown in Table 1. The mean ± SD age for the group was 52 ± 8 years with a range of 15-70 years. Subjects 55-64 years of age (28.2%) were most affected followed by those 45-54 years, 26.3%; the least affected age group included participants less than 25 years of age, 4.1%.

The majority of subjects were female 244 (58.2%). Most were married 280 (66.9%) with 56 (13.4%) widowed and 42 (10.1%) single. The majority, 365 (87.2%) had a prior diagnosis of asthma with the median (IQR) age at first asthma diagnosis being 29(22-36) years. A family history of asthma was present in 149 (35.6%) of subjects.

Current and previous history of smoking was reported by 36 (8.6%) participants and secondhand smoking was reported by 23 (5.5%) subjects. A majority of study participants 304 (72.6%) had a history of biomass exposure.

Table 1: Socio-demographic characteristics of study participants, Tikur Anbessa Specialized Hospital, 2016-18

Socio-demographic Characteristics	Frequency (%)
Age in Year	
<15	6 (1.4)
15-24	11 (2.6)
25-34	31 (7.4)
35-44	70 (16.7)
45-54	110 (26.3)
55-64	118 (28.2)
65+	73 (17.4)
Mean Age	52 Years
Median age of onset of asthma(IQR)	29(22 - 36) years
Gender	
Male	175 (41.8)
Female	244 (58.2%)
Marital status	
Single	42 (10.1)
Married	279 (66.91)
Divorced	32 (7.8)
Widowed	56 (13.4)
Family History of Asthma	
Yes	149(35.6)
No	255(61.0)
I don't know	14(3.4)
Smoking History	
Current /Former smoker	36(8.6%)
Second hand smoke	23(5.5)
Never Smoked	381(91.4)
Biomass Exposure history	
Yes	304(72.6)
No	115(27.5)

The majority of the patients 243 (58.0%) had severe persistent asthma; 134 (32.0%) had moderate persistent asthma, 36 (0.6%) had mild persistent asthma, and 5 (1.2%) had mild intermittent asthma (Figure 1). Approximately 90% of study subjects had moderate to severe asthma. The most common respiratory symptoms were cough (189, 45.1%) and wheeze (158, 37.7%). On average, study participants used systemic steroids for asthma control three times per year and had at least one yearly exacerbation and emergency room visit. A large number of asthmatics, 196 (47.0%), had three or more exacerbations in one year; a smaller number, 103 (24.6%), had at least one hospital admission per year.

The number of asthma exacerbation was greater in the uncontrolled group than the controlled asthma group (P=0.007). Overall, 93.8% of the cohort reported uncontrolled asthma symptoms (ACQ >1.5) on study entry. Self-report of medication adherence was high in 67.7% of study participants, medium in 17.2%, and low in 15.1%. Despite this high adherence, 90 % of subjects had moderate to severe asthma. Allergy testing using skin prick was positive in only 19(6.9%) of the participants.

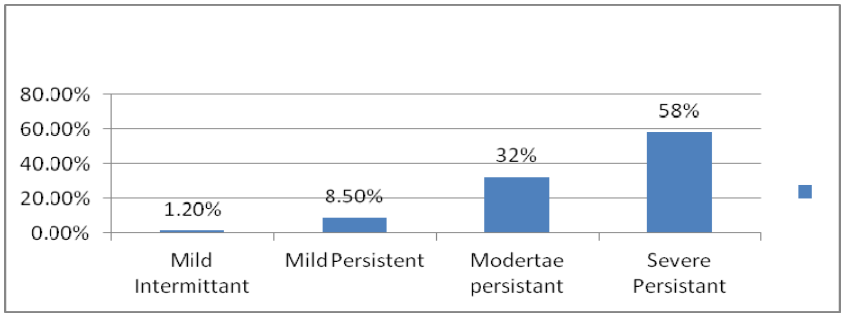

Figure 1: Asthma classification based on severity among study participants, Tikur Anbessa Specialized Hospital, 2016-18.

Medication use is shown in Table 2. Salbutamol MDI was the most common medication used (56.6%) followed by theophylline/aminophylline tablets (23.2%), oral steroids (22.7%), injectable steroids (13.4%), inhaled corticosteroid/long-acting beta agonist combination MDI (12.2%), inhaled steroid alone (Beclomethasone) (12.2%), Salbutamol tablets/syrup (11%).

A small number of subjects, 46 (11%) were not using any asthma medication despite their diagnosis. Poor asthma control was associated with use of salbutamol in any form (P=0.048) and use of theophylline as a controller medication (P=0.01).

Table 2: Asthma medications use among study participants, Tikur Anbessa Specialized Hospital, 2016-18

Medication use	**Frequency (%)**	
Currently on the following medications:	N = 419	100%
Salbutamol tabs/syrup	46	11.0
Salbutamol inhaler	237	56.6
Theophylline/Aminophylline tablets	97	23.2
Theophylline /Aminophylline injections	30	7.2
Nebulized salbutamol	2	0.5
Nebulized salbutamol/ipratropium	3	0.7
Nebulized steroid	2	0.5
Oral steroids such as prednisolone, dexamethasone	95	22.7
Injectable steroids such as hydrocortisone, dexamethasone	7	1.7
Inhaled steroids such as beclomethasone inhaler	51	12.2
Combination inhalers (steroids and long acting beta agonists)	56	13.4
Combination inhaler(salbutamol/ipratropium)	1	0.2
Leukotriene modifiers such as montelukast and zafirlukast	1	0.2
On systemic steroids (Oral & injectable steroids)	95	22.7
Not taking any asthma medication	46	11.0

Common asthma triggers are shown in Figure 2. Cold weather (88.1%), dust (86.6%), upper respiratory infections (82%), and strong smells and perfumes (70%) were the most frequently reported triggers. Exercise (59%), emotional situations (45.6%), cigarette smoke exposure (43%) and household pets were less often reported as triggers (3.34%)

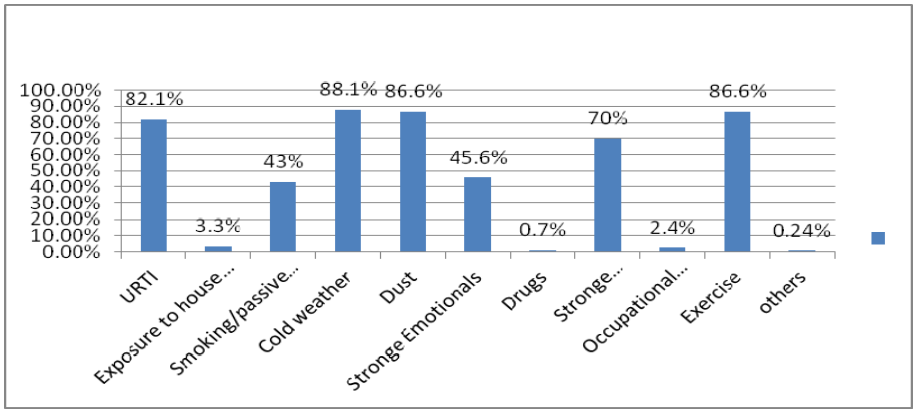

Figure 2: Reported common asthma triggers among study participants, Tikur Anbessa Specialized Hospital, 2016-18

A total of 147 (35%) of subjects had at least one comorbidity (Figure 3). Depression (86%) was the most common finding; minimal, mild, and moderate/severe depression were seen in 62.5%, 17%, and 4% subjects, respectively. Other less common comorbidities included: Hypertension (36%), obesity (10.7%), GERD (7.6%), rhinosinusitis (4.1%), and eczema/dermatitis (4.1%). The assessment of quality of life based on quality of life using Asthma Quality of Life Questionnaire (AQoL) was poor in uncontrolled asthma than controlled Asthma (P=0-000)

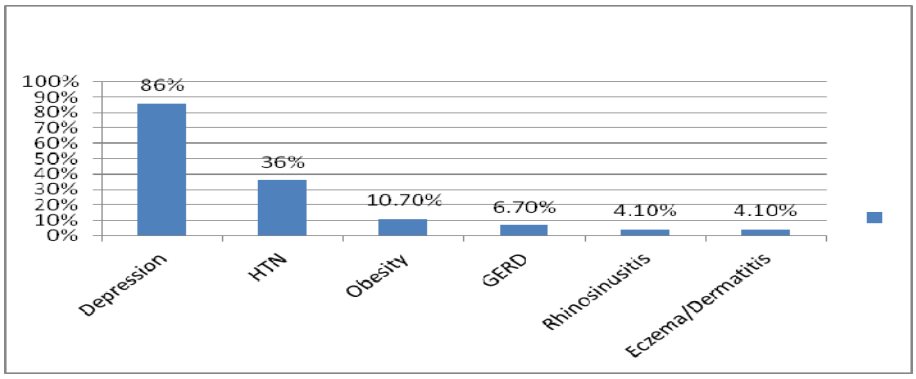

Figure 3: Comorbidities among study participants, Tikur Anbessa Specialized Hospital, 2016-18.

DISCUSSION

This study is the largest comprehensive evaluation of the characteristics of asthmatics living in Ethiopia. Spirometry was performed on all subjects and the diagnosis of asthma was confirmed using strict criteria. Many of our results are in concert with other published research. We found a predominance of older female asthmatics with late onset disease and infrequent atopy, as measured by skin prick testing. This can be explained by improved life expectancy, urbanization, increases rate of obesity and increased rate of air pollution in our population (34, 37) Studies from the United States and Europe have found similar findings; adult-onset asthma and adult-onset phenotypes were associated with factors such as female gender, obesity, occupational exposure, rhinitis, respiratory infections, smoking, stressful life events, and low level of lung function (38-41).

Asthmatics in this study appear to have more severe disease than reported in other studies from high resource countries (42-44).

A majority of the study patients (90%) had moderate to severe asthma and reported frequent respiratory symptoms, asthma exacerbations, use of systemic steroids, and hospital admissions.

In addition, 393 (93.8%) of the group reported uncontrolled asthma symptoms (ACQ >1) despite reporting high medication adherence. The number of asthma exacerbation was more in uncontrolled group than controlled asthma group (P=0.007). The percent of uncontrolled asthma was higher than in studies from high resources countries (45, 46) but in keeping with other research done in Africa (47-54-) and a smaller study done in Ethiopia (55).

This is also reflected by poor quality of life based on quality of life assessment using Asthma Quality of Life Questionnaire (AQoL) (P=0.000) Several factors may explain the observed disease severity and poor asthma control. In our study, short acting beta agonists served as the mainstay of treatment; only 25% were on proper controller medications. Poor asthma control was associated with use of salbutamol of any form and use of theophylline as a controller medication.

Previous studies done in Ethiopia found that the cost of inhaled corticosteroids and limited access to this class of medications played a critical role in undertreatment of asthma; our findings are in concert with those results (56-58). Also, improper inhaler technique, fear of inhaler use, and physician fear of unaffordability of inhaled ICS to prescribe for their patients may have also contributed to the observed poor asthma control (55-60). In addition, many of our asthmatics came to medical attention at a later stage of disease which reflects the health seeking behavior of the population in Ethiopia (61, 62). Development of national guidelines, additional education of patients and physicians on asthma and its proper management, and the availability and affordability of controller medications are necessary if asthma control is to improve in Ethiopia.

The prevalence of comorbidities in those with severe asthma was high in our study, as in others (63-65) and may also help explain the severity of disease seen. However, a more unique observation was the high rate of depression in our analysis, possibly reflecting impaired quality of life due to poor asthma control. Further investigations are needed to confirm this finding.

Unlike other studies, a history of rhinosinusitis and eczema was very low likely reflecting the infrequent presence of atopic asthma.

Conclusions

In Ethiopia, asthmatics presenting to a tertiary care hospital are characterized as predominantly female with late onset disease, a strong family history, minimal atopy, and limited exposure to cigarette smoke. In addition, there is a high percent of uncontrolled, moderate/severe disease associated with one or more comorbidities. Development of national guidelines, patient and physician education on asthma and its management, and increased availability and affordability of controller medications are urgently needed.

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