Determinants of Uncontrolled Asthma Among Adult Asthmatic Patients on Follow-Up at Chest Clinic of Jimma Medical Center: Unmatched Case-Control Study

Leta Adugna Geleta (✉ letaadugna72@gmail.com)
Salale University   https://orcid.org/0000-0002-7099-0420

Lelisa Sena Dadi
Jimma University

Alemayehu Atomsa Sona
Jimma University

Abstract

Background

Uncontrolled asthma is a notorious public health problem throughout the world despite the presence of effective treatments. Characterizing phenotypes of patients with uncontrolled asthma and searching for risk factors of uncontrolled asthma have been suggested as priority research agenda in the prevention of chronic respiratory diseases. This study aimed to identify the determinants of uncontrolled asthma.

Methods

Institution-based case-control study was conducted on asthmatic patients who were on follow-up at chest clinic of Jimma University Medical (JMC) from March to May, 2020. A total of 59 cases and 118 controls were included in the study. Logistic regression was employed to identify determinants of uncontrolled asthma. Adjusted odds ratios (AORs) with their corresponding confidence intervals (CI) were used to assess the strengths of association between uncontrolled asthma and its determinants at p values ≤ 0.05.

Results

Age of the patients [AOR: 2.78; 95% CI: 1.14, 6.81], age of the cases' residential houses [AOR: 3.65; 95% CI: 1.30, 10.28], presence of pets within the houses [AOR: 2.78; 95% CI: 1.29, 5.96], having rhinitis [AOR: 3.34; 95% CI: 1.17, 9.52], past asthma exacerbation [AOR: 2.38, 95% CI: 1.05, 5.40], non-adherence to treatment [AOR: 2.81; 95% CI: 1.30, 6.08] and smoking [AOR: 7.09; 95% CI: 1.84, 27.33] were found to be determinants of uncontrolled asthma.

Conclusions

Uncontrolled asthma is resulted from multiple sociodemographic, environmental, clinical, and behavioral factors. Therefore, interventions targeting to improve asthma control should consider those factors comprehensively.

Background

The Global Initiative for Asthma (GINA) defined asthma as a heterogeneous disease, usually characterized by chronic airway inflammation and is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity together with variable expiratory airflow limitation (1). Asthma control is the degree to which the manifestations of asthma are minimized and the goals of therapy are met (2).

Uncontrolled asthma has multiple effects and severe consequences on asthmatic patients. It poses substantial economic impacts on patients which is driven by hospitalizations, emergency department visits, and sick days (3). The direct health care cost of patients with uncontrolled asthma is four to eight

times that of controlled (15, 16). Shreds of evidence also revealed that uncontrolled asthma results in higher rates of depression, insomnia, sleep disturbances, and significant derangement in health-related quality of life of asthmatic patients (6−9). Furthermore, patients with asthma will lose an estimated 15.46 million Quality Adjusted Life Years Lost (QALYs) because of uncontrolled asthma in the coming 20 years (10).

According to the World Health Organization (WHO) asthma report of 2018, despite imposing a high burden on the health of the global population, asthma research lags behind research for other Non-communicable Diseases (NCDs) and needs further investment (11). Characterizing the phenotypes of patients with uncontrolled asthma and searching for specific risk factors has been suggested as priority research agenda for the prevention and control of chronic respiratory diseases (12).

Despite the existence of effective treatments, Asthma remains uncontrolled everywhere throughout the world (3, 13−16). Similarly, a significant proportion of asthmatic patients suffer from uncontrolled asthma in Africa (17−20). Studies conducted in Ethiopia showed different prevalence of uncontrolled asthma ranging from 64.5−85.2%, implying high prevalence of uncontrolled asthma in Ethiopia (21−23).

The fact that adequate control was not achieved in a significant proportion of asthmatic patients, despite the presence of effective medications, emphasizes the importance of identifying the determinants of uncontrolled asthma. Even though a couple of studies have been conducted in Ethiopia (12−14, 24), majority of them were cross-sectional in nature focusing mainly on socio-demographic, clinical, and some behavioral factors. The studies didn't give attention to housing factors, which play a major role in asthma control as the cases pass most of their time in the home environment. Therefore, this study aimed to assess the determinants of uncontrolled asthma among asthmatic patients on follow-up at chest clinic of Jimma Medical Center (JMC).

Methods

Study area and period

The study was conducted at JMC. The center is located in Jimma Town, which is 356 km away from Addis Ababa to southwest Ethiopia. It is one of the largest teaching university hospitals in Ethiopia. The center covers about fifteen million people under its catchment area in the southwest part of Ethiopia. Chest clinic is one of the departments of the center where patients with various respiratory disorders including asthma are treated. The study was conducted from March to May, 2020.

Study design and population

Unmatched case-control study design was employed among adult asthmatic patients on follow-up at chest clinic of JMC. Cases were asthmatic patients whose asthma was uncontrolled as defined by asthma control test score ≤ 19 and controls were those whose asthma was controlled as defined by asthma control test score of above 19.

Inclusion and Exclusion criteria

Asthmatic patients attending follow-up at the chest clinic aged 18 or above years and on follow-up for the last consecutive three months preceding the study were included in the study. Asthma patients who were diagnosed with interstitial lung diseases, Chronic Obstructive Pulmonary Diseases (COPDs), bronchiectasis, lung cancer, and cardiac illnesses were excluded from the study due to similarity of the symptoms. Pregnant asthmatic patients were also excluded due to the variable effects of pregnancy on asthma.

Sample size

The sample size was estimated based on the double population proportion approach. STAT CALC application of Epi info version 7 was used to calculate the sample size with 2:1 ratio of controls to cases, and with the assumptions of 95% confidence interval, 80% power and a minimum of 0.24 odds ratio to be detected. Thus, taking 28.57% of controls with low monthly income taken from a previous study (23) and adding 10% non-response rate 59 cases and 118 controls were included in the study.

Sampling procedure

All asthmatic patients who came during the study period and fulfilled eligibility criteria were enrolled in the study. Accordingly, the study participants were selected consecutively for both cases and controls until the calculated sample size was attained.

Data collection techniques and procedures

Data were collected using a structured questionnaire adopted from different literatures (2, 25–30). The English version of the questionnaire was translated into the local language and back-translated to English to maintain its consistencies. The questionnaire was also pretested outside of the study hospital on 5% of the sample size, which was not included in the final data. Modifications were made accordingly after the pre-test. Data was collected through face to face interview and chart review by trained two nurses who work in the chest clinic of the JMC.

Asthma control was evaluated using standardized and international asthma control test. The questionnaire has five items, including asthma symptoms (daytime and nocturnal), use of rescue medications, the effect of asthma on daily functioning, and self-assessed level of control over the past four weeks. Each item includes five response options corresponding to a 5-point rating scale. A value of ACT ≤ 19 defines uncontrolled asthma (25, 31). Asthma severity was classified as intermittent, mild persistent, moderate persistent, and severe persistent according to National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3 (2).

Medication adherence was evaluated using the Medication Adherence Report Scale (MARS-5) which is a five-item questionnaire rated on a five-point Likert scale. Asthmatic patients who scored 23 or above were categorized as adherent to medication while those who scored less than 23 were categorized as non-adherent (27).

Asthma knowledge was evaluated using consumer questions (CQ) for asthma knowledge. The questionnaire has 12 "true/false" questions of equal weight. Those who score nine or above were categorized as having good knowledge and below nine as having poor knowledge (28).

Attitude towards asthma was assessed using five questions to be rated on a five-point Likert scale. The score ranges from 5–25; patients' attitudes were categorized into two groups as "positive attitude" if the score is ≥ 15 and "negative attitudes" if the score < 15 (29).

Data processing and analysis

The collected data were checked for completeness, coded and entered to Epi data version 3.1, and then exported to statistical package for social sciences (SPSS), version 25 for analysis. Then, it was cleaned and analyzed. Descriptive statistics like frequencies, tables, and figures were used to describe background variables. A principal component analysis was done to quantify the wealth index. Accordingly, four components were created with varimax rotation and Eingen value greater than 1 where the total variance of 67.8% was explained by the model.

The data were also analyzed using multiple logistic regression model to identify determinants of uncontrolled asthma. First, bivariate logistic regression analysis was done for each independent variable and then, those variables with p-values ≤ 0.25 were entered into multivariable logistic regression to control possible confounders. Backward elimination method was employed in the multivariable logistic regression analysis where adjusted odds ratios (AORs) with their corresponding CIs were used to assess the strength of the associations between dependent and its determinants at P-Value ≤ 0.05 cut off points. The model fitness was checked using Hosmer-Lomeshow goodness fit test and the model was found to be fit.

Results

Sociodemographic characteristics

A total of 177 (59 cases and 118 controls) asthmatic patients on follow-up were included in the study. The mean ages (± standard deviation) of the cases and controls were 50.97 (± 15.52) and 39.56 (± 14.37) years, respectively. More than half (54.2%) of cases and controls (50.8%) were males. Majority (71.2%) of the cases and two-third (66.9%) of the controls were urban residents. More than one-fourth of cases (28.8%) and thirty percent of controls had attended college or above education. Concerning the occupation of the respondents, below one-third of cases (30.5%) and controls (28.8%) were government employees.

Housing condition

More than half (61%) of the cases and the controls (58%) reported that they live in houses they owned privately. The median (IQR) age of houses of the cases and controls were 15 (10 to 25) and 7 (4 to 15) years, respectively. Majority of both the cases (91.5%) and controls (96.6%) reported that their bedrooms

had windows. Similarly, ninety-one percent of the cases and ninety-seven percent of the controls live in houses made of corrugated iron sheet. Nearly half (47.5%) of cases but only less than three in ten (28.8%) of controls reported that the walls of their houses were mud and cracked. About two-thirds (66.1%) of the cases and (67.8%) the controls live in houses with cemented floors. More than half of cases (50.8%) and the controls (54.2%) reported that electricity was their main source of energy. Regarding the presence of pets, more than half (55.9%) of cases reported that they had domestic animals while more than two-thirds (70.3%) of controls reported that they hadn't domestic animals.

Table 1
Sociodemographic and housing condition characteristics of asthmatic patients on follow-up at JMC, 2020

Characteristics	Categories	Cases, N (%)	Controls, N (%)	Total, N (%)
Age	18–34	11 (18.6)	48 (40.4)	59 (33.3)
	35 and above	48 (81.4)	70 (59.3)	118 (66.7)
Sex	Male	32 (54.2)	60 (50.8)	92 (52.0)
	Female	27 (45.8)	58 (49.2)	85 (48.0)
Residence	Urban	42 (71.2)	79 (66.9)	121 (68.4)
	Rural	17 (28.8)	39 (33.1)	56 (31.6)
Wealth Index	Poor	26 (44.1)	45 (38.1)	71 (40.1)
	Middle	10 (16.9)	17 (14.4)	27 (15.3)
	Rich	23 (39.0)	56 (47.5)	79 (44.6)
Ownership of house	Privately owned	36 (61)	69 (58.5)	105 (59.3)
	Rented from private	12 (20.3)	28 (23.7)	40 (22.6)
	Rented from government	11 (18.6)	21 (17.8)	32 (18.1)
Age of house	⬚ 20 years	44 (74.6)	109 (92.4)	153 (86.4)
	≥ 20 years	15 (25.4)	9 (7.6)	24 (13.6)
Presence of window in the bedroom	Yes	54 (91.5)	114 (96.6)	168 (94.9)
	No	5 (8.5)	4 (3.4)	9 (5.1)
Roof	Corrugated iron sheet	54 (91.5)	115 (97.5)	169 (95.5)
	Thatch/grass	5 (8.5)	3 (2.5)	8 (4.5)
Wall	Mud/cracked	28 (47.5)	34 (28.8)	62 (35.0)
	Mud/well plastered	19 (32.2)	45 (38.1)	64 (36.2)
	Cemented	12 (20.3)	39 (33.1)	51 (28.8)
Floor	Earth	14 (23.7)	30 (25.4)	44 (24.9)

Characteristics	Categories	Cases, N (%)	Controls, N (%)	Total, N (%)
	Wood	6 (10.2)	8 (6.8)	14 (7.9)
	Cemented	39 (66.1)	80 (67.8)	119 (67.2)
Usual source of Energy	Wood	20 (33.9)	39 (33.1)	59 (33.3)
	Gas stoves	9 (15.3)	15 (12.7)	24 (13.6)
	Electricity	30 (50.8)	64 (54.2)	94 (53.1)
Household size	< 3	23 (39.0)	50 (42.4)	73 (41.2)
	≥ 3	36 (61.0)	68 (57.6)	104 (58.8)
Presence of pets	Yes	33 (55.9)	35 (29,7)	68 (38.4)
	No	26 (44.1)	83 (70.3)	109 (61.6)

Clinical characteristics

The median (IQR) duration with asthma among the cases and the controls were 16.0 (7.0 to 25.0) and 6.5 (2.0 to 12.3) years, respectively. Regarding the severity of the disease among the cases, 27.1% had intermittent, 35.6% had mild persistent, 27.1% had moderate persistent and the rest 10.2% had severe persistent asthma while 25.5%, 32.2%, 28.8%, and 11.3% of the controls had intermittent, mild persistent, moderate persistent and severe persistent asthma, respectively. Short-acting β-agonists with low-dose oral corticosteroids were the most commonly used drugs by the cases whereas short-acting β-agonists with inhaled corticosteroids were the most commonly used drugs by the controls. More than one-third (37.3%) of the cases and three in ten (29.9%) of the controls had exacerbations of asthma in the last 12 months preceding the study. Nearly half (47.5%) of the cases had comorbid illnesses while only below a third (30.5%) of the controls had comorbid illnesses. Above one-third (33.9%) of the cases but a small proportion (14.4%) of the controls had unscheduled health care visits.

Behavioral characteristics

Concerning the knowledge about asthma, less than half (40.7%) of cases had good knowledge while closely two-third (65.3%) of controls had good knowledge about asthma. Two-third (66.1%) of cases and the majority (84.7%) of controls had a positive attitude towards asthma treatment/control. On the basis of adherence to medications, only about a third (37.3%) of cases were adherent to medications; however, more than half of controls (58.5%) were adherent to medications. With regard to the level of physical activity, majority of both cases (79.7%) and controls (82.2%) were not sufficiently active physically. Concerning the history of smoking cigarette, close to one in five (18.6%) of cases but only 3.4% of controls reported that they have used to smoke cigarette.

Table 2
Clinical and behavioral characteristics of asthmatic patients on follow-up at JMC, 2020

Characteristics	Categories	Cases, N (%)	Controls, N (%)	Total, N (%)
Severity	Intermittent	15 (25.5)	32 (27.1)	47 (26.6)
	Mild persistent	19 (32.2)	42 (35.6)	61 (34.5)
	Moderate persistent	17 (28.8)	32 (27.1)	49 (27.7)
	Severe persistent	8 (13.6)	12 (10.2)	20 (11.3)
Medication type	SABA only	15 (25.4)	29 (24.6)	44 (24.9)
	SABA + ICS	15 (25.4)	34 (28.8)	49 (27.7)
	SABA + low dose OCS	19 (32.2)	31 (26.3)	50 (28.2)
	SABA + high dose OCS	10 (16.9)	24 (20.3)	34 (19.2)
Comorbidity	Yes	28 (47.5)	36 (30.5)	64 (36.2)
	No	31 (52.5)	82 (69.5)	113 (63.8)
Exacerbation	Yes	22 (37.3)	27 (22.9)	49 (27.7)
	No	37 (62.7)	91 (77.1)	128 (72.3)
Family history	Yes	17 (28.8)	45 (38.1)	62 (35.0)
	No	42 (71.2)	73 (61.9)	115 (65.0)
Visit	Scheduled	39 (66.1)	101 (85.6)	140 (79.1)
	Unscheduled	20 (33.9)	17 (14.4)	37 (20.9)
Asthma knowledge	Good	24 (40.7)	77 (65.3)	101 (57.1)
	Poor	35 (59.3)	41 (34.7)	76 (42.9)
Attitude towards Asthma	Positive	39 (66.1)	100 (84.7)	139 (78.5)
	Negative	20 (33.9)	18 (15.3)	38 (21.5)
Adherence to treatment	Adherent	22 (37.3)	69 (58.5)	91 (51.4)
	Non-adherent	37 (62.7)	49 (41.5)	86 (48.6)
Physical activity	Sufficient	12 (20.3)	21 (17.8)	33 (18.6)
	Insufficient	47 (79.7)	97 (82.2)	144 (81.4)
Smoking	No	48 (81.4)	114 (96.6)	162 (91.5)
	Yes	11 (18.6)	4 (3.4)	15 (8.5)

Determinants of uncontrolled asthma

After controlling for possible cofounders, older asthmatic patients (≥ 35 years of age) were about three times [AOR: 2.78; 95% CI: 1.14, 6.81] more likely to have uncontrolled asthma compared those patients between the age of 18 and 34 years. Uncontrolled asthma was more than three times [AOR: 3.65; 95% CI: 1.30, 10.28] higher among patients who reported to have lived in old houses constructed 20 years ago compared to those who have lived in houses constructed since the past 20 years. The presence of pets within the household was also found to be determinant of uncontrolled asthma where patients who own pets were about three times [AOR: 2.78; 95% CI: 1.29, 5.96] more likely to have uncontrolled asthma compared to their counterparts.

Again, uncontrolled asthma was more than three times [AOR: 3.34; 95% CI: 1.17, 9.52] higher among patients diagnosed with rhinitis compared to patients who were not diagnosed to have rhinitis. Uncontrolled asthma was more than two times [AOR: 2.38, 95% CI: 1.05, 5.40] higher among patients who had exacerbation compared with those who did not have exacerbation in the last 12 months before the study. Uncontrolled asthma was also about three times [AOR: 2.81; 95% CI: 1.30, 6.08] higher among medication non-adherent patients compared to those who were adherent. Lastly, patients who smoke cigarette were found to have seven times [AOR: 7.09; 95% CI: 1.84, 27.33] a higher risk of uncontrolled asthma compared to non-smokers (Table 3).

Table 3
Determinants of uncontrolled asthma among asthmatic patients on follow-up at JMC, 2020

Variables	Categories	Controls	Cases	COR [95% CI]	AOR [95%CI]	P-value
Age	18−34	48	11	1	1	
	≥ 35	70	48	2.99 [1.41, 6.34]	2.78 [1.14, 6.81]	0.025
Age of house	🔲 20 years	109	44	1	1	
	≥ 20 years	9	15	4.13 [1.68, 10.13]	3.65 [1.30, 10.28]	0.014
Pet ownership	Yes	35	33	3.01 [1.57, 5.76]	2.78 [1.29, 5.96]	0.009
	No	83	26	1	1	
Rhinitis	Yes	12	11	2.05 [0.84, 4.97]	3.34 [1.17, 9.52]	0.024
	No	106	48	1	1	
Exacerbation	Yes	27	22	2.00 [1.02, 3.96]	2.38 [1.05, 5.40]	0.039
	No	91	37	1	1	
Adherence to treatment	Adherent	69	22	1	1	
	Non-adherent	49	37	2.37 [1.25, 4.50]	2.81 [1.30, 6.08]	0.009
Smoking	No	114	48	1	1	
	Yes	4	11	6.53 [1.98, 21.53]	7.09 [1.84, 27.33]	0.004

Discussion

This study intended to identify determinants of uncontrolled asthma. Age of patients, age of the patients' living houses, presence of pets in the houses, having rhinitis, exacerbation in the last 12 months, adherence to treatment, and smoking were found to be determinants of uncontrolled asthma.

In this study, asthmatic patients whose age was 35 or above were nearly three times more likely to have uncontrolled asthma when compared with those whose age was between 18 and 34. This finding is supported by studies done in Spain (32), China (33), and Saudi Arabia (15). Similarly, a study done in Jimma, Ethiopia, also stated that the probability of getting well-controlled asthma was more than three times higher in the age group of 14−34 years than older age groups (21). The possible explanation for

this might be due to the worsening of the physiology of lungs parallel to aging lung and variability in how asthma responds to treatment as a result of differences in airway inflammation in aged people (34).

In this study, patients who reported to have lived in old houses were more likely to have uncontrolled asthma compared to those who have lived in houses constructed in the past 20 years. This result is supported by a study done in Poland (35), which demonstrated that there is a statistically significant difference with respect to asthma control between people who live in older houses and those who live in recently constructed houses. This might be because old houses increase dampness and facilitate mold growth that precipitates and worsen asthma symptoms resulting in uncontrolled asthma.

This study also demonstrated that the presence of pets within living houses was another determinant of uncontrolled asthma. Studies done in Congo and Morocco also reported a higher risk of uncontrolled asthma among patients who owned pets (11, 36). This could be due to an increment in asthma symptoms attributed to airway hyperresponsiveness, inflammation, and irritation of airways as a result of an allergy to the animals.

Another finding of this study was a significant association between uncontrolled asthma and comorbidity of rhinitis. This finding is in agreement with studies conducted in Brazil (36) and China (33). The study conducted in Brazil stated that asthmatic patients with symptoms of rhinitis were more than three times more likely to have uncontrolled asthma (36). Similarly, the Chinese study revealed that the risk of uncontrolled asthma was higher among patients with concomitant rhinitis (33). This might be due to the reason that allergic rhinitis is related to the worsening of asthma symptoms by enhancing the lower airway inflammation (37).

Having exacerbation in the last 12 months preceding the study was also found to increase the likelihood of having uncontrolled asthma attacks. The result of a study conducted in Addis Ababa; Ethiopia, was in line with this finding. The study showed that asthmatic patients who had exacerbation were more than two times more likely to develop uncontrolled asthma (22). The possible explanation could be due to the fact that past exacerbation predicts future exacerbation that might increase asthma symptoms (38). It might also be due to the effect of exacerbation on lung function i.e. accelerated loss of lung function as a result of asthma exacerbation (39).

This study also depicted that non-adherence to treatment was another determinant of uncontrolled asthma. This finding is in line with studies conducted in China (33), UK (40), North African and Middle East countries (41), Morocco (35), and Nigeria (18). A previous study conducted at Jimma Medical Center, Ethiopia, also showed that the odds of uncontrolled asthma was about 8.5 times higher among non-adherent patients when compared to the adherent ones (24). The possible explanation for this might be a rapid decline in lung function as a result of non-adherence to medications (42).

Lastly, patients who smoke cigarette were found to have a higher probability of uncontrolled asthma. This is supported by different studies conducted in Saudi Arabia (15), England (43), Hungary (44), and Nigeria (18). This might be because smoking is significantly associated with the decline in lung function

(45). Another possible reason might be due to the fact that response to inhaled corticosteroids is attenuated among patients who smoke cigarette, hence, reduces the effectiveness of the drugs (46).

Limitation of the study

Even though the study tried to reduce the effect of the seasonality of asthma on its control through assessing the control over four weeks, it might not depict the distribution of uncontrolled asthma throughout the year. Self-report of some of the variables like behavioral variables (alcohol consumption, chewing khat, and smoking) and housing condition could introduce social desirability bias. Assessment of housing conditions based on self-response rather than expert evaluation might not depict the real standard of the housing.

Conclusions

This study has identified different sociodemographic, environmental, clinical, and behavioral determinants of uncontrolled asthma. This shows that uncontrolled asthma is resulted from multiple factors. Therefore, it is important to consider those factors while targeting and designing interventions to improve asthma control comprehensively.

Measures like asthma education program, counseling, and health education should be taken to alleviate the problem. Longitudinal studies are also needed to assess the distribution and determinants of uncontrolled asthma considering seasonal variations, more socioeconomic and demographic factors.

Abbreviations

ACT
Asthma Control Test; CI:Confidence interval; **GERD**:Gastro-Esophageal Reflux Disease, **GINA**:Global Initiative for Asthma; **JMC**:Jimma Medical Center; **QALY**:Quality Adjusted Life Years Lost.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from Jimma University Institute of Health Institutional Review Board (IRB). The purpose of the study was informed to the patients and written informed consent was obtained from each participant prior to the interview. Additionally, all the information obtained from each study participant was kept confidential throughout the process of the study.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LA: involved from inception to design, acquisition of data, analysis and interpretation, drafting, and reviewing the manuscript. **LSD**: involved from inception to design, acquisition of data, analysis and interpretation, drafting, and reviewing the manuscript. **AA**: involved from inception to design, acquisition of data, analysis and interpretation, drafting, and reviewing the manuscript.

Consent for publication

Not applicable.

References

1. Global initiative for asthma: Asthma management and prevention, 2019. Pract Nurse. 2019;49(5).
2. National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma Full Report 2007. Children. 2007.
3. Su N, Lin J, Chen P, Li J, Wu C, Yin K, et al. Evaluation of asthma control and patient's perception of asthma: Findings and analysis of a nationwide questionnaire-based survey in China. J Asthma. 2013;50(8):861–70.
4. Doz M, Chouaid C, Com-Ruelle L, Calvo E, Brosa M, Robert J, et al. The association between asthma control, health care costs, and quality of life in France and Spain. BMC Pulm Med. 2013;13(1).
5. Santos LA, Oliveira MA, Faresin SM, Santoro IL, Fernandes ALG. Direct costs of asthma in Brazil: A comparison between controlled and uncontrolled asthmatic patients. Brazilian J Med Biol Res. 2007;40(7):943–8.
6. Woledesenbet MA, Shumet Mekonen S, Sori LM, Abegaz TM. Epidemiology of Depression and Associated Factors among Asthma Patients in Addis Ababa, Ethiopia. Psychiatry J. 2018;2018:1–7.

7. Sundbom F, Malinovschi A, Lindberg E, Almqvist C, Janson C. Insomnia symptoms and asthma control – interrelations and importance of comorbidities. Clin Exp Allergy. 2019;0–2.

8. Mastronarde JG, Wise RA, Shade DM, Olopade CO, Scharf SM. Sleep quality in asthma: Results of a large prospective clinical trial. J Asthma. 2008;45(3):183–9.

9. Dean BB, Calimlim BM, Kindermann SL, Khandker RK, Tinkelman D. The impact of uncontrolled asthma on absenteeism and health-related quality of life. J Asthma. 2009;46(9):861–6.

10. Yaghoubi M, Adibi A, Safari A, FitzGerald JM, Sadatsafavi M. The projected economic and health burden of uncontrolled asthma in the United States. Am J Respir Crit Care Med. 2019;200(9):1102–12.

11. WHO. Global Asthma Network The Global Asthma Report [Internet]. Auckland, New Zealand. 2018. 92 p. Available from: www.globalasthmanetwork.org

12. Bousquet J, Kiley J, Bateman ED, Viegi G, Cruz AA, Khaltaev N, et al. Prioritised research agenda for prevention and control of chronic respiratory diseases. Eur Respir J. 2010;36(5):995–1001.

13. Demoly P, Annunziata K, Gubba E, Adamek L. Repeated cross-sectional survey of patient-reported asthma control in Europe in the past 5 years. Eur Respir Rev. 2012;21(123):66–74.

14. Marchioro J, Gazzotti MR, Nascimento OA, Montealegre F, Fish J, Jardim JR. Level of asthma control and its relationship with medication use in asthma patients in Brazil. J Bras Pneumol. 2014;40(5):487–94.

15. BinSaeed AA. Asthma control among adults in Saudi Arabia study of determinants. Saudi Med J. 2015;36(5):599–604.

16. Turktas H, Mungan D, Uysal MA, Oguzulgen K. Determinants of asthma control in tertiary level in Turkey: A cross-sectional multicenter survey. J Asthma. 2010;47(5):557–62.

17. Benkheder A, Bouacha H, Nafti S, Taright S, El Ftouh M, Yassine N, et al. Control of asthma in the Maghreb: results of the AIRMAG study. Respir Med [Internet]. 2009;103(SUPPL. 2):S12–20. Available from: http://dx.doi.org/10.1016/S0954-6111(09)70023-X

18. Desalu OO, Fawibe AE, Salami AK. Assessment of the level of asthma control among adult patients in two tertiary care centers in Nigeria. J Asthma. 2012;49(7):765–72.

19. Serugendo AN, Kirenga BJ, Hawkes M, Nakiyingi L, Worodria W, Okot-Nwang M. Evaluation of asthma control using Global Initiative for Asthma criteria and the Asthma Control Test in Uganda. Int J Tuberc Lung Dis. 2014;18(3):371–6.

20. Kabengele BO, Kayembe JMN, Kayembe PK, Kashongue ZM, Kaba DK, Akilimali PZ. Factors associated with uncontrolled asthma in adult asthmatics in Kinshasa, Democratic Republic of Congo. PLoS One. 2019;14(4):1–13.

21. Zemedkun K, Woldemichael K, Tefera G. Assessing control of asthma in Jush, Jimma, South West Ethiopia. Ethiop J Health Sci. 2014;24(1):49–58.

22. Gebremariam TH, Binegdie AB, Mitiku AS, Ashagrie AW, Gebrehiwot KG, Huluka DK, et al. Level of asthma control and risk factors for poor asthma control among clinic patients seen at a Referral

Hospital in Addis Ababa, Ethiopia. BMC Res Notes. 2017;10(1):4–9.

23. Fanta K, Bekele F. Uncontrolled asthma and associated factors among adult asthmatic patients on follow-up at chest clinic of Jimma University Specialized Hospital, South-West Ethiopia. Indo Am J Pharm Res. 2016;6(11).

24. Zewudie A, Nigussie T, Mamo Y, Kumela K. Determinants of poorly controlled asthma among asthmatic patients in Jimma University Medical Center, Southwest Ethiopia: A case control study. BMC Res Notes [Internet]. 2019;12(1):1–6. Available from: https://doi.org/10.1186/s13104-019-4571-y

25. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the Asthma Control Test: A survey for assessing asthma control. J Allergy Clin Immunol. 2004;113(1):59–65.

26. Chakraborty NM, Fry K, Behl R, Longfield K. Simplified asset indices to measure wealth and equity in health programs: A reliability and validity analysis using survey data from 16 countries. Glob Heal Sci Pract. 2016;4(1):141–54.

27. Chan AHY, Horne R, Hankins M, Chisari C. The Medication Adherence Report Scale (MARS-5): a measurement tool for eliciting patients' reports of non-adherence. Br J Clin Pharmacol [Internet]. 2019 Dec 10;bcp.14193. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/bcp.14193

28. Kritikos V, Krass I, Hui SC, Bosnic-Anticevich SZ. The validity and reliability of two asthma knowledge questionnaires. J Asthma. 2005;42(9):795–801.

29. H.P.D M, Subasinghe S. Knowledge attitudes and practices of asthma-Does it associate with demographic factors of adult patients. Asian Pacific J Heal Sci. 2016;3(Supplimentary 2016):94–9.

30. Marshall AL, Smith BJ, Bauman AE, Kaur S. Reliability and validity of a brief physical activity assessment for use by family doctors. Br J Sports Med. 2005;39(5):294–7.

31. Thomas M, Kay S, Pike J, Williams A, Carranza Rosenzweig JR, Hillyer E V., et al. The Asthma Control Test^{TM} (ACT) as a predictor of GINA guideline-defined asthma control: Analysis of a multinational cross-sectional survey. Prim Care Respir J. 2009;18(1):41–9.

32. Munoz-Cano R, Torrego A, Bartra J, Sanchez-Lopez J, Picado RP, Valero A. Follow-up of patients with uncontrolled asthma: Clinical features of asthma patients according to the level of control achieved (the COAS study). Eur Respir J [Internet]. 2017;49(3). Available from: http://dx.doi.org/10.1183/13993003.01885-2015

33. Zhong N, Lin J, Zheng J, Lai K, Xie C, Tang KJ, et al. Uncontrolled asthma and its risk factors in adult Chinese asthma patients. Ther Adv Respir Dis. 2016;10(6):507–17.

34. Budde J, Skloot GS. Is aging a "comorbidity" of asthma? Pulm Pharmacol Ther [Internet]. 2018 Oct;52:52–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S109455391830138X

35. Ghanname I, Chaker A, Cherkani Hassani A, Herrak L, Arnaul Ebongue S, Laine M, et al. Factors associated with asthma control: MOSAR study (Multicenter Observational Study of Asthma in Rabat-Morocco). BMC Pulm Med. 2018;18(1):1–13.

36. Barros LL, Souza-Machado A, Corrêa LB, Santos JS, Cruz C, Leite M, et al. Obesity and poor asthma control in patients with severe asthma. J Asthma. 2011;48(2):171–6.

37. Oka A, Matsunaga K, Kamei T, Sakamoto Y, Hirano T, Hayata A, et al. Ongoing Allergic Rhinitis Impairs Asthma Control by Enhancing the Lower Airway Inflammation. J Allergy Clin Immunol Pract [Internet]. 2014 Mar;2(2):172-178.e1. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213219813004364

38. Miller MK, Lee JH, Miller DP, Wenzel SE. Recent asthma exacerbations: A key predictor of future exacerbations. Respir Med. 2007;101(3):481–9.

39. Bai TR, Vonk JM, Postma DS, Boezen HM. Severe exacerbations predict excess lung function decline in asthma. Eur Respir J. 2007;30(3):452–6.

40. Clatworthy J, Price D, Ryan D, Haughney J, Horne R. The value of self-report assessment of adherence, rhinitis and smoking in relation to asthma control. Prim Care Respir J. 2009;18(4):300–5.

41. Tarraf H, Al-Jahdali H, Al Qaseer AH, Gjurovic A, Haouichat H, Khassawneh B, et al. Asthma control in adults in the Middle East and North Africa: Results from the ESMAA study. Respir Med [Internet]. 2018;138:64–73. Available from: https://doi.org/10.1016/j.rmed.2018.03.024

42. Vähätalo I, Ilmarinen P, Tuomisto LE, Tommola M, Niemelä O, Lehtimäki L, et al. 12-Year Adherence To Inhaled Corticosteroids in Adult-Onset Asthma. ERJ Open Res [Internet]. 2020;6(1):00324–2019. Available from: http://dx.doi.org/10.1183/23120541.00324-2019

43. Nguyen K, Zahran H, Iqbal S, Peng J, Boulay E. Factors associated with asthma control among adults in five New England states, 20062007. J Asthma. 2011;48(6):581–8.

44. Tomisa G, Horváth A, Szalai Z, Müller V, Tamási L. Prevalence and impact of risk factors for poor asthma outcomes in a large, specialist-managed patient cohort: A real-life study. J Asthma Allergy. 2019;12:297–307.

45. Tommola M, Ilmarinen P, Tuomisto LE, Haanpää J, Kankaanranta T, Niemelä O, et al. The effect of smoking on lung function: A clinical study of adult-onset asthma. Eur Respir J [Internet]. 2016;48(5):1298–306. Available from: http://dx.doi.org/10.1183/13993003.00850-2016

46. Lazarus SC, Chinchilli VM, Rollings NJ, Boushey HA, Cherniack R, Craig TJ, et al. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma. Am J Respir Crit Care Med. 2007;175(8):783–90.