ORIGINAL ARTICLE

Assessment of Factors Affecting Symptom Control in Asthmatic Patients

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ABSTRACT

Objective: To assess the level of symptoms control achieved by Asthmatic Patients in Pakistan and the associated factors making an impact on symptom control.

Methods: A prospective cross-sectional study was carried out at Darul Sehat Hospital from December 2018 till December 2019. All patients irrespective of age and gender diagnosed as bronchial asthma were consecutively included. Symptom control was assessed according to Global Initiative for Asthma (GINA) assessment tool. Prevalence of asthma symptom control was determined while association of risk factors with uncontrolled asthma was also evaluated.

Results: Of 113 patients, the mean age was 36.8 ±16.6 years. There were 76 (67.3%) patients who had uncontrolled asthma. A significant association of uncontrolled asthma was observed with incorrect inhaler technique (p value of 0.039), more than 10 years asthma duration (p value <0.001), lack of inhaled corticosteroid (ICS) use (p value 0.004), Gastroesophageal Reflux Disease (GERD) (p value <0.001), more than 1 episode of asthma exacerbation in last 12 months (p value <0.001), and with high use of short acting beta agonists (p value <0.001).

Conclusion: A higher prevalence of uncontrolled asthma was observed in our cohort with significant association of uncontrolled asthma with poor inhaler technique, lack of ICS use, GERD, more than 10 years asthma duration, and more than 1 asthma exacerbation episode in last 12 months.

Keyword: Asthma, bronchial spasm, bronchoconstriction, bronchodilator agents, bronchial diseases.

INTRODUCTION

Asthma is a common disease of airways characterized by chronic inflammation and usually presents with symptoms like shortness of breath, cough, chest tightness and wheezing and these symptoms do vary over time in intensity.[1] Asthma has a great global impact. Estimated prevalence of Asthma in Pakistan as highlighted by report on Global burden of Asthma is 4.3%.[2] There are multiple factors that trigger asthma symptoms which include allergen exposure, smoking, allergic rhinitis, sinusitis, gastroesophageal reflux disease (GERD), inadequate use of inhaled corticosteroids (ICS) that include poor adherence to medication and inappropriate inhaler technique.[3,4] Asthma has a great impact on population and when poorly controlled leads to considerable economic impact with loss of work days, school attendance, frequent hospital admissions, poor quality of life and ultimately death.[5] According to a study, approximately 24.2% of the patients with asthma have well controlled asthma.[6] There are multiple studies from different parts of the world that reflect asthma control and also the influence of these factors over symptom control but no such study has been conducted in Pakistan.[7-10] According to a study, 45% patients had uncontrolled asthma.[7] Therefore, the objective behind conducting this study was to assess the level of symptoms control achieved by asthmatic patients in developing country like Pakistan and to assess the factors which are making an impact on symptom control so that these factors can be focused and managed effectively in order to achieve good control over symptoms and lead a healthy life.

METHODS

A prospective cross sectional study was undertaken at Darul Sehat Hospital for duration of December 2018 till December 2019 after Institutional Review Board (IRB) approval. Taking frequency of asthma control as 24.2%[6], confidence interval (CI) as 95% and precision as 8%, the estimated sample size came out to be 111 but total 113 patients were included. Non Probability Consecutive sampling technique was used for sample collection. Both male and female patients of either age, presenting with respiratory symptoms such as cough, shortness of breath, chest tightness and wheezing and were diagnosed as having bronchial asthma by physician on the basis of appropriate clinical history and examination or proved by spirometry were included. Patients were excluded if they refused to give consent, had clinical features that suggested other diagnoses,

on treatment of pulmonary tuberculosis or previously treated for pulmonary tuberculosis, or had severe exacerbation requiring hospitalization. Written informed consent was obtained from all patients after explaining pros and cons of the study. Patients fulfilling inclusion criteria were interviewed. Demographic data including age, gender, height, weight, comorbid conditions such as diabetes mellitus, hypertension, ischemic heart disease, smoking status, time since asthma diagnosis, family history of asthma, history of atopy (self-reported history of allergic rhinitis or eczema and occupation were noted.

Symptom control was assessed according to Global Initiative for Asthma (GINA) symptom control assessment tool.[11] (Table 1) This tool comprise frequency of symptoms reported in daytime, night awakening due to asthma, any activity limitation as a result of asthma, and number of times reliever medication taken per week over the period of 4 weeks. Symptom control was labeled as "well controlled" if all of these features were absent. In the presence of 1 or 2 features, symptom control was labeled as "partially controlled". If 3 or more of these features were present then symptom control was labeled as "uncontrolled". Record of current medications in patient's use was obtained by either seeing prescription of patients own chest physician or patient showing medicines at the time of interview.

Presence of different risk factors was also noted. GERD was recorded as self-reported sensation of retrosternal burning requiring medication. Allergic rhinitis was recorded as self-reported recurrent episodes of nasal discharge and sneezing related to allergen exposure or seasonal change. Asthma exacerbations were defined as worsening of symptoms requiring addition of a course of oral corticosteroids, according to the recommendation of patient's own chest physician.[11] The number of asthma exacerbations experienced over past 12 months was retrospectively assessed by asking the patients the number of times patient needed to modify usual treatment or had to take courses of oral corticosteroids. Eosinophil counts were recorded from patients' complete blood count (CBC). Exposure to the occupational agents leading to development of symptoms and the use of drugs that may precipitate symptoms such as salicylates, nonsteroidal anti-inflammatory drugs (NSAIDs) or beta-blockers were also noted as potential asthma triggering factors. Patient's current medications were also noted. High use of reliever medicine was assessed by asking the patient about consumption of short acting beta agonist (SABA) inhaler within 1 month. Inadequate use of inhaled corticosteroids was assessed by presence of either of the following: Not ever prescribed or poor compliance or incorrect inhaler technique. Inhaler technique for the use of a metered-dose or dry powder inhaler was evaluated by the investigator by asking the patients to demonstrate their usual inhaler technique and recorded as incorrect or correct according to previously reported evaluation of inhaler use.[12] Respiratory infections were defined as self-reported episodes of increasing cough and purulent sputum for which a course of antibiotic medications was prescribed to the patient by the primary chest physician.

Data entry and analysis was done using statistical package for social sciences (SPSS) version 22.0. All qualitative variables were expressed in terms of frequency and percentages While all quantitative variables were expressed in terms of mean and standard deviation (SD). Prevalence of different levels of symptom control in asthma patients was also calculated. Effects modifiers were controlled by stratification to see their effect on poor symptom control in asthma patients. Chi-square test/Fisher-exact was applied and p value of ≤0.05 was taken as significant.

Table 1: Asthma control according to Global Initiative for Asthma (GINA) for adults

Symptoms in the past 4 weeks	Asthma symptom control		
	Well Controlled	Partly Controlled	Uncontrolled
Daytime symptoms more than 2×/week	No criterion applies	1–2 criteria apply	3–4 criteria apply
Nocturnal awakening due to asthma at any time			
Reliever >2×/week			
Any limitation of daily activity due to asthma			

RESULTS

Total 113 patients were included in this study. Mean age of the patients was 36.8 ± 16.6 years. Mean duration of asthma was 18.0 ± 12.0 years. Family history of asthma was positive in 82 (72.6%). Among co-morbid conditions, hypertension was common and was present in 23 (20.4%) of the patients. Among presenting symptoms, shortness of breath was the most common symptom and was present in 111 (98.2%) patients. Chest tightness was present in all patients. Among patients with atopy, allergic rhinitis was present in 108 (95.6%) patients. Total 68 (60.2%) had greater than 1 episode of asthma exacerbation in last 12 months. Total 35 (31.0%) were smokers and 78 (69.0%) were nonsmokers. All the patients used inhalers and among them, 108 (95.6%) had the incorrect technique of using inhaler. Total 85 (75.2%) had gastroesophageal reflux disease (GERD). Moreover, uncontrolled asthma was present in 76 (67.3%) of the cases.

Among patients taking medications for asthma, short acting beta agonist (SABA) was used by 97 (85.8%) patients, inhaled corticosteroid (ICS) was used by 46 (40.7%) patients, long acting beta agonist (LABA) was used by 46 (40.7%) patients and leukotriene receptor agonist (LTRA) was used by 70 (61.9%) patients. Table 2 describes briefly the medications used.

Uncontrolled asthma was significantly higher in patients without any history of diabetes mellitus (p value of 0.002), in patients using inhalers incorrectly (p value of 0.039), in patients with more than 10 years asthma duration (p value <0.001), in patients with GERD (p value <0.001) and in patients having >1 episode of asthma exacerbation in last 12 months (p value <0.001) (Table 3). Uncontrolled asthma was significantly higher in patients not taking ICS (p value of 0.004) and in patients with high use of SABA (p value <0.001) (Table 4).

DISCUSSION

Asthma is a major prevalent disease globally accounting for its presence in approximately 300 million people, and is responsible for almost 250,000 deaths prematurely annually.[13] Asthma has a negative impact on the patients as well as their communities by causing loss of work and school hours, impaired quality of life, frequent hospitalizations, frequent visit to the emergency department (ED) and in severe cases death may also occur. A significant portion of costs related to asthma has been attributed to severe as well as uncontrolled asthma. In the present study we determined a developing country's perspective from Asia for evaluating symptom control in asthmatic patients. Moreover, factors related to poor symptom control in asthma were also assessed.

The results of our study demonstrated a high prevalence of uncontrolled asthma in our population. A high prevalence of uncontrolled asthma has been reported by other studies but the reported prevalence was lower as compared to our study.[6] This could be due to larger sample size of the previous studies. Another study with physician diagnosed asthma demonstrated a high prevalence of uncontrolled asthma.[14] In our study, GINA assessment tool was labeled to evaluate asthma symptom control which yielded high prevalence of uncontrolled asthma, whereas an international study reported a lower prevalence of uncontrolled asthma.[15]

Our study has shown that well controlled asthma has a lower prevalence in our population. This contrasts with the results reported by other authors.[6] Such a difference in results could be due to the reason that these previous studies were conducted on a larger sample size. Moreover, the difference in genetic and ethnic factors between the study populations could be another postulated reason for difference in asthma symptom control.

Table 2: Medication use in study population

	n	%
Short acting beta agonist (SABA)	97	85.8
High use of SABA	34	30.1
Inhaled corticosteroid	32	28.3
Long acting beta agonist	46	40.7
Leukotriene receptor agonist	70	61.9
Methylxanthine	3	2.7
Long acting muscarinic antagonist	2	1.8
Nonsteroidal anti-inflammatory drugs	3	2.7
Beta blocker	12	10.6
Salicylates	1	0.9

SABA: Short Acting Beta Agonist

Table 3: Baseline factors significantly associated with asthma control

| Factors | Total | Asthma Symptom Control | | p-value |
		Uncontrolled (n=76)	Well/Partially controlled (n=37)	
Diabetes Mellitus				
Present	15 (13.3)	15 (100)	0 (0)	0.002**
Absent	98 (86.7)	61 (62.2)	37 (37.8)	
Hypertension				
Present	23 (20.4)	21 (29.3)	2 (8.7)	0.006*
Absent	90 (79.6)	55 (61.1)	35 (38.9)	
Inhaler technique				
Correct	5 (4.4)	1 (20)	4 (80)	0.039**
Incorrect	108 (95.6)	75 (69.4)	33 (30.6)	
GERD				
Present	85 (75.2)	65 (76.5)	20 (23.5)	<0.001*
Absent	28 (24.8)	11 (39.3)	17 (60.7)	
Duration of symptoms				
≤10 years	31 (27.4)	7 (22.6)	24 (77.4)	<0.001*
>10 years	82 (72.6)	69 (84.1)	13 (15.9)	
Number of exacerbations				
≤1	45 (39.8)	19 (25)	26 (70.3)	<0.001*
>1	68 (60.2)	57 (75)	11 (29.7)	
Cough				
Absent	22 (19.5)	9 (11.8)	13 (35.1)	0.003*
Present	91 (80.5)	67 (88.2)	24 (64.9)	
Shortness of breath				
Absent	2 (1.8%)	0 (0)	2 (5.4)	0.105
Present	111 (98.2)	76 (100)	35 (94.6)	
Wheezing				
Present	105 (92.9)	73 (96.1)	32 (86.5)	0.111**
Absent	8 (7.1)	3 (3.9)	5 (13.5)	

-GERD: Gastroesophageal Reflux Disease
- Following factors were found insignificantly associated with asthma control: Gender (p-value 0.289*), Family history of asthma (p-value 0.703*), Ischemic heart disease (p-value 0.155*), Atopy (p-value 0.155*), Eosinophil count (p-value 0.312*) - *Chi-square test applied, **Fisher's exact test applied

A high prevalence of uncontrolled asthma was reported in women in our study. Studies have also reported a higher prevalence of uncontrolled asthma in females.[16,17] In childhood, asthma has a higher prevalence in boys, but at puberty there is an increase in sex hormones that causes in increase in asthma in females.[18] Moreover, females have high IgE levels at puberty and this may result in triggering of symptoms by dust or pollen exposure with associated reduced ratio of FEV1/FVC.[19] In our study, uncontrolled asthma was higher in patients having family history of asthma. An important risk factor of asthma is having its family history and evaluation of familial risk can help identify the patients who have a high risk of asthma. However, a study has shown that patients having family history of asthma have best controlled asthma.[20] The pathogenesis of asthma involves a complex interaction of various ethnic, genetic and life style factors and this could be the reason behind a varying prevalence of asthma control between these studies.

Our study results reported that patients with uncontrolled asthma had lower incidence of diabetes. Another study has reported that diabetes has not a significantly high prevalence in patients with difficult to treat asthma.[21] Insulin resistance, metabolic syndrome and diabetes have an important pathophysiological role in development of asthma.[22]

The results of our study have shown that history of

Table 4: Comparison of asthma control with medication use

| | Total | Asthma Symptom Control | | p-value |
		Uncontrolled	Well/Partially controlled	
SABA				
Present	97 (85.8)	67 (88.2)	30 (81.1)	0.390[*]
Absent	16 (14.2)	9 (11.8)	7 (18.9)	
ICS				
Present	32 (28.3)	15 (19.7)	17 (45.9)	0.004[*]
Absent	81 (71.7)	61 (80.3)	20 (54.1)	
LABA				
Present	46 (40.7)	35 (46.1)	11 (29.7)	0.097[*]
Absent	67 (59.3)	41 (53.9)	26 (70.3)	
LTRA				
Present	70 (61.9)	45 (59.2)	25 (67.6)	>0.999[**]
Absent	43 (38.1)	31 (40.8)	12 (32.4)	
LAMA				
Present	2 (1.8)	2 (2.6%)	0 (0)	>0.999[**]
Absent	111 (98.2)	74 (97.4)	37 (100)	
Methylxanthine				
Present	3 (2.7)	2 (2.6)	1 (2.7)	>0.999[**]
Absent	110 (97.3)	74 (97.4)	36 (97.3)	
NSAIDs				
Present	3 (2.7)	3 (3.9%)	0 (0)	0.550[**]
Absent	110 (97.3)	73 (96.1)	37 (100)	
Beta blocker				
Present	12 (10.6)	11 (14.5%)	1 (2.7)	>0.999[**]
Absent	101 (89.4)	65 (85.5)	36 (97.3)	
High use of SABA				
Present	34 (30.1)	34 (44.7)	0 (0)	<0.001[*]
Absent	79 (69.9)	42 (55.3)	37 (100)	

- ICS: Inhaled Corticosteroid, LABA: Long Acting Beta Agonist, LAMA: Long Acting Muscarinic Antagonist, LTRA: Leukotriene Receptor Agonist. NSAISs: Nonsteroidal Anti-Inflammatory Drugs, SABA: Short Acting Beta Agonist
-*Chi-square test applied, **Fisher's exact test applied

atopy was higher in patients with uncontrolled asthma as compared with partially controlled/well controlled asthma. Similar results have been shown by a previous study.[23] According to a study, atopic patients usually have onset of asthma at an earlier age; however the study concluded that aeroallergens were not the predictors of asthma control.[24] Among atopy, nasal diseases such as allergic rhinitis or rhinosinusitis are among prevalent chronic respiratory illnesses.

Our study has shown that uncontrolled asthma was significantly higher in patients with incorrect inhaler technique. A regional study has reported a similar observation that poorly controlled asthma patients and those patients whose FEV1 is less than 70% have error in their technique of using inhalers.[25] Another study reported a high prevalence of incorrect inhaler

technique which reduced at the follow up visit indicating the importance of proper educating regarding the inhaler technique.[26]

According to our study results, patients with uncontrolled asthma had significantly higher GERD. A previous study has shown that in patients with uncontrolled asthma, GERD prevalence was higher.[27] Another study has demonstrated that GERD was the third most common comorbid condition in patients with asthma after rhinitis or sinusitis and cardiovascular diseases.[28] A significantly higher number of patients in our study with uncontrolled asthma had duration of asthma of more than 10 years. Another study also reported a statistically significant difference between duration of asthma and asthma control, with uncontrolled asthma population having a longer

asthma duration.[29] Longer asthma duration has been linked to poor asthma control due to irreversible obstruction to airflow. IgE, cytokines derived from T cells and mast cells start the early asthma reaction whereas activation of eosinophils have their role in persistent asthma symptoms characterizing chronic obstruction to airflow which later becomes irreversible after a longer duration.

Our study results also demonstrated that asthma exacerbations were significantly higher in patients having uncontrolled asthma. Another study also reported that exacerbation in last 12 months is a significant risk factor for poor asthma control.[6] Asthma exacerbations have a negative impact on quality of life and are a source of burden on healthcare. Therefore, intense management should be addressed for its management and prevention of future exacerbations.

Our study has shown that proportion of patients not using ICS was significantly high in cases of uncontrolled asthma. Another study has reported that patients reported good asthma control with the consistent use of ICS.[14] ICS has a good role in management of asthma by reducing its symptoms and improving quality of life by reducing the number of exacerbations, asthma related hospitalizations and improving pulmonary function. In addition, our study has further shown that excessive use of SABA was significantly higher in patients with uncontrolled asthma, a finding also reported by other studies.[6,15] Use of short acting beta agonist as a rescue is a marker for severity of asthma and its high rate in uncontrolled asthma could suggest that the patients might not be using the maintenance medications or the dosage of the maintenance medications might not be enough.

Our study is not without certain limitations. First of all, this study was undertaken on a small sample size. Another limitation of this study was that some patients reported use of herbal medications for asthma control, and the content of such medicines is obscured. It may contain bronchodilator or steroids which remain unrevealed, so this may have certain impact on symptom control which couldn't be highlighted in the present study. Another limitation is that spirometry wasn't done in every patient labeled as having asthma, some patients were physician diagnosed so this may raise query on asthma diagnosis of such patients. Moreover many patients reported to have asthma may have persistent airflow limitation or asthma chronic obstructive pulmonary disease (COPD) overlap (ACO) which requires spirometry for differentiation.

These limitations aside, we believe to the best of our knowledge that this study was the initial step in determining the level of asthma control in a developing country like Pakistan. Moreover, factors associated with poor asthma control were also evaluated. It is recommended that further studies on larger sample size should be carried out.

CONCLUSION

A high proportion of patients had uncontrolled asthma in our population. Level of uncontrolled asthma was significantly higher in patients with incorrect inhaler usage technique, GERD, duration of symptoms more than 10 years, more than 1 episode of asthma exacerbation in past 12 months, absent use of ICS and high use of SABA.

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