Impact of Treatment on Asthma Control in Quetta Pakistan

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Abstract

Background: Poorly controlled asthma may lead to decreased lung function, increase the risk of complications and more episodes of exacerbations, increased healthcare utilization, including more frequent hospitalizations and emergency room visits. Regular monitoring of asthma symptoms and lung function can help identify any potential issues in asthma control and ensure optimal management. **Objectives:** The study aims to assess the asthma control by the usage of asthma controller medications especially, corticosteroids, bronchodilators and leukotriene modifiers, among patients receiving treatment through well-validated questionnaire. **Materials and Methods:** A cross-sectional study with a sample of 361 was conducted in different public hospitals outpatient departments and clinics of Quetta Pakistan by using a convenience sampling technique. The Asthma Control Questionnaire (ACQ) was used to measure the asthma control of the asthmatic patients. The descriptive and inferential statistics have been done by using SPSS version 20 with a *p* value <0.05. **Results:** The study found that an average score of asthma control was 3.1±1.10 thereby indicating uncontrolled asthma with also 62.3% of study participants had uncontrolled asthma, no patient had controlled asthma. An increased number of medications including the use of corticosteroids and leukotriene modifiers posed an impact on asthma control of the study population. **Conclusion:** The study concluded that corticosteroids and leukotriene modifiers can be effective in asthma control and it is suggested for the future studies that route of administration and treatment guidelines must also be determined along with the asthma control to gain a complete picture of impact of treatment and management on any health outcomes.

Keywords: Asthma Control, Asthma Control Questionnaire, Treatment, Quetta, Pakistan.

INTRODUCTION

Asthma is a chronic respiratory disease characterized by inflammation and narrowing of the airways, leading to difficulty breathing. As of 2021, the estimated prevalence of asthma worldwide is 235 million people.[1] In Pakistan, the prevalence of asthma is reported to be around 7-10% of the population.[2-4] It is caused by a combination of genetic and environmental factors, such as exposure to air pollution, allergens, and viral infections.

Hospitalizations and mortality due to asthma are significant public health concerns. Hospitalizations for asthma can be triggered by various factors such as exposure to allergens, air pollution, respiratory infections, and poor management of the condition.[5] In some cases, hospitalization may be necessary to control severe asthma attacks, which can be life-threatening if not treated promptly. Asthma-related mortality is also a significant concern, with deaths resulting from severe asthma attacks. Although asthma death rates have decreased over the past few decades, asthma still remains a leading cause of death from respiratory diseases.[6] Factors such as poor access to health care, limited access to effective treatments, and inadequate management of the condition can increase the risk of death from asthma.[7]

Asthma can be managed through medication, lifestyle changes, and avoiding triggers, but it is not curable. The underlying mechanism of asthma involves inflammation of the airways, increased production of mucus, and narrowing of the airways due to muscle contractions. Effective management and control of asthma is crucial to prevent exacerbations and improve quality of life for individuals with the condition.[8]

Pharmacotherapy for asthma includes Bronchodilators (Short-acting beta-agonists (SABA), Long-Acting Beta-Agonists (LABA), Antimuscarinics), Anti-inflammatory drugs (Corticosteroids (oral, inhaled), Leukotriene modifiers, Monoclonal antibodies), Combination therapy (Inhaled corticosteroids with LABA) and other medications such as Theophylline and Cromones.[9] According to the Global Initiative for Asthma (GINA) classification, patients with mild asthma can effectively manage their symptoms with the use of a reliever medication as needed or a low-dose Inhaled Corticosteroid (ICS) inhaler. For individuals with moderate asthma, the use of a low-dose ICS combined with a long-acting beta 2 agonist (LABA) can effectively control symptoms. In the case of severe asthma, the combination of high-dose ICS and LABA is used for symptom control.[10]

Treatment plays a crucial role in controlling asthma and improving quality of life for individuals with this chronic respiratory condition. Effective treatment can help reduce symptoms, prevent asthma attacks, and improve lung function. Appropriate and effective treatment is crucial in controlling asthma, improving lung function, and reducing the frequency and severity of symptoms. Regular medical evaluation and adherence to the prescribed treatment plan are crucial in achieving optimal asthma control.

Poorly controlled asthma can also lead to more frequent and severe asthma attacks, also known as exacerbations, which can be life-threatening. Poor asthma control can also result in decreased lung function and reduced quality of life, impacting daily activities and work performance.[11] In addition, poorly controlled asthma can increase the risk of complications such as pneumonia, bronchitis, and sinusitis. It can also lead to increased healthcare utilization, including more frequent hospitalizations and emergency room visits.[12] To prevent poorly controlled asthma, it is crucial to adhere to the prescribed treatment plan, including regular use of medications, avoiding triggers, and seeking prompt medical attention for worsening symptoms. Regular monitoring of asthma symptoms and lung function can help identify and address any potential issues in asthma control and ensure optimal management.

Assessing asthma control is an important aspect of managing this chronic respiratory condition. Effective asthma control can improve quality of life, reduce the frequency and severity of symptoms, and prevent asthma attacks. [13] Asthma control can be assessed by symptom assessment, lung function testing, using rescue medications and Asthma Control Questionnaire (ACQ). The ACQ is a self-administered questionnaire that assesses asthma control based on symptoms, rescue medication use, and daily activities.[14]

A systematic review highlighted several studies which evaluate and assess asthma control among patient receiving treatment.[15] Studies conducted in Pakistan emphasize on childhood asthma and asthma control test.[16,17] Literature suggests there are no studies conducted in Pakistan which assess asthma control in adult population through questionnaire approach. The present study aims to assess the asthma control by the usage of asthma controller medications especially, corticosteroids, bronchodilators and leukotriene modifiers, among patients receiving treatment through well-validated questionnaire.

MATERIALS AND METHODS
Study Design, Sample and Study Settings

The cross-sectional study of determining the control of asthma by the treatment modalities was conducted in Pulmonary out-patient departments of two public tertiary hospitals of Quetta Pakistan i.e., Bolan Medical Complex, Hospital; Sandeman Provisional Hospital, Quetta Pakistan and several out-patients private primary health care centers of Quetta, Pakistan by employing a was non-probability convenience sampling technique to acquire patients. A total of 361 patients was made after the fulfillment of inclusion and exclusion criteria for the study.

Inclusion and Exclusion Criteria

The eligible patients, to be included in the study, had to have confirmed diagnosis of asthma from at least six months or more and were prescribed the asthma treatment. Moreover, they could read and write Urdu language (national language of Pakistan) and consented to participate in the study. Patients who were smokers, mechanically ventilated with comorbid conditions like hypertension, heart diseases, intermittent claudication or any accompanied rib fracture and congenital ribcage deformities were excluded.

Methods for Measuring Control

Asthma control can also be patient reported as they also cover many aspects of a disease such as related to treatment and symptom control but their use can be under or overvalued due to scoring criteria. Quite a few validated instruments for assessing asthma control are currently available such as Asthma Control Test (ACT), Childhood Asthma Control Test (cACT), Asthma Control Questionnaire (ACQ), Asthma Therapy Assessment Questionnaire (ATAQ), and Lara Asthma Symptom Scale (LASS),[18] each capturing multiple aspects of asthma burden. Amongst the abovementioned tools Asthma Control Questionnaire was the commonly used tool[18] comprising only 7 items about recent (past week) symptoms, consequences of asthma i.e., night time awakening and limitations in performing daily activities and lung functioning which is to be filled by the clinician as FEV1 values were derived in that particular question.[18,19] Asthma control was measured on a 7point scale ranging from 0 as no impairment to 6 as maximum impairment. For each questionnaire, a score of 0 indicates fully controlled, 1-2 indicates partially controlled 3-4 as uncontrolled and 5-6 suggests severely uncontrolled.[19,20] However, there are other studies where different scoring method of ACQ has also been reported. Those studies did not derived average rather they summed up scores obtained in all 6 items making 36 as a maximum score.[21] In addition to this there is another study reported which claimed to use any of the scoring method i.e., either summation of the responses or taking a mean by dividing the sum of all responses with total number of questions.[22]

Ethical Consideration

This National Bioethics Committee Pakistan's guidelines[23] were followed to conduct the study and therefore according to the guidelines the study was approved by the Research Committee of Faculty of Pharmacy and Health Sciences of University of Baluchistan. Moreover, written consent followed by oral agreement from the patients was acquired and they were given assurance about the confidentiality of their responses and they were informed about their right to leave the questionnaire at any time.

Statistical Analysis

The data was analyzed by using SPSS version 20 (SPSS, 2011). Descriptive statistics were used to summarize the demographic and disease characteristics of the study participants and also the level of asthma control among study population. Inferential statistical tests, Mann–Whitney U test and Kruskal Wallis tests, with a significant p-value < 0.05 were applied to assess the impact of treatment on asthma control.

RESULTS
Demographic Characteristics of a study population

A total of 400 questionnaires were filled out of which 361 questionnaires were completely filled. Out of 361 majority of the study participants were of age 21-30years (n=95) and were male (n=229). The ethnicity of Pathan with a percentage of 39.1% was majorly reported by the patients and large number of study population was from urban cities i.e., 295 patients. 82% reported no smoking and 250 respondents also reported of being married. Table 1 summarizes the characteristics of the study population.

Table 1: Demographics characteristics of Study Population.

Demographic Characteristics	Frequency (*n* = 361)	Percentage (%)
Age Group		
21-30	95	26.3
31-40	68	18.8
41-50	85	23.5
51-60	64	17.7
Above 60	49	13.6
Gender		
Male	229	63.4
Female	132	36.6
Ethnicity		
Baloch	107	29.6
Pathan	141	39.1
Punjabi	57	15.8
Sindhi	13	3.6
Others	43	11.9
Marital status		
Unmarried	88	24.4
Married	250	69.3
Separated/Divorced	13	3.6
Widow	10	2.8
Education		
Uneducated	20	5.5
Only religious education	52	14.4
Primary	59	16.3
Matric	60	16.6
Intermediate	53	14.7
Graduate	77	21.3
Higher education	40	11.1
Occupation		
Student	44	12.2
Unemployed	75	20.8
Government employee	59	16.3
Private employee	31	8.6
Retired	19	5.3
Personal business	69	19.1
Others	64	17.7
Income		
No income	112	31.0
Don't want to disclose	82	22.7
Less than 10000	09	2.5
10000 to 20000	27	7.5
20000 to 30000	47	13.0
More than 30000	84	23.3
Locality		
Urban	295	81.7
Rural	66	18.3
Smoking history		
Yes	65	18.0
No	296	82.0

Table 2: Disease Related Characteristics of Study Participants.

Characteristics	Frequency (*n* = 361)	Percentage (%)
Duration of Asthma		
Less than 6 months	18	5.0
1 to 3 years	102	28.3
More than 3 years	241	66.8
Disease Severity		
Moderate	217	60.1
Severe	144	39.9
Allergy		
Yes	320	88.6
No	41	11.4
Type of Allergy		
Dust	55	15.2
Smoke	43	11.9
Fumes	18	5.0
Pollen	23	6.4
Other	28	7.8
All	155	42.9
None	39	10.8

Table 3: Assessment of level of asthma control.

Asthma control	Frequency	Percentage
Fully controlled	0	0
Partially controlled	62	17.2
Uncontrolled	225	62.3
Severely controlled	74	20.5

Disease Related Characteristics of a study population

Table 2 gives an overview of disease characteristics of study population. 66.8% of asthmatics were suffering from asthma for more than 3 years but majority of them had moderate asthma with a percentage of 60.1%. Atopic asthma was reported by 88.6% (*n*=320) asthmatic patients participated in the present study.

Assessment of level of asthma control

Table 3 describes the present level of asthma control of study subjects. The average scores for patient-rated asthma control was 3.1±1.10. Out of 361 respondents, 225 (62.3%) had uncontrolled asthma and none of the patient was fully controlled.

Table 4 demonstrates that majority of study participants (*n*=96, 26.6%) faced problems in performing their usual activities and 96 (26.6%) patients reported that their asthma is not adversely controlled that they have to remain awake at night time nor do they showed morning symptoms as given by 94 (26.0%). Large number i.e., 219 (60.7%) of the patients' spirometry tests to determine the asthma control were not conducted by the physicians or Pulmonologists as recommended by the guidelines.

Impact of treatment of patients on AQLQ score

According to the Table 5, except the bronchodilators, corticosteroids and mast cell stabilizers and total number of medications used had significant effect on ACQ score. In addition, those who were using more than 5 medications were showing better ACQ scores rather than those who were using less medications and those who were using corticosteroids and mast cell stabilizers also had better scores although scores were not lying in the range of controlled asthma scores.

DISCUSSION

Asthma is a public health problem and when it is not adequately managed despite of the treatment poorly controlled asthma, as defined by poor symptom control and failure of response to treatment,[24] may lead to high morbidity due to exacerbations, mortality and also lower productivity.[25] Since pandemic of COVID-19, asthmatic patients became more vulnerable because of increased number of exacerbations in a year imposing a greater burden on health care system in managing the disease. Furthermore, treatment strategies also differ with varying knowledge and expertise of physicians by which the ultimate goal of asthma treatment is sometimes cannot be fulfilled due to number of confounding factors involved therefore, in the current study asthma control was determined in order to provide a picture by which treatment and management of the disease is to be carried out in such a way that the disease is not aggravated to severe conditions and to reduce the health care utilization by asthmatic patients.

The study found that scores of the asthma control questionnaire were quite high indicating poor control of asthma despite of the treatments given

Items	0 n (%) no impairment	1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)	6 n (%) severely uncontrolled
1. Night time awakenings	15 (4.2)	38 (10.5)	77 (21.3)	96 (26.6)	70 (19.4)	46 (12.7)	19 (5.3)
2. Asthma symptoms in morning	16 (4.4)	59 (16.3)	93 (25.8)	94 (26.0)	57 (15.8)	29 (8.0)	13 (3.6)
3. Limitations in activities	18 (5.0)	54 (15.0)	77 (21.3)	67 (18.6)	96 (26.6)	42 (11.6)	07 (1.9)
4. Shortness of breath	11 (3.0)	49 (13.6)	61 (16.9)	84 (23.3)	76 (21.1)	65 (18.0)	15 (4.2)
5. Wheezing	15 (4.2)	36 (10.0)	66 (18.3)	69 (19.1)	87 (24.1)	66 (18.3)	22 (6.1)
6. Number of puffs taken per day	71 (19.7)	118 (32.7)	137 (38.0)	13 (3.6)	16 (4.4)	0	06 (1.7)
7. FEV1 predicted*	03 (0.8)	23 (6.4)	57 (15.8)	25 (6.9)	16 (4.4)	09 (2.5)	09 (2.5)

Table 4: Responses of the study population for all items of the Asthma Control Questionnaire.

* 219 (60.7%) patients' FEV1 predicted values were not determined

Table 5: Impact of Treatment of Patients on ACQ Score.

Treatment Characteristics	Overall ACQ Score (3.13 ± 1.10)	*P*-value
Number of current medicines^a 1 2-3 4-5 More than 5	2.18 ± 0.82 2.97 ± 1.08 3.18 ± 1.09 3.83 ± 1.07	**0.003**
Bronchodilator^b Yes No	3.14 ± 1.10 2.80 ± 1.31	0.525
Mast cell stabilizers^b Yes No	3.22 ± 1.07 2.46 ± 1.14	**0.000**
Corticosteroids^b Yes No	3.23 ± 1.09 2.68 ± 1.06	**0.000**

a Kruskall-Wallis Test
b Mann-Whitney U Test

i.e., corticosteroids, mast cell stabilizers and bronchodilators. Majority of the patients were lying in the range of uncontrolled asthma. Furthermore, it was also found in the current study that except bronchodilators only corticosteroids and mast cell stabilizers affect asthma control of patients. Moving towards each question of ACQ it was revealed that majority had moderate symptoms like shortness of breath and wheezing, were very limited in performing daily activities, and had to wake up several times in night due to asthma symptoms. In addition to this one aspect which came forward by this study was that there were large number of patients whose FEV1 by which functioning of lungs are determined were not reported.

The majority of the studies previously conducted worldwide were based on comparison of asthma control tools rather than determining the asthma control[26,27] and many studies were also there which compared Asthma Control Questionnaire responses to the GINA criteria for asthma control.[28,29] Quite a few studies were found with which current study findings were compared and within this context the current study reported average score lying in between values that demonstrate uncontrolled asthma whereas the only study which reported asthma control determined by ACQ did not use the same scoring method as of the present study but the patients had same uncontrolled asthma.[21] The uncontrolled asthma may be because of inability to understand the use of inhalers or maybe due to increased number of medications which would cause the patients to not buy the inhalers until the occurrence of exacerbations.

Another thing which was revealed after extensive literature review was the different scoring method used in all studies, moreover, the cut-off points of scores were also different for categorizing controlled, partially uncontrolled and severely uncontrolled asthma.[19,21,22,26,30] Therefore, it is recommended to perform a review study to determine actual scoring method and criteria that best fit all categories related to asthma control.

The large number of asthmatics in the present study had uncontrolled asthma which are not similar to the study conducted on European population although cutoff points were different from the current study in which majority of the participants showed controlled asthma.[1] This could be attributed to the difference in countries and compliance to the guidelines in the European countries as compared to the developing country where the current study was conducted.

It was also observed in the study that majority of the patients' spirometry tests to determine the asthma control were not conducted by the physicians or respirologists as recommended by the guidelines which are in line to the other studies conducted in different places or countries.[9,21,22] The reason for not using these tests would be the inaccessibility of the required equipment and technical aid.[23,24] The problem can be resolved by increasing the availability of pulmonary function tests, educating physicians and their personnel about the usefulness and importance of these tests and to provide physicians trainings regarding their use.[31,32]

Nevertheless, the impact of treatment which was the main objective of the study was determined and it was concluded by the results of this study that bronchodilators does not cause asthma to control rather corticosteroids and leukotriene modifiers does show an influence on asthma control. However, the current study did not determined that all these treatment modalities were given as monotherapies or given in combination and moreover which route and type of dosage form were utilized by the patients. Therefore, it cannot be concluded that how bronchodilators does not cause asthma control while leukotriene modifiers did have impact. There are other studies in which asthma control due to medications was determined but not by ACQ and those studies found that inhaled corticosteroids influence asthma control but not bronchodilators as a monotherapy. Furthermore, it was also found that those patients who did not take bronchodilators have better scores of asthma control as compared to those who were using bronchodilators.

CONCLUSION
It was concluded in the study that increased number of medications including the use of corticosteroids and leukotriene modifiers posed an impact on asthma control of the study population. The study data got itself limited as

the compliance to specific guidelines, medication adherence and the type of treatment used were not determined. Therefore, it is suggested for the future studies that route of administration and treatment guidelines must also be determined along with the asthma control to gain a complete picture of impact of treatment and management on any health outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, *et al*. Global Initiative for Asthma Strategy 2021: Executive summary and rationale for key changes. American Journal of Respiratory and Critical Care Medicine. 2022;205(1):17-35.

2. Khan MA. Monthly and seasonal prevalence of asthma and chronic obstructive pulmonary disease in the District Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan. The Egyptian Journal of Bronchology. 2022;16(1):63.

3. Amin I, ZhongXia C, Ullah I, Haq IU, Ali I. Study on risck factors of childhood asthma in Karachi, Pakistan. IJSIT. 2022.

4. Khan S, Iqbal S, Azam A, Qadeer S, Khanam S. Prevalence and determinants of Asthma in adults in Khyber Pakhtunkhwa, Pakistan. Abasyn Journal of Life Sciences. 2022;5(2):26-32.

5. Wei Y, Qiu X, Sabath MB, Yazdi MD, Yin K, Li L, *et al*. Air pollutants and asthma hospitalization in the Medicaid population. American Journal of Respiratory and Critical Care Medicine. 2022;205(9):1075-83.

6. Delgado-Romero J, Pereyra-Rodriguez J. Asthma mortality in Spain from 1980 to 2019. Trends and perspectives in new treatment era. J Investig Allergol Clin Immunol. 2023;33(2):2.

7. Liu W, Wei J, Cai M, Qian Z, Long Z, Wang L, *et al*. Particulate matter pollution and asthma mortality in China: A nationwide time-stratified case-crossover study from 2015 to 2020. Chemosphere. 2022;308:136316.

8. Melhorn J, Howell I, Pavord ID. Should we apply a treatable traits approach to asthma care? Annals of Allergy, Asthma and Immunology. 2022.

9. Cazzola M, Rogliani P, Naviglio S, Calzetta L, Matera MG. An update on the currently available and emerging synthetic pharmacotherapy for uncontrolled asthma. Expert Opinion on Pharmacotherapy. 2022;23(10):1205-16.

10. Chipps BE, Murphy KR, Oppenheimer J. 2020 NAEPP guidelines update and GINA 2021—asthma care differences, overlap, and challenges. The Journal of Allergy and Clinical Immunology: In Practice. 2022;10(1):S19-S30.

11. Ioniuc I, Miron I, Lupu VV, Starcea IM, Azoicai A, Alexoae M, *et al*. Challenges in the Pharmacotherapeutic Management of Pediatric Asthma. Pharmaceuticals. 2022;15(12):1581.

12. Dengela TA, Sorato MM. Evaluation of Asthma Pharmacotherapy and Treatment Outcome Among Asthmatic Patients Undergoing Follow-Up at the Chest Clinic at AUSH (Ambo University Specialized Hospital), Oromia Region, West, Ethiopia. Research and Review: Management of Emergency and Trauma Nursing (e-ISSN: 2582-0494). 2023:1-16.

13. Canonica GW, Spanevello A, De Llano LP, Ribas CD, Blakey JD, Garcia G, *et al*. Is asthma control more than just an absence of symptoms? An expert consensus statement. Respiratory Medicine. 2022;202:106942.

14. Juniper EF, Bousquet J, Abetz L, Bateman ED, Committee G. Identifying 'well-controlled'and 'not well-controlled'asthma using the Asthma Control Questionnaire. Respiratory Medicine. 2006;100(4):616-21.

15. Jia CE, Zhang HP, Lv Y, Liang R, Jiang YQ, Powell H, *et al*. The Asthma Control Test and Asthma Control Questionnaire for assessing asthma control: Systematic review and meta-analysis. Journal of Allergy and Clinical Immunology. 2013;131(3):695-703.

16. Shoukat S, Gowani SA, Khowaja AA, Khan J. Assessment of asthma control using the asthma control test at a tertiary care centre in Karachi, Pakistan. Journal of the Pakistan Medical Association. 2009;59(3):173.

17. Jabeen U, Zeeshan F, Bano I, Bari A, Rathore AW. Adherence to asthma treatment and their association with asthma control in children. J Pak Med Assoc. 2018;68(5):725-8.

18. Alzahrani YA, Becker EA. Asthma control assessment tools. Respiratory Care. 2016;61(1):106-16.

19. Juniper E, O'byrne P, Guyatt G, Ferrie P, King D. Development and validation of a questionnaire to measure asthma control. European Respiratory Journal. 1999;14(4):902-7.

20. Barnes P, Casale T, Dahl R, Pavord I, Wechsler M. The Asthma Control Questionnaire as a clinical trial endpoint: Past experience and recommendations for future use. Allergy. 2014;69(9):1119-40.

21. Boulet LP, Phillips R, O'Byrne P, Becker A. Evaluation of asthma control by physicians and patients: Comparison with current guidelines. Canadian Respiratory Journal. 2002;9(6):417-23.

22. Nieuwenhof LVD, Schermer T, Eysink P, Halet E, Van Weel C, Bindels P, *et al*. Can the Asthma Control Questionnaire be used to differentiate between patients with controlled and uncontrolled asthma symptoms? A pilot study. Family Practice. 2006;23(6):674-81.

23. Committee-Guidelines. NBCPER. National Bioethics Committee Pakistan: Ethical Research Committee-Guidelines. 2011. Available from: http://www.pmrc.org.pk/erc_guidelines.htm.

24. Chipps BE, Zeiger RS, Dorenbaum A, Borish L, Wenzel SE, Miller DP, *et al*. Assessment of asthma control and asthma exacerbations in the epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) observational cohort. Current Respiratory Care Reports. 2012;1(4):259-69.

25. Pavord ID, Mathieson N, Scowcroft A, Pedersini R, Isherwood G, Price D. The impact of poor asthma control among asthma patients treated with inhaled corticosteroids plus long-acting β2-agonists in the United Kingdom: a cross-sectional analysis. NPJ primary care respiratory medicine. 2017;27(1):17.

26. Olaguibel JM, Quirce S, Juliá B, Fernández C, Fortuna AM, Molina J, *et al*. Measurement of asthma control according to Global Initiative for Asthma guidelines: A comparison with the Asthma Control Questionnaire. Respiratory Research. 2012;13(1):1-10.

27. O'Byrne PM, Reddel HK, Eriksson G, Östlund O, Peterson S, Sears MR, *et al*. Measuring asthma control: A comparison of three classification systems. European Respiratory Journal. 2010;36(2):269-76.

28. Dalcin PDTR, Grutcki DM, Laporte PP, Lima PBd, Viana VP, Konzen GL, *et al*. Impact of a short-term educational intervention on adherence to asthma treatment and on asthma control. Jornal Brasileiro de Pneumologia. 2011;37:19-27.

29. Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, *et al*. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL study. American Journal of Respiratory and Critical Care Medicine. 2004;170(8):836-44.

30. Braido F, Brusselle G, Guastalla D, Ingrassia E, Nicolini G, Price D, *et al*. Determinants and impact of suboptimal asthma control in Europe: The international cross-sectional and longitudinal assessment on asthma control (LIAISON) study. Respiratory Research. 2016;17(1):1-10.

31. Jin R, Choi BC, Chan BT, McRae L, Li F, Cicutto L, *et al*. Physician asthma management practices in Canada. Canadian Respiratory Journal. 2000;7(6):456-65.

32. Grant EN, Moy JN, Turner-Roan K, Daugherty SR, Weiss KB, Team CASIP. Asthma care practices, perceptions, and beliefs of Chicago-area primary-care physicians. Chest. 1999;116:145S-54S.