Original Article

The Effect of Obesity on Severity of Asthma: An Observational Prospective Study from Pakistan

Sara Shahid[1,2], Saad S. Alqahtani[3], Mishal Bajwa[1], Mahnoor Rashid[4], Anosh Sana[1], Amna Bajwa[1], Abdul N. Ali[5], Ahmad K. Ariffin[6], Mahgull Mahmood[2], Fahad Ahmed[7], Muhammad Abid Mustafa[4]

[1]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan, [2]Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan, [3]Department of Clinical Pharmacy, College of Pharmacy, King Khalid University, Abha, Saudi Arabia, [4]Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan, [5]Department of Pharmacy Practice, Geethanjali College of Pharmacy, Cheeryal (V), Keesara (M), Hyderabad, Telangana, India, [6]Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, UniSZA, Besut, Terengganu, Malaysia, [7]Faculty of Pharmacy, University of Sargodha, Sargodha, Punjab, Pakistan

Submitted: 11-Mar-2023
Revised: 24-Apr-2023
Accepted: 20-May-2023
Published: 21-Mar-2024

ABSTRACT

Objective: The current research study aimed to access the relationship between obesity and asthma exacerbations and severity among adult patients at the outpatient section of a federal hospital (PIMS) in Islamabad, Pakistan. **Methods:** A cross-sectional research study was carried out on 207 asthma adult patients belonging to different areas and ethnic groups from the country. The study setting was the PIMS hospital, which attracts patients from all over the country due to its facilities and cost-effective treatments. The body mass index (BMI) of asthma patients was calculated using the heights and weights of the study subjects. However, the pulmonary functions were calculated using a computerized spirometer i-e Spirolab III S/N 303681 in line with Winspiro PRO 7.1.version software. It presents the patient's forced vital capacity that expires in the first second of expiration to full (FEV1) in comparison to forced vital capacity (FVC) ratio, that is, Tiffeneau–Pinelli index was also recorded to determine the asthma severity. **Results:** According to recent surveys, the overall prevalence of patients with overweight and obesity was 29.0% and 23.7%, respectively. A Chi-square test was used, and a statistically significant relationship was observed between BMI and asthma severity ($P < 0.001$). The adult obese female patients presented poor pulmonary functions. The average FEV1/FVC ratio presented significant variance among four different categories of BMI with $P < 0.05$. This difference was due to the normal BMI category as the Tiffeneau–Pinelli index, that is, FEV1/FVC in the normal BMI group was significantly lower as compared to that in underweight and obese patients. **Conclusion:** The study subjects presented raised asthma severity in accordance with the raised BMI. Obese patients presented comparatively raised asthma exacerbations. Moreover, a statistically significant association of gender difference was observed between obesity and asthma severity. It was concluded that adult asthmatic women with obesity presented raised asthma severity as compared to adult asthmatic males.

KEYWORDS: *Asthma, body mass index (BMI), forced expiratory volume (FEV1), forced vital capacity (FVC), obesity*

INTRODUCTION

Asthma is a chronic disease of air passages, which is characterized by the presenting symptoms of wheezing, shortness of breath, coughing, chest tightness, and decreased forced expiratory volume (FEV).[1] Both symptoms and airflow limitations differ with time and intensity and these symptoms are often exaggerated by trigger factors that differ from person to person.[1] The word asthma was derived from a Greek word meaning "hard breathing" and therefore it represents a series

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jpbs

DOI: 10.4103/jpbs.jpbs_238_23

Address for correspondence: Dr. Sara Shahid, Department of Pharmacy Practice, Lahore Pharmacy College, Lahore Medical and Dental College, University of Health Sciences, Lahore, Pakistan.
E-mail: sarashahid498@gmail.com

How to cite this article: Shahid S, Alqahtani SS, Bajwa M, Rashid M, Sana A, Bajwa A, *et al.* The effect of obesity on severity of asthma: An observational prospective study from Pakistan. J Pharm Bioall Sci 2024;16:38-43.

of breathing problems rather than a single respiratory disease.[2]

Globally, around 334 million adults are expected to be suffering from asthma.[3] However, in Pakistan, according to a 2012 survey, approximately 6 million people are suffering from asthma.[4] Karachi, Pakistan's largest city, according to population, comprises about 8–10% chronic asthma-suffering population; every 250th death in this large city is due to severe asthma exacerbations.[4]

Pulmonary function testing along with spirometry plays an important role in the differential diagnosis of asthma. Moreover, other characteristic features of asthma are evaluated for the purpose of diagnosis.[5] Chronic airway inflammation with elevated production of T-lymphocytes and cell-released mediators is responsible for mucous secretion, bronchoconstriction, and airway irresponsiveness.[6] Asthma is illustrated as a phenotype of variant phenotypes based on family history, responsiveness as the result of treatment, and severity of the disease.[7]

The pulmonary function test (PFT) is the basis for the diagnosis of asthma. Spirometry is performed using a computerized spirometer to access FEV and peak expiratory flow (PEF) measurements based on which the FEV1/FVC ratio, that is the Tiffeneau–Pinelli index is calculated.[8] It presents the patient's forced vital capacity that expires in the first second of expiration to full (FEV1) in comparison to forced vital capacity (FVC). Normal values lie in the range of 75% and are expressed as FEV1%.[9]

The Global Initiative for Asthma (GINA) system of classification is used to access the severity of the disease, dividing the pulmonary functions into four categories, namely, normal spirometry, mild restriction, moderate restriction, moderate severe restriction, severe restriction, and very severe restriction in breathing.[10]

The variant types of asthma according to the pathophysiology include many variant types, among which obesity-associated asthma is rapidly increasing day by day worldwide.[11] Obesity-induced asthma is the emerging phenotype of asthma in recent times.[12] Although this disease can never be cured completely, appropriate treatment along with prevention and management can control the disease substantially and allow people with asthma to gain improved quality of life.[13]

Every asthma patient must learn what triggers should be avoided to gain control over asthma severity.[4] During asthma management, failure to use appropriate medications or loss of adherence to adequate treatment can lead to severe symptoms and consequently death.[3]

In accordance with the survey conducted by the World Health Organization (WHO), the body mass index (BMI) of an individual is categorized into four groups, namely underweight with BMI ≤18.5 kg/m^2, BMI is considered normal if it lies within the range 18.5 kg/m^2–24.9 kg/m^2, BMI is considered overweight if it is ≥25 kg/m^2 <30 kg/m^2, and obese if BMI is ≥30 kg/m^2.[14] Overweight and obesity are termed when an abnormal amount of fat (adipose tissue) is accumulated that imposes a substantial risk to health.[4] The common complications of excessive adipose tissue accumulation include the elevated risk of diabetes, hypertension, asthma, and hyperlipidemia.[15] Obesity is related to the non-allergic asthma phenotype and is associated with incidence as well as the course of the disease. In Pakistan, there is an increase in the proportion of obese women from 22.5% (1993–94) to 34% (2011) and 39% (2012–13).[16]

To evaluate whether there is a relationship between obesity and asthma in the northwest Pakistani population (Islamabad and adjacent areas), this prospective study was conducted, in which physician-diagnosed adult asthma patients were included, whereas obesity has been defined in accordance with the reference categories of BMI by the WHO. The association of the potential confounder, that is, gender with obesity and asthma was discussed.

Materials and Methods

Study design and settings and duration

This observational prospective study included asthma adult patients enrolled from the Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. Its pulmonary department is well established, due to which it attracts patients from all over the country.

This research was carried out for evaluating the asthma severity in adult patients, as well as the association of obesity with asthma severity. The ethical approval of our study was taken from SZABMU Islamabad, Pakistan, under PIMS hospital having allotted approval number SZABMU/220M.

Inclusion criteria

The adult patients (age >10 years) diagnosed with asthma by the physician were recruited into this study. Study subjects who failed to undergo spirometry were excluded, patients with age greater than 50 years along with foreign patients (non-Pakistanis), and patients unwilling to participate were excluded from the present study.

Sample size calculation

According to the G power calculator formula statistics,[5] the sample size was set at 207 study subjects. The minimum sample size was 200, and 207 sample size was included. G power calculations, along with two arm proportions, α-value was 0.05, β-value was 0.80, and the calculated odds ratio (OR) was 2.089 having a 95% confidence interval (CI).

Data collection methodology

The data of study subjects were recorded on a data collection form. Study subjects' demographics along with disease history were recorded from their medical record files.

BMI calculation

The patients' BMIs were calculated by the hospital's clinical staff through proper height measurement while standing straight without shoes, along with the digital weight measurement in kilograms, without shoes. BMI (kg/m^2) of patients was calculated individually by the principal investigator using weight and height and the following formula: BMI = weight (kilograms)/ height (meters squared).

The international standards of BMI categorization presented by the WHO were used.[17] The BMI of study subjects was categorized into four categories, that is, underweight, normal, overweight, and obese.

Assessment of respiratory function

Asthma patients were asked to undergo pulmonary function tests (spirometry) on the prescription of a licensed physician. Pulmonary functions were calculated through a computerized spirometer, that is, Spirolab III S/N 303681 in line with WinspiroPRO 7.1.version. Hospital clinical staff did the spirometry procedures to determine the pulmonary functions of asthma patients. In spirometry result values of asthmatic patients FEV and PEF measurements were noted and recorded for asthma assessment. Moreover the FEV1/FVC ratio, that is, the Tiffeneau–Pinelli index was recorded.

Statistical analysis

The statistical analyzing software used for this study was SPSS, v21.0. For inferential statistics, the Chi-square test, as well as the two-way analysis of variance (ANOVA), was used to find the *P*-values (post-hoc analysis using Games Howell's procedure). Values of $P < 0.05$ were presented as statistically significant.

Results

Table 1 depicts the demographic variables of the study subjects. The education status of the study subjects is depicted in Figure 1.

Classification of BMI as frequency of asthma patients is summarized in Figure 2.

Most of the study subjects were observed to have normal weight, whereas only 21 patients (10.1%) were underweight.

Pulmonary function test (PFT) reports

Spirometry results of 207 adult asthmatic patients are illustrated in Figure 3.

Majority of the patients, that is, 23.7% (49) of total asthma patients presented normal spirometry results, whereas 18.8% (39) of patients were observed to have mild restriction in breathing. Moderate restriction was reported in 12.6% (26) of patients. The frequency of spirometry results is graphically presented in Figure 3.

The statistical association of BMI with the gender of patients is demonstrated in Table 2. Females were more prone to obesity, whereas males were observed to have normal BMI.

Table 3 presents the statistical association of BMI with the ratio of the FEV in the first 1 s to the FVC of the lungs (FEV1/FVC).

Table 4 statistically presents that the average FEV1/FVC ratio was significantly different in the four categories of BMI with $P < 0.05$.

The average FEV1/FVC ratio was significantly different in the four categories of BMI with $P < 0.05$. This

Table 1: Demographics of asthma patients (study subjects)

Variables	Categories	*n* (%)
Gender	Male	103 (49.8)
	Female	104 (50.2)
Age	18-24 years	32 (15.5)
	25-44 years	58 (28.0)
	45-64 years	78 (37.7)
	65 & above	39 (18.8)
Area	Rural	116 (56.0)
	Urban	91 (44.0)
Ethnicity	Punjabi	109 (52.7)
	Pathan	64 (30.9)
	Others	34 (16.4)
Socioeconomic Status	Low class	51 (24.6)
	Middle class	153 (73.9)
	Upper class	3 (1.4)

Table 2: BMI association with gender

Variable	Categories	Under weight (%)	Normal (%)	Overweight (%)	Obese (%)	*P*
Gender	Male	10	49	33	11	0.001
	Female	10	30	25	39	

difference was due to the normal BMI category as FEV1/FVC in the normal BMI group was significantly lower as compared to that in underweight and obese patients.

Discussion

Asthma is illustrated as variant phenotypes based on family history, responsiveness to treatment, and severity of the disease.[9] The variant types of asthma according to the pathophysiology include different types that include allergic broncho-pulmonary mycosis as well as asthma with obesity.[11] We believe that this is the first study that associates asthma control and its comorbidity, that is, obesity, in the northeastern area of Pakistan.

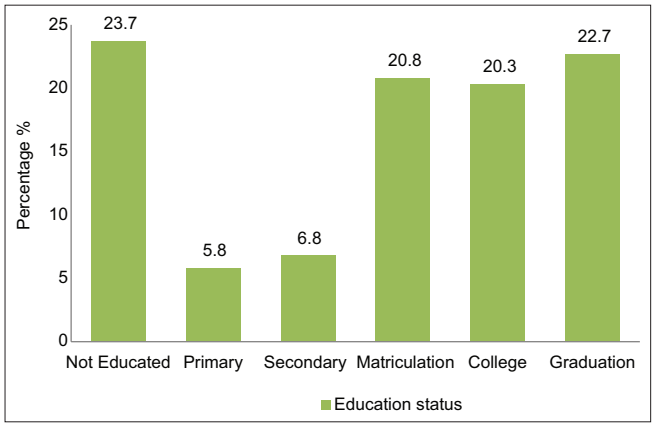

Figure 1: Education status of study subjects

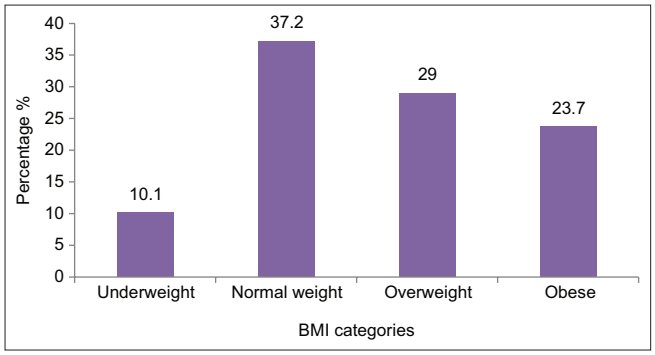

Figure 2: Body mass index (BMI) descriptive ratio

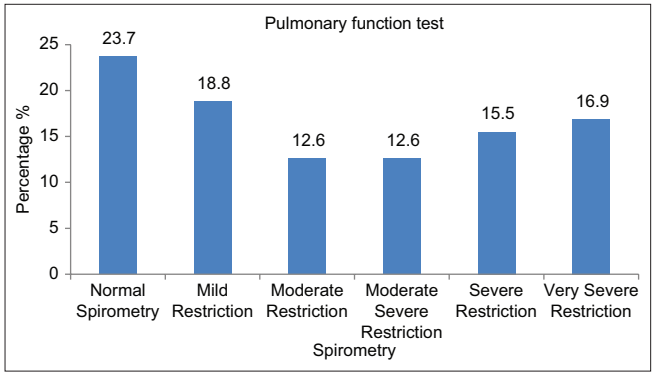

Figure 3: Spirometry ratio of study subjects

According to the present study, FEV1/FVC in the normal BMI group was significantly lower as compared to that in underweight and obese patients. The possible reason could be the differences in alveolar macrophages of overweight and obese patients with asthma. Alveolar macrophages of obese asthmatic patients are extremely sensitive to leptin. This phenotype of macrophages along with a higher concentration of leptin could contribute to airway responsiveness.[16] Furthermore, the presence of fat tissues around the thorax and abdominal cavity exerts pressure over the thoracic wall and decreases functional residual capacity (FRC).[16] This results in a higher risk for expiration flow limitation and airway closure. Kapadia *et al*.[18] conducted a clinical trial to access the association between asthma and obesity. The sample size for this study was 601. It was observed that patients with obesity did not have efficient control over asthma exacerbations and presented poor asthma-specific QoL (quality of life) as compared to non-obese asthmatic patients. These findings comply with the findings of the present study.[18] Moreover, a study conducted on adult asthmatic patients from South Carolina presented similar results. Patients with a higher BMI (>35 kg/m^2) were categorized as obese patients and presented higher asthma prevalence as compared to non-obese patients.[19]

In contrast to the present study, research evaluating 200 adults with age >20 years from the clinic of asthma "Paulista State University"-Botucatu, Brazil, presented that study subjects with BMI >35 kg/m^2 (obese patients) indicated a reduction in FEV1-(forced expiratory volume in the first second) along with a reduction in FVC. Moreover, obese patients presented a higher prevalence of wheezing despite a remarkable variance in the FEV1/FVC ratio, in contrast to the asthmatics having normal BMI. Thus, there was no significant association of bronchial obstruction with obesity.[20]

In the current study, the univariate analysis of ANOVA presented that obesity is related to raised asthma severity. This is because obesity is an etiological factor of

Table 3: BMI association with FEV_1/FVC

Variable	Underweight (%)±SD	Normal (%)±SD	Overweight (%)±SD	Obese (%)±SD	*P*
FEV_1/FVC	112.80±13.40	104.38±14.58	106.98±14.02	109.80±10.85	0.035

Table 4: Spirometry outcomes

Outcome Variable	Mean±SD	95% Confidence interval		*t*-Statistic (df)	*P*	Effect size (η^2)
		Lower bounds	Upper bounds			
Normal spirometry	27.76±6.49	25.96	29.53	3.528 (1, 206)	0.004	0.081
Mild restriction	27.20±6.79	25.09	29.38			
Moderate restriction	25.85±5.69	23.67	28.14			
Moderate severe Restriction	24.92±6.97	22.40	27.81			
Severe restriction	23.74±3.96	22.35	25.12			
Very severe restriction	23.29±5.30	21.67	25.26			

Analysis of Variance (ANOVA) was used to find the *P*-values (post-hoc analysis using Games-Howell's procedure). The *t*-statistic is farther from 0 than the critical values considered reject Null Hypothesis. C.I=Confidence Interval (Group Statistics), SD=Standard Deviation, df=Degrees of freedom. Partial eta-squared (η^2) was used to calculate the effect size. However, the effect size was classified in accordance with Cohen's category. if $0.01 \leq \eta^2 \leq 0.06$=small, if $0.06 \leq \eta^2 \leq 0.14$=medium, $\eta^2 \geq 0.14$=large

asthma. Adipose tissues promote the production of leptin and adipokines, which leads to airway irresponsiveness. Moreover, bronchodilative and bronchoprotective effects of deep breath are absent in obese asthmatic patients, resulting in raised airway resistance.[21]

In conformity with the current study, research conducted on 12,465 asthma patients belonging to the age group of 18–74 years presented similar results.[22] The study was conducted on the Hispanic/Latinos population from Hispanic community health centers in the United States. A statistically significant relationship has been observed between obesity and increased asthma exacerbations.[22] However, in contrast to the present study, research conducted on 607 adult asthma adults presented the results that only 12% of adult asthmatic patients had a BMI >25 kg/m^2 (obese patients). According to this study, obesity was not associated with asthma control.[14]

The present study accessed the correlation of gender with obesity in adult asthmatic patients. It was observed that females were more prone to obesity as compared to male study subjects.

Gender differences in obesity have been observed worldwide. Asthma becomes more severe and prevalent around puberty in women as compared to men. Therefore, it has been observed that estrogen plays a significant role in the modulation of Th2 cytokine development. Moreover, estrogen affects airway responsiveness and influences inflammatory processes.[21]

Similarly, a research study conducted in the southwestern Pakistani population presented that women are three times obese as compared to being underweight. That might be because the major proportion of the women is housewives, who are more prone to lipid-rich diets and fatty food consumption.[16] Similar results were observed from the study conducted at Hospital "du-Sacre-Coeur-de-Montreal," Canada, where the majority of the female asthmatic patients recruited into the study were obese.[19] In conformity to the present study, an observational study conducted on adult asthmatic patients of the Malabar region of Kerala, India, depicts that most of the obese asthmatics, that is, 63% of the total sample were female patients.[17] Moreover, a prospective study conducted by the Clinic of Lung Diseases in Zagreb, Croatia, recruited 92 women and 52 men with 18–88 years of age. The correlation of BMI and lung functions of asthmatic patients presented a statistically significant association of obesity with asthma. However, it was observed that asthmatic women are more prone to obesity in contrast to asthmatic men.[21] However, in contrast to the present study, a cross-sectional questionnaire-based survey on Japanese preschool children presented no specific gender association with obesity.[23]

Conclusion

The present study presented a clear association between obesity of current asthma severity. Elevated BMI, that is, overweight along with obesity was related to poor asthma control as well as raised asthma severity. However, when stratified according to gender, obesity was more prevalent in women as compared to adult asthmatic men. These current findings emphasize the advantage of weight loss in obese asthmatics. Obesity is emerging as a recent phenotype of asthma due to their relationship worldwide.

Limitations

As this study is a single-centered study conducted in Islamabad; therefore; the results cannot be generalized nationwide. Because it was a cross-sectional study, it did not determine whether obesity precedes the development of asthma or not.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. Am J Respir Crit Care Med 2017:195:557-82.
2. Iqbal MS, Al-Saikhan FI, Ahmed NJ, Iqbal MZ. How do out-of-pocket expenditures affect healthcare: A qualitative insight of acute exacerbation among asthma patients. J Pharm Res Int 2020;32:67-73.
3. Van Gemert F, van der Molen T, Jones R, Chavannes N. The impact of asthma and COPD in sub-Saharan Africa. Prim Care Respir J 2011;20:240-8.
4. Lalani NS. A study of knowledge assessment and competence in asthma and inhaler technique of nurses employed at university teaching hospital. Health 2012;316-8.
5. Shahid S, Ahmed F, Shahnaz G, Saqlain M, Ans M, Sana A, *et al*. The impact of theoretical and practical guidance regarding metered dose inhaler technique on asthma patients. J Young Pharm 2022;14:327.
6. Schreiber J, Sonnenburg T, Luecke E. Inhaler devices in asthma and COPD patients–A prospective cross-sectional study on inhaler preferences and error rates. BMC Pulmon Med 2020;20:1-12. doi: 10.1186/s12890-020-01246-z.
7. Shahid S, Ahmed F, Bajwa A, Ans M, Sana A, Abbas S, *et al*. The impact of an educational intervention on the skill of community pharmacists in the use of a pressurized metered-dose inhaler: A covert simulated patient approach in Pakistan. Int J Pharm Investigation 2022;12:380-5.
8. Lavoie KL, Bacon SL, Labrecque M, Cartier A, Ditto B. Higher BMI is associated with worse asthma control and quality of life but not asthma severity. Respir Med 2006;100:648-57.
9. Gauthier M, Ray A, Wenzel SE. Evolving concepts of asthma. Am J Respir Crit Care Med 2015;192:660-8.
10. Ma J, Strub P, Xiao L, Lavori PW, Camargo CA, Wilson SR, Lv N. Behavioral weight loss and physical activity intervention in obese adults with asthma. A randomized trial. Ann Am Thorac Soc 2015;12:1-11. doi: 10.1513/AnnalsATS.201406-271OC.
11. Vermeulen F, De Meulder I, Paesmans M, Muylle I, Bruyneel M, Ninane V. Asthma control measurement using five different questionnaires: A prospective study. Respir Med 2013;107:1314-21.
12. Iqbal MS, Al-Saikhan FI, Iqbal MZ, Ahmed NJ. The burden of illness of acute exacerbation of asthma. Asian J Pharm 2020;14:183-7.
13. Mubarak N, Hatah E, Khan TM, Zin CS. A systematic review and meta-analysis of the impact of collaborative practice between community pharmacist and general practitioner on asthma management. J Asthma Allergy 2019;12:109-53.
14. Sastre J, Olaguíbe JM, Viña AL, Vega JM, Del Pozo V, Picado C. Increased body mass index does not lead to a worsening of asthma control in a large adult asthmatic population in spain. J Investig Allergol Clin Immunol 2010;20:551-5.
15. Taylor B, Mannino D, Brown C, Crocker D, Twum-Baah N, Holguin F. Body mass index and asthma severity in the National Asthma Survey. Thorax 2008;63:14-20.
16. Janjua NZ, Mahmood B, Bhatti JA, Khan MI. Association of household and community socioeconomic position and urbanicity with underweight and overweight among women in Pakistan. PLoS One 2015;10:1-15. doi: 10.1371/journal.pone.0122314.
17. Chandrasekhar D, Parambil AK, Puthur A, Manikuttan M, Mangadanchery M, Izudheen Irshad M, *et al*. An observational study to assess the prevalence and impact of obesity in asthma management. J Young Pharm 2019;11:291-6.
18. Kapadia SG, Wei C, Bartlett SJ, Lang J, Wise RA, Dixon AE. Obesity and symptoms of depression contribute independently to the poor asthma control of obesity. Respir Med 2014;108:1100-7.
19. Liu Y, Pleasants RA, Croft JB, Lugogo N, Ohar J, Heidari K, *et al*. Body mass index, respiratory conditions, asthma, and chronic obstructive pulmonary disease. Respir Med 2015;109:851-9.
20. Pelegrino NRG, Faganello MM, Sanchez FF, Padovani CR, Godoy ID. Relationship between body mass index and asthma severity in adults. J Bras Pneumol Publicacao 2007;33:641-6.
21. Lampalo M, Majer M, Ferara N, Milošević M, Barišić Kutija M, Jukić I. Gender differences in relationship between body mass index and asthma. Psychiatr Danub 2019;31:786-91.
22. Thakur N, Borrell LN, Ye M, Oh SS, Eng C, Meade K, *et al*. Acculturation is associated with asthma burden and pulmonary function in Latino youth: The GALA II study. J Allergy Clin Immunol 2019;143:1914-22.
23. Okabe Y, Adachi Y, Itazawa T, Yoshida K, Ohya Y, Odajima H, *et al*. Association between obesity and asthma in japanese preschool children. Pediatr Allergy Immunol 2012;23:550-5.