

Role of Common Variables: Age, Gender, BMI, Rhinosinusitis, and Smoking among Asthmatic and Severe Asthmatic Patients

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Background: This study was done to determine the role of common variables, including age, gender, body mass index (BMI), rhinosinusitis, and smoking among a group of asthmatic and severe asthmatic patients in 2016.

Materials and Methods: This retrospective study was carried out from mid-June to the end of September 2016. Of 678 patients with asthma referred to private asthma clinics in Tehran, 163 subjects were selected. Severe asthma (SA) cases were diagnosed according to the SA definition (severe shortness of breath, chest tightness or pain, and coughing or wheezing, low peak expiratory flow (PEF) using a peak flow meter, and more than two days of wheezing and coughing per week). Patients with the presence of concomitant diseases, such as gastroesophageal reflux disease, sleep apnea, hypo- and hyperthyroidism, as well as users of nonsteroidal anti-inflammatory drugs (NSAIDs) were excluded. According to the signs and symptoms and classic criteria of asthma, the subjects with SA were assigned to the case group and subjects with asthma to the control group. Besides, general information, including age, gender, BMI, smoking history, and the presence of Rhinosinusitis was collected.

Results: Of 163 subjects, 92 patients (56.4%) were in the control, and 71 patients (43.6%) in the case group. The rate of SA among 678 patients was 10.47%. The mean age of the case group was 49.08 ±11.66 and the control group was 50.05 ±15.65 years. There was a significant difference in BMI between the case and control groups (p=0.034), especially among females in the case group (p=0.001). BMI was significantly higher in females than in males (p=0.002). Also, smoking status was not significant between the case and control groups (p=0.751). Rhinosinusitis was significantly higher in the case groups compared with the control groups (p= .014).

Conclusion: Rhinosinusitis was higher in SA patients (case group). SA was more observed among females than males and those who were more overweight. It seems that rhinosinusitis and obesity are more important risk factors. Moreover, obese female patients require more serious attention.

Key words: Asthma; Prevalence; Age Groups; Gender Identity; Body Mass Index; Rhinosinusitis; Smoking

INTRODUCTION

Asthma is a common chronic inflammatory disease of the airway that is affected by environmental and

hereditary factors. Severe asthma (SA) is difficult to treat and it seems that its rate is increasing, particularly in low- and middle-income countries (1). Based on the World

Health Organization (WHO) SA definition, SA is uncontrolled asthma, which can lead to frequent complications, including chronic illnesses, like lung function impairment or reduced lung growth in children (or even death) or side effects caused by used medications. SA consists of three groups with different public health messages and challenges: untreated SA due to undiagnosed asthma or a lack of access to treatment; difficult-to-treat SA (due to adherence issues, improper or incorrect use of medications, environmental triggers, or comorbidity); and treatment-resistant SA, including asthma, for which control is not achieved in spite of the highest level of recommended treatment or asthma that is controlled using the highest level of recommended treatment (2,3).

On the other hand, SA is widely accepted as a heterogeneous disease, and the use of targeted biofeedback phenotypes has been effective in its treatment. AS is associated with factors, such as occupational exposure, personal smoking, obesity, female sex, eosinophil recurrent inflammation, nasal polyps and sinusitis, aspirin sensitivity, and respiratory tract infections (4-11). Genetic variation may interact with factors affecting lung function and asthma sensitivity and severity (11). The prevalence of asthma in countries Eastern Mediterranean Region (EMRO) is 4.5-25.9% (12). The overall asthma prevalence was approximately 8% in Sweden (13). The prevalence of asthma in Asia is 3 - 7% and is expected to increase (14,15). Cigarette smoking caused more severe symptoms of asthma and a decline in lung function. The prevalence of SA among students in Ahwaz, Iran was 8.9% in the age group of 13-14 and 6.8% among those aged 6-7 years old (16). SA occurs among a small proportion of asthmatic patients; however, due to frequent severe exacerbations and persistence of symptoms, it is associated with a higher rate of morbidity and mortality and also higher cost and burden on the patient and the society.

Although the effects of risk factors on SA have previously been documented, more attention should be paid to the age, gender, body mass index (BMI), rhinosinusitis, and smoking risk factors. The present study aimed at determining the role of common variables, such

as age, gender, BMI, rhinosinusitis, and smoking among a group of asthmatic and severe asthmatic patients in 2016 as well as shedding light on the most important risk factor among asthmatic patients.

MATERIALS AND METHODS

This retrospective study was carried from mid-June to the end of September 2016. Of 678 patients with asthma referring to the private asthma clinics in Tehran, 163 subjects with asthma were selected. In this study, we tried to investigate the role of common basic factors and indicators that are routinely gathered during clinical evaluation of asthmatic patients.

SA cases were diagnosed according to the SA definition (severe shortness of breath, chest tightness or pain, coughing or wheezing, low peak expiratory flow (PEF) using a peak flow meter, and more than two days of wheezing and coughing per week). Patients with concomitant diseases, such as gastroesophageal reflux disease (GERD), sleep apnea, hypo- and hyperthyroidism, as well as users of nonsteroidal anti-inflammatory *drugs* (NSAIDs) were excluded.

All patients had the results of pulmonary function tests (PFTs) para-nasal sinus x-ray. According to the signs and symptoms and classic criteria of asthma, the subjects with SA were assigned to the case group and subjects with asthma to the control group. The subjects' information, including age, gender, BMI, smoking history, and presence of rhinosinusitis was collected.

Data were analyzed using the SPSS software version 16 and are expressed as mean \pm standard deviation (SD) for continuous and frequencies (%) for categorical variables. Continuous variables were assessed using T-test, whereas categorical variables were measured by the Chi-square. $P < 0.05$ was considered statistically significant. Various factors were considered to investigate the effect of factors affecting SA and were evaluated by regression analysis

RESULTS

A total of 163 subjects were studied, of whom 92 cases (56.4%) were in the control and 71 patients (43.6%) were in the case group. The rate of SA among the total population

was 10.47%. Table 1 presents the distribution of the case and control groups. The Chi-square test showed no differences between the case and control groups regarding sex ($p=0.509$).

Table 1. Distribution of case and control groups by sex

Groups	Number (%)		Total
	Female	Male	
Control	55(59.8%)	37(40.2%)	92(100%)
Case	46(64.8%)	25(35.2%)	71(100%)
Total	101(62.0%)	62(38.0%)	163(100.0%)

According to the results of the t-test, there was a significant difference in BMI between the case and control groups ($p=0.034$) (Table 2) and the case group had a higher BMI.

The subjects (both genders) were homogenous regarding age; however, BMI was significantly higher in females than males (t-test, $p=0.002$) (Table 3) and the difference was more meaningful in the case group ($p=0.001$) (Table 4).

Table 3. Mean \pm SD age and BMI by sex

Sex		Number	Mean \pm SD	Std. Error Mean	P. Value
Age	Female	101	49.31 \pm 13.43	1.3364	0.707
	Male	62	50.16 \pm 15.02	1.9081	
BMI	Female	101	28.26 \pm 5.23	0.5204	0.002
	Male	62	25.74 \pm 4.61	0.5857	

Table 4. Mean \pm SD BMI among case group by sex

Case Group	Sex	Number	Mean \pm SD	Std. Error Mean	P. Value
BMI	Female	46	29.96 \pm 6.04	0.8901	0.001
	Male	25	25.30 \pm 4.69	0.9397	

Table 5. Distribution of smoking status by sex among case and control groups

Groups		Smoker				Total
		Non	Positive	Passive	Ex	
Control	Female	44(80.0%)	1(1.8%)	9(16.4%)	1(1.8%)	55(100.0%)
	Male	31(83.8%)	0(0.0%)	3(8.1%)	3(8.1%)	37(100.0%)
	Total	75(81.5%)	1(1.1%)	12(13.0%)	4(4.3%)	92(100.0%)
Case	Female	35(76.1%)	0(0.0%)	10(21.7%)	1(2.2%)	46(100.0%)
	Male	19(76.0%)	2(8.0%)	2(8.0%)	2(8.0%)	25(100.0%)
	Total	54(76.1%)	2(2.8%)	12(16.9%)	3(4.2%)	71(100.0%)

There were no differences between smoking status between the case and control groups (Chi-square test, $p=0.751$) (Table 5).

Both case and control groups had rhinosinusitis; however, it was significantly more observed in the case groups ($p=.014$). There was no association between the studied variables and SA (Table 6).

Logistic regression test showed that there were no differences between smoking, BMI, age, rhinosinusitis, marital status, and the number of children by considering sex as the reference group.

Table 2. Mean \pm SD age and BMI among case and control groups

Groups		Number	Mean \pm SD	Std. Error	P.
				Mean	Value
Age	Control	92	50.05 \pm 15.65	1.63129	0.651
	Case	71	49.08 \pm 11.66	1.38412	
BMI	Control	92	26.52 \pm 4.23	0.44550	0.034
	Case	71	28.32 \pm 6.00	0.71236	

Table 6. Rhinitis status among case and control groups

Groups	Rhinitis		Total	
	No	Yes		
Control	Female	21(38.2%)	34(61.8%)	55(100.0%)
	Male	18(48.6%)	19(51.4%)	37(100.0%)
	Total	39(42.4%)	53(57.6%)	92(100.0%)
Case	Female	7(15.2%)	39(84.8%)	46(100.0 %)
	Male	7(28.0%)	18(72.0%)	25(100.0 %)
	Total	14(19.7%)	57(80.3%)	71(100.0 %)
Total	53(32.5%)	110(67.5%)	163(100.0%)	

DISCUSSION

The obtained results showed that the rate of SA in the total population was 10.47%. The number of females was more than males and the prevalence of asthma among female adult cases was higher than males. Both groups were homogenous regarding age. BMI in females was significantly higher than males and this difference was more meaningful in the case group. There were no differences between smoking status between the case and control groups. Rhinosinusitis was more observed in the case group. Hekking et al. showed that in the Netherlands as a Western European country, 17.4% of asthmatic patients had difficult-to-control asthma, whereas a smaller proportion of 3.6% showed the criteria of severe refractory asthma (17). Also, 8.1% of a nationwide population of current patients with asthma was classified as severe asthmatic patients. Von Bülow et al. showed that among Danish adults, 8.1% of patients with asthma had SA (18). The prevalence of SA among school children (13–14 years old) in Ahvaz (Iran) was 9.8% (16).

Our findings were in line with other studies. We found that the prevalence of SA was higher among females. Zein and Erzurum showed that the overall prevalence of asthma was 12.7% in females and 11.4% in males. Other studies have also revealed that SA was more prevalent among the older population and females (19). Gibson et al. showed that in the elderly, more attention to asthma problems and obstructive airway disease is needed to provide effective care systems, appropriate clinical guidelines, and a research program resulting in improved health outcomes (20).

Female cases had a higher BMI than males. Jensen et al. showed that understanding the manifestations and mechanisms of

asthma in childhood obesity in both genders will help direct clinical management and targeted therapeutic interventions (21). Barros et al. reported that the prevalence of asthma in obese subjects was more than in uncontrolled patients with normal BMI (22). In contrast with our findings, Chen et al. showed that sex was not associated with the disease course. Other risk factors may play a major role in asthmatic patients, which we were not investigated in this study and it was the weakness of the current study (23).

Although there was a significant difference in BMI in the studied groups, the association between the studied variables and SA was not observed and other variables may play a major role. Therefore, more studies are needed in this regard in the population of Iranian patients with asthma.

According to our results, the prevalence of active smoking in asthmatic individuals was low and patients with asthma refrain from smoking, which is significantly different from the general population of Iranian society. Also, women are more at because of their exposure to secondhand smoke from male smokers. McLeish et al. showed that improvements in lung functioning and asthma symptoms are associated with smoking cessation (24). Tobacco caused 33% of all male deaths at the ages of 25–69 years in Hong Kong in 1998. It has been shown that if current smoking patterns continue by 2030, cigarettes will cause 3 million deaths annually in the western world and 7 million deaths in the low- and middle-income countries (25).

Jha et al. showed that compared with people who have never smoked, smokers lose at least a decade of life expectancy. Quitting smoking before the age of 40 years could reduce the death rate up to 90% (26).

Rhinosinusitis was common in all patients; however, it was more prevalent among SA cases. Asthma and chronic rhinosinusitis are associated with an allergic airway, which is a common issue in pathophysiology, epidemiology, and treatment of asthma (27). Our findings were in line with other studies.

The WHO definition of SA should be applicable to low- and middle-income countries. Hence, complicated cases could be identified through global collaboration as databases of international biobanks. The number of cases and the lack of advanced molecular biological study in this group was one of the

major limitations. Given the increasing global prevalence of asthma, observing more cases with SA can be expected. Therefore, the prevention of risk factors can be very effective in reducing mortality and associated costs of this disorder. Paying attention to women, especially women with SA, weight control, and reduction of BMI, avoiding exposure to secondhand smoke, and controlling rhinosinusitis could be simple but effective measures to reduce the risk of developing asthma. Thus, the high costs of treatment of this disorder, especially frequent admissions and precious drugs can be reduced.

CONCLUSION

The prevalence of rhinosinusitis was more among SA patients (case groups). SA was observed more among females than males and those who were more overweight. It seems that rhinosinusitis and obesity are more important risk factors. Moreover, obese female patients require more serious attention.

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Conflict of Interest

There is no conflict of interest.

REFERENCES

1. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43(2):343-73.
2. Bush A, Zar HJ. WHO universal definition of severe asthma. *Curr Opin Allergy Clin Immunol* 2011;11(2):115-21.
3. Bousquet J, Mantzouranis E, Cruz AA, Ait-Khaled N, Baena-Cagnani CE, Bleecker ER, et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol* 2010;126(5):926-38.
4. Haldar P, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, et al. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 2008;178(3):218-224.
5. Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med* 2010;181(4):315-23.
6. Miranda C, Busacker A, Balzar S, Trudeau J, Wenzel SE. Distinguishing severe asthma phenotypes: role of age at onset and eosinophilic inflammation. *J Allergy Clin Immunol* 2004;113(1):101-8.
7. ten Brinke A, Zwinderman AH, Sterk PJ, Rabe KF, Bel EH. Factors associated with persistent airflow limitation in severe asthma. *Am J Respir Crit Care Med* 2001;164(5):744-8.
8. ten Brinke A, van Dissel JT, Sterk PJ, Zwinderman AH, Rabe KF, Bel EH. Persistent airflow limitation in adult-onset nonatopic asthma is associated with serologic evidence of Chlamydia pneumoniae infection. *J Allergy Clin Immunol* 2001;107(3):449-54.
9. Knutsen AP, Bush RK, Demain JG, Denning DW, Dixit A, Fairs A, et al. Fungi and allergic lower respiratory tract diseases. *J Allergy Clin Immunol* 2012;129(2):280-91; quiz 292-3.
10. Vicencio AG, Muzumdar H, Tsirilakis K, Kessel A, Nandalike K, Goldman DL. Severe asthma with fungal sensitization in a child: response to itraconazole therapy. *Pediatrics* 2010;125(5):e1255-8.
11. 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.
12. Masjedi M, Ainy E, Zayeri F, Paydar R. Assessing the Prevalence and Incidence of Asthma and Chronic Obstructive Pulmonary Disease in the Eastern Mediterranean Region. *Turk Thorac J* 2018;19(2):56-60.
13. Larsson K, Ställberg B, Lisspers K, Telg G, Johansson G, Thuresson M, et al. Prevalence and management of severe asthma in primary care: an observational cohort study in Sweden (PACEHR). *Respir Res* 2018;19(1):12.

14. Anderson HR, Gupta R, Kapetanakis V, Asher MI, Clayton T, Robertson CF, et al. International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children. *Int J Epidemiol* 2008;37(3):573-82.
15. Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S; International Study of Asthma and Allergies in Childhood Phase Three Study Group. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009;64(6):476-83.
16. Shakurnia AH, Assar S, Afra M, Latifi M. Prevalence of asthma among schoolchildren in Ahvaz, Islamic Republic of Iran. *East Mediterr Health J* 2010;16(6):651-6.
17. Hekking PP, Wener RR, Amelink M, Zwinderman AH, Bouvy ML, Bel EH. The prevalence of severe refractory asthma. *J Allergy Clin Immunol* 2015;135(4):896-902.
18. von Bülow A, Kriegbaum M, Backer V, Porsbjerg C. The prevalence of severe asthma and low asthma control among Danish adults. *J Allergy Clin Immunol Pract* 2014;2(6):759-67.
19. Zein JG, Erzurum SC. Asthma is Different in Women. *Curr Allergy Asthma Rep* 2015;15(6):28.
20. Gibson PG, McDonald VM, Marks GB. Asthma in older adults. *Lancet* 2010;376(9743):803-13.
21. Jensen ME, Wood LG, Gibson PG. Obesity and childhood asthma - mechanisms and manifestations. *Curr Opin Allergy Clin Immunol* 2012;12(2):186-92.
22. 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.
23. Chen W, Marra CA, Lynd LD, FitzGerald JM, Zafari Z, Sadatsafavi M. The natural history of severe asthma and influences of early risk factors: a population-based cohort study. *Thorax* 2016;71(3):267-75.
24. McLeish AC, Zvolensky MJ. Asthma and cigarette smoking: a review of the empirical literature. *J Asthma* 2010;47(4):345-61.
25. To T, Daly C, Feldman R, McLimont S. Results from a community-based program evaluating the effect of changing smoking status on asthma symptom control. *BMC Public Health* 2012;12:293.
26. Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013;368(4):341-50.
27. Feng CH, Miller MD, Simon RA. The united allergic airway: connections between allergic rhinitis, asthma, and chronic sinusitis. *Am J Rhinol Allergy* 2012;26(3):187-90.