

Association of Obesity with Asthma Severity, Control and Quality of Life

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Background: The association between asthma and obesity is becoming increasingly established but the mechanism that might explain the observed differences in asthma severity, control and quality of life between obese and non-obese adult asthmatics is not clear.

The purpose of this study was: 1) to determine asthma severity, control and quality of life in obese asthmatics and 2) to explore, according to the body mass index (BMI), the systemic inflammatory state of asthmatic people.

Materials and Methods: A cross-sectional study was conducted between 2009 and 2010. Two hundred adult asthmatic patients were included. Data analysis consisted of univariate analysis with chi-square comparison test followed by a multivariate logistic regression.

Results: Obesity worsens the severity of asthma. This finding was more strongly observed among women than men. Obesity and overweight are associated with a poorer control of asthma. According to BMI, obese asthmatics had 6 times more frequent emergency visits, 5 times more frequent hospitalizations for asthma related complaints, increased missed work days and greater dose of inhaled corticosteroids (1025µg/day vs. 759µg/day of beclometasone equivalent). Mean serum level of C-reactive protein (CRP) and leptin was significantly correlated with asthma severity based on GINA classification (5.75 vs. 2.81 mg/l; 20.5 vs. 5.38 ng/ml; respectively).

Conclusion: In summary, it appears that obesity is significantly associated with a greater asthma severity and a poorer asthma control and quality of life. Chronic systemic inflammation state may explain the relationship between obesity and asthma.

Key words: Asthma, Obesity, Severity, Control, Quality of life, Leptin

INTRODUCTION

Asthma and obesity are both chronic diseases constituting important health problems worldwide. Their prevalence has widely increased over the past decade. Asthma currently affects over 3.24% of men and 3.82 % of women in Tunisia (1). The prevalence of obesity is 14.2% (2). Many studies have confirmed the positive association between body mass index (BMI) and asthma (3-5). Thus, obesity might be associated with greater prevalence of

asthma. Some studies suggest that asthma, in obese subjects, may have a particular phenotype. Therefore, obesity could contribute to greater severity of asthma and its poorer control.

Although the association of asthma with obesity is becoming increasingly established, the mechanism that might explain the observed differences in asthma severity, control and quality of life between obese and non-obese

subjects is not clear. In recent studies, authors have reported that obesity promotes a systemic inflammatory state that could contribute to the increase of asthma severity and its poor control.

The purpose of this study was: 1) to determine whether obesity contributes to a worse asthma severity, control and quality of life in adult Tunisian population with asthma and 2) to explore, according to the BMI, the systemic inflammatory state in asthmatic people.

MATERIALS AND METHODS

A cross sectional study was conducted between 2009 and 2010. Participants were subjects from inpatient and outpatient Respiratory Departments of Abderrahman Mami Hospital, the largest Respiratory Hospital in Tunisia. A total of 200 adult asthmatic patients were included in this study. Understudy subjects were aged 18 years or older and met GINA criteria for more than one year. Subjects, who were pregnant, had any additional respiratory disease or asthma exacerbation ≤ 4 weeks were excluded from the study.

The primary dependent variables were as follows:

Asthma severity was classified according to the criteria of the 2008 GINA (Global Initiative for Asthma) classification as intermittent, mild persistent, moderate persistent or severe persistent.

Asthma control was assessed by using the 2008 GINA criteria as controlled, partly controlled and uncontrolled. The Quality of life was evaluated by the AQVAT questionnaire (asthma quality of life questionnaire in Tunisia) (6). The AQVAT questionnaire is an Arabic version of the asthma quality of life questionnaire (AQLQ) (4). The AQVAT, a validated instrument from which one can generate an overall score and 4 domain scores (symptoms, emotions, activity, and environment), evaluates quality of life in asthmatics across four domains: activity limitation, symptoms, emotional distress and environmental stimuli. It contains 33 items rated on a 10-point scale (0: no impairment, 10: maximal impairment). An average AQVAT score higher than 6 indicated that patient had poor quality of life.

The primary independent variable was BMI, which was calculated using patients' height and weight. BMI status was analyzed as a 3-level categorical measure based on established guidelines for defining normal weight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), and obesity (≥ 30 kg/m²) (5).

The secondary independent variables were gender, age, body weight, height, waist circumference, smoking habit, profession, spirometry results, health care utilization in the past 12 months (emergency room, hospitalization), missed work days and prescribed medications which were all recorded. The serum samples were analyzed for levels of leptin (by an immunoenzymatic assay LEPTIN EASIA kit From Biosource) TM and C - reactive protein (CRP) by immunoturbidimetry (BiosystemsTM). Leptin and CRP were not measured in the fasted state.

This study was approved by the Ethics Committee of Abderrahmen Mami Hospital.

Statistical Analysis

All analyses were performed using SPSS software. We examined bivariate associations of BMI status with each outcome measure using Pearson χ^2 analysis. Multiple logistic regression models were used to analyze the independent effect of BMI status on asthma outcomes after adjustment for possible confounding factors, where BMI status was treated as a 3-level categorical variable (18.5-24.9 [reference group], 25.0-29.9, and ≥ 30 kg/m²). Each outcome measure was regressed on BMI status, adjusting for gender, age, body weight, height, waist circumference, smoking habit, profession, spirometry results, health care utilization in the past 12 months (emergency room, hospitalization), missed work days and prescribed medications.

RESULTS

Two-hundred patients (84 men, 116 women) were entered the study.

The mean age was 46.14 \pm 13.83 years (range 18-80 years). The majority of subjects were women (58%), 21.5 % were current smokers. The mean BMI among the population was 27.79 \pm 5.76 (18 - 44.95 kg/m²). Thirty

percent (30%) of patients had a BMI >30 Kg /m², 31.5% had a BMI between 25 and 30 and 38.5% had a BMI <25 Kg/m². The general characteristics of understudy patients based on BMI values are presented in Table 1.

Analysis of BMI categories showed that obese subjects were mostly female, non smoker, had no job and had higher prevalence of comorbidities.

The asthma characteristics are summarized in Tables 2 and 3. Concerning the disease severity, 16 (8%) had intermittent asthma, 65 (32%) had mild persistent asthma, 91 (45.5 %) had moderate persistent asthma and 28 (14 %) had severe persistent asthma.

Table 1. Distribution of patients according to their body mass index.

Variables	Overall (n=200)	Normal (n=77)	Over weight (n=63)	Obese (n=60)	P
Age (years)*	46.14±18.83	43.1±15.6	46.6±12.6	49.7±12.6	0.016
Male, n (%)	84 (42)	43 (21.5)	28 (14)	13 (6.5)	0.018
Female, n (%)	116 (58)	34 (17)	35 (17.5)	47 (23.5)	
Current smoker, n (%)	43 (21.5)	20 (26.5)	8 (12.5)	4 (6.7)	0.001
Employed, n (%)	78 (39)	44 (57.14)	31 (49.2)	17 (28.3)	0.005
Diabetes, n (%)	17 (8.5)	3 (3.9)	4 (6.3)	10 (16.6)	0.005
Hypertension, n (%)	17 (8.5)	2 (2.6)	4 (6.3)	11 (18.3)	0.001
Hypercholesterolemia (%)	5 (2.5)	0	0	5 (8.3)	0.001
GERD, n (%)	9 (4.5)	1 (1.2)	2 (3.1)	6 (10)	0.001
Rhinitis, n (%)	587 (29)	45 (58.5)	6 (9.5)	5 (8.3)	0.001
Sinusitis n (%)	14 (7)	10 (13)	2 (3.1)	2 (3.3)	0.03

*: Mean ± standard deviation / GERD: Gastroesophageal reflux disease.

Table 2. Asthma severity and control according to BMI

Variables	Normal (n=77)	Over weight (n=63)	Obese (n=60)	p
Asthma severity, n (%)				<0.001
Intermittent	10 (12.98)	4 (6.34)	2 (3.33)	
Mild Persistent	33 (42.85)	25 (39.68)	7 (11.66)	
Moderate Persistent	30 (38.96)	29 (46.03)	32 (53.33)	
Severe Persistent	4 (5.19)	5 (7.93)	19 (31.33)	
Asthma control, n (%)				<0.001
Controlled	64 (83.11)	47 (74.6)	15 (25)	
Partly controlled	11 (14.28)	14 (22.22)	38 (63.33)	
Uncontrolled	2 (2.59)	2 (3.17)	7 (11.66)	

Table 3. Asthma characteristics and pulmonary function in asthmatic patients

Variables	Overall (n=200)	Normal (n=77)	Over weight (n=63)	Obese (n=60)	p
Atopy n (%)	107 (53.5)	44 (22)	38 (19)	25 (12.5)	< 0.001
Age of onset *	29.6±13.48	26.6±14.16	29.29±12.55	33.65±12.70	< 0.001
Daily ICS dose**	870±293	759.7±330.5	857.1±260.7	1025±193.6	< 0.001
AQVAT score*	-	11.34±0.34	21.98±0.66	64.35±2.04	< 0.001
FEV ₁ , % Pred*	75.85±15.30	79.78±12.66	78.11±16.5	68.42±14.72	< 0.001
FVC, % Pred *	86.55±12.32	79.78±12.66	78.11±16.5	68.42±14.72	< 0.001
FEV ₁ /FVC % pred *	80.19±9.98	82.16±0.98	80.38±10.14	77.47±9.92	< 0.001
ER / urgent*	0.35±0.65	0.13±0.44	0.21±0.44	0.78±0.84	< 0.001
Hospitalization *	0.08±0.31	0.1±0.11	0.2±0.10	0.53±0.31	< 0.001
Missed work days	6	1	2	3	0.01

*: Mean ± standard deviation / **: 1µg / day of Beclometasone or an equivalent

The median FEV1 / FVC ratio was 80.19 ± 9.98 , median FEV1 % of predicted was 75.85 ± 15.30 and FVC % of predicted was 86.55 ± 12.32 .

The univariate analysis showed that obesity and overweight were associated with a higher GINA severity classification, lower GINA control classification and poorer quality of life (AQVAT score of more than 6). FEV1, FVC and FEV1/FVC were significantly lower in the obese group.

Based on BMI, the onset of asthma was later in the obese group, with less atopy, more frequent emergency visits and hospitalizations for asthma related complaints in the year preceding enrollment, increased missed work days and greater dose of inhaled corticosteroids (ICS).

BMI and inflammatory parameters:

Mean serum levels of CRP and leptin were significantly higher in the obese subjects (Figures 1 and 2).

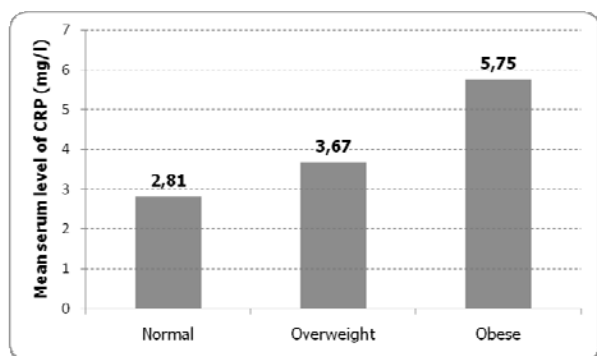


Figure 1. Mean serum level of CRP according to BMI

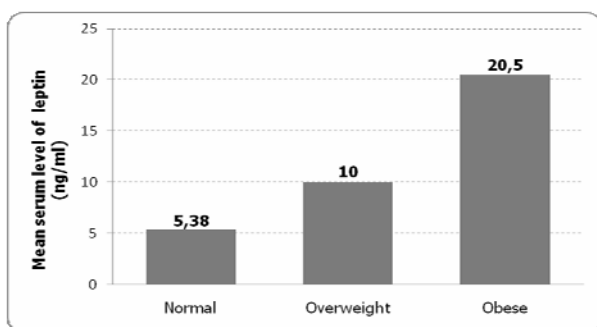


Figure 2. Mean serum level of leptin (ng/ml)

Also, the mean serum level of CRP and leptin was significantly correlated with asthma severity based on GINA classification (Figures 3 and 4).

The multivariable logistic regression showed that obese subjects were significantly more likely to have a more severe asthma. After adjustment for age, smoking status, gender and co-morbidities, the odds ratio of the correlation between obesity and asthma severity was 6.1 (95% CI 2.4-15.2; $p < 0.001$).

The association between obesity and asthma severity among women also revealed a statistically significant difference (OR 11.2; 95% CI 2.9-42.4; $p = 0.001$) but, there was no such correlation among men (OR 0.7; 95% CI 3-51; $p = 0.98$). Also, the multivariate analysis showed a significant correlation between obesity and worse asthma control using the GINA classification (OR 20; 95% CI 7.5-53).

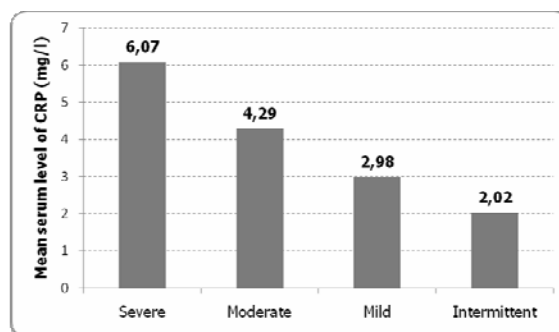


Figure 3. Serum level of CRP in each asthma severity category

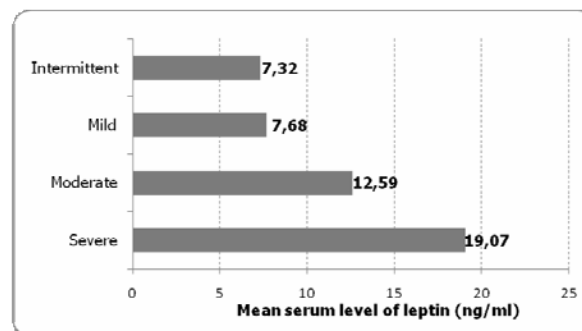


Figure 4. Serum level of leptin in each asthma severity category

DISCUSSION

The results of the present study showed that in adult asthmatics of Tunisian population, a higher BMI was associated with worse severity, control and quality of life. To our knowledge, this is the first study to find a concomitant relationship between BMI and asthma severity, control and quality of life.

While the majority of studies support an association between obesity and asthma severity in children, the literature examining obesity and asthma severity in adults remains controversial. In agreement with our results, indicating that obese subjects have more severe asthma than non obese subjects, Taylor et al. (5) found a significant association between the increase of BMI and the worsening of asthma severity in 3,095 asthmatics. Contrarily, other studies have failed to demonstrate such association between obesity and asthma severity (7, 8). In a study similar to the present investigation, 200 adult asthmatic patients were evaluated (7). The authors found no correlation between obesity and asthma severity (7). Similarly, Lavoie et al. (8) demonstrated no relationship between BMI and asthma severity. Certain differences between our study and that of those authors (7,8) can partially be explained as follows: the prevalence of obesity among asthmatics (8) was lower than that observed in our study (25% vs 30%) whereas the prevalence of smoking (7) was greater (35% vs 21.5%).

The present study revealed significant sex differences in the relationship between BMI and asthma severity which is consistent with the results of other studies (8-11). Thus, in these studies, when the group of asthmatics was divided according to gender, this association was found among women but not among men. On the contrary, Lavoie (8) observed no sex difference in the relationship between BMI and asthma severity. This finding is consistent with the results of many studies (8, 12- 16).

Previous studies had reported that obesity worsens asthma control. Lavoie (8) in his study on 382 adults found that patients with higher BMI scored higher in asthma control questionnaire (ACQ) independent of their age and sex. Our study approved this finding, and found similar correlations in terms of medication use, risk of hospitalization, emergency visits related to asthma exacerbation and missed work days. But, Clerisme- Beaty et al. (17), using 4 validated asthma control questionnaires among 292 adult asthmatics failed to find an association between obesity and asthma control.

The association between obesity and asthma control has been demonstrated to be independent of the asthma severity (8, 18). Lessard et al. found that obese people with asthma had poorer asthma control than non obese asthmatics with the same degree of bronchoconstriction (15).

The relationship between obesity and asthma related quality of life is controversial. Similar to our results, Mosen et al. (19) in their study on 1,113 asthmatics found that obesity is associated with worse asthma related quality of life independent of sex. Contrarily, Lavoie study is the only one to report that men experience a sharper decline in asthma-related quality of life compared to women with increasing BMI (8). They explain this finding by the fact that the loss of functional capacity with increasing BMI may have greater meaning for men than women.

Although a number of studies have demonstrated a significant association between obesity and asthma severity, control and quality of life, the mechanism still remains unclear. Many studies, based on the blood level of C-reactive protein and leptin, which are two inflammatory markers, had reported that the systemic inflammation state in obese asthmatics is a plausible mechanism that could explain the relationship between asthma and obesity. Thus, in agreement with our results indicating a positive correlation between the blood level of CRP and leptin and the BMI. Considine et al. (20) found a significant association between BMI and blood level of leptin. Guler et al. (21) showed that the blood level of leptin was correlated with asthma severity.

In the present study, we found that leptin and CRP levels were higher among obese subjects particularly in women which was in accord with other studies (22). This finding could explain the sex differences in the relationship between obesity and asthma revealed in our study and in many other researches.

In summary, it appears that obesity is significantly associated with a greater asthma severity and poorer asthma control and quality of life. Chronic systemic inflammation state may explain the relationship between

obesity and asthma. Dietary modification and weight loss must be considered for overweight and obese asthmatics because it may help to achieve a better health status and improve asthma related quality of life.

REFERENCES

1. Prévalence de l'asthme dans les pays du Maghreb : étude AIRMAG. *Rev Mal Resp* 2009; 26:33.
2. Xème congrès maghrébin Tunis 2006. Profil épidémiologique et clinique de l'obésité en Tunisie. Pr Samira Blouza institut national de nutrition de Tunis. Available from <http://www.stmi.org.tn>
3. Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992; 47 (2): 76- 83.
4. Elamin EM. Asthma and obesity: a real connection or a casual association? *Chest* 2004; 125 (6): 1972- 4.
5. 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 (1): 14- 20.
6. Thèse de doctorat en médecine. Dr Cherif Rahma. Conception et validation d'un questionnaire d'altération de la qualité de vie dans l'asthme en Tunisie (AQVAT). Faculté de Médecine de Tunis, 2 /7/2007.
7. Pelegrino NR, Faganello MM, Sanchez FF, Padovani CR, Godoy I. Relationship between body mass index and asthma severity in adults. *J Bras Pneumol* 2007; 33 (6): 641- 6.
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 (4): 648- 57.
9. Chen Y, Dales R, Tang M, et al. Obesity may increase the incidence of asthma in women but not in men: longitudinal observations from the Canadian National Population Health Surveys. *Am J Epidemiol* 2002; 155:191-7.
10. Tantisira KG, Weiss ST. Complex interactions in complex traits: obesity and asthma. *Thorax* 2001; 56 Suppl 2: ii64- 73.
11. Loerbroks A, Apfelbacher CJ, Amelang M, Stürmer T. Obesity and adult asthma: potential effect modification by gender, but not by hay fever. *Ann Epidemiol* 2008; 18 (4): 283- 9.
12. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999; 14 (4): 902- 7.
13. Chanez P, Varin P, Bourdin A et al. Body mass index (BMI) discriminates patients with severe asthma. *Proc Am Thorac Soc* 2006; 3: A790.
14. Dixon AE, Shade DM, Cohen RI, Skloot GS, Holbrook JT, Smith LJ, et al. Effect of obesity on clinical presentation and response to treatment in asthma. *J Asthma* 2006; 43 (7): 553- 8.
15. Lessard A, Turcotte H, Cormier Y, Boulet LP. Obesity and asthma: a specific phenotype? *Chest* 2008; 134 (2): 317- 23.
16. de Marco R, Marcon A, Jarvis D, Accordini S, Almar E, Bugiani M, et al. Prognostic factors of asthma severity: a 9-year international prospective cohort study. *J Allergy Clin Immunol* 2006; 117 (6): 1249- 56.
17. Clerisme-Beaty EM, Karam S, Rand C, Patino CM, Bilderback A, Riekert KA, et al. Does higher body mass index contribute to worse asthma control in an urban population? *J Allergy Clin Immunol* 2009; 124 (2): 207- 12.
18. Saint-Pierre P, Bourdin A, Chanez P, Daures JP, Godard P. Are overweight asthmatics more difficult to control? *Allergy* 2006; 61 (1): 79- 84.
19. Mosen DM, Schatz M, Magid DJ, Camargo CA Jr. The relationship between obesity and asthma severity and control in adults. *J Allergy Clin Immunol* 2008; 122 (3): 507- 11.e6.
20. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 1996; 334 (5): 292- 5.
21. Guler N, Kirerleri E, Ones U, Tamay Z, Salmayenli N, Darendeliler F. Leptin: does it have any role in childhood asthma? *J Allergy Clin Immunol* 2004; 114 (2): 254- 9.
22. Kim S, Camargo CA Jr. Sex-race differences in the relationship between obesity and asthma: the behavioral risk factor surveillance system, 2000. *Ann Epidemiol* 2003; 13 (10): 666- 73.