ORIGINAL ARTICLE

Asthma Diagnosis Is Not Associated With Obesity in a Population of Adults From Madrid

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Abstract

Background: Several studies have suggested a relationship between asthma and obesity; however, this relationship is unclear when obesity is compared with bronchial hyperresponsiveness to methacholine.
Aim: To determine whether obesity is associated with a diagnosis of asthma.
Methods: We conducted a cross-sectional study in a population of Spanish adults in the north of Madrid, Spain between 2003 and 2007. The patients included had experienced asthma symptoms during the previous year, but had a ratio of forced expiratory volume in the first second of expiration (FEV_1) to forced vital capacity (FVC) of >70%. Diagnosis was confirmed by the presence of symptoms and demonstration of bronchial hyperresponsiveness to methacholine. Obesity was measured by body mass index (BMI). Adjusted odd ratios (OR) were obtained by logistic regression.
Results: Of a total of 1424 patients included, 251 (17.6%) were diagnosed with asthma. These patients were younger (P<.001) and had lower BMI (P<.001) and lung function parameters (FEV_1 and FEV1/FVC ratio) than individuals without asthma (P<.001). After adjusting the model for age, gender, baseline FEV_1, and FEV_1/FVC ratio, patients with overweight or obesity were not more frequently diagnosed with asthma than those with normal weight (OR, 0.848 [95% confidence interval (CI), 0.59-1.20]; and OR, 0.616 [95% CI, 0.38-0.99], respectively). In addition, obese males were more frequently diagnosed with asthma than obese females (P<.041).
Conclusions: In this study, obesity and overweight were not associated with a diagnosis of asthma based on the presence of consistent symptoms and demonstration of airway responsiveness to methacholine.

Key words: Asthma. Obesity. Body mass index. Airway hyperresponsiveness.

Resumen

Fundamento: Varios estudios sugieren que la obesidad es un factor de riesgo para padecer asma, lo que no siempre se confirma cuando se compara la obesidad con la hiperreactividad bronquial (HRB) en pacientes con síntomas de asma.
Objetivo: Determinar si la obesidad se asocia con el diagnóstico de asma, confirmado por presencia de síntomas e HRB a metacolina.
Pacientes y Métodos: Se realizó un estudio transversal en población adulta del Área Norte de Madrid entre 2003 y 2007. Se incluyeron sujetos que habían padecido síntomas de asma en el último año, con un FEV_1/FVC>70% y que precisaban una prueba de metacolina para confirmar el diagnóstico. La obesidad se definió según el índice de masa corporal (IMC). Se aplicó un modelo de regresión logística para calcular odd ratios (OR) ajustadas.
Resultados: Se estudiaron 1.424 sujetos y se diagnosticaron de asma 251 sujetos (17,6%) que, comparados con los 1.173 no diagnosticados de asma, eran más jóvenes y presentaban un IMC y parámetros de función pulmonar (FEV_1, FEV_1/FVC) más bajos (p<0,001). Tras ajustar el modelo por edad, sexo, FEV_1 basal y FEV_1/FVC el diagnóstico de asma no fue más prevalente en los sujetos obesos o con sobrepeso que en los sujetos con peso normal (OR 0,848, IC95% 0,59-1,20 y OR 0,616, IC95% 0,38-0,99, respectivamente). El diagnóstico de asma fue más frecuente en hombres obesos que en mujeres obesas (p=0,041).
Conclusiones: La obesidad y el sobrepeso no se asociaron con el diagnóstico de asma establecido por la presencia de síntomas e HRB a metacolina.

Palabras clave: Asma. Obesidad. Índice de masa corporal. Hiperreactividad bronquial.

Introduction

Asthma and obesity are common disorders with an enormous impact on public health. It has been estimated that up to 65% of the adult population of the United States of America is obese or overweight [1], while in Spain about 15% of the population is obese and 39% is overweight [2]. These figures have increased progressively in recent years. Although bronchial asthma affects a smaller proportion of people, its prevalence has also increased in the last few decades. According to the Centers for Disease Control and Prevention, the prevalence of asthma in North American children increased from 3.6% in 1980 to 5.8% in 2003 [3]. In Spain, the prevalence of asthma increased by 0.26% per year from 1991 to 2001 [4].

Epidemiological data have led some researchers to suggest that obesity is a risk factor for the development of new-onset asthma, with odds ratios (OR) of between 1.1 and 3.0—when comparing the highest body mass index (BMI) with the lowest BMI categories—and the effect is apparently stronger in women [5]. A meta-analysis investigating overweight and obesity as risk factors for incidental asthma showed that both conditions progressively increased the odds of incident asthma and that the strength of this relationship was similar in men and women [6].

The exact nature of this association has not been fully elucidated, and methodological issues such as determining who has asthma compared with who has symptoms that mimic asthma hamper many studies [3]. However, mechanical factors or aspects of systemic inflammation related to obesity may contribute to the pathogenesis of asthma [2,7,8]. Simple obesity can cause an increase in airway resistance and a mild degree of airflow limitation [9]. Therefore, establishing a firm diagnosis of asthma in obese patients with or without airflow limitations would require confirmation by an objective procedure, such as measurement of airway hyperresponsiveness. We report the results of a cross-sectional study of a population of adults from the north of Madrid, Spain who were investigated for suspected asthma between 2003 and 2007. The aim of this study was to determine whether obesity, measured by BMI, is associated with a diagnosis of asthma, as established by the presence of symptoms and demonstration of airway responsiveness to methacholine.

Methods

Study Population

Patients were consecutively recruited from outpatient asthma clinics at the Allergy and Pulmonology Departments of La Paz Hospital, Madrid between 2003 and 2007. All patients were adults who, according to their allergist or pulmonologist, had presented with symptoms suggestive of asthma (cough, shortness of breath, or wheezing) in the last year, with a ratio of forced expiratory volume in the first second of expiration (FEV_1) to forced vital capacity (FVC) of >70%, and in whom it was necessary to establish the diagnosis of asthma by measuring airway hyperresponsiveness (AHR) to methacholine. Patients with contraindications for methacholine challenge testing as outlined in the American Thoracic Society (ATS) guidelines [10] were excluded.

All patients gave their written informed consent, and the study was approved by the Ethics Subcommittee of the Research Committee of Hospital Universitario La Paz, Madrid, Spain (code: HULP:PI-619).

Variables

The variables studied were age, gender, smoking status, height (m), weight (kg), BMI, and lung function (FVC, FEV_1, and FEV_1/FVC), which was measured immediately before the methacholine challenge test. The results of the methacholine challenge test were considered positive or negative.

Definitions

Asthma: Asthma was defined as a categorical dichotomous variable based on the presence of both consistent symptoms in the previous 12 months and a demonstration of AHR to methacholine.

Obesity: The weight and height of each patient were measured in street clothes without shoes immediately before performing the methacholine challenge test. BMI (kg/m^2) was calculated for each patient and categorized as follows: normal weight, BMI <25 kg/m^2; overweight, BMI 25.0-29.9 kg/m^2; and obese, BMI ≥30 kg/m^2.

Spirometry and Methacholine Challenge Test

Spirometry was performed according to ATS recommendations [11].

Methacholine challenge tests were performed in both departments of the hospital according to current guidelines [10], and the spirometric reference values used were those reported by the European Community of Coal and Steel and the European Respiratory Society in 1993 [12]. The methacholine challenge test was performed according to ATS recommendations following the 5-breath dosimeter protocol [10]. In the Allergy Department, testing was conducted using an electronic dosimeter (Spira Elektro, Respiratory Care Centre, Hameelinna, Finland), with an output of 0.45 µL and a nebulization time of 0.6 seconds, and the provocative concentration causing a 20% drop in FEV_1 (PC_{20}) was calculated. In the Pulmonology Department, testing was performed using a bronchial aerosol provocation system (APS, Jaeger, Würzburg, Germany), with a Medic-Aid SideStream nebulizer (Medic-Aid Ltd, Bognor Regis, UK), and the provocative dose causing a 20% drop in FEV_1 (PD_{20}) was calculated. This nebulizer was calibrated to produce an output of 160 mg/mL with an airflow rate of 100 mL/s. A flow sensor in the expiratory port triggers a solenoid that exposes the nebulizer to compressed air at 138 kPa for about 0.6 seconds to give a calibrated output per puff of 9.0 µL. The nebulizer generates heterodisperse droplets with a median aerodynamic mass diameter of 0.5 to 4 µm. AHR was considered positive or present if there was a ≥20% fall in FEV_1 from baseline with a PD_{20} ≥2.0 mg (9.9 µmol) of methacholine [13] or PC_{20} (5-breath dosing) of ≤16 mg/mL of methacholine [10].

Statistical Analysis

Data are expressed as mean (SD) and percentages. Univariate relationships between dependent and independent variables were explored using the *t* test. One-way analysis of variance was used to compare normally distributed variables, the Wilcoxon rank sum test for skewed variables, and the χ^2 test for categorical variables. Univariate and multivariate conditional logistic regression models were constructed to determine the odds of having asthma in different BMI categories after adjusting for the other variables. For all analyses, a 2-tailed $P<.05$ was considered significant. All analyses were performed with the SAS statistical software package, version 9.1.3 (SAS Institute, Cary, North Carolina, USA).

Results

Study Population

We included 1424 patients, of whom 981 (86.9%) were from the Pulmonology Department and 443 (31.1%) were from the Allergy Department. Mean BMI was 25.96 kg/m^2 (SD, 4.94). Normal weight was recorded in 666 patients (46.7%), overweight in 481 (33.8%), and obesity in 277 (19.5%).

Asthma was diagnosed in 251 patients (17.6%). The results of a univariate analysis according to asthma diagnosis are shown in Table 1. Asthma patients were younger and had a

Table 1. Baseline Characteristics

	No. Asthma	Asthma	Total	*P* Value
Patients, n	1173	251	1424	
Age, y, mean (SD)	41.96 (16.94)	33.96 (14.67)	40.55 (16.83)	<.001[a]
BMI, kg/m^2, mean (SD)	26.27 (5.01)	24.48 (4.27)	25.96 (4.94)	.001[a]
Gender, n (%)				.549[b]
Male	364 (81.4)	83 (18.6)	447	
Female	809 (82.8)	168 (17.2)	977	
Smoking status, n (%)				.625[b]
Nonsmoker	810 (83.6)	159 (16.4)	969	
Current smoker	184 (82.1)	40 (17.9)	224	
Ex-smoker	139 (80.8)	33 (19.2)	172	
FVC, L, mean (SD)	3.800 (1.142)	4.229 (3.406)	3.875 (1.773)	.156[a]
FEV_1, L, mean (SD)	3.274 (.986)	3.321 (.850)	3.283 (.963)	.440[a]
FEV_1, % predicted, mean (SD)	86.48 (9.66)	82.88 (11.16)	85.84 (10.03)	<.001[a]
FEV_1/FVC, mean (SD)	0.867 (.115)	0.829 (.111)	0.860 (.112)	<.001[a]

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in the first second of expiration; FVC, forced vital capacity.
[a]*t* test.
[b]χ^2 test.

Table 2. Association Between Body Mass Index and Asthma Diagnosis (Symptoms and Bronchial Hyperresponsiveness)

BMI category	Asthma[a] No. (%)	No asthma No. (%)	Total No. (%)	OR (95% CI)	Adjusted OR (95% CI)[b]
Normal weight, BMI<25 kg/m^2	125 (22.7%)	515 (77.3%)	666 (46.8%)		
Overweight, BMI 25-29.9 kg/m^2	72 (15%)	409 (85%)	481 (33.8%)	0.6 (0.44-0.82)	0.848 (0.59-1.20)
Obese, BMI ≥30 kg/m^2	28 (10.1%)	249 (89.9%)	277 (19.4%)	0.3841 (0.25-0.59)	0.616 (0.38-0.99)
All BMI categories	251 (17.6%)	1173 (82.4%)	1424 (100%)		

Abbreviations: BMI, body mass index; CI, confidence interval; FEV_1, forced expiratory volume in the first second of expiration; FVC, forced vital capacity; OR, odds ratio; PC_{20}, provocative concentration causing a 20% drop in FEV_1; PD_{20}, provocative dose causing a 20% drop in FEV_1.
[a]Geometric mean: PC_{20}, 3.58 mg/mL; PD_{20}, 0.77 mg.
[b]Model adjusted for age, sex, FEV_1, and FEV_1/FVC at baseline.

lower BMI than those without asthma (P<.001). No significant differences were observed in smoking status according to asthma diagnosis. Lung function spirometric parameters (FEV_1 as percent predicted and FEV_1/FVC ratio) were significantly lower in asthma patients than in those without asthma (Table 1).

Relation of Asthma to Body Mass Index

The distribution of patients with confirmed asthma is shown in Table 2. After adjustment for age, gender, baseline FEV_1, and FEV_1/FVC ratio, patients with overweight or obesity were not more frequently diagnosed with asthma than those with normal weight (OR, 0.848 [95% confidence interval (CI), 0.59-1.20]; and OR, 0.616 [95% CI, 0.38-0.99], respectively).

Effects of Other Variables

A multivariate analysis of gender distribution (Table 3) for patients classified according to BMI and asthma showed that obese males were more frequently diagnosed with asthma than obese females (P=.041). Smoking data (Table 4) revealed no significant differences. Increasing BMI had no significant

Table 3. Gender Classified According to Body Mass Index and Asthma

BMI Category	Asthma No. (%)	No Asthma No. (%)	Total No. (%)	*P* Value
Normal weight				.176[a]
Male	34 (18.9%)	146 (81.1%)	180 (27%)	
Female	117 (24.1%)	369 (75.9%)	486 (73%)	
Total	151	515	666	
Overweight				.051
Male	37 (19%)	158 (81%)	195 (40.5%)	
Female	35 (12.2%)	251 (87.8%)	286 (59.5%)	
Total	72	409	481	
Obese				.041
Male	12 (17%)	60 (83%)	72 (26%)	
Female	16 (7.8%)	189 (92.2%)	205 (74%)	
Total	28	249	277	
All patients	251	1173	1424	

[a]χ^2 test.

Table 4. Smoking Status Classified According to Body Mass Index and Asthma

BMI Category	Asthma No. (%)	No Asthma No. (%)	Total No. (%)	*P* Value
Normal weight				.731[a]
Nonsmoker	99 (22.6)	340 (77.4)	439 (69.5)	
Current smoker	26 (20.2)	103 (79.8)	129 (20.4)	
Ex-smoker	16 (25)	48 (75)	64 (10.1)	
Total	141 (22.3)	491 (77.7)	632	
Overweight				.700
Nonsmoker	42 (13.5)	270 (86.5)	312 (67.7)	
Current smoker	10 (14.9)	57 (85.1)	67 (14.5)	
Ex-smoker	14 (17.1)	68 (82.9)	82 (17.8)	
Total	66 (14.3)	395 (85.7)	461	
Obese				.530
Nonsmoker	18 (8.3)	200 (91.7)	218 (80.1)	
Current smoker	4 (14.3)	24 (85.7)	28 (10.3)	
Ex-smoker	3 (11.5%)	23 (88.5)	26 (9.6)	
Total	25 (9.2)	247 (90.8)	272	
All patients	232	1133	1365	

[a]χ^2 test.

Table 5. FEV_1, FEV_1, and FEV_1/FVC Data of Asthma Patients Classified According to BMI[a]

	Normal Weight No. (%)	Overweight No. (%)	Obese No. (%)	*P* Value[b]
FEV_1, L	3.33 (0.791)	3.38 (0.100)	3.10 (0.719)	.32
FEV_1, % predicted	83.7 (11)	81.01 (9.6)	83 (14.3)	.23
FEV_1/FVC	0.83 (0.11)	0.81 (0.96)	0.83 (14)	.23

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in the first second of expiration; FVC, forced vital capacity.
[a]Results expressed as mean (SD).
[b]Analysis of variance.

effect on spirometric results (FEV_1, FEV_1/FVC ratio) in asthma patients (Table 5).

Discussion

We found that obesity and overweight, defined as a BMI of ≥30 kg/m^2 and 25-29.9 kg/m^2, respectively, were not associated with a higher prevalence of confirmed asthma diagnosis in a population of adults from Madrid. Similar results were found in another Spanish study [14]. The distribution of BMI in this sample was similar to the distribution in the general population of Spain [2].

Although obesity has been associated with severe asthma [15], the results of the Severe Asthma Research Program [16], did not find obesity to be more prevalent in severe asthma than in milder asthma; therefore, further studies are necessary in this area.

The population we describe had an FEV_1/FVC ratio >70% and similar characteristics to those of the population reported in the main articles [17-19] on the association between excess weight and AHR in patients with symptoms of asthma.

In the European Community Respiratory Health Survey, AHR increased with BMI in men but not in women [17]. In a case-control study from participants in the Normative Aging Study, a high initial BMI was associated with the development of AHR to methacholine (OR, 10; 95% CI, 2-6-37.9) when patients in the highest BMI quintile were compared with those in the middle quintile. There was also a linear relationship between increasing BMI during the study period and subsequent development of AHR [18].

In contrast, Schachter et al [19] showed that, in a group of 1971 adults, BMI was associated with asthma symptoms (dyspnea and wheezing) but not with airflow obstruction or AHR. Tantisira et al [20] showed similar results in a pediatric population.

Changes in anatomical and respiratory function could cause increased symptoms of cough, shortness of breath, and wheezing without altering airway behavior. Sutherland et al [21] studied 30 obese and nonobese adult women with asthma and observed that changes in respiratory function, especially dynamic hyperinflation, were more pronounced in obese individuals with bronchoconstriction; however, BMI was independently associated with changes in lung volume and AHR. In our study, no significant effects of increasing BMI on spirometric results were observed in asthma patients. Salome et al [22] studied the effect on breathlessness and AHR to methacholine in 49 nonasthmatic patients (23 obese and 26 nonobese) aged between 18 and 70 years. The authors found that obesity reduced lung volume, but did not alter the sensitivity of or maximal response to methacholine. However, obese patients had an enhanced perception of dyspnea—associated with greater apparent stiffness of the respiratory system—and may therefore be at greater risk of symptoms. Similar results were encountered by Machado et al [23]. In addition, simulated obesity-related changes in lung volume increased airway responsiveness in lean nonasthmatic patients [24].

Some prospective studies have suggested that the relationship between obesity and asthma is stronger in women [25]; however, the difference in estimates of effect between men and women is usually small. In a random-effects meta-analysis of data from 7 studies, a similar increase in the odds of incident asthma due to overweight and obesity was observed in men (OR, 1.46; 95% CI, 1.05-2.02) and women (OR, 1.68; 95% CI, 1.45-1-94) [6]. In the present study, a diagnosis of asthma was more common in obese men than obese women classified according to BMI.

The cause of bronchial inflammation in obese patients with asthma appears to be different from that of atopy [8,24]. It is now well established that obesity is characterized by a state of chronic low-grade systemic inflammation. Adipose tissue secretes important regulatory adipokines such as leptin, a proinflammatory adipokine, and adiponectin, which has anti-inflammatory properties [8]. It has been suggested that leptin may contribute to the increased prevalence of asthma observed among obese persons [8]; however, recent studies indicate that the association between obesity and asthma is unlikely to be due to a direct effect of leptin on airway smooth muscle [26].

In the present study, a diagnosis of asthma was confirmed in 17.6% of patients based on symptoms of cough, shortness of breath, or wheezing. Aaron et al [27] found that about one-third of obese and nonobese individuals with physician-diagnosed asthma did not have asthma when objectively assessed. Therefore, asthma may be overdiagnosed in developed countries. Moreover, if symptoms in this group are due to causes unrelated to asthma, then asthma medication would be unlikely to affect their symptoms. In fact, symptoms alone do not appear to be a good guide for the diagnosis and treatment of asthma.

In conclusion, although our study is subject to the limitations of cross-sectional studies, obesity was not associated with asthma in a population of adults from the north of Madrid.

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