

# Clinical impact of obesity on respiratory diseases: A real-life study

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## ABSTRACT

**Background:** Obesity has become an epidemic that affects Mexico; significantly interferes with respiratory physiology by decreasing lung volumes, therefore, might be considered as a relevant risk factor associated with the development of respiratory diseases. **Objective:** Our primary outcome was to analyze the frequency and risk factors between obesity and respiratory disease in the Mexican population. **Materials and Methods:** An observational, single-center, descriptive study, which included the totality of patients who were referred for medical attention at the Respiratory and Thorax Surgery Unit at the Hospital Regional de Alta Especialidad de la Península de Yucatán during the period from January 2015 to December 2018. The cases were grouped based on the existence or not of respiratory disease and the presence or absence of obesity (body mass index [BMI] >30 kg/m<sup>2</sup>). **Results:** A total of 1167 patients were included; about 39% of the population had average BMI 36.5 kg/m<sup>2</sup>. The primary respiratory diseases in obese patients were Obstructive Sleep Apnea Syndrome (OSAS, 19%) and asthma (15%). The logistic regression analysis showed a direct association between the presence of obesity with respiratory disease (odds ratio 1.58, 95% confidence interval 1.22–2.03,  $P < 0.001$ ), the strength of this association was related with asthma and OSAS. **Conclusion:** The presence of obesity is an independent risk factor for respiratory disease, primarily for OSAS and asthma.

**KEY WORDS:** Asthma, lung function, obesity, obstructive sleep apnea syndrome, respiratory disease

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## INTRODUCTION

According to the World Health Organization (WHO), we are facing the most serious obesity epidemic unprecedented. The majority of the population reside in countries where overweight and obesity take more lives than underweight.<sup>[1,2]</sup> According to the WHO data, Mexico is the second country in the world with the highest number of obese people, since it comprises >70% of the population.<sup>[1,3]</sup> In Yucatan, the prevalence of obesity has increased considerably in the past

6 years, reaching 40.6% in men and 22.2% in women.<sup>[4,5]</sup> These epidemiological changes have led to several phenotypes of expression and etiology of obesity-related diseases than previously known, suggesting a reanalysis in several areas including the impact of obesity on lung disease.<sup>[6]</sup>

So far, the excess of adipose tissue have showed to generate changes in the intestinal microbiome, cellular metabolism,

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immune function, lipid metabolism, and insulin resistance among others; together, they establish a proinflammatory state that has been linked to the development of pulmonary and systemic diseases and leads to a deterioration of the pulmonary immune response, altering the onset and progression of respiratory diseases.<sup>[7,8]</sup>

Obesity is considered an independent risk factor for the development or greater number of complications of different respiratory diseases. Among the main causes of death from respiratory disease in 2015 in Mexico, multiple have a close association with obesity and the same could be said of the main causes of death in the world.<sup>[9-11]</sup> It is clear that facing the obesity epidemic, it is necessary to analyze the presentation in populations of regions with greater obesity/disease interaction. Thus, the purpose of this study is to describe the frequency of association between obesity and cases treated with respiratory diseases in a third-level reference center in Mexico.

## MATERIALS AND METHODS

This is an observational, single-center, descriptive study that included all adult patients >18-year-old referred to the Respiratory and Thoracic Surgery Unit at the Hospital Regional de Alta Especialidad de la Península de Yucatán (HRAEPY) during the period January 2015–December 2018. Due to the retrospective nature of the study, it was not necessary to generate an informed consent letter. However, at all times confidentiality was preserved according to the Declaration of Helsinki;<sup>[12]</sup> moreover, to increase the security of the information, the data were recorded in a spreadsheet with access coded on the computer of the principal investigator. Number of ethics committee approval 2018-028.

HRAEPY is a third-level reference center, which primarily evaluate patients without social security and has the capacity for systematic diagnostic approach of respiratory disorders, which in addition to patient care carries out undergraduate and postgraduate teaching and research laboratories.

### Patients

All the medical files of patients over 18 years old who attended the outpatient clinic during the period previously indicated were included in the study. Only the data from the first evaluation were considered.

The following variables were systematically obtained: age, gender, height, body mass index (BMI), and vital signs: blood pressure (systolic/diastolic), heart rate, respiratory rate, temperature, and oxygen saturation (pulse oximetry). Each diagnosis was established according to current standards. For example, the diagnosis of asthma was established by meeting each requirement outlined by the Global Initiative for Asthma, chronic obstructive pulmonary disease (COPD) meeting the requirements of global strategy for the diagnosis, management, and prevention of COPD.<sup>[13,14]</sup>

The cases were grouped based on the existence of a confirmed respiratory disease at the end of the systematic evaluation. The following diagnoses were included: asthma, COPD, pulmonary hypertension, Obstructive Sleep Apnea Syndrome (OSAS), diffuse interstitial lung disease, lung infections (including sequelae of pneumonia or tuberculosis), pleural disease, bronchiectasis, and cancer (primary lung and metastatic to lung). Likewise, all patients who were evaluated in the study period were classified based on the BMI in two groups: cases with defined obesity with a BMI >30 kg/m<sup>2</sup> and cases without obesity BMI <30 kg/m<sup>2</sup>.

### Statistical analysis

Continuous variables are described as means with standard deviation (SD), on the other hand, categorical variables as frequencies with percentages. Comparisons were done according to the nature of variables, among categorical variables using Chi-square test; meanwhile, continuous variables through *t*-test for independent groups.

We used logistic regression models to know the association between the primary variable of the study (obesity) with the existence of the respiratory disease, all the associated factors that showed a *P* < 0.1 were significantly incorporated into a multivariate analysis. The results are expressed as odds ratio (OR) with their respective 95% confidence intervals (CIs). A two-sided *P* < 0.05 was considered statistically significant. All analyses underwent with STATA version 13 (Statacorp, College Station, Texas, USA).

## RESULTS

This report includes a total of 1,167 patients who were evaluated during the study period; the mean age was 51-year-old (SD ± 14) and 70% were women. Thirty-nine percent of the population were obese (BMI ≥30 kg/m<sup>2</sup>), with a mean BMI of 36.5 kg/m<sup>2</sup> (SD ± 7.6) and 21% classified as Grade 3 Obesity (BMI ≥40 kg/m<sup>2</sup>). The waist and hip measurements were 108 cm and 117 cm, respectively. The overall description of the population is detailed in Table 1. Among previous medical conditions, patients with obesity were more prevalent in high blood pressure (18% vs. 8%), gastrointestinal disorders (5% vs. 2%), and chronic rhinosinusitis disease (5% vs. 1.2%). The majority of patients with a respiratory disorder in Yucatan came from the Northwest region and 38% of the cases have obesity Grade III; in frequency, the Southern region followed, of which 26% had Grade III obesity [Table 1].

### Causes of respiratory evaluation

Among patients with obesity, the main respiratory illness was OSAS (19%) and asthma (15%). On the other hand, in patients without obesity, the most frequent cause of care was diffuse interstitial disease (19%) followed by cancer (7.5%). Other respiratory diseases are listed in Table 2. In the group of patients who complaint about respiratory symptoms, however, not related to a

**Table 1: General characteristics of the study population (n=1167)**

Variable	Obese patients (n=453), n (%)	Nonobese patients (n=714), n (%)	P
Age (years)	51 (14)	53 (18)	0.013
Female sex	316 (70)	380 (54)	<0.001
Yucatán geographic area			
West	3	7	0.025
Northwest	49	47	
Center	6	6	
Downtown coastline	5	6	
Northeast	5	7	
East	8	11	
South	23	16	
Morbidities			
Diabetes mellitus 2	45 (10)	65 (9)	0.636
Hypertension	81 (18)	55 (8)	<0.001
Cardiovascular disease	13 (3)	23 (3)	0.732
Renal disease	2 (0.5)	7 (1)	0.305
Gastrointestinal disease	21 (5)	16 (2)	0.038
Rheumatological disease	21 (5)	45 (6)	0.568
Neuromuscular disease	2 (0.5)	11 (1.5)	0.081
Rhinosinusitis disease	22 (5)	9 (1.2)	<0.001
Anthropometry			
Weight (kg)	84 (25)	58 (11)	<0.001
Height (m)	1.51 (0.11)	1.53 (0.11)	0.001
BMI (kg/m <sup>2</sup> )	36.5 (7.6)	24.6 (3.6)	
3034.9	266 (59)	N/A	<0.001
3539.9	92 (20)	N/A	
≥40	95 (21)	N/A	
Neck perimeter (cm)	40 (4.8)	N/A	
Waist (cm)	108 (18)	N/A	
Hip (cm)	117 (16)	N/A	
Waist-to-hip ratio	0.93 (0.09)	N/A	
Systolic BP	119 (16)	112 (17)	<0.001
Diastolic BP	76 (11)	70 (10)	<0.001
Heart rate	81 (14)	84 (17)	0.008
Respiratory rate	20 (3)	20 (7)	0.675
Oxygen saturation	96 (3)	96 (3)	0.886

The results are presented as mean with SD and frequencies with percentages. BMI: Body mass index, BP: Blood pressure, SD: Standard deviation, N/A: Not available

specific lung disease, they have gastroesophageal reflux disease, postinfectious cough, rhinosinusitis disease, or were evaluated prior to surgery. Some were defined as healthy [Table 2].

### Distribution of respiratory diseases based on obesity grade

Asthma and OSAS patients were more prevalent as degree of obesity increased. Moreover, 17% of patients with asthma and 42% of patients with OSAS were obese Grade III [Table 3].

Finally, the logistic regression analysis showed that the presence of obesity was associated as a risk factor for a respiratory disease (OR 1.58, 95% CI 1.22–2.03,  $P < 0.001$ ), in particular with asthma and OSAS; on the other hand, patients who have cancer (OR 0.32, 95% CI 0.16–0.61,  $P = 0.001$ ) and diffuse interstitial pneumonia (OR 0.63, 95% CI 0.45–0.87,  $P = 0.006$ ) were more probable to be a nonobese patients. In the multivariate analysis, obesity remained as a strong predictor in cases with asthma and OSAS [Table 4].

## DISCUSSION

It is remarkable that 4 out of 10 patients who were evaluated for a respiratory disorder have some degree of obesity and predominates in female sex. The main association of obesity and respiratory disease was with OSAS and asthma patients. Therefore, obesity should be considered as a risk factor for respiratory disease in the population of the Southeast of Mexico.

In the world, about 1400 million adults are overweight and 500 million obese. According to the health observatory (Global Health Observatory), Mexico is one of the five countries in Latin America with the highest prevalence of overweight and obesity.<sup>[1,3,5]</sup> Mexico's National Health and Nutrition Surveys (ENSANUT) report that the prevalence of overweight and obesity in children and adults has increased in the past three decades, therefore, it is currently one of the two countries with the highest prevalence of obesity in the world. The 2016 analysis allowed to identify that adults older than 20 years of age have a combined frequency of overweight and obesity of 72.5%.<sup>[5]</sup> When categorizing by sex, the prevalence of overweight and obesity was higher in women (75.6% and 38.6%,

**Table 2: Distribution of respiratory disease among the study groups**

Variable	Obese patients (n=453), n (%)	Nonobese patients (n=714), n (%)	P
<b>Respiratory disease</b>			
Asthma	69 (15)	44 (6)	<0.001
Bronchiectasis	7 (1.5)	22 (3)	0.102
Oncological disorders	11 (2.5)	52 (7.5)	<0.001
Pleural disease	16 (3.5)	36 (5)	0.223
COPD	32 (7)	56 (8)	0.623
Pulmonary hypertension	11 (2.5)	27 (4)	0.204
History of pneumonia/TBP	18 (4)	36 (5)	0.397
GERD rhinitis	32 (7)	59 (8)	0.536
Neuromuscular disorders	7 (1.5)	30 (4)	0.012
Diffuse interstitial pneumonia	59 (13)	138 (19)	0.005
OSAS	89 (19.5)	15 (2)	<0.001
Healthy patients	4 (1)	11 (1.5)	0.376
Respiratory symptoms without specific disease	35 (8)	40 (5.5)	0.207
Preoperative pulmonary Evaluation	6 (1.5)	19 (2.5)	0.457
Solitary pulmonary nodule	8 (2)	8 (1)	0.226

The data are presented as frequencies with percentages. COPD: Chronic obstructive disease, GERD: Gastroesophageal reflux disease, TBP: Pulmonary tuberculosis, OSAS: Obstructive sleep apnea syndrome

**Table 3: Distribution of the main respiratory diseases based on the degree of obesity**

VARIABLES	Obesity Grade I (n=266), n (%)	Obesity Grade II (n=92), n (%)	Obesity Grade III (n=95), n (%)	P
Asthma	24 (9)	29 (32)	16 (17)	0.005
COPD	25 (9.5)	6 (6.5)	1 (1)	0.479
Respiratory symptoms without specific disease	23 (8.5)	4 (4.5)	6 (6)	0.814
Interstitial lung disease	41 (15.5)	9 (10)	9 (9.5)	0.576
Pulmonary hypertension	7 (2.5)	1 (1)	7 (2.5)	0.966
OSAS	31 (11.5)	8 (8.5)	40 (42)	<0.001

The data are presented as frequencies with percentages. COPD: Chronic obstructive disease, OSAS: Obstructive sleep apnea syndrome

**Table 4: Logistic regression analysis between obesity and respiratory disease**

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Respiratory disease (overall)	1.58	1.22–2.03	<0.001			
Asthma	2.75	1.84–4.10	<0.001	3.23	2.16–4.84	<0.001
OSAS	9.89	5.61–17.42	<0.001	10.88	6.15–19.23	<0.001
Diffuse interstitial pneumonia	0.63	0.45–0.87	0.006			
Neuromuscular disorder	0.36	0.16–0.82	0.016			
Respiratory oncology	0.32	0.16–0.61	0.001	0.48	0.22–0.85	0.015

OSAS: Obstructive sleep apnea syndrome, OR: Odds ratio, CI: Confidence interval

respectively); on the other hand, by categorizing according to the degree of obesity, the morbid obesity ratio (BMI  $\geq 40$  kg/m<sup>2</sup>) female: male reaches 2.4:1.<sup>[3,5]</sup> The relevance of our results is because Yucatán has the highest childhood obesity rate in the country (20.5% in the 2012 registry) and among adult population, 8 out of 10 are overweight or obese.<sup>[15]</sup> We identified that 4 out of 10 cases who were evaluated for lung disease had obesity with an average BMI of 36.5 kg/m<sup>2</sup>, that is, Grade II obesity and 70% were women. Within Yucatan, obesity seems higher in the northwest and south geographic area. Although, BMI is an indirect measure of metabolic health, in the respiratory system it compromises the mechanical and pulmonary homeostasis due to the interaction of hormonal, metabolic, inflammatory, neurological, and dietary factors.<sup>[8,10]</sup>

Among the mechanisms that contribute to the development of respiratory symptoms, patients with obesity have a premature closure of the airway with each breath.

Consequently, it has been observed that breathing is more superficial with greater effort and respiratory work that can affect the development of bronchial hyperreactivity.<sup>[16]</sup> Explanations of this functional phenomenon included a decrease in the smooth muscle load of the airway with lower lung volumes allowing an increase in the actin-myosin crosslinking that tends to reduce the patency of the open airway. These lineal changes can be observed with lower expiratory mid-flows at higher BMI. Finally, premature closure of the airway can lead to a significant mismatch between ventilation and perfusion, expressing a greater proportion of hypoxemia and dyspnea.<sup>[17]</sup>

Obesity is identified as an important risk factor for the development of a series of respiratory diseases. Among the best known in the nonLatino population included: asthma, pulmonary hypertension, sleep apnea, obesity hypoventilation syndrome, pneumonia, and acute respiratory distress syndrome.<sup>[18]</sup> Moreover, it has a close



relationship with important imbalances in the pathogenesis of other diseases such as COPD. The results obtained in this report allow us to analyze that obesity conferred an additional risk of 58% for the existence of some respiratory disease in the Latino population of Mexico. In particular, the highest specific association was observed in cases with OSAS (OR 9.89) and asthma (OR 2.75). Possible mechanisms of interaction might include that adipose tissue is an active endocrine organ that produces cytokines and hormones that regulate metabolism and immune responses.<sup>[18,19]</sup> In obesity, there is an imbalance in the production of pro/anti-inflammatory cytokines, the most striking is the decrease in the production of adiponectin.<sup>[19]</sup> Under steady-state conditions, adiponectin negatively regulates the recruitment of eosinophils in the respiratory tract by inhibiting allergic inflammation in the respiratory tract. In the obese, the levels of adiponectin are markedly reduced, consequently, systemic inflammation markers are increased gradually, which affects a greater number of respiratory exacerbations.<sup>[18]</sup>

The relationship between obesity and asthma is one of the most studied and understood, with the participation of “metabolic inflammation.”<sup>[20]</sup> Furthermore, an imbalance between adipokine levels in obesity that could skew the immune response toward a Th-1 phenotype. When contrasting healthy participants, patients with normal weight, and obese asthma, it is observed that there is an association between obesity and Th-1 polarized inflammation that was related to higher levels of inflammatory markers such as leptin and interleukin-6.<sup>[7]</sup>

Among the limitations of the present study, we can point out the retrospective nature, without measurements of biomarkers and cytokines associated with obesity. In the same way, the recruitment of the patients was carried out in a single reference center, however, all the patients referred to the clinic were analyzed, and the evaluation was deepened in the search for some respiratory disorders were research is detailed and carried out by experts so precision is expected in the final diagnosis. It highlights the relevance of obesity in relation to respiratory diseases, which results in several important conclusions, both from the point of view of care and teaching. Physicians attending the respiratory population require training in the diagnosis and management of obesity and its related problems and in treating patients with various comorbidities. From a public health point of view, strategies to reduce obesity, promote a healthier diet, with fewer calories for quick access, and more exercise, can be considered as having a broad impact including respiratory disorders.

## CONCLUSION

Among population in the Southeast of Mexico, the presence of obesity is an independent risk factor for respiratory disease, primarily for OSAS and asthma. The diagnosis and treatment of respiratory complications in obese patients represent a challenge for health systems.

Knowing the regional expression can strengthen the justification to develop the research processes aimed at clarifying the pathogenesis and provide the necessary resources that safeguard the correct care for these patients.

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## Conflicts of interest

There are no conflicts of interest.

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