

OBESITY

Central Obesity and Asthma Outcomes in Adults Diagnosed with Asthma

SANAZ TAVASOLI, M.D.,^{1,2} SHAHRYAR EGHTESEADI, PH.D.,¹ HASSAN HEIDARNAZHAD, M.D.,^{2,3,*}
AND MAZIAR MORADI-LAKEH, M.D., M.P.H.^{4,5}

¹Department of Nutrition and Biochemistry, Tehran University of Medical Sciences, Tehran, Iran.

²Immunology, Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Iran.

³National Research Institute of Tuberculosis and Lung Disease, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁴Department of Community Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

⁵Gastro-Intestinal and Liver Disease Research Center (GILDRC), Tehran University of Medical Sciences, Tehran, Iran.

Objective. The potential role of central obesity in asthma outcomes has been examined in a few studies. The aim of this study was to examine the relationship between central obesity and asthma outcomes in a group of Iranian asthma patients. **Methods.** One hundred and forty-two outpatients with asthma were studied. Central obesity was defined according to National Institute of Health (NIH) and Asian waist circumference (WC) and waist-to-hip ratio (WHR) cut-offs. Asthma outcomes including asthma control, pulmonary function, and morbidity were evaluated. The association between central obesity and asthma outcomes was studied by linear and logistic regression analyses. **Results.** Linear regression analysis showed a significant association of WHR-based central obesity with forced expiratory volume in 1 s (FEV₁) ($\beta = -9.04$; p -value = .044) and forced vital capacity (FVC) ($\beta = -10.52$; p -value = .012). Logistic regression analysis showed a significant increased risk of asthma attacks in 3 months with Asian WC-based central obesity [odds ratio (OR) = 6.31, 95% confidence interval (CI): 1.16–34.41]; emergency room (ER) visits with NIH WC-based (OR = 5.15, 95% CI: 1.36–19.55) and Asian WC-based (OR = 18.72, 95% CI: 1.92–182.63) central obesity; and hospitalization in 1 year with NIH WC-based (OR = 5.28, 95% CI: 1.28–21.84) and Asian WC-based (OR = 12.39, 95% CI: 1.29–119.53) central obesity. **Conclusions.** Our study shows that the Asian WC-based central obesity is a better predictor of asthma morbidity. The results of this study emphasize, when studying the relationship between asthma control and obesity, the importance of selecting the proper definitions for asthma control or central obesity and appropriate cutpoints. Further study in this field using other asthma control and quality of life questionnaires is warranted.

Keywords Asians, asthma control, asthma morbidity, pulmonary function tests, waist circumference, waist-to-hip ratio

INTRODUCTION

Asthma and obesity are important public health issues (1–3). Although the prevalence of asthma has decreased in certain countries in recent years, it is a different story in Iran (4). Recent data show that asthma is more prevalent in Iran than that estimated in national reports (5). These data warrant a need for further studies on asthma in this country. As a result of recent nutritional transitions in Iran, obesity and diet-related chronic diseases are more common (6,7). It has been shown that there is an ethnic variation in fat distribution with the Asian populations having greater visceral fat deposition than Europeans (8). As a result, central obesity might be considered more prevalent in the Asian populations.

According to the epidemiological studies, the association between obesity or central obesity and asthma is quite complex (9–12). Studies suggest that general obesity might be associated with asthma severity and may also lead to poor asthma control (13–15). Although central obesity has more effect on health outcomes and all-cause mortality (8), very limited data about association between central obesity and asthma severity or control are available (16).

There are two major mechanisms explaining the relationship between asthma and obesity (17). First is the mechanical effect; obesity has been shown to decrease lung volumes and negatively affect lung function in general population (18,19). However, such a relationship is yet to be investigated in patients with asthma. Another possible mechanism is through systemic inflammation (9). It is believed that obesity, especially central obesity, is associated with systemic inflammation. Central obesity is a major risk factor for many chronic diseases, such as type 2 diabetes and dyslipidemia (9,20). Therefore, one might hypothesize that central obesity may lead to worse clinical outcomes in patients with asthma. The best predictive indicator of such a relationship, however, has yet to be determined. Waist-to-hip ratio (WHR) and waist circumference (WC) are two alternative measures that reflect abdominal obesity. Each provides different information and has different values in predicting disease risk and thus may not be interchangeable (8). Moreover, the universal cut-off points for WC are not applicable, given ethnic or population-specific differences. In fact, different WC cut-offs are suggested for Asians to predict disease risk (8,20). The aim of this study was to evaluate the relationship between central obesity and asthma outcomes, including asthma control, pulmonary function, and morbidity, in adults with asthma in Iran.

*Corresponding author: Hassan Heidarnazhad, M.D., Masih Daneshvari Hospital, Bahonar St., Darabad, Tehran 19556, Iran; Fax: +98 26109680-26109484; E-mail: Heidarnazhad@nritld.ac.ir

METHODS

Study Population

This cross-sectional study was conducted in an outpatient asthma clinic in Milad Hospital (Tehran, Iran) between May 2006 and September 2007, with the approval of the Institutional Review Board. The subjects were 18 to 65 years old. Asthma was diagnosed according to National Asthma Education and Prevention Program (NAEPP) guidelines (21), using clinical data as well as spirometry or metacholine challenge testing. Treatment had been initiated based on the Asthma Management and Prevention guidelines (2) at least 3 months prior to the study by the same physician. Subjects were excluded if they were current smokers or had smoked within past 2 years, had evidence of any respiratory illness other than asthma, history of cardiovascular disease, congestive heart failure, thyroid dysfunction, or a body mass index (BMI) less than 18.5 kg/m² (22). Informed written consent was obtained from all subjects.

Data Collection

Demographic data [age, gender, and education (less or more than elementary school education)], duration of disease (less or more than 8 years) (23), asthma severity and control (24), anthropometric measurements (weight, height, WC, and hip circumference), and pulmonary function test (PFT) indices including forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), peak expiratory flow (PEF), and FEV₁ to FVC ratio (FEV₁/FVC) were collected.

Anthropometric Measurement

Weight was measured to the nearest 0.5 kg and height was measured to the nearest 0.1 cm, according to the standard protocols (25). WC was measured to the nearest 0.1 cm, using a nonelastic tape measure, at the midpoint between the lower costal margin and iliac crest, without applying pressure on the soft tissues by pulling the tape. During WC measurement, the examinees were asked to relax and exhale, while standing. Hip circumference was measured using a nonelastic tape measure, at the level of the maximum posterior extension of the buttocks, to the nearest 0.1 cm (26). All measurements were conducted by the same physician. BMI (kg/m²) and WHR were calculated. BMI was categorized as normal, overweight, and obese according to the National Institute of Health (NIH) criteria (26). Central obesity was defined according to WC and WHR cut-offs. WC of greater than 102 cm in men and 88 cm in women was designated as NIH WC-based central obesity (26). WHR of greater than 0.80 in women and 0.95 in men was defined as WHR-based central obesity (27).

Asian Abdominal Obesity

We also used Asian-based central obesity cut-off points as several studies have suggested lower WC and BMI cut-off values for Asians (20). This alternative classification is suggested and used by some investigators, because of higher prevalence of chronic diseases such as hypertension

and diabetes at normal BMI levels in Asians. In this classification, the central obesity cut-off points are 80 cm and 90 cm for women and men, respectively.

Asthma Outcomes

The evaluated asthma outcomes included asthma severity and control, pulmonary function, and asthma morbidity. Asthma severity and control were defined based on the Global Initiative for Asthma (GINA) 2004 and 2006 guidelines, using clinical symptoms including daytime and nighttime symptoms and PFT parameters (24). Pulmonary function was measured by spirometry according to American Thoracic Society (ATS) standard methods (28–30). Asthma morbidity was evaluated by three variables: asthma attacks in 3 months, emergency room (ER) visits in 1 year, and hospitalization in 1 year.

Statistical Analysis

Independent sample *t* test and chi-square test were used to investigate the relationship of abdominal obesity indices and patients' socio-demographic data with asthma outcomes. Binary logistic regression analysis was conducted between dichotomous asthma control (controlled vs. partially controlled and uncontrolled) as the dependent variable and central obesity and potential confounding variables (age, gender, literacy level, and BMI) as predictors. In another model, we substituted asthma morbidity variables as the dependent variables. The association of pulmonary function indices as quantitative dependent variable with central obesity was examined via multiple linear regression analysis with adjustment for potential confounding variables (age, gender, literacy level, duration of disease, asthma control, and BMI). In all the analyses, central obesity indicators were entered as independent variables and asthma outcomes were considered as dependent variables. The level of significance was set at 5%. All analyses were performed using the SPSS statistical package 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient's Characteristic

Clinical characteristics of the subjects are described in Table 1. One hundred eighty-nine subjects were enrolled in the study, 155 of whom met the inclusion criteria and 142 patients (66.9% female and 33.1% male; mean age 47.34 ± 10.67 years) completed the PFT.

Based on BMI, 78.9% of patients were found to be overweight or obese. Central obesity was detected in 73.94% of subjects when using the Asian WC, as opposed to 40.14% with the NIH WC indicator. Comparatively, 78.17% of patients were determined to have central obesity by WHR.

There was a significant difference between central obese and normal patients in terms of age, literacy level, and gender, in both WC-based and WHR-based central obesity categorizations (Table 1). There was a significant difference in BMI categories according to WC-based but not WHR-based central obesity categorization. There was a significant difference in mean FEV₁ and FVC according

TABLE 1.—Characteristics of the study population by central obesity categories.

	NIH WC-based central obesity			WHR-based central obesity			Asian WC-based central obesity		
	Normal	Obesity	p value	Normal	Obesity	p value	Normal	Obesity	p value
Number (%)	85 (59.86)	57 (40.14)		31 (21.83)	111 (78.17)		37 (26.06)	105 (73.94)	
Age, years (SD)	45.80 (11.78)	49.63 (8.35)	0.002*	42.10 (10.73)	48.80 (10.23)	0.036*	43.65 (13.64)	48.64 (9.14)	0.014*
Literacy level (%)			0.016*			0.015*			0.914
Less than 5 years	37 (43.5)	37 (64.9)		10 (32.3)	64 (57.7)		19 (51.4)	55 (52.4)	
More than 5 years	48 (56.5)	20 (35.1)		21 (67.7)	47 (42.3)		18 (48.6)	50 (47.6)	
Duration of disease			0.378			0.538			0.555
Less than 8 years (%)	56 (65.9)	33 (57.9)		21 (67.7)	68 (61.3)		25 (67.6)	64 (61.0)	
More than 8 years (%)	29 (34.1)	24 (42.1)		10 (32.3)	43 (38.7)		12 (33.4)	41 (39.0)	
Gender			<0.0001*			<0.0001*			0.008*
Female (%)	46 (54.1)	49 (86.0)		26 (83.9)	69 (62.2)		18 (48.6)	77 (73.3)	
Male (%)	39 (45.9)	8 (14.0)		5 (16.1)	42 (37.8)		19 (51.4)	28 (26.7)	
BMI			<0.0001*			0.440			<0.0001*
Normal (%)	30 (35.3)	0 (0.0)		9 (29.0)	21 (18.9)		27 (73.0)	3 (2.9)	
Overweight (%)	53 (62.4)	14 (24.6)		14 (45.2)	53 (47.7)		10 (27.0)	57 (54.3)	
Obese (%)	2 (2.4)	43 (75.4)		8 (25.8)	37 (33.3)		0 (0.0)	45 (42.9)	
Oral corticosteroid use			0.786						
Yes (%)	18 (21.2)	11 (19.3)		2 (6.5)	27 (24.3)	0.29	7 (18.9)	22 (21.0)	0.792
No (%)	67 (78.8)	46 (80.7)		29 (93.5)	84 (75.7)	0.823	30 (81.1)	83 (79.0)	0.230
Asthma severity			0.861						
Intermittent (%)	15 (17.6)	7 (12.3)		6 (19.4)	16 (14.4)		8 (21.6)	14 (13.3)	
Mild persistent (%)	11 (12.9)	8 (14.0)		5 (16.1)	14 (12.6)		2 (5.4)	17 (16.2)	
Moderate Persistent (%)	28 (32.9)	20 (35.1)		9 (29.0)	39 (35.1)		11 (29.7)	37 (35.2)	
Severe persistent (%)	31 (36.5)	22 (38.6)		11 (35.5)	42 (37.8)		16 (43.2)	37 (35.2)	
Asthma control			0.407			0.406			0.209
Controlled (%)	16 (18.8)	6 (10.5)		7 (22.6)	15 (13.5)		9 (24.3)	13 (12.4)	
Partially controlled (%)	32 (37.6)	24 (42.1)		10 (32.3)	46 (41.4)		14 (37.8)	24 (42.1)	
Uncontrolled (%)	37 (43.5)	27 (47.4)		14 (45.2)	50 (45.0)		14 (37.8)	50 (47.6)	
Asthma attacks in 3 months			0.591			0.525			0.549
Yes (%)	28 (32.9)	22 (38.6)		9 (29.0)	41 (36.9)		11 (29.7)	39 (37.1)	
No (%)	57 (67.1)	35 (61.4)		22 (71.0)	70 (63.1)	0.817	26 (70.3)	66 (62.9)	0.131
Emergency room visits in one year			0.121						
Yes (%)	18 (21.2)	19 (33.3)		7 (22.6)	30 (27.0)		6 (16.2)	31 (29.5)	
No (%)	67 (78.8)	38 (66.7)		24 (77.4)	81 (73.0)	0.488	31 (83.8)	74 (70.5)	0.522
Hospitalization in one year			0.245						
Yes (%)	19 (22.4)	18 (31.6)		6 (19.4)	31 (27.9)		8 (21.6)	29 (27.6)	
No (%)	66 (77.6)	39 (68.4)		25 (80.6)	80 (72.1)		29 (78.4)	76 (72.4)	
FEV ₁ , % of predicted (SD)	80.09 (25.67)	78.91 (19.41)	0.769	88.47 (17.91)	77.15 (24.07)	0.016*	80.75 (27.84)	79.22 (21.60)	0.733
FVC, % of predicted (SD)	83.47 (21.91)	81.32 (18.04)	0.539	92.15 (16.53)	79.94 (20.65)	0.003*	84.80 (24.12)	81.84 (19.00)	0.449
PEF, % of predicted (SD)	78.58 (31.29)	72.18 (22.41)	0.186	82.76 (25.13)	74.09 (28.73)	0.130	75.78 (28.96)	76.07 (27.97)	0.956
FEV ₁ /FVC ratio (SD)	81.28 (13.96)	82.94 (11.17)	0.471	85.41 (11.61)	81.18 (12.95)	0.119	80.10 (14.98)	82.58 (12.08)	0.366

Notes: BMI – body mass index; NIH – National Institute of Health; WC – waist circumference; WHR – waist-to-hip ratio; FEV₁ – forced expiratory volume in 1 s; FVC – forced vital capacity; PEF – peak expiratory flow.

**p* < .05.

to WHR-based but not WC-based central obesity categorization. No significant difference was found regarding the duration of disease, asthma severity and control, and other asthma morbidity variables (Table 1).

According to Asian central obesity categorization, there was a significant difference between central obese and normal patients in terms of age, gender, and BMI categories (Table 1) but not in terms of asthma status and morbidity or pulmonary function variables.

Association between Central Obesity and Asthma Control

Because of the strong correlation between asthma severity and control, we omitted asthma severity from the analysis. No association between central obesity (NIH or Asian WC and WHR) and asthma control was appreciated after adjustment for the confounders (Table 2).

Association between Central Obesity and Pulmonary Function

There was a significant association between WHR-based central obesity and both FEV₁ ($\beta = -9.04$, p -value = .044) and FVC ($\beta = -10.52$, p -value = .012) (Tables 3 and 4).

On the other hand, there was no significant association between NIH and Asian WC-based central obesity and PFT indices before and after adjustment for the other variables.

Association between Central Obesity and Asthma Morbidity

Table 5 shows the binary logistic regression for asthma morbidity. It shows a significant association between NIH and Asian WC-based central obesity with both ER visits [odds ratio (OR) = 5.15, 95% confidence interval

TABLE 2.—Binary logistic regression derived OR and 95% CI for partially and uncontrolled asthma.

Variable	Category or increment	Control of asthma		
		Model 1 [OR (95% CI)]	Model 2 [OR (95% CI)]	Model 3 [OR (95% CI)]
Central obesity ^a	Normal	Baseline	Baseline	Baseline
	Obese	1.02 (0.21–4.91)	2.74 (0.61–12.41)	1.62 (0.54–4.87)
Age	1 year more	1.01 (0.97–1.06)	1 (0.96–1.05)	1.01 (0.96–1.06)
Gender	Male	Baseline	Baseline	Baseline
	Female	1.06 (0.37–3.01)	1.06 (0.38–2.95)	1.18 (0.41–3.36)
Literacy level	≤5 years	Baseline	Baseline	Baseline
	>5 years	0.71 (0.25–2.02)	0.63 (0.22–1.81)	0.73 (0.26–2.05)
BMI	Normal	Baseline	Baseline	Baseline
	Overweight	0.44 (0.06–3.25)	1.09 (0.15–8.11)	0.48 (0.11–2.07)
	Obese	0.51 (0.1–2.66)	0.6 (0.17–2.14)	0.5 (0.15–1.71)

Notes: BMI – body mass index; OR – odds ratio; CI – confidence interval.

^aCentral obesity stands for NIH WC-based central obesity in model 1, Asian WC-based central obesity in model 2, WHR-based central obesity in model 3. None of the p -values were <.05.

TABLE 3.—Multiple linear regression analysis derived coefficients (β), 95% CI, and p -value for the association between central obesity and socio-demographic with FEV₁ % predicted.

Variable	Category or increment	FEV ₁ % predicted					
		Model 1 ^a		Model 2 ^b		Model 3 ^c	
		β (95% CI)	p	β (95% CI)	p	β (95% CI)	p
Central obesity ^d	Normal	Baseline		Baseline		Baseline	
	Obese	−9.7 (−21.46 to 2.07)	0.105	−3.35 (−16.04 to 9.35)	0.603	−9.04 (−17.83 to −0.24)	0.044*
Age	1 year more	0.23 (−0.14 to 0.61)	0.219	0.25 (−0.14 to 0.63)	0.208	0.29 (−0.09 to 0.67)	0.133
Gender	Male	Baseline		Baseline		Baseline	
	Female	9.94 (1.98 to 17.9)	0.015*	8.54 (0.68 to 16.4)	0.033*	6.92 (−.99 to 14.83)	0.14
Literacy level	≤5 years	Baseline		Baseline		Baseline	
	>5 years	3.99 (−3.89 to 11.86)	0.319	5.45 (−2.42 to 13.32)	0.173	4.3 (−3.44 to 12.05)	0.274
BMI	Normal	Baseline		Baseline		Baseline	
	Overweight	−0.48 (−9.89 to 8.93)	0.920	0.21 (−12.99 to 13.42)	0.974	−0.95 (−10.15 to 8.25)	0.839
	Obese	10.28 (−4.35 to 24.91)	0.167	4.68 (−10.59 to 19.94)	0.546	3.21 (−7.15 to 13.57)	0.542
Duration of disease	≤8 years	Baseline		Baseline		Baseline	
	>8 years	−8.34 (−15.93 to −0.75)	0.032*	−8.79 (−16.43 to −1.15)	0.024*	−9.05 (−16.57 to −1.53)	0.019*
Asthma control	Controlled	Baseline		Baseline		Baseline	
	Partially controlled	−14.90 (−25.15 to −4.64)	0.005*	−14.89 (−25.29 to −4.5)	0.005*	−14.13 (−24.38 to −3.89)	0.007*
	Uncontrolled	−27.4 (−37.64 to −17.16)	<0.001*	−26.78 (−37.17 to −16.39)	<0.001*	−26.63 (−36.81 to −16.44)	<0.001*

Notes: BMI – body mass index; CI – confidence interval; FEV₁ – forced expiratory volume in 1 s

^aModel R^2 : 0.268.

^bModel R^2 : 0.265.

^cModel R^2 : 0.285.

^dCentral obesity stands for NIH WC-based central obesity in model 1, Asian WC-based central obesity in model 2, and WHR-based central obesity in model 3.

* $p < .05$.

TABLE 4.—Multiple linear regression analysis derived coefficients (β), 95% CI and p -value for the association between central obesity and socio-demographic with FVC% predicted.

Variable	Category or increment	FVC % predicted					
		Model 1 ^a		Model 2 ^b		Model 3 ^c	
		β (95% CI)	p	β (95% CI)	p	β (95% CI)	p
Central obesity ^d	Normal	Baseline		Baseline		Baseline	
	Obese	-9.25 (-20.21 to 1.71)	0.097	-2.36 (-14.2 to 9.48)	0.694	-10.52 (-18.65 to -2.39)	0.012*
Age	1 year more	0.17 (-0.18 to 0.52)	0.328	0.18 (-0.18 to 0.54)	0.325	0.24 (-0.11 to 0.59)	0.174
Gender	Male	Baseline		Baseline		Baseline	
	Female	7.27 (-0.15 to 14.69)	0.055	5.94 (-1.39 to 13.27)	0.111	4.04 (-3.27 to 11.35)	0.277
Literacy level	≤5 years	Baseline		Baseline		Baseline	
	>5 years	4.54 (-2.79 to 11.88)	0.223	5.88 (-1.46 to 13.21)	0.089	4.66 (-2.5 to 11.81)	0.2
BMI	Normal	Baseline		Baseline		Baseline	
	Overweight	-3.93 (-12.7 to 4.84)	0.376	-3.9 (-16.22 to 8.42)	0.533	-4.11 (-12.6 to 4.39)	0.341
	Obese	7.04 (-6.59 to 20.67)	0.309	0.96 (-13.28 to 15.19)	0.895	0.6 (-8.98 to 10.17)	0.902
Duration of disease	≤8 years	Baseline		Baseline		Baseline	
	>8 years	-5.72 (-12.79 to 1.36)	0.112	-6.17 (-13.3 to 0.95)	0.089	-6.43 (-13.38 to 0.52)	0.07
Asthma control	Controlled	Baseline		Baseline		Baseline	
	Partially controlled	-9.47 (-19.03 to 0.09)	0.052	-9.53 (-19.23 to 0.16)	0.054	-8.53 (-17.99 to 0.94)	0.077
	Uncontrolled	-17.26 (-26.8 to -7.72)	<0.0001*	-16.74 (-26.44 to -7.05)	0.001*	-16.42 (-25.83 to -7.01)	0.001*

Notes: BMI – body mass index; CI – confidence interval; FVC – forced vital capacity.

^aModel R^2 : 0.158.

^bModel R^2 : 0.161.

^cModel R^2 : 0.197.

^dCentral obesity stands for: NIH WC-based central obesity in model 1, Asian WC-based central obesity in model 2, and WHR-based central obesity in model 3.

* $p < .05$.

(CI): 1.36–19.55 for NIH WC; OR = 18.72, 95% CI: 1.92–182.63 for Asian WC] and hospitalization in 1 year (OR = 5.28, 95% CI: 1.28–21.84 for NIH WC; OR = 12.39, 95% CI: 1.29–119.53 for Asian WC). Asian WC-based central obesity shows a statistically significant association with asthma attacks in 3 months (OR = 6.31, 95% CI: 1.16–34.41), whereas NIH WC-based central obesity did not.

DISCUSSION

Our study demonstrates that there is no significant association between central obesity; defined by NIH WC-based, Asian WC-based, and WHR-based central obesity; and asthma control. However, this study reveals that Asian WC-based central obesity is a better predictor of asthma morbidity in Iranian asthma patients.

Interestingly, our study shows a significant difference between the number of the subjects found obese in NIH WC-based central obesity (40.14%) versus WHR-based (78.17%) and Asian WC-based (73.94%) central obesity. One plausible explanation could be that the optimal cut-off points to define obesity and fat distribution patterns vary across different ethnicities and populations (8). The authors of this article agree with Nyamdorj et al.'s (31) suggestion that region-specific cut-off points may be required to define obesity cut-off points accurately.

Our results show that there is no relationship between central obesity and asthma control defined by the GINA 2006 guidelines (24). There are several studies on the association between BMI and asthma control (10, 22), and the significant role of obesity in asthma control and its severity continues to unfold (15, 32–36). It seems that the data on

central obesity and asthma control are scant and less convincing. For instance, Lessard et al. (37) found a significant correlation between asthma control and WC but not WHR, using the asthma control questionnaire (ACQ) (38). Similarly, Barros et al. (39) found no association between asthma control (using ACQ) and WHR. Inconsistency in defining asthma control and asthma severity may be a confounding factor. Although asthma severity and control have been used interchangeably in some studies, they are two distinct concepts (22). Asthma control is defined as a way to monitor asthma management goals (40). However, the severity of asthma is used to categorize patients at the time of diagnosis (2). In our study, using asthma control to describe asthma status seems accurate, because all enrolled subjects have received at least 3 months of standard therapy prior to the study. Another factor contributing to differing results is the method used to define asthma control. We used the GINA asthma control classification, whereas other studies that demonstrated a significant association between asthma control and obesity utilized validated questionnaires, such as the Juniper ACQ (15, 37, 39). Further investigation with well-designed studies using different questionnaires for the same subjects would be needed to make recommendations on the association between asthma control and the type of questionnaires used.

This study reveals a relationship of WHR with FEV₁, and FVC, independent of BMI and asthma control. The association between central obesity and pulmonary function has been investigated in the general population in several studies (10, 18, 41–44). However, there are only limited data on a similar association in asthma patients. To our knowledge, this is the first study using three different indices for central obesity, adjusted for BMI. Our study

TABLE 5.—Binary logistic regression derived OR and 95% CI for asthma morbidity.

Dependent variable	Variable	Category or increment	Asthma morbidity		
			Model 1 [OR (95% CI)]	Model 2 [OR (95% CI)]	Model 3 [OR (95% CI)]
Asthma attacks in last 3 months	Central obesity ^a	Normal	Baseline	Baseline	Baseline
		Obese	2.1 (0.62–7.17)	6.31 (1.16–34.41)*	1.9 (0.73–4.98)
	Age	1 year more	0.96 (0.92–1)	0.95 (0.91–0.99)*	0.96 (0.92–1)
	Gender	Male	Baseline	Baseline	Baseline
		Female	1.45 (0.61–3.46)	1.63 (0.68–3.88)	1.81 (0.75–4.35)
	Literacy level	≤5 years	Baseline	Baseline	Baseline
		>5 years	0.7 (0.31–1.61)	0.63 (0.22–1.81)	0.68 (0.3–1.56)
	Duration of disease	≤8 years	Baseline	Baseline	Baseline
		>8 years	3.19 (1.42–7.14)*	3.3 (1.44–7.55)*	3.32 (1.48–7.43)
	BMI	Normal	Baseline	Baseline	Baseline
		Overweight	2.91 (0.62–13.58)	7.71 (1.15–51.61)*	1.7 (0.56–5.16)
		Obese	1.86 (0.56–6.21)	1.38 (0.57–3.36)	1.16 (0.48–2.8)
ER outpatient visit in last year	Central obesity ^a	Normal	Baseline	Baseline	Baseline
		Obese	5.15 (1.36–19.55)*	18.72 (1.92–182.63)*	1.63 (0.59–4.54)
	Age	1 year more	0.95 (0.9–0.99)*	0.93 (0.89–0.98)*	0.95 (0.91–0.99)*
	Gender	Male	Baseline	Baseline	Baseline
		Female	0.87 (0.34–2.24)	1.17 (0.45–3.02)	1.2 (0.48–3.02)
	Literacy level	≤5 years	Baseline	Baseline	Baseline
		>5 years	1 (0.4–2.47)	0.71 (0.28–1.77)	0.89 (0.37–2.15)
	Duration of disease	≤8 years	Baseline	Baseline	Baseline
		>8 years	3.14 (1.27–7.32)*	3.3 (1.44–7.55)*	3.25 (1.35–7.82)*
	BMI	Normal	Baseline	Baseline	Baseline
		Overweight	3.7 (0.7–19.48)	10.65 (0.99–114.23)	0.96 (0.29–3.12)
		Obese	2.48 (0.7–8.72)	1 (0.43–2.81)	0.87 (0.34–2.22)
Hospitalization in last year	Central obesity ^a	Normal	Baseline	Baseline	Baseline
		Obese	5.28 (1.28–21.84)*	12.39 (1.29–119.53)*	2.75 (0.89–8.49)
	Age	1 year more	0.95 (0.91–1)	0.94 (0.89–0.99)*	0.95 (0.91–1)*
	Gender	Male	Baseline	Baseline	Baseline
		Female	1.63 (0.57–4.63)	2.12 (0.74–6.11)	2.35 (0.83–6.7)
	Literacy level	≤5 years	Baseline	Baseline	Baseline
		>5 years	1.44 (0.54–3.85)	0.99 (0.37–2.63)	1.34 (0.5–3.55)
	Duration of disease	≤8 years	Baseline	Baseline	Baseline
		>8 years	8.15 (2.97–22.36)*	8.26 (2.95–23.11)*	8.22 (3.08–21.97)*
	BMI	Normal	Baseline	Baseline	Baseline
		Overweight	8.34 (1.41–48.87)*	17.02 (1.52–191.08)*	2.26 (0.64–7.91)
		Obese	2.84 (0.73–10.99)	1.23 (0.44–3.44)	1.03 (0.37–2.91)

Notes: BMI: body mass index; OR – odds ratio; CI – confidence interval.

^aCentral obesity stands for: NIH WC-based central obesity in model 1, Asian WC-based central obesity in model 2, and WHR-based central obesity in model 3.

* $p < .05$.

shows that WHR-based central obesity may be superior in predicting impairment of pulmonary function in asthma patients. This finding is similar to some findings in the general population (41). Obesity can affect respiratory function via various mechanisms including accumulation of fat and impairing the diaphragm's movement. Although low FEV₁ and FVC suggest restrictive lung disease, chronically obese people usually present with both obstructive (severe and morbid obesity) and restrictive (in mild to moderate obesity) ventilatory patterns (45). The question remains unanswered whether such a relationship is a mechanical effect of obesity on lung function independent of asthma mechanism. Further study in this field is needed.

By evaluating the relationship between asthma morbidity and abdominal obesity, it seems that central obesity (both NIH and Asian WC) increases the risk of morbidity independent of BMI. It is also concluded that the Asian cut-offs are better predictors than the NIH cut-offs. Only a few studies have examined the potential role of central

obesity in asthma morbidity (46). Although their results are in agreement with our findings, there is a correlation between central obesity and asthma morbidity; this is the first study examining three central obesity indices.

Although we showed an association between central obesity and asthma outcomes, there is a dichotomy in the findings; PFTs are associated with WHR-based central obesity, whereas asthma morbidity is associated with the NIH and Asian WC-based central obesity. This dichotomy may stem from the cut-off points used to define central obesity. These cut-offs are used in relation to other chronic disease risk estimations such as cardiovascular disease or diabetes rather than asthma outcomes and may not be appropriate for asthma outcome risk estimation.

Our findings, once again, emphasize the complexity of the association between asthma and obesity. Certain differences between our study and other similar studies with different results may partially be explained by the prevalence of various confounders such as smoking, as well as the definition of obesity using different central obesity

indices or cut-off points. It is also important to realize that most of the clinical trials examining the effect of weight loss programs (including nutrition therapy or bariatric surgery) on asthma control show significant improvement after weight loss (47, 48). In addition, a number of studies (cross sectional or clinical trial) have demonstrated a poor quality of life in obese asthma patients in comparison to non-obese patients (15, 47, 49).

To our knowledge, this was the first study that examined the association between central obesity using three indices: WC, WHR, and Asian WC with asthma control, morbidity, and pulmonary function. To limit treatment bias, all subjects received standard therapy according to the GINA guideline, and their asthma was managed by one physician. There were limitations in this study that should be considered. Our findings were obtained only from Iranian asthma patients; hence, our findings may not be applicable to other populations. Furthermore, the likelihood of explaining any causal relationship is limited due to the nature of the study. We also realized that including a non-asthmatic population would have strengthened the study.

CONCLUSIONS

In conclusion, our study demonstrates that there is a relation between the NIH and Asian WC central obesity and asthma morbidity, independent of BMI. It also reveals that the Asian cut-offs are more predictive than the NIH cut-offs, although the findings may not be applicable to other populations or ethnicities. The authors of this article recommend that region-specific cut-off points may be required for defining obesity accurately. The study also emphasizes the importance and complexity of defining asthma outcome variables precisely. Further study in this field including subjects from different ethnic backgrounds and using different questionnaires is warranted.

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DECLARATION OF INTEREST

All authors of this article "Asthma outcomes and central obesity in adults diagnosed with asthma" declare that they do not have any conflict of interest to declare.

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REFERENCES

- Peters JI, McKinney JM, Smith B, Wood P, Forkner E, Galbreath AD. Impact of obesity in asthma: evidence from a large prospective disease management study. *Ann Allergy Asthma Immunol* 2011; 106:30–35.
- Global Initiative for Asthma. Global strategy for asthma management and prevention. Revised 2006. Available at: www.ginasthma.org. Accessed July 20, 2006.
- World Health Organization. Obesity: preventing and managing the global epidemic. WHO Technical Report Series 894. Revised 2000. Available at: http://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/index.html. Accessed November 26, 2007.
- Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, Robertson C, and the ISAAC Phase Three Study Group. Worldwide trends in the prevalence of asthma symptoms: phase III of the international study of asthma and allergies in childhood (ISAAC). *Thorax* 2007; 62:758–766.
- Entezari A, Mehrabi Y, Varesvazirian M, Pourpak Z, Moin M. A systematic review of recent asthma symptom surveys in Iranian children. *Chron Respir Dis* 2009; 6:109–114.
- Ghassemi H, Harrison G, Mohammad K. An accelerated nutrition transition in Iran. *Public Health Nutr* 2002; 5:149–155.
- Rashidi A, Mohammadpour-Ahramani B, Vafa MR, Karandish M. Prevalence of obesity in Iran. *Obes Rev* 2005; 6:191–192.
- World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation. Revised 2011. Available at: http://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/index.html. Accessed April 15, 2012.
- Shore SA. Obesity and asthma: possible mechanisms. *J Allergy Clin Immunol* 2008; 121:1087–1093.
- Grammatopoulou E, Haniotou A, Douka A, Koutsouki D. Factors associated with BMI in Greek adults with asthma. *J Asthma* 2010; 47:276–280.
- Brumpton B, Langhammer A, Romundstad P, Chen Y, Mai XM. General and abdominal obesity and incident asthma in adults: the hunt study. *Eur Respir J*, in press.
- Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007; 175:661–666.
- Akerman MJH, Calacanis CM, Madsen MK. Relationship between asthma severity and obesity. *J Asthma* 2004; 41:521–526.
- Thomson CC, Clark S, Camargo CA. Body mass index and asthma severity among adults presenting to the emergency department. *Chest* 2003; 124:795–802.
- 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; 100:648–657.
- Appleton SL, Adams RJ, Wilson DH, Taylor AW, Ruffin RE. Central obesity is associated with nonatopic but not atopic asthma in a representative population sample. *J Allergy Clin Immunol* 2006; 118:1284–1291.
- Zammit C, Liddicoat H, Moonsie I, Makker H. Obesity and respiratory diseases. *Int J Gen Med* 2010; 3:335–343.
- Thyagarajan B, Jacobs DR Jr, Apostol GG, Smith LJ, Jensen RL, Crapo RO, Graham Barr R, Lewis CE, Williams OD. Longitudinal association of body mass index with lung function: the CARDIA study. *Respir Res* 2008; 9:31.
- Wannamethee SG, Shaper AG, Whincup PH. Body fat distribution, body composition, and respiratory function in elderly men. *Am J Clin Nutr* 2005; 82:996–1003.
- James PT. Obesity: the worldwide epidemic. *Clin Dermatol* 2004; 22:276–280.
- National Heart Lung and Blood Institute. National asthma education and prevention program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Revised 2007. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/index.com>. Accessed May 20, 2009.
- Clerisme-Beatty EM, Karam S, Rand C, Patino CM, Bilderback A, Riekert KA, Okelo SO, Diette GB. Does higher body mass index contribute to worse asthma control in an urban population? *The J Allergy Clin Immunol* 2009; 124:207–212.
- Grammatopoulou E, Stavrou N, Myrianthefs P, Karaterliotis K, Baltopoulos G, Behrakis P, Koutsouki D. Asthma control in Greece: validity and reliability evidence of the asthma control test—ACT in Greece. *J Asthma* 2010; 48:57–64.
- Global Initiative for Asthma. Pocket guide for asthma management and prevention. Revised 2006. Available at: <http://www.ginasthma.org>. Accessed December 12, 2006.

25. Jelliffe DB, Jelliffe EFP. Community Nutritional Assessment: With Special Reference to Less Technically Developed Countries. 1st ed. Oxford: Oxford University Press, 1989.
26. National Institutes of Health. NIH Publication No. 98-4083: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Revised September 1998. Available at: http://www.nhlbi.nih.gov/guidelines/obesity/ob_gdlns.htm. Accessed April 15, 2012.
27. Azizi F, Rahmani M, Emami H, Mirmiran P, Hajipour R, Madjid M, Ghanbili J, Ghanbarian A, Mehrabi Y, Saadat N, Salehi P, Mortazavi N, Heydari P, Sarbazi N, Allahverdian S, Saadati N, Ainy E, Moeini S. Cardiovascular risk factors in an Iranian urban population: Tehran lipid and glucose study (phase 1). *Sozial- und Preventivmedizin* 2002; 47:408–426.
28. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, Casaburi R, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Hankinson J, Jensen R, Johnson D, MacIntyre N, McKay R, Miller MR, Navajas D, Pellegrino R, Viegi G. Standardisation of the measurement of lung volumes. *Eur Respir J* 2005; 26:511–522.
29. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen R, Pellegrino R, Viegi G, Wanger J; ATS/ERS Task Force. General considerations for lung function testing. *Eur Respir J* 2005; 26:153–161.
30. Standardization of Spirometry. 1994 Update. American thoracic society. *Am J Respir Crit Care Med* 1995; 152:1107–1136.
31. Nyamdorj R, Qiao Q, Lam TH, Tuomilehto J, Ho SY, Pitkanen J, Nakagami T, Mohan V, Janus ED, Ferreira SR. BMI compared with central obesity indicators in relation to diabetes and hypertension in Asians. *Obesity (Silver Spring)* 2008; 16:1622–1635.
32. Laforest L, Van Ganse E, Devouassoux G, Bousquet J, Chretien S, Bauguil G, Pacheco Y, Chamba G. Influence of patients' characteristics and disease management on asthma control. *J Allergy Clin Immunol* 2006; 117:1404–1410.
33. Siroux V, Boudier A, Bousquet J, Bresson JL, Cracowski JL, Ferran J, Gormand F, Just J, Le Moual N, Morange S, Nadif R, Oryszczyn MP, Pison C, Scheinmann P, Varraso R, Vervloet D, Pin I, Kauffmann F. Phenotypic determinants of uncontrolled asthma. *J Allergy Clin Immunol* 2009; 124:681–687.
34. 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.
35. Saint-Pierre P, Bourdin A, Chanez P, Daures JP, Godard P. Are overweight asthmatics more difficult to control? *Allergy* 2006; 61:79–84.
36. Boulet LP, Franssen E. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. *Respir Med* 2007; 101:2240–2247.
37. Lessard AA, Turcotte HLN, Cormier Y, Boulet LP. Obesity and asthma: a specific phenotype? *Chest* 2008; 134:317–323.
38. 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; 14:902–907.
39. Barros LL, Souza-Machado A, Correa LB, Santos JS, Cruz C, Leite M, Castro L, Coelho AC, Almeida P, Cruz AA. Obesity and poor asthma control in patients with severe asthma. *J Asthma* 2011; 48:171–176.
40. Humbert M. Asthma control or severity: that is the question. *Allergy* 2007; 62:95–101.
41. Canoy D, Luben R, Welch A, Bingham S, Wareham N, Day N, Khaw KT. Abdominal obesity and respiratory function in men and women in the EPIC-Norfolk Study, United Kingdom. *Am J Epidemiol* 2004; 159:1140–1149.
42. Chen R, Tunstall-Pedoe H, Bolton-Smith C, Hannah MK, Morrison C. Association of dietary antioxidants and waist circumference with pulmonary function and airway obstruction. *Am J Epidemiol* 2001; 153:157–163.
43. Chen Y, Rennie D, Cormier YF, Dosman J. Waist circumference is associated with pulmonary function in normal-weight, overweight, and obese subjects. *Am J Clin Nutr* 2007; 85:35–39.
44. Harik-Khan RI, Wise RA, Fleg JL. The effect of gender on the relationship between body fat distribution and lung function. *J Clin Epidemiol* 2001; 54:399–406.
45. Parameswaran K, Todd DC, Soth M. Altered respiratory physiology in obesity. *Can Resp J* 2006; 13:203–210.
46. Appleton SL, Wilson DH, Tucker G, Ruffin RE, Taylor AW, Adams RJ. Sex differences in asthma morbidity associated with obesity in a representative population sample. *J Allergy Clin Immunol* 2008; 121:1285–1287.
47. Stenius-Aamiala B, Poussa T, Kvamstrom J, Gronlund EL, Ylikahri M, Mustajoki P. Immediate and long term effects of weight reduction in obese people with asthma: Randomised controlled study. *BMJ* 2000; 320:827–832.
48. Maniscalco M, Zedda A, Faraone S, Cerbone MR, Cristiano S, Giardiello C, Sofia M. Weight loss and asthma control in severely obese asthmatic females. *Respir Med* 2008; 102:102–108.
49. 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; 122:507–511.