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Authors

Rastogi, Deepa
Jung, Molly
Strizich, Garrett
et al.

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Association of systemic inflammation, adiposity, and metabolic dysregulation with asthma burden among Hispanic adults

Deepa Rastogi[1], **Molly Jung**[1], **Garrett Strizich**[1], **Pamela A. Shaw**[2], **Sonia M. Davis**[3], **Oana L. Klein**[4], **Frank J. Penedo**[5], **Andrew L. Ries**[6], **Martha L. Daviglus**[7], **Juan J. Moreiras**[8], **Matthias A. Salathe**[8], **Juan C. Celedón**[9], **Carmen R. Isasi**[1], and **Robert C. Kaplan**[1]

[1]Albert Einstein College of Medicine, Bronx, NY

[2]University of Pennsylvania, Philadelphia, PA

[3]University of North Carolina, Chapel Hill, NC

[4]University of California San Francisco, CA

[5]Northwestern University, Chicago, IL

[6]University of California, San Diego, CA

[7]University of Illinois at Chicago, Chicago, IL

[8]University of Miami, Miami, FL

[9]University of Pittsburgh, PA

Abstract

Rationale—Obesity-related asthma is associated with higher disease burden than normal-weight asthma among Hispanics. Adiposity, metabolic dysregulation, and inflammation are all implicated in pathogenesis of obesity-related asthma, but their independent contributions are poorly understood.

Objective—To examine the independent contributions of body fat distribution, metabolic abnormalities and inflammation on asthma symptoms and pulmonary function among Hispanics.

Methods—Participants of the Hispanic Community Health Study/Study of Latinos with doctor-diagnosed asthma who completed an asthma symptom questionnaire and performed a valid spirometry were included in the analysis (n=1,126). Multivariate analysis was used to examine the independent association of general adiposity (assessed using body mass index), truncal adiposity (assessed by waist circumference), metabolic dysregulation (presence of insulin resistance and low

Corresponding author: Deepa Rastogi MBBS, MS, Albert Einstein College of Medicine, 3415 Bainbridge Ave, Bronx, NY 10467, Telephone: 718-515-2330, Fax: 718-515-2608, drastogi@montefiore.org.

Author contributions:

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HDL) and inflammation (high-sensitivity C-Reactive Protein≥3mg/L) with reported asthma symptoms or pulmonary function measures (FEV_1, and FVC) while adjusting for demographic and clinical covariates.

Results—Of the 1,126 participants, 334 (29.5%) were overweight, and 648 (57.8%) were obese. FEV_1 and FVC were lower in obese compared to normal-weight asthmatics. In analyses controlling for metabolic and adiposity factors, high hs-CRP (>7 mg/L) was associated with more symptoms (prevalence-ratio 1.27 (95%CI 1.05, 1.54), and lower FVC (β −138ml (95%CI −27ml, −249ml)) and FEV_1 (β −155ml (95% CI −38ml, −272ml). Low HDL was also associated with lower FVC (β −111ml (−22ml, −201ml) and FEV_1 (β −100ml (−12ml, −188ml)). Results were similar in men and women.

Conclusions—Our findings suggest that hs-CRP and low HDL, rather than general and truncal adiposity, are associated with asthma burden among overweight and obese Hispanic adults.

Keywords

Asthma; Obesity; Hispanics; Pulmonary function; Inflammation

Introduction

Studies suggest that obesity-related asthma is distinct from asthma in normal-weight individuals [1]. Obese asthmatics have greater disease severity [2], lower pulmonary function [3, 4] and lower response to medications [5] than normal-weight asthmatics. The disease burden is higher in Hispanics [6, 7], in whom obesity [8], and asthma [7] are more prevalent than in non-Hispanic whites [9].

Obesity may affect asthma through several mechanisms, including truncal adiposity [10], obesity-mediated metabolic dysregulation [11, 12] or systemic inflammation [1]. Truncal adiposity is associated with higher asthma prevalence [13] and lower pulmonary function[14, 15]. However, truncal adiposity is also linked to higher circulating inflammatory mediators [16], and insulin resistance [17], which itself increases asthma risk [11], asthma-like symptoms [18], and influences pulmonary function [19, 20]. Since not all obese individuals have asthma, examining the independent contributions of body fat distribution, metabolic abnormalities, and inflammation on asthma symptoms and pulmonary function may elucidate the relative importance of these obesity-mediated risk factors for asthma, particularly among Hispanics.

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) offered a unique opportunity to examine these associations in a cohort of over 1,100 individuals with asthma. We hypothesized that adiposity (assessed using body mass index (BMI) and waist circumference), metabolic dysregulation (assessed by insulin resistance and low high density lipoprotein (HDL) cholesterol) and systemic inflammation (assessed by high sensitivity C-Reactive Protein (hs-CRP)), are independently associated with symptoms and lower pulmonary function among US Hispanic adults with asthma. We additionally explored whether these associations differ between Puerto Ricans, who have a higher disease burden [9], and members of other Hispanic subgroups.

Methods

Study participants

Details on the HCHS/SOL study have been previously published [21, 22]. Briefly, 16,415 Hispanic adults ages 18 to 74 years, were recruited in four U.S. cities, (the Bronx ((NY), Chicago (IL), Miami (FL), and San Diego (CA)) between 2008 and 2011. Participants were selected by population-based multistage probability sampling of households within census blocks. Persons eligible for the study were community-dwelling individuals who self-identified as being Hispanic or Latino, were able to travel to the local field center, were not pregnant, or on active military duty, and did not have plans to move out of the area. Of screened eligible individuals, 41.7% enrolled [23] and completed questionnaires, including a standardized respiratory questionnaire developed for epidemiologic studies [24], provided blood and urine specimens, and underwent a physical exam and spirometry testing at an in-person clinic visit. The Institutional Review Boards at each institution approved the study and all participants provided written informed consent.

Of the 1,275 participants with self-reported current physician-diagnosed asthma [25], 142 were excluded because of incomplete (n=88) or invalid (n=50) spirometry, or missing height or weight measurements (n=4). The underweight (n=7) group was also excluded for several reasons including its association with higher asthma morbidity [1], the current study's focus on the effect of overweight and obese, and because the small sample size precluded a sub-set analysis. These exclusion criteria restricted the current analysis to 1,126 participants.

Asthma symptoms, medication use, and pulmonary function testing

Based on weekly frequency of coughing and wheezing in prior 12 months [24], two symptom categories were created: No symptoms (no cough or wheeze) and any symptoms (presence of cough most days of the week and/or wheeze at least once a week). Current asthma medication use was assessed by medications that the participant reported currently using and brought in at the time of the research study visit. The medications were grouped into inhaled short-acting beta agonists, oral steroids or controller medications, comprised of 1) inhaled corticosteroids alone, 2) leukotriene modifiers alone, 3) combination therapy of inhaled steroids and long acting beta agonists, 4) combination of groups 1 and 2, or 5) combination of groups 2 and 3 [26].

Spirometry was performed by trained technicians on a SensorMedics model 1022 spirometer with a digital volume encoder, temperature sensor, and RS232 serial computer interface as per the American Thoracic Society guidelines [27]. Data was processed using OMI spirometry software (version 5.05.11). The best of three attempts was retained for analysis. Raw values of forced vital capacity (FVC), and forced expiratory volume in the first second (FEV_1) were analyzed because the current predicted values generated using National Health and Nutritional Examination Survey (NHANES) prediction equations [28], may not be generalizable to all Hispanic subgroups [9]. However, for clinical interpretation of the study findings, percent-predicted values of FVC and FEV_1 were generated using NHANES prediction equations [28] and their analysis, which was similar to that of the raw values, are included in Supplemental Tables 2 and 3. Of the 305 participants with pre-bronchodilator

FEV_1/FVC ratio <0.7 or less than the lower limit of normal [28], post-bronchodilator spirometry was conducted in 250 (82%) participants. A positive bronchodilator response was defined as an increase in FEV_1 of ≥200 ml and ≥12% [27].

Adiposity and metabolic markers

Height, waist, and hip circumference (all rounded to the nearest centimeter), and weight (rounded to the nearest 0.1 kg) were measured by trained technicians according to standardized protocols [29]. Established BMI cutoffs were used to define normal-weight (BMI 18.5–24.99 kg/m^2), overweight (BMI ≥25–30 kg/m^2) and obesity (BMI≥30 kg/m^2) [29]. Abnormal waist circumference was classified as >102 cm for men and >88 cm for women based on WHO guidelines [30].

Laboratory tests were performed by the HCHS/SOL Central Laboratory at the University of Minnesota. hs-CRP and HDL levels and Homeostatic model assessment of insulin resistance (HOMA-IR) (fasting glucose × fasting insulin/405) [31] were included in the analysis. hsCRP and glucose were measured on a Roche Modular P Chemistry Analyzer (Roche Diagnostics Corporation) using an immunoturbidimetric method. HDL cholesterol was measured using a direct magnesium/dextran sulfate method. Fasting insulin was measured using two commercial immunoassays (ELISA, Mercodia AB, Uppsala, Sweden; and sandwich immunoassay on a Roche Elecsys 2010 Analyzer, Roche Diagnostics, Indianapolis, IN); early measures conducted with the Mercodia assay were calibrated, and values were equivalent to the Roche method.

Statistical Analysis

Analyses were weighted to account for the selection of HCHS/SOL participants with unequal probabilities [21] and were performed using SAS version 9.3 (SAS Institute, Cary, NC) and SUDAAN release 11.0.1 (RTI International, Research Triangle Park, NC). hs-CRP was classified into the low/reference group (<3mg/L) [32] and values ≥3mg/L were split evenly between “moderate” (hs-CRP 3–7mg/L) and “high” (hs-CRP>7mg/L) categories. HOMA-IR was analyzed in quartiles, and HDL was analyzed as a dichotomous variable, with abnormal values defined as <40 mg/dL for men and <50 mg/dL for women [33]. Multivariable-adjusted prevalence ratios for asthma symptoms associated with each predictor variable (BMI categories, waist circumference, hs-CRP, HOMA-IR, and HDL), were derived from Poisson regression models with robust variance estimators, while adjusting for age, gender, height, current smoking status and lifetime pack- years [34], employment status [35], co-morbid conditions (coronary artery disease, and congestive heart failure) [36] and asthma medication use; the results are reported as Model 1. We then modeled all predictor variables (BMI categories, waist circumference, hs-CRP, HOMA-IR, and HDL) simultaneously to examine their independent effects on symptoms; the results are reported as Model 2. Similar linear regression models of each predictor variable (Model 1) and of all predictor variables together (Model 2) were constructed with raw values of FEV_1, and FVC and bronchodilator responsiveness as the dependent variables. In addition, a multiple imputation approach was taken to address the missing bronchodilator evaluation. Since all predictor variables (BMI categories, waist circumference, hsCRP, HOMA-IR and HDL) are associated with obesity, we ran diagnostic tests for all models to assess for

multicollinearity. The variance inflation factor (VIF) ranged from 1 to 4.9, suggesting that variances in beta estimates were not unduly impacted by correlations between predictor variables [37]. Further, several sensitivity analyses were carried out for co-existent COPD. We subsequently examined whether the above stated effects were modified by Puerto Rican status. Effect estimates specific to those of Puerto Rican and non-Puerto Rican background were derived from fully adjusted models constructed separately for each independent variable of interest, with interaction terms for Puerto Rican heritage. We also examined effect modification by gender and BMI categories in a similar manner.

Results

Characteristics of the study population

Tables 1 and 2 summarize the main characteristics of study participants. Compared to normal-weight participants, overweight and obese participants were older, more likely to be Puerto Rican, and have heart failure, but less likely to report current alcohol consumption; there were no significant differences in gender, employment status or coexisting COPD between the three BMI categories. As expected, overweight and obese participants had higher waist circumference, hs-CRP, and HOMA-IR, and lower HDL, than normal-weight participants.

Association of adiposity status with asthma burden

Table 3 shows a comparison of asthma symptoms, medication use, and pulmonary function according to BMI categories. Compared to normal-weight participants, overweight and obese participants were more likely to report cough on most days of the week and/or wheeze at least once a week. This symptom burden was accompanied by higher use of rescue and controller medications. More overweight and obese asthmatics were on inhaled steroids or combination therapy of inhaled steroids with long-acting beta agonists. Moreover, FVC and FEV_1 were lower in overweight and obese than normal-weight participants.

Association of adiposity, inflammation, and metabolic dysregulation with asthma symptoms

Overweight participants had 1.45-fold higher (95%CI 1.05, 2.01) and obese participants had 1.27-fold higher (95%CI 0.92, 1.76) prevalence of asthma symptoms than normal-weight participants (Table 4, Model 1). Participants with high hs-CRP had 1.29-fold (95%CI 1.06, 1.57) higher prevalence of symptoms than those in the low hs-CRP group (Table 4, Model 1). After adjustment for BMI categories, waist circumference, HOMA-IR and HDL (Table 4, Model 2), only hs-CRP persisted as a predictor of symptoms with prevalence ratio of 1.27 (95%CI 1.05, 1.54). This association did not differ by sex (P-interaction=0.56). Repeat sensitivity analyses after excluding participants with coexisting COPD yielded similar results (data not shown).

Association of adiposity, inflammation, and metabolic dysregulation with spirometry indices

Obese status, abnormal waist circumference, moderate and high hs-CRP, the highest quartile of insulin resistance, and abnormal HDL were individually associated with lower FVC

(Table 5, Model 1). However, after adjustment for BMI categories, waist circumference, and HOMA-IR, moderate and high hs-CRP, and low HDL remained significantly associated with a lower FVC (Table 5, Model 2).

Similar associations were observed for FEV_1 (Table 6). Abnormal waist circumference, hs-CRP in moderate and high categories, and abnormal HDL were individually associated with lower FEV_1 (Table 6, Model 1). After adjusting for BMI categories, waist circumference, and HOMA-IR, high hs-CRP and low HDL remained significant predictors of FEV_1 (Table 6, Model 2). We did not observe an association of BMI, waist circumference, hs-CRP, HOMA-IR, or HDL with bronchodilator responsiveness in both the complete case analysis (Supplementary Table 1) and imputed analyses accounting for those with incomplete post-bronchodilator spirometry (data not shown). The association of BMI categories and waist circumference with FVC and FEV_1 did not differ by sex (P-interaction=0.74 and 0.44 respectively) or when those with COPD were excluded from the analysis. Furthermore, the associations of BMI categories, waist circumference, metabolic dysregulation and inflammation with raw values of FEV_1 and FVC were retained for the percent-predicted values as well (Supplementary Tables 2 and 3).

Interaction of BMI with hs-CRP in predicting asthma burden

Given the above observations, we further examined the interaction between BMI and hs-CRP levels on asthma symptoms and pulmonary function (Figure 1). There was heterogeneity in the association of hs-CRP with asthma symptoms, FVC, and FEV_1 between the BMI categories (P-interaction ranging from 0.02 for FVC to 0.10 for symptoms). Although overweight and obese participants with low hs-CRP reported 52% (95%CI 2%, 127%) and 49% (95%CI 1%, 122%) higher prevalence of symptoms, respectively, and reduced FVC compared to normal-weight participants, higher hs-CRP among obese individuals was not associated with further increase in morbidity or decrease in pulmonary function. Normal weight and overweight individuals in the highest category of hs-CRP had FVC similar to obese individuals.

Differential association of hs-CRP with asthma burden among Puerto Ricans as compared to those of other Hispanic background

We further found that Puerto Ricans with moderate hs-CRP levels had 7% lower FVC (95%CI −1%, −12%) and high hs-CRP had 8% lower FVC (95%CI −3%, −13%), than those with low hs-CRP (Figure 2). A similar trend was not observed among those of other Hispanic background; those with moderate hs-CRP had 2% lower FVC (95%CI −6%, 2%) and those with high hs-CRP had 1% lower FVC (95%CI −5%, 4%)(P-interaction=0.04) (Figure 2). Similar but non-statistically significant results were obtained for FEV_1 (P-interaction=0.23, Figure 2) but not for symptoms.

Discussion

In the Study of Latinos, a representative sample of Hispanic adults from four metropolitan areas in the US, we found that hs-CRP, rather than general or truncal adiposity, was associated with disease symptoms or lower pulmonary function among overweight and

obese participants with asthma. In keeping with prior studies, we found that obesity was associated with higher symptom burden [38], and that low HDL [12, 39] and high HOMA-IR [19] were associated with pulmonary function abnormalities. However, when mutually controlled for adiposity and metabolic measures, hs-CRP was the only variable associated with both more symptoms and lower pulmonary function. Thus, while we confirmed previously reported individual associations of adiposity, metabolic dysregulation and systemic inflammation [40, 41] with asthma disease burden and pulmonary function deficits, by simultaneously modeling these variables in a multivariate analysis, we found that systemic inflammation is independently associated with, and modifies the association of adiposity or insulin resistance with asthma symptomatology and pulmonary function abnormalities in a Hispanic cohort.

There is substantial evidence that systemic, rather than airway inflammation, underlies obesity-related asthma [42]. Although several studies have linked leptin, a pro-inflammatory adipokine, and its related cytokines IL-6 and TNF, with asthma burden in obese individuals, these inflammatory markers are not routinely used in clinical care. Studies have reported elevated CRP among obese asthmatics [43], which correlates with lower pulmonary function [41] and airway hyper-responsiveness [44]. CRP decreases with weight loss and is associated with improved asthma control and quality of life [45]. Since truncal adiposity and metabolic dysregulation are intricately linked with systemic inflammation [16], our findings of the independent association of inflammation and its attenuating effect on the association of adiposity and insulin resistance with asthma burden, reinforce that inflammation, rather than adiposity and/or insulin resistance, is associated with asthma disease burden among the obese. Moreover, we are the first to show these associations in a representative sample of US Hispanic population. Although the direct mechanism by which hs-CRP may impact the lungs is not known, once validated, our results suggest that hs-CRP may serve as potential biomarker of asthma disease burden in obese individuals.

Further, we identified heterogeneity in the effect of hs-CRP across BMI categories with the linear trend between hs-CRP levels and asthma outcomes less evident among obese participants with high hs-CRP than among those of normal-weight and overweight status. Although obese participants with low hs-CRP levels already had 50% higher symptom prevalence and lower FVC than normal-weight participants, higher hs-CRP was not associated with progressively higher probability of symptoms or lower pulmonary function. This intriguing finding may potentially be explained by a threshold effect of hs-CRP associated with longstanding obesity. Since our study is cross sectional, longitudinal studies are needed to identify the role of both rapidity of weight gain and its persistence among the obese on the association of hs-CRP with pulmonary morbidity. Furthermore, since few studies have sub-classified hs-CRP beyond the 3mg/L threshold, whether the effect of hs-CRP in other chronic inflammatory diseases is similarly less prominent at higher levels is not known.

We also found a stronger association of hs-CRP with pulmonary function among Puerto Ricans, although this finding was statistically significant only for FVC. Given the higher asthma burden among Puerto Ricans [9], who also had higher overweight and obesity prevalence in our study, additional studies are needed to elucidate mechanisms specific to

Puerto Ricans, which may explain a higher susceptibility to obesity-related pulmonary morbidity.

In addition to hsCRP, low HDL remained an independent correlate of low pulmonary function, after adjusting for hs-CRP, suggesting that dyslipidemia influences pulmonary health by a mechanism distinct from systemic inflammation. HDL levels have been inversely associated with wheezing [12] and directly correlated with FEV_1 [39]. Conversely, high fat intake was associated with reduced HDL and elevated fractional exhaled nitric oxide (FeNO) within 2 hours [46], and increased neutrophilic airway inflammation and an attenuated response to bronchodilators in the long term [47]. These studies, in conjunction with our results, suggest that HDL may influence pulmonary function by modifying airway-specific inflammation rather than systemic inflammation. Together, the association of hs-CRP and low HDL with pulmonary function deficits, independent of adiposity, begins to identify biomarkers that may potentially be useful to identify obese individuals at risk for pulmonary morbidity.

Unlike prior reports [19], we did not find an independent association of insulin resistance with asthma symptoms or pulmonary function. The relatively low HOMA-IR levels in our population-based epidemiologic study as compared to a study where participants were recruited at an obesity clinic [19] or another that included Native Americans [20], known to have high diabetes prevalence, may explain these disparate results. Hence, it is likely that the HOMA-IR level or threshold that may be predictive of pulmonary involvement in obese individuals [19] may have been absent among our study participants.

Although our findings for general adiposity and symptoms extend those of prior studies [48–50] to U.S. Hispanics, we did not replicate a linear association between BMI and asthma symptoms found in non-Hispanic whites [49]. Further, attenuation of the association of abnormal waist circumference with FVC and FEV_1, when adjusted for hs-CRP and HDL, suggest that systemic inflammation and metabolic dysregulation, intricately linked to truncal adiposity, drive its association with asthma burden. Lastly, the lack of association between bronchodilator responsiveness and our obesity-related measures suggest that altered airway mechanics, rather than increased airway reactivity, may underlie obesity-related asthma [51] among Hispanics as well.

We recognize several study limitations. First, hs-CRP is a non-specific measure of inflammation and thus, does not increase our understanding of the type of inflammation involved in obese asthma among Hispanics. Although measures specific to systemic or airway atopic inflammation (total IgE, FeNO) or obesity-mediated inflammation (leptin, IL-6 and TNF) were not available to delineate distinct inflammatory subtypes, given the routine clinical use of hs-CRP, our results highlight its utility as a test to investigate pulmonary morbidity among obese individuals. However, airway-specific mechanisms by which hs-CRP influences the obese asthma phenotype need to be investigated. We had a high proportion of overweight and obese individuals in our sample but it was in keeping with national prevalence of overweight/obese status in Hispanics [8]. We also recognize the inherent limitations of using BMI as a measure of adiposity. However, the size of our study did not allow for inclusion of more sophisticated measures of adiposity. Moreover, the

overlap between percent body fat and BMI in a subset of SOL participants suggests that BMI in our participants is reflective of adiposity rather than high muscle mass [52]. We had a seventeen percent overlap between COPD and asthma in our cohort. However, sensitivity analysis confirmed that co-existent COPD did not influence the association of asthma morbidity with adiposity, hs-CRP and metabolic dysregulation. Furthermore, specific asthma questionnaires including Asthma Control Test were not used in the study and limited our ability to classify symptoms as per the NHLBI Asthma guidelines [26]. Finally, the cross sectional nature of our study conducted only in a Hispanic population, limits deductions of causality and generalizability to a non-Hispanic population. However, given the higher burden of both obesity and asthma among Hispanics, our findings are pertinent and facilitate an improved understanding of the biological processes that may underlie pulmonary morbidity in an ethnic group disproportionately burdened with obesity.

Conclusions

We found that systemic inflammation is associated with symptoms, and inflammation and low HDL are associated with lower pulmonary function among obese Hispanics with asthma, suggesting that inflammation plays a major role in obese asthma in Hispanics, with additional influences of dyslipidemia. The independent contributions of these adiposity-related complications suggest that quantification of inflammation and dyslipidemia among overweight and obese Hispanics may facilitate identification of those with higher pulmonary disease burden.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation list

BMI	Body mass index
HOMA-IR	Homeostatic model assessment of insulin resistance
HDL	High density lipoprotein
HCHS/SOL	Hispanic Community Health Study/Study of Latinos

FVC	Forced vital capacity
FEV_1	Forced expiratory volume in the first second
FeNO	Fractional exhaled nitric oxide

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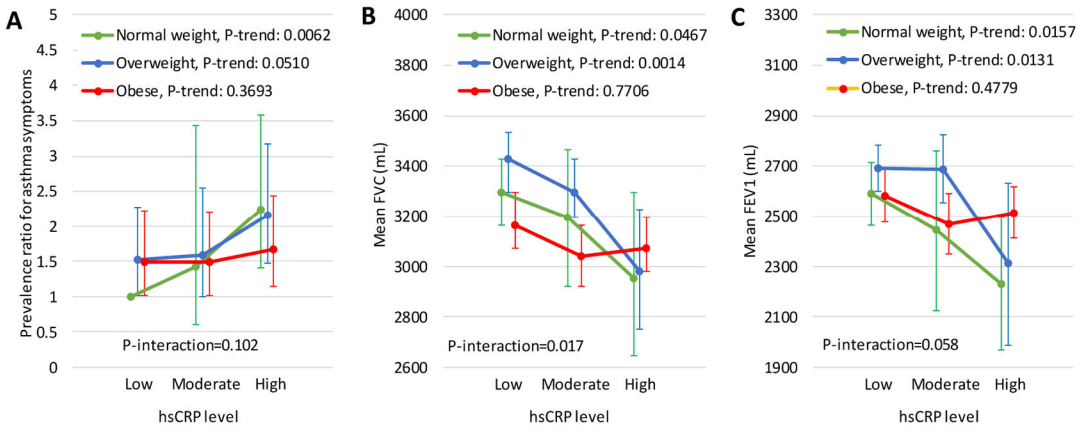

Figure 1.

Association of BMI with hs-CRP in predicting asthma burden among Hispanic adults. The association of low, moderate and high hs-CRP with A) asthma symptoms B) mean FVC C) mean FEV_1 among normal weight, overweight and obese participants. The curves depict the mean prevalence ratio, and mean raw FVC and FEV_1 values and their 95% confidence interval.

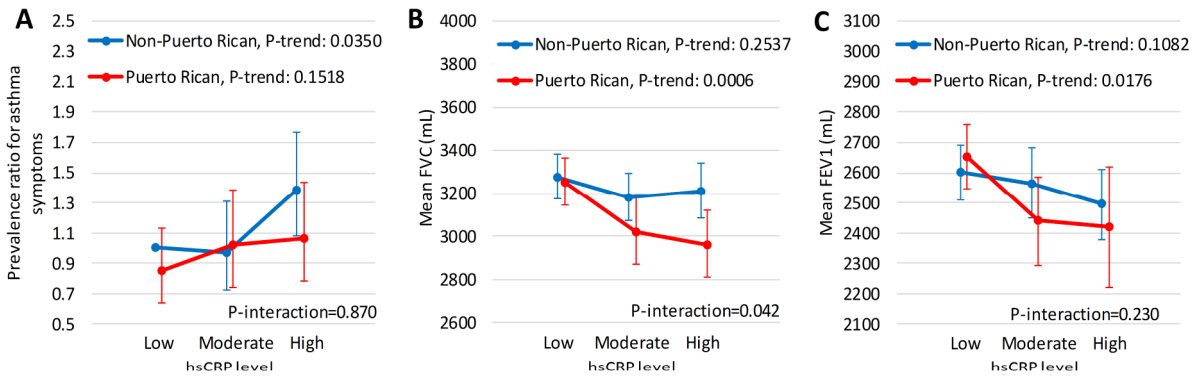

Figure 2.

Interaction of BMI with hs-CRP in predicting asthma burden among Puerto Rican as compared to non-Puerto Rican Hispanic adults. The association of low, moderate and high hs-CRP with A) asthma symptoms B) mean FVC C) mean FEV_1 among Puerto Rican and non-Puerto Rican participants. The curves depict the mean prevalence ratio, and mean raw FVC and FEV_1 values and their 95% confidence interval.

Table 1

Socio-demographic and clinical characteristics by BMI category among US Hispanic adults with asthma, HCHS/SOL 2008–2011

	Normal-weight	Overweight	Obese	
	N=144	N= 334	N= 648	
Variable	**Percent (95% CI)**	**Percent (95% CI)**	**Percent (95% CI)**	**P value**
Socio-demographic characteristics				
Age category				<0.001
18–29	40.8 (31.2, 51.2)	16.3 (10.7, 23.9)	10.8 (7.7, 15.1)	
30–39	14.9 (8.3, 25.3)	18.9 (11.4, 29.6)	18.4 (14.1, 23.5)	
40–49	13.2 (7.7, 21.6)	20.9 (15.1, 28.0)	20.2 (15.9, 25.3)	
50–59	11.5 (7.7, 16.7)	19.2 (14.7, 24.8)	23.9 (19.9, 28.4)	
60–69	14.7 (10.2, 20.6)	13.1 (9.9, 17.1)	17.6 (10.7, 27.7)	
70+	5.0 (1.9, 12.5)	11.7 (7.1, 18.8)	9.2 (6.7, 12.4)	
Males	35.2 (26.1, 45.6)	31.9 (25.1, 39.6)	31.3 (23.8, 39.9)	0.82
Latino heritage group				0.03
Puerto Rican	38.1 (28.6, 48.7)	48.5 (39.7, 57.3)	47.0 (39.4, 54.9)	
Cuban	26.5 (17.3, 38.4)	18.0 (12.5, 25.3)	15.8 (11.5, 21.4)	
Dominican	10.8 (5.8, 19.4)	7.1 (4.7, 10.6)	10.9 (7.9, 14.8)	
Mexican	14.3 (8.6, 22.8)	16.5 (11.0, 24.0)	16.0 (11.6, 21.6)	
Central American	3.9 (1.6, 9.2)	4.2 (2.5, 7.0)	3.2 (2.0, 4.9)	
South American	0.1 (0.0, 0.8)	2.8 (1.4, 5.4)	2.2 (1.2, 4.0)	
Other	6.3 (2.6, 14.4)	3.0 (1.4, 6.3)	4.8 (2.8, 8.2)	
Employed	37.3 (27.7, 48.1)	39.5 (32.0, 47.6)	32.3 (26.5, 38.6)	0.33
Smoking Status				0.05
Never	60.2 (50.8, 69.0)	49.6 (41.2, 58.0)	49.8 (42.8, 56.8)	
Former	9.7 (5.7, 15.9)	20.6 (12.5, 32.0)	24.6 (17.3, 33.7)	
Current	30.1 (22.2, 39.3)	29.9 (23.2, 37.5)	25.7 (21.0, 31.0)	
Cigarette pack-years * (mean (95% CI)	22.1 (14.9, 29.3)	15.7 (11.6, 19.8)	18.0(14.4, 21.5)	0.26
Alcohol consumption				0.07
Never	14.5 (9.1, 22.4)	22.2 (16.2, 29.7)	17.6 (13.8, 22.1)	
Former	32.3 (22.8, 43.5)	33.4 (26.1, 41.5)	44.5 (37.3, 51.9)	
Current	53.2 (42.5, 63.6)	44.4 (36.0, 53.2)	37.9 (31.9, 44.3)	
Medical history				
Childhood wheeze (age 5 years or younger)	15.1 (8.9, 24.5)	15.8 (8.8, 26.7)	11.5 (8.4, 15.6)	0.5
COPD	15.3 (10.7, 21.4)	16.4 (11.7, 22.3)	17.9 (10.7, 28.4)	0.9
Coronary heart disease	2.5 (1.1, 5.5)	6.3 (3.6, 10.7)	5.3 (3.5, 7.9)	0.1
Congestive heart failure	0.6 (0.1, 4.1)	2.9 (1.1, 7.5)	4.7 (3.0, 7.2)	0.004

All values represent population estimates and account for complex survey design.

P values were obtained from Wald F-statistics and test for any difference across groups. Percentages may not add to 100 due to rounding.

*Among ever smokers

Table 2

Prevalence of truncal adiposity, systemic inflammation and metabolic dysregulation by BMI category among US Hispanic adults with asthma

Variable	BMI Category			P value
	Normal weight	Overweight	Obese	
	Mean/Percent (95% CI)	Mean/Percent (95% CI)	Mean/Percent (95% CI)	
Measures of adiposity				
Waist circumference (cms) (mean)	82 (81, 83)	94 (93, 95)	115 (113, 116)	
Abnormal * (n=853), %	8.1 (4.8, 13.4)	61.2 (53.4, 68.5)	97.7 (96.1, 98.7)	<0.0001
Normal * (n=271), %	91.9 (86.7, 95.2)	38.8 (31.5, 46.6)	2.3 (1.3, 3.9)	
Measures of inflammation				
hs-CRP (mg/L) (mean)	1.0 (0.8, 1.3)	2.7 (2.1, 3.7)	4.6 (4.2, 5.0)	<0.0001
Low, 0– <3 (n=525), %	80.7 (71.5, 87.5)	60.2 (51.0, 68.7)	31.6 (27.4, 36.2)	<0.0001
Moderate, 3– <7 (n=310), %	11.7 (6.8, 19.3)	20.3 (14.5, 27.7)	37.0 (31.8, 42.6)	
High, ≥7 (n=278), %	7.6 (3.8, 14.6)	19.5 (12.0, 30.1)	31.3 (27.3, 35.7)	
Percent blood neutrophils †	55 (49, 63)	57 (52, 63)	57 (49, 63)	
Neutrophil count ($\times 10^9$) †	3.4 (2.7, 4.5)	3.8 (3.1, 4.7)	4.1 (2.9, 5.2)	
Percent blood eosinophils †	2.4 (1.0, 3.8)	2.8 (1.8, 4.0)	2.8 (1.9, 3.9)	
Eosinophil count ($\times 10^9$) †	0.11 (0.05, 0.21)	0.14 (0.06, 0.24)	0.14 (0.06, 0.24)	
Measures of glucose metabolism and serum lipids				
HOMA-IR (mean)	1.4 (1.3, 1.6)	2.2 (2.0, 2.5)	4.1 (3.8, 4.4)	<0.0001
Q1: 0– <1.59 (n=235), %	60.4 (49.8, 70.1)	31.3 (24.2, 39.5)	9.2 (6.5, 12.9)	<0.0001
Q2: 1.59– <2.57 (n=216), %	26.5 (18.7, 36.3)	23.1 (17.6, 29.8)	15.9 (12.7, 19.9)	
Q3: 2.57– <4.21 (n=304), %	9.8 (5.1, 18.1)	29.7 (21.2, 40.0)	29.3 (24.9, 34.2)	
Q4: ≥4.22 (n=352), %	3.2 (1.4, 7.4)	15.8 (11.1, 21.9)	45.6 (40.8, 50.4)	
HDL (mg/dl) (mean)	54.4 (51.7, 57.1)	49.9 (47.4, 52.4)	46.4 (45.2, 47.7)	<0.0001
Abnormal ≠ (n=524), %	27.1 (19.3, 36.7)	38.0 (29.6, 47.2)	57.1 (51.9, 62.2)	<0.0001
Normal ≠ (n=589), %	72.9 (63.3, 80.7)	62.0 (52.8, 70.4)	42.9 (37.8, 48.1)	

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All values represent population estimates and account for complex survey design.

Percentages may not add to 100 due to rounding

*Waist circumference: normal, ≤102 cm for men and ≤ 88 cm for women; abnormal, >102 cm for men and >88 cm for women.

†Percent blood neutrophils and eosinophils and their counts are reported as median (interquartile range) and were obtained from complete blood count analysis.

‡HDL: normal, ≥40 mg/dL for men and ≥50 mg/dL for women; abnormal, <40 mg/dL for men and <50 mg/dL for women.

Abbreviations: hs-CRP= high sensitivity C reactive protein; HOMA-IR= homeostatic measurement of insulin resistance; HDL= high density lipoprotein

Table 3

Asthma burden by BMI category in US Hispanic adults with asthma

Variable	BMI Category			
	Normal-weight	**Overweight**	**Obese**	***P* value**
Self-report asthma symptoms (% (95%CI))				
Asthma symptoms				0.03
None (n=624)	68.8 (59.1, 77.2)	50.2 (41.7, 58.6)	54.9 (47.9, 61.8)	
Cough and/or wheeze (n=502)				
Asthma medication use (% (95%CI))				
Short acting bronchodilators (n=477)	29.4 (21.5, 38.9)	44.3 (36.0, 53.0)	46.8 (40.0, 53.6)	0.02
Oral steroids (n=43)	1.8 (0.6, 5.6)	3.8 (1.1, 12.7)	4.7 (3.0, 7.3)	0.16
Controller medications				
None (n=771)	83.2 (75.9, 88.7)	69.4 (61.0, 76.7)	64.9 (56.7, 72.2)	0.001
ICS alone (n=53)	1.5 (0.5, 4.6)	2.3 (1.3, 4.2)	3.9 (2.5, 6.1)	0.14
Leukotriene receptor antagonist alone (n=89)	6.0 (3.1, 11.4)	10.2 (6.0, 16.9)	7.9 (5.4, 11.6)	0.45
ICS/LABA combination (n=124)	5.2 (3.0, 9.0)	10.6 (7.0, 15.8)	10.2 (7.4, 13.9)	0.05
ICS and leukotriene receptor antagonist (n=17)	0.6 (0.1, 3.7)	2.8 (0.5, 14.0)	1.0 (0.5, 1.9)	0.59
ICS/LABA combination and leukotriene receptor antagonist (n=56)	2.7 (0.8, 8.9)	3.1 (1.6, 5.8)	5.7 (3.5, 9.2)	0.27
Pulmonary function (mean (95% CI))				
FVC (ml)	3702 (3452, 3951)	3416 (3278, 3553)	3160 (3046, 3274)	<0.001
FVC (percent predicted)	93.4 (90.6, 96.1)	91.7 (89.0, 94.3)	84.0 (80.9, 87.2)	<0.0001
FEV_1 (ml),	2814 (2625, 3002)	2596 (2465, 2726)	2400 (2246, 2553)	0.003
FEV_1 (percent predicted)	85.0 (81.9, 88.1)	84.8 (81.3, 88.2)	78.4 (73.4, 83.3)	0.0579
FEV_1/FVC ratio	73.5 (71.3, 75.7)	75.2 (73.3, 77.2)	76.2 (73.6, 78.9)	<0.05

All values represent population estimates and account for complex survey design.

P value test for differences in means or geometric means across BMI groups for continuous variables, or any differences between groups for classification variables; for individual drug classes, P-values test differences in probabilities of using each drug class across BMI groups, versus all other categories.

Abbreviations: ICS= Inhaled corticosteroiod, LABA= Long acting beta agonists FVC = forced vital capacity, FEV_1 = forced expiratory volume in 1^{st} second

Table 4

Association of self-reported asthma symptoms with measures of adiposity, inflammation, and metabolic dysregulation in US Hispanic adults with asthma

Predictor Variables	Model 1* (n=1,105) PR for any symptoms vs none (95% CI)	Model 2† (n=1,083) PR for any symptoms vs none (95% CI)
Measures of adiposity		
BMI Category		
Normal-weight	Ref	Ref
Overweight	1.45 (1.05, 2.01) ǂ	1.37 (0.99, 1.91)
Obese	1.27 (0.92, 1.76)	1.27 (0.87, 1.86)
Waist circumference		
Normal	Ref	Ref
Abnormal	1.04 (0.80, 1.36)	1.03 (0.78, 1.37)
Measures of inflammation		
hs-CRP, mg/L		
Low, 0– <3	Ref	Ref
Moderate, 3– <7	1.08 (0.87, 1.34)	1.08 (0.86, 1.36)
High, ≥7	1.29 (1.06, 1.57) ǂ	1.27 (1.05, 1.54) ǂ
Measures of metabolic dysregulation		
HOMA-IR		
Q1: 0– <1.59	Ref	Ref
Q2: 1.59– <2.57	0.87 (0.67, 1.13)	0.82 (0.63, 1.06)
Q3: 2.57– <4.23	1.03 (0.80, 1.31)	0.92 (0.72, 1.17)
Q4: ≥4.23	0.90 (0.70, 1.16)	0.77 (0.59, 1.00)
HDL		
Normal	Ref	Ref
Abnormal	1.13 (0.95, 1.34)	1.11 (0.93, 1.32)

*Model 1 investigated the individual association of each predictor variable (BMI categories, waist circumference, hs-CRP, HOMA-IR and HDL) with asthma symptoms, adjusting for age, sex, height, field center, cigarette use, cigarette pack-years, self-reported coronary heart disease (including myocardial infarction, coronary artery bypass surgery, and stent or balloon angioplasty), self-reported history of heart failure, and anti-asthmatic medication use.

†Model 2 investigated the independent association of each predictor variable with asthma symptoms by including all predictor variables in one model in addition to adjusting for all covariates as detailed above in Model 1.

All values represent population estimates and account for complex survey design.

ǂp value<0.05 based on Poisson regression

Abbreviations: PR = Prevalence Ratio; CI = confidence interval; BMI= body mass index; hs-CRP = high-sensitivity C-Reactive protein; HOMA-IR= Homeostatic measurement of insulin resistance; HDL = high-density lipoprotein

Table 5

Association of FVC with measures of adiposity, inflammation, and metabolic dysregulation in US Hispanic adults with asthma

	Model 1*	Model 2†
	n=1,105	n=1,083
Predictor Variables	**β (95% CI)**	**β (95% CI)**
Measures of adiposity		
BMI Category		
Normal-weight	Ref	Ref
Overweight	25 (−128, 178)	126 (−31, 284)
Obese	−201 (−340, −62) ǂ	60 (−148, 268)
Waist circumference		
Normal	Ref	Ref
Abnormal	−253 (−369, −136) §	−98 (−254, 57)
Measures of inflammation		
hs-CRP, mg/L		
Low, 0– <3	Ref	Ref
Moderate, 3– <7	−208 (−309, −106) ǂ	−134 (−232, −36) ǂ
High, ≥7	−224 (−326, −121) ǂ	−138 (−249, −27) ǂ
Measures of metabolic dysregulation		
HOMA-IR		
Q1: 0– <1.59	Ref	Ref
Q2: 1.59– <2.57	−2 (−115, 110)	38 (−76, 152)
Q3: 2.57– <4.23	−106 (−227, 15)	−31 (−156, 95)
Q4: ≥4.23	−242 (−347, −137) §	−104 (−226, 18)
HDL		
Normal	Ref	Ref
Abnormal	−173 (−259, −87) §	−111 (−201, −22) ǁ

All values represent population estimates and account for complex survey design.

P values:

ǁ = <0.05;

ǂ = <0.01;

§ = < 0.001 based on linear regression.

* Model 1 investigated the individual association of each predictor variable (BMI categories, waist circumference, hs-CRP, HOMA-IR and HDL) with FVC, adjusting for age, sex, height, field center, cigarette use, cigarette pack-years, self-reported coronary heart disease (including myocardial infarction, coronary artery bypass surgery, and stent or balloon angioplasty), self-reported history of heart failure, and anti-asthmatic medication use

† Model 2 investigated the independent association of each predictor variable with FVC by including all predictor variables in one model in addition to adjusting for all covariates as detailed above in Model 1.

β is derived from linear regression analysis and represent change in FVC (ml) for unit change in predictor variable categories.

Abbreviations: FVC = forced vital capacity; CI = confidence interval; BMI= body mass index; hs-CRP = high-sensitivity C-Reactive protein; HOMA-IR= Homeostatic measurement of insulin resistance; HDL = high-density lipoprotein.

Table 6

Association of FEV_1 with measures of adiposity, inflammation, and metabolic dyregulation in US Hispanic adults with asthma

	Model 1* (n=1,105)	Model 2† (n=1,083)
Predictor Variables	**β (95% CI)**	**β (95% CI)**
Measures of adiposity		
BMI Category		
Normal-weight	Ref	Ref
Overweight	89 (−58, 236)	125 (−12, 263)
Obese	−56 (−184, 73)	93 (−111, 297)
Waist circumference		
Normal	Ref	Ref
Abnormal	−132 (−256, −9) ǂ	−63 (−213, 87)
Measures of inflammation		
hs-CRP, mg/L		
Low, 0– <3	Ref	Ref
Moderate, 3– <7	−111 (−212, −11) ǂ	−100 (−197, −3)
High, ≥7	−172 (−286, −58) §	−155 (−272, −38) §
Measures of metabolic dysregulation		
HOMA-IR		
Q1: 0– <1.59	Ref	Ref
Q2: 1.59– <2.57	64 (−46, 175)	85 (−32, 202)
Q3: 2.57– <4.23	31 (−92, 155)	76 (−51, 202)
Q4: ≥4.23	−36 (−132, 60)	56 (−56, 168)
HDL		
Normal	Ref	Ref
Abnormal	−120 (−204, −36) §	−100 (−188, −12) ǂ

All values represent population estimates and account for complex survey design.

P values:

ǂ = <0.05;

§ = <0.01 based on linear regression analysis

* Model 1 investigated the individual association of each predictor variable (BMI categories, waist circumference, hs-CRP, HOMA-IR and HDL) with FEV_1, adjusting for age, sex, field center, cigarette use, cigarette pack-years, self-reported coronary heart disease (including myocardial infarction, coronary artery bypass surgery, and stent or balloon angioplasty), self-reported history of heart failure, and anti-asthmatic medication use.

^ Model 2 investigated the independent association of each predictor variable with FEV_1 by including all predictor variables in one model in addition to adjusting for all covariates as detailed above in Model 1.

β is derived from linear regression analysis and represent change in FEV_1 (ml) for unit change in predictor variable categories.

Abbreviations: FEV_1 = forced expiratory volume in first second; CI = confidence interval; BMI= body mass index; hs-CRP = high sensitivity C-Reactive protein; HOMA-IR = homeostatic model assessment of insulin resistance; HDL = high-density lipoprotein.