Respiratory Medicine 125 (2017) 72–81

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

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

Deepa Rastogi [a, *], Molly Jung [a], Garrett Strizich [a], Pamela A. Shaw [b], Sonia M. Davis [c], Oana L. Klein [d], Frank J. Penedo [e], Andrew L. Ries [f], Martha L. Daviglus [g], Juan J. Moreiras [h], Matthias A. Salathe [h], Juan C. Celedón [i], Carmen R. Isasi [a], Robert C. Kaplan [a]

[a] Albert Einstein College of Medicine, Bronx, NY, United States
[b] University of Pennsylvania, Philadelphia, PA, United States
[c] University of North Carolina, Chapel Hill, NC, United States
[d] University of California, San Francisco, CA, United States
[e] Northwestern University, Chicago, IL, United States
[f] University of California, San Diego, CA, United States
[g] University of Illinois at Chicago, Chicago, IL, United States
[h] University of Miami, Miami, FL, United States
[i] University of Pittsburgh, PA, United States

ARTICLE INFO

Article history:
Received 20 December 2016
Received in revised form
28 February 2017
Accepted 2 March 2017
Available online 6 March 2017

Keywords:
Asthma
Obesity
Hispanics
Pulmonary function
Inflammation

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 = 1126). 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 HDL) and inflammation (high-sensitivity C-Reactive Protein≥3 mg/L) with reported asthma symptoms or pulmonary function measures (FEV_1, and FVC) while adjusting for demographic and clinical covariates.
Results: Of the 1126 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 −138 ml (95%CI -27 ml, −249 ml)) and FEV_1 (β −155 ml (95% CI -38 ml, −272 ml). Low HDL was also associated with lower FVC (β −111 ml (−22 ml, −201 ml) and FEV_1 (β −100 ml (−12 ml, −188 ml)). 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.

1. 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

* Corresponding author. Albert Einstein College of Medicine, 3415 Bainbridge Ave, Bronx, NY 10467, United States.
E-mail address: drastogi@montefiore.org (D. Rastogi).

http://dx.doi.org/10.1016/j.rmed.2017.03.003
0954-6111/

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 1100 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.

2. Methods

2.1. Study participants

Details on the HCHS/SOL study have been previously published [21,22]. Briefly, 16,415 Hispanic adults ages 18–74 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 1275 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 1126 participants.

2.2. 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].

2.3. 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 x 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.

2.4. 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 (<3 mg/L) [32] and values ≥3 mg/L were split evenly between “moderate” (hs-CRP 3–7 mg/L) and “high” (hs-CRP>7 mg/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