Published in final edited form as:

Allergy. 2018 July ; 73(7): 1547–1550. doi:10.1111/all.13450.

Genetic Predisposition to Obesity is associated with Asthma in US Hispanics/Latinos: Results from the Hispanic Community Health Study/Study of Latinos

Yanjun Guo^{1,2,#}, Jee-Young Moon^{3,#}, Cathy C Laurie⁴, Kari E North⁵, Lisa AP Sanchez-Johnsen⁶, Sonia Davis⁵, Bing Yu⁷, Sharmilee M Nyenhuis⁸, Robert Kaplan³, Deepa Rastogi^{9,*}, and Qibin Qi^{3,*}

¹School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Department of Occupational and Environmental Health, Wuhan, China

²Harvard T.H. Chan School of Public Health, Department of Epidemiology, Boston, MA, USA

³Albert Einstein College of Medicine, Department of Epidemiology and Population Health, Bronx, NY

⁴University of Washington, Department of Biostatistics, Seattle, WA

⁵University of North Carolina, Collaborative Studies Coordinating Center, Department of Biostatistics, Chapel Hill, NC

⁶University of Illinois at Chicago, Department of Psychiatry, Chicago, IL

⁷UT Health, Department of Epidemiology and Human Genetics Center, Houston, TX

⁸University of Illinois at Chicago, Department of Medicine, Chicago, IL

⁹Albert Einstein College of Medicine, Department of Pediatrics, Bronx, NY

Keywords

Obesity; Asthma; Genetic predisposition; U.S. Hispanics/Latinos; Genetics

Obesity and asthma are two significant public health issues worldwide. Accumulating evidence has related high body mass index (BMI) and obesity with asthma (1), although a causal role of obesity in the development of asthma remains uncertain. A recent study reported a significant association between genetic predisposition to obesity, estimated by a genetic risk score (GRS) based on 32 BMI-associated variants, and increased risk of

*To whom correspondence should be addressed: Dr. Deepa Rastogi (drastogi@montefiore.org), Department of Pediatrics; and Dr. Qibin Qi (qibin.qi@einstein.yu.edu), Department of Epidemiology and Population Health, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461.

#These authors contribute to this work equally

DR. YANJUN GUO (Orcid ID: 0000-0002-5927-778X)

Conflict of interest statement: The authors declare no competing interests.

Author Contribution: Conducted data analysis, interpreted the results, and wrote the manuscript: Y.G., J.M. Interpreted the results and revised the manuscript: C.L., K.N., L.J., S.D., B.Y., S.N., and R.K., Designed the study, analyzed and interpreted the results, provided clinical explanation, and revised the manuscript: D.R., Q.Q.

childhood asthma in 4,835 European children, supporting a potential causal relationship between obesity and asthma (2). However, it remains unknown whether genetic predisposition to obesity is associated with later-onset asthma which is different from childhood-onset asthma (3). Data is also limited in other ethnic groups, especially in US Hispanics/Latinos who have both high prevalence of obesity and asthma (4). Therefore, we aimed to examine whether genetic predisposition to obesity is associated with asthma and explore potential differences by sex and age of asthma onset in U.S. Hispanics/Latinos.

This study included 12,465 individuals aged 18–74 years from the Hispanic Community Health Study (HCHS)/Study of Latinos (SOL) (5). Information on presence of physician-diagnosed asthma and age of asthma onset were gathered from a standard respiratory questionnaire (5). A total of 1996 participants reported physician-diagnosed asthma, and were further separated into childhood-onset asthma ($n=1148$) and later-onset asthma ($n=841$) by asthma onset age <16 years old vs. ≥ 16 years. A BMI GRS was calculated by summing up the number of BMI-increasing alleles of 97 BMI-associated variants identified by genome-wide association studies (GWAS) (6). Details in study design and methods are available in Supplementary Data.

In this study, individuals with asthma were more likely to be females, born in US, and current smokers, and had lower levels of education, family income and pulmonary function (FVC, FEV₁, and FEV₁/FVC), and higher BMI and BMI GRS compared to those without asthma (Table S1). We also confirmed that higher BMI GRS was significantly associated with higher BMI ($P<0.001$), and higher BMI was significantly associated with increased odds of asthma ($P<0.001$) (Figure S1).

In all participants, higher BMI GRS was significantly associated with increased risk for asthma (OR=1.08[1.03, 1.14] per SD increment of GRS; $P=0.002$) and childhood-onset asthma (OR=1.12[1.06, 1.18]; $P<0.001$), but not later-onset asthma (OR=1.05[0.98, 1.13]; $P=0.182$) (Table 1). The ORs for asthma and childhood-onset asthma increased across tertiles of the BMI GRS ($P_{\text{trend}}=0.02$ and 0.004 , respectively). In females, higher BMI GRS showed significant associations with asthma (OR= 1.12[1.04, 1.19]; $P=0.001$), childhood-onset asthma (OR=1.15[1.06, 1.24]; $P=0.001$), and later-onset asthma (OR=1.09[1.00, 1.19]; $P=0.045$). In males, no significant associations between the BMI GRS and asthma were observed in both continuous and categorical analyses. However, no significant interactions between the BMI GRS and sex were observed (all $P_{\text{interaction}}>0.05$).

We then carried out stratified analyses by Hispanic/Latino background subgroups (Figure 1). Overall, the BMI GRS showed consistent associations with asthma across Hispanic/Latino background subgroups and little heterogeneity was observed (all $I^2=0.0\%$; all $P_{\text{heterogeneity}} \geq 0.59$), though most associations were not significant in each group. In addition, we also examined the association between the BMI GRS and asthma by smoking status in all participants as well as in females and males separately (Table S2). Results were consistent among never, former, and current smoker, and there was no evidence of effect modification by smoking status (all $P_{\text{interaction}}>0.05$).

In this population-based cohort of US Hispanics/Latinos, we found that the association between the BMI GRS and risk of asthma was more evident for childhood-onset asthma than later-onset asthma. Indeed, asthma that starts in childhood differed from adulthood-onset asthma (7). Later-onset asthma is proposed to be more complicated and is associated with worse prognosis, but also less is known about its prevalence, risk factors, and mechanisms as compared to childhood asthma (3). The lack of association of later-onset asthma with the BMI GRS is in line with prior GWAS-identified asthma-associated variants which also showed more pronounced effects on childhood-onset asthma than on later-onset asthma (7), together suggesting a relatively weaker role of genetic predisposition in later-onset asthma as compared to childhood-onset asthma. In addition, later-onset asthma is frequently non-atopic, suggesting that atopic might be involved in the relationship between obesity and asthma. However, our study was limited by lacking information on atopic status.

Another interesting finding of this study is that the BMI GRS was significantly associated with risk of asthma in females but not in males. This potential sex difference is consistent with some but not all prior studies. Granell et al. (2) found that the association between BMI and asthma was stronger in girls compared to boys, but there was no strong evidence for sex stratification in the association between a GRS based on 32 BMI-associated variants and asthma. In light of inconsistencies regarding sex difference in the relationship between obesity and asthma from observational studies (1), it is likely that factors such as sex hormones, adipokines, inflammatory cytokines from adipose tissue, and hormone-related events (e.g., menarche) potentially explain the sex differences (8).

Variations in the prevalence of asthma across different Hispanic/Latino subgroups have been observed in our HCHS/SOL (9) and other studies (4). In this analysis, the associations between genetic predisposition to obesity and asthma were generally consistent across Hispanic/Latino background subgroups, and little heterogeneity was observed. These results from subgroup analyses support the robustness of the observed association between genetic predisposition to obesity and risk of asthma and suggest that differences in asthma burden between different Hispanic/Latino subgroups in the context of obesity is likely driven by factors other than genetic predisposition.

In conclusion, our study showed a significant association between genetic predisposition to obesity and increased risk of asthma in US Hispanics/Latinos, providing evidence for a potential causal relationship between obesity and asthma. In addition, we found that the genetic association was more evident for childhood-onset asthma than later-onset asthma, and for females than males, but these findings need to be validated in future studies, including among individuals of diverse ethnic backgrounds.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: The baseline examination of the Hispanic Community Health Study/Study of Latinos was carried out as a collaborative study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the

University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following Institutes/Centers/Offices contributed to the HCHS/SOL first funding period through a transfer of funds to the NHLBI: National Institute on Minority Health and Health Disparities, the National Institute of Deafness and Other Communications Disorders, the National Institute of Dental and Craniofacial Research, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, and the NIH Office of Dietary Supplements. The Genetic Analysis Center at the University of Washington was supported by NHLBI and NIDCR contracts (HHSN268201300005C AM03 and MOD03). Genotyping efforts were supported by NHLBI HSN 26220/20054C, NCATS CTSI grant UL1TR000123, and NIDDK Diabetes Research Center (DRC) grant DK063491. Dr. Qi is supported by a Scientist Development Award (K01HL129892) from the NHLBI.

The authors thank the staff and participants of HCHS/SOL for their important contributions. A complete list of staff and investigators has been provided by Sorlie P., et al. in *Ann Epidemiol.* 2010; 20:642–649 and is also available on the study website <http://www.cscce.unc.edu/hchs/>.

References

1. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med.* 2007; 175(7):661–666. [PubMed: 17234901]
2. Granell R, Henderson AJ, Evans DM, Smith GD, Ness AR, Lewis S, et al. Effects of BMI, fat mass, and lean mass on asthma in childhood: a Mendelian randomization study. *PLoS Med.* 2014; 11(7):e1001669. [PubMed: 24983943]
3. de Nijs SB, Venekamp LN, Bel EH. Adult-onset asthma: is it really different? *Eur Respir Rev.* 2013; 22(127):44–52. [PubMed: 23457164]
4. Rosser FJ, Forno E, Cooper PJ, Celedon JC. Asthma in Hispanics. An 8-year update. *Am J Respir Crit Care Med.* 2014; 189(11):1316–1327. [PubMed: 24881937]
5. Lavange LM, Kalsbeek WD, Sorlie PD, Aviles-Santa LM, Kaplan RC, Barnhart J, et al. Sample design and cohort selection in the Hispanic Community Health Study/Study of Latinos. *Ann Epidemiol.* 2010; 20(8):642–649. [PubMed: 20609344]
6. Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Felix R, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature.* 2015; 518(7538):197–U401. [PubMed: 25673413]
7. Moffatt MF, Gut IG, Demenais F, Strachan DP, Bouzigon E, Heath S, et al. A large-scale, consortium-based genomewide association study of asthma. *N Engl J Med.* 2010; 363(13):1211–1221. [PubMed: 20860503]
8. Varraso R, Siroux V, Maccario J, Pin I, Kauffmann F, et al. Epidemiological Study on the G. Asthma severity is associated with body mass index and early menarche in women. *Am J Respir Crit Care Med.* 2005; 171(4):334–339. [PubMed: 15557134]
9. Barr RG, Aviles-Santa L, Davis SM, Aldrich TK, Gonzalez F, Henderson AG, et al. Pulmonary Disease and Age at Immigration among Hispanics Results from the Hispanic Community Health Study/Study of Latinos. *American Journal of Respiratory and Critical Care Medicine.* 2016; 193(4):386–395. [PubMed: 26451874]

Figure 1. Associations between BMI genetic score and asthma across Hispanic/Latino background groups

A, asthma; **B**, childhood-onset asthma; and **C**, later-onset asthma. Data are ORs (95% CI) for BMI genetic score on asthma, adjusted for sampling weight, sex, field center, US born, and 3 Hispanic background specific PCs. For asthma (A) and later-onset asthma (C), age, age of immigration, smoking, education, and income were further adjusted. Overall results were combined by fixed-effects meta-analysis.

Table 1

Associations of the BMI genetic risk score with asthma, childhood-onset asthma, and later-onset asthma in US Hispanics/Latinos.

	Case/Control	Continuous		P for interaction (GRS ×sex)	Tertiles			
		OR (95% CI)*	P Value		T1	T2	T3	
								P Trend
BMI genetic score (range)								
Asthma [†]								
All	1996/10469	1.08 (1.03,1.14)	0.002	0.14	1.00	0.98 (0.86,1.11)	1.16 (1.02,1.31)	0.02
Female	1351/5993	1.12 (1.04,1.19)	0.001		1.00	1.01 (0.86,1.19)	1.26 (1.08,1.48)	0.004
Male	645/4476	1.03 (0.94,1.11)	0.553		1.00	0.94 (0.77,1.17)	1.00 (0.82,1.22)	0.993
Childhood-onset Asthma								
All	1148/10469	1.12 (1.06,1.18)	<0.001	0.25	1.00	1.08 (0.94,1.25)	1.23 (1.07,1.41)	0.004
Female	687/5993	1.15 (1.06,1.24)	0.001		1.00	1.17 (0.96,1.42)	1.36 (1.13,1.65)	0.001
Male	461/4476	1.08 (0.99,1.18)	0.10		1.00	0.97 (0.77,1.22)	1.07 (0.86,1.34)	0.509
Later-onset Asthma [‡]								
All	841/10469	1.05 (0.98,1.13)	0.182	0.06	1.00	0.89 (0.74,1.07)	1.14 (0.95,1.36)	0.134
Female	659/5993	1.09 (1.00,1.19)	0.045		1.00	0.88 (0.71,1.10)	1.24 (1.00,1.52)	0.041
Male	182/4476	0.93 (0.80,1.07)	0.301		1.00	0.95 (0.67,1.35)	0.87 (0.61,1.24)	0.456

Definition of abbreviation: CI = confidence interval, GRS= genetic risk score, T= tertile, BMI=body mass index.

Models adjusted for sampling weight, sex, field center, 5 PCs, US born.

Controls were participants without asthma.

* Per 1 SD of BMI genotype score (6 units).

[†] Additionally adjusted for age, age of immigration, smoking, education, income.