**Name of Journal: *World Journal of Diabetes***

**Manuscript NO: 32589**

**Manuscript Type:** **Original Article**

***Observational Study***

**Risk factors for low high-density lipoprotein among Asian Indians in the United States**

Lucke-Wold B *et al*. Low HDL in immigrant Asian Indians

**Brandon Lucke-Wold, Ranjita Misra,Thakor G Patel**

**Brandon Lucke-Wold,** Department of Social and Behavioral Sciences, School of Public Health, West Virginia University, WV 26505, United States

**Ranjita Misra,** Social and Behavioral Sciences, West Virginia University School of Public Health, Morgantown, WV 26505, United States

**Thakor G Patel,** Uniformed University of Health Sciences, Bethesda, MD 20814, United States

**Author contributions:** All authors contributed equally to this work, read and approved the final manuscript; Misra R and Patel TG designed the research and completed the data collection; Misra R supervised the project, carried out the data analysis and drafted/edited the manuscript; Lucke-Wold B completed the literature review, created the tables and drafted/ edited the manuscript; Patel TG drafted and edited the manuscript.

**Institutional review board statement:** The study was approved by the institutional review board of two universities, for data collection and for data analysis (de-identified) for this current manuscript by West Virginia University.

**Informed consent statement:** Participation was voluntary, and informed consent was obtained from all subjects prior to participation. The study was approved by the institutional review board of Texas AM University. In order to protect anonymity, unique participant codes were created based on initials of first and last name and numbers for each participant.

**Conflict-of-interest statement:** The authors declare they have no conflict of interest.

**Data sharing statement:** The DIA study used an 18-page survey to assess various constructs and anthropometric and clinical data to assess prevalence and risk for diabetes. Clinical information and demographic questions pertaining to this study are referenced in the paper; details were also provided in the method section. The authors do not wish to share their data in such repositories because of the unique nature of this only large scale population-level data on immigrant Asian Indians in the US. However, the authors are willing to provide additional supporting files (in SPSS) on which the conclusions of the manuscript have been based.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Correspondence to: Ranjita Misra, PhD, Professor, MPH Program Coordinator,** Department of Social and Behavioral Sciences, School of Public Health, West Virginia University,  1500 University Avenue, Morgantown, WV 26506-9190, United States. [ramisra@hsc.wvu.edu](mailto:ramisra@hsc.wvu.edu)

**Telephone:** +1-304 2934168

**Fax:** +1**-**304 2936685

**Received:** January 16, 2017

**Peer-review started:** January 16, 2017

**First decision:** March 8, 2017

**Revised:** May 9, 2017

**Accepted:** May 22, 2017

**Article in press:**

**Published online:**

**Abstract**

***AIM***

To examine the differences in metabolic risk factors (RFs) by gender in the Asian Indian (AI) population in the United States.

***METHODS***

Using cross-sectional data from 1038 randomly selected Asian Indians, we investigated the relationship between metabolic syndrome (MetS) RFs, cardiovascular disease, and diabetes.

***RESULTS***

A greater percent of women in this group had increased waist circumference and low high density lipoprotein (HDL) levels than men, but AI males had increased blood glucose, increased blood pressure, and increased triglycerides compared to females. Those individuals who met the MetS criteria had increased cardiovascular disease. One of the biggest single RFs for cardiovascular disease and diabetes reported in the literature for AIs is low HDL.

***CONCLUSION***

Our results show that lack of knowledge about diabetes, low physical activity, increased body mass index, and age were the factors most significantly correlated with low HDL in this population. Future studies and prospective trials are needed to further elucidate causes of the MetS and diabetes in AIs.

**Key words:** Asian Indians; Diabetes; Cardiovascular disease; Metabolic syndrome; Low high density lipoprotein

© **The Author(s) 2017**. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Low high density lipoprotein (HDL) in American Indians is a significant risk factor for the metabolic syndrome. In particular, women with lack of knowledge about diabetes, decreased physical activity, and who have an increased body mass are at increased risk of low HDL.

Lucke-Wold B, Misra R,Patel TG.Risk factors for low high-density lipoprotein among Asian Indians in the United States. *World J Diabetes* 2017; In press

**INTRODUCTION**

South-Asians who live in the United States have an increased risk for developing the metabolic syndrome (MetS)[1]. A proposed reason is poor dietary habits consistent with sedentary western lifestyle[2]. Few studies have looked at this unique population, but data from the Indian Americans national study suggests that Asian Indians (AIs) may be more susceptible to certain components that make up the MetS[3]. For example, Vasudevan and colleagues found that obesity was prominent in people from South-Asian descent but was often times underdiagnosed[4]. Furthermore, AIs have increased risk for cardiovascular disease due to genetic predisposition and low high density lipoprotein (HDL)[5]. What is unknown however is if gender plays a significant role in increasing susceptibility for the MetS in this population. Furthermore, it is unknown what individual components of the MetS are more closely associated with diabetes in this population.

In this paper, we investigate these important questions utilizing data collected from a cross-sectional survey in the United States. Although causative factors cannot be determined, this study provides valuable insight into the differences observed between genders in relation to individual components of the MetS. More importantly, it highlights, which components of the MetS are more closely correlated with diabetes in this population. Previous studies in India have found that women have lower HDL than men and that cardiovascular risk factors (RFs) such as diabetes, hypertension, and smoking are highly prevalent[6,7]. Herein we report that a greater percent of AI males have increased fasting glucose, blood pressure, and triglycerides compared to females and that a greater percent of AI females have increased waist circumference and decreased HDL compared to males.

**MATERIALS AND METHODS**

***Sample and data collection***

The sample consisted of 1,038 randomly selected AIs aged ≥ 18 years from seven US cities (Houston, TX; Phoenix, AZ; Washington, DC; Boston, MA; San Diego, CA; Edison, NJ and Parsippany, NJ); sampling frame and data collection methodology was previously reported[8]. All participants consented for the study prior to completing phone interviews and subsequent anthropometric/fasting blood work. In order to protect anonymity, participant codes were created based on letter codes and numbers unique to each participant. Non-participants did not differ in gender, educational level, family history of diabetes and cardiovascular disease, or smoking status, but were significantly older than participants. Survey data were collected *via* telephone interviews by trained, multilingual AI staff; the response rate was 37%. All participants completed blood work (after a 10 h fast) and anthropometric measurements. Blood samples were centrifuged to separate plasma or serum, and shipped on ice to three core laboratories for biochemical analysis (Atherotech Laboratory (Birmingham, AL), Diabetes Diagnostic Laboratory (Columbia, MO), and Translational Metabolism Unit, Baylor College of Medicine (Houston, TX)). The Institutional Review Board of Texas A&M University approved the study.

***Measures***

**Demographic information:**Demographic information included age, gender, marital status, education, income, and access to conventional health care (health insurance coverage). Income was assessed as a categorical variable with response options ranging from < $10000 to ≥ $150000.Body mass index (BMI) was calculated from height and weight (kg/m2).

**Knowledge ofMetS RFs:**Knowledge of 11 MetS RFs (age, high cholesterol, DM, male gender, menopause, fat intake, overweight/obesity, family history, sedentary lifestyle, smoking, and stress) was assessed. Response options for each RF were 0 = no and 1 = yes. A MetS knowledge score was computed by summing the number of correct answers (Cronbach’s α = 0.78); a higher score indicated greater knowledge.

**Fasting glucose:** Fasting capillary glucose (mg/dL) was measured using Accucheck Advantage (Roche Diagnostics, Indianapolis, IN). Although fasting serum glucose was collected and stored, analysis indicated abnormal levels with large standard deviations from the capillary glucose for one-third of the respondents. Hence fasting capillary glucose was used for calculating CMetS in the current analysis.

**RFs for MetS:** Plasma samples were assayed for TG, HDL using the vertical auto profile test at the Atherotech Laboratory (Birmingham, AL) as described previously[9]. The LDL-R subfraction was determined by subtracting Lp(a) and IDL from total LDL.

**Waist circumference:** For males/females, the cut-off of WC = 35.4/31.5 inches was used to define elevated WC in this study, based on the IDF criteria for South Asians; also it has a high sensitivity (0.901/0.923) and specificity (0.836/0.768) for identifying South Asians with BMI ≥ 25 kg/m2 [10].

# *Definitions*

**MetS:** MetS was assessed according to the Harmonization criteria, *i.e.*, presence of ≥ 3 of the MetS RFs: central obesity, elevated triglycerides (≥ 150 mg/dL), low HDL (< 40 mg/dL in males, < 50 mg/dL in females, or specific treatment for these lipid abnormalities), elevated BP (≥ 130/≥ 85 mmHg or treatment of previously diagnosed hypertension), and elevated fasting glucose (≥ 100 mg/dL or previously diagnosed type 2 diabetes). Central obesity was defined as ethnicity-specific elevated WC (for South Asians: ≥ 35.4 inches for males, ≥ 31.5 inches for females, where South Asian included Chinese, Malay and Asian-Indian populations)[11].

**Diabetes:** Diabetes was defined as fasting blood glucose ≥ 126 mg/dL or a self-report of previously diagnosed diabetes. Impaired fasting glucose was defined as fasting blood glucose between 100-125 mg/dL.

***Statistical analysis***

All analyses were performed using IBM SPSS version 24.0 (Chicago, IL) by the authors. The statistical analysis was reviewed by an expert biostatistician at WVU for adequacy, appropriateness, homogeneity of the data including missingness prior to the multivariate analysis. Basic descriptive statistics were obtained for demographic variables and MetS RFs. Analysis of variance was used to examine the difference in MetS RFs by gender for the total sample and by those with type 2 diabetes mellitus (T2DM). The acceptance level for statistical significance was α = 0.05. Multiple logistic regression analysis was used to predict low HDL controlling for traditional RFs such as age, gender, BMI, lifestyle behaviors, family history of chronic diseases, and MetS knowledge, and diabetes status. Sample size calculations indicated that 656 participants would provide over 80% power to detect important differences in HDL risk.

**RESULTS**

***MetS variables***

Lauderdale and colleagues found that the MetS was significantly higher at all BMIs in Asian Americans *vs* non-Hispanic Whites[12]. In those surveyed for our study, 62.7% had elevated fasting blood glucose (651/1038), 28.7% had elevated blood pressure (298/1038), and 41.3% had elevated triglycerides (429/1038). Sixty percent had an elevated waist circumference (623/1038) and 35.9% had low levels of HDL cholesterol (373/1038). These values were similar to those reported by Misra *et al*[13] from AIs living in northern California.

***Variables by gender***

Recent evidence indicates that AIs have genetic single nucleotide polymorphisms that make them susceptible to developing the MetS in the context of poor diets and western sedentary lifestyles[14]. What has not been adequately investigated however is the role of gender as increasing risk for metabolic criteria. We report in Table 1 significant differences between male and females for individual components of the MetS. Interestingly, males were more likely to have elevated blood glucose, elevated blood pressure, and elevated triglycerides compared to females whereas females were more likely to have elevated waist circumference and low HDL cholesterol.

***Heart disease and T2DM***

Trude *et al*[15] reported that AIs had a 7.8% prevalence of cardiovascular disease. In our cohort, we found that 7.2% of survey participants had been diagnosed with cardiovascular disease. MetS can increase the risk for cardiovascular disease and subsequent adverse outcomes[16]. Similarly, diabetes is increasingly prevalent in this population. Seventeen point four percent of survey participants had diabetes and 32.9% of participants had pre-diabetes. Like cardiovascular disease, diabetes increases the risk for long-term morbidity and mortality[17].

***Diabetes and individual components of the MetS***

Anjana *et al*[18] found that low HDL in Indians is a predictor for the progression to T2DM. In Table 1, we report that a greater percentage of AI females had low HDL than males. In Table 2, we look specifically at participants with diagnosed or undiagnosed T2DM. The majority (60.71%) of females diagnosed with diabetes had low HDL compared to only 39.32% of males. Hence, further investigation is warranted to determine if low HDL in females might contribute to the onset and progression of diabetes in this population.

***Multivariate analysis of RFs for low HDL***

Mani *et al*[19] found that low HDL is a primary predictor of progression towards diabetes and the MetS. We were interested in what factors were significantly associated with low HDL in our AI population (Table 3). A significant effect was found for age of respondent (*P* = 0.03), physical activity level (*P* = 0.014), knowledge about diabetes risk factors (*P* = 0.017), and the BMI (*P* = 0.01). Other groups have shown similar correlations between these risk factors and low HDL in other populations with high prevalence of the MetS[20].

**DISCUSSION**

Cardiovascular disease mortality is significantly higher among AIs and MetS, a proxy to predict the development of CVD, is of concern in this high-risk group. A study in South Asia recently found that ethnic Chinese had the lowest incidence of the MetS whereas ethnic Indians had the highest rate[21]. The MetS in this population can lead to an increase in vascular inflammatory markers such as C reactive protein, which can accelerate the progression of T2DM[22]. Indians as a whole have increased risk for developing diabetes due to genetic predisposition for poor insulin secretion[23]. This predilection for diabetes is even present in AIs with low body weight[24]. Little is known about gender differences in individual MetS components among AIs; our results highlight significant differences among male and female AIs for the five MetS criteria in a large Asian Indian sample in the United States. The results have broad-reaching implications for public health education, primary prevention, and improving unhealthy behavior.

A greater percentage of AI males had increased blood glucose, increased blood pressure, and increased triglycerides compared to females. Interestingly however, females had increased waist circumference and lower HDL compared to males. Recent evidence suggests that low HDL has a strong genetic component and can significantly increase the risk for cardiovascular disease, diabetes, and mortality[25]. Although this study is cross-sectional in design, it does show an important finding in that AI women with diabetes are much more likely to have low HDL than males.

Our study results showed that the obesity was associated with low HDL levels among AIs. One plausible explanation might be the westernized lifestyle adapted upon immigration or acculturation to the United States society. In addition, the increased vulnerability to metabolic diseases including the MetS may be due to the unique body composition, which is marked by increase in abdominal obesity and percent body fat. This is termed the “Yudkin Yajnik paradox” where AIs with low BMI have higher percent body fat than African Americans and Europeans increasing their risk for metabolic diseases[26]. The typical AI phenotype is one of higher percent body fat, higher truncal, sub-cutaneous, and intra-abdominal fat, and less lean body mass[27]. These features are even noted in AI neonates[28]. These genetic findings coupled with biochemical indicators such as high levels of inflammatory markers, low levels of adiponectin, the co-existence of hyperinsulinemia, insulin resistance, hypertriglyceridemia, abnormal lipid profiles, endothelial dysfunction and hyperhomocystenemia set the stage for chronic low grade inflammation that exacerbates morbidity and mortality among AIs. Since muscle mass is an indicator of insulin sensitivity, a lower muscle mass re-routes energy from large carbohydrate meals typical in the Asian Indian diet into hepatic lipogenesis compromising muscle glycogen synthesis. The outcome is atherogenic dyslipidemia[29], a menacing combination that is metabolically linked to insulin resistance, promotes sub-clinical chronic inflammation, and is strongly associated with type 2 diabetes and cardiovascular disease. Underlying genetic factors such as gene variants and polymorphisms further exacerbate the risk for AIs. These factors include the ectonucleotide pyrophosphate phosphodiesterase 1 (ENPP1) 121Q variant implicated in negatively influencing insulin receptor signaling[30], the *DOK5* gene[31] that increases the risk for diabetes in immigrant AIs[30], apolipoprotein E gene polymorphisms and the Myostatin gene linked to abdominal obesity[32], the AMDI variant in homocysteine metabolism that predisposes children to obesity[33], and finally the PPAR-gamma polymorphisms that contribute to non-alcoholic fatty liver disease[34]. Research shows low HDL level is a strong and independent risk factor for cardiovascular disease[35]. A meta-analysis showed one mg/dL increase of HDL-C levels is associated with a 2%–3% decreased CVD risk[36]. It may be one of the primary reasons why AIs are disproportionately burdened by coronary artery disease at younger ages and in more severe forms[37,38]. Our results concur with prior studies that AIs have amplified low levels of HDL as compared to Non-Hispanic Whites and Europeans. Furthermore, the higher prevalence of low HDL among AI females (61%) than AI males in this study (39%) support prior literature on a higher prevalence among AI women ranging from 65%-79%[37,39,40] than among AI men 35%-67% [37,39-41].

Low HDL can be exacerbated in the context of sedentary habits and a poor diet in Indian populations[42]. We found that obesity, decreased physical activity, lack of knowledge about diabetes, and advanced age are significantly associated with low HDL in this population. AIs who have lived in the United States for greater than 10 years are more likely to have a sedentary lifestyle, increased obesity, and increased risk of diabetes type 2[43]. Ghai and colleagues compared an AI cohort to a White non-Hispanic cohort. They noted that AIs were less likely to eat 5 servings of fruit and vegetables a day and less likely to engage in physical activity. They were more likely however to have a lower calorie diet, not smoke, and not consume alcohol[44]. The authors concluded that genetics in addition to lifestyle factors contributed to the development of the MetS in AIs.

Going forward, it will be important to isolate key genetic components that increase the susceptibility of low HDL in AI women. Once these components are identified, it will be possible to develop a tailored treatment approach and education with personalized medicine. Additionally, public health initiatives can provide an important element for training individuals to engage in health promoting behavior. Diabetes prevention and management programs can help individuals learn key skills on how to prevent and manage the MetS. These programs can be especially influential for the AI population[45].

The MetS affects the AI population and may contribute to the increased prevalence of diabetes. Interestingly, we found a significant difference in metabolic components between men and women. A greater percent of women met the waist circumference and low HDL criteria than men. Furthermore, in this cohort we found a high prevalence of diagnosed cardiovascular disease, which has been linked to increased adverse vascular events. Understanding the genetic and environmental components that contribute to the increased MetS in this population will be essential in order to improve and tailor public health and pharmacologic treatment approaches.

**COMMENTS**

***Background***

American Indians are prone to develop the metabolic syndrome (MetS) once they adapt a western lifestyle.

***Research frontiers***

This article addresses the importance of low high density lipoprotein for the development of diabetes and the MetS in American Indians.

***Innovations and breakthroughs***

Improving education about the MetS for this population will be beneficial.

***Applications***

In particular, diabetes prevention and management programs will be highly important to implement for this population.

***Terminology***

The authors specifically focused on the components of the MetS.

***Peer-review***

The authors utilized data collected from a cross-sectional survey from 1038 randomly selected Asian Indians in the U.S to investigate the relationship between metabolic syndrome risk factors, cardiovascular disease, and diabetes. The article implicates that one of the biggest single risk factors for cardiovascular disease and diabetes reported in the literature for Asian Indians is low HDL. It is suitable to the Journal and could be helpful in clinic application.

**REFERENCES**

1 **Needham BL**, Kim C, Mukherjee B, Bagchi P, Stanczyk FZ, Kanaya AM. Endogenous sex steroid hormones and glucose in a South-Asian population without diabetes: the Metabolic Syndrome and Atherosclerosis in South-Asians Living in America pilot study. *Diabet Med* 2015; **32**: 1193-1200 [PMID: 25443798 DOI: 10.1111/dme.12642]

2 **Ali R**, Lee ET, Knehans AW, Zhang Y, Yeh J, Rhoades ER, Jobe JB, Ali T, Johnson MR. Dietary Intake among American Indians with Metabolic Syndrome - Comparison to Dietary Recommendations: the Balance Study. *Int J Health Nutr* 2013; **4**: 33-45 [PMID: 26594109]

3 **Kotha P**, Patel CB, Vijayaraghavan K, Patel TG, Misra R. Modified criteria for determining cardiometabolic syndrome in Asian Indians living in the USA: report from the diabetes among Indian Americans national study. *Int J Cardiol* 2012; **155**: 343-345 [PMID: 22261694 DOI: 10.1016/j.ijcard.2011.12.040]

4 **Vasudevan D**, Stotts AL, Mandayam S, Omegie LA. Comparison of BMI and anthropometric measures among South Asian Indians using standard and modified criteria. *Public Health Nutr* 2011; **14**: 809-816 [PMID: 21247513 DOI: 10.1017/S1368980010003307]

5 **Enas EA**, Kuruvila A, Khanna P, Pitchumoni CS, Mohan V. Benefits & amp; risks of statin therapy for primary prevention of cardiovascular disease in Asian Indians - a population with the highest risk of premature coronary artery disease & amp; diabetes. *Indian J Med Res* 2013; **138**: 461-491 [PMID: 24434254]

6 **Gupta A**, Gupta R, Sharma KK, Lodha S, Achari V, Asirvatham AJ, Bhansali A, Gupta B, Gupta S, Jali MV, Mahanta TG, Maheshwari A, Saboo B, Singh J, Deedwania PC. Prevalence of diabetes and cardiovascular risk factors in middle-class urban participants in India. *BMJ Open Diabetes Res Care* 2014; **2**: e000048 [PMID: 25489485 DOI: 10.1136/bmjdrc-2014-000048]

7 **Gupta R**, Sharma M, Goyal NK, Bansal P, Lodha S, Sharma KK. Gender differences in 7 years trends in cholesterol lipoproteins and lipids in India: Insights from a hospital database. *Indian J Endocrinol Metab* 2016; **20**: 211-218 [PMID: 27042418 DOI: 10.4103/2230-8210.176362]

8 **Misra R**, Modawal A, Panigrahi B. Asian-Indian physicians' experience with managed care organizations. *Int J Health Care Qual Assur* 2009; **22**: 582-599 [PMID: 19957420 DOI: 10.1108/09526860910986858]

9 **Kulkarni KR**. Cholesterol profile measurement by vertical auto profile method. *Clin Lab Med* 2006; **26**: 787-802 [PMID: 17110240]

10 **Misra A**, Misra R. Asian indians and insulin resistance syndrome: global perspective. *Metab Syndr Relat Disord* 2003; **1**: 277-283 [PMID: 18370652 DOI: 10.1089/1540419031361390]

11 **Bainey KR**, Norris CM, Gupta M, Southern D, Galbraith D, Knudtson ML, Graham MM. Altered health status and quality of life in South Asians with coronary artery disease. *Am Heart J* 2011; **162**: 501-506 [PMID: 21884867 DOI: 10.1016/j.ahj.2011.06.009]

12 **Palaniappan LP**, Wong EC, Shin JJ, Fortmann SP, Lauderdale DS. Asian Americans have greater prevalence of metabolic syndrome despite lower body mass index. *Int J Obes (Lond)* 2011; **35**: 393-400 [PMID: 20680014 DOI: 10.1038/ijo.2010.152]

13 **Misra KB**, Endemann SW, Ayer M. Measures of obesity and metabolic syndrome in Indian Americans in northern California. *Ethn Dis* 2006; **16**: 331-337 [PMID: 17682232]

14 **Arnaiz-Villena A**, Fernández-Honrado M, Rey D, Enríquez-de-Salamanca M, Abd-El-Fatah-Khalil S, Arribas I, Coca C, Algora M, Areces C. Amerindians show association to obesity with adiponectin gene SNP45 and SNP276: population genetics of a food intake control and "thrifty" gene. *Mol Biol Rep* 2013; **40**: 1819-1826 [PMID: 23108996 DOI: 10.1007/s11033-012-2236-1]

15 **Trude AC**, Kharmats A, Jock B, Liu D, Lee K, Martins PA, Pardilla M, Swartz J, Gittelsohn J. Patterns of Food Consumption are Associated with Obesity, Self-Reported Diabetes and Cardiovascular Disease in Five American Indian Communities. *Ecol Food Nutr* 2015; **54**: 437-454 [PMID: 26036617 DOI: 10.1080/03670244.2014.922070]

16 **Lucke-Wold BP**, Turner RC, Lucke-Wold AN, Rosen CL, Huber JD. Age and the metabolic syndrome as risk factors for ischemic stroke: improving preclinical models of ischemic stroke. *Yale J Biol Med* 2012; **85**: 523-539 [PMID: 23239952]

17 **Giugliano D**, Maiorino MI, Bellastella G, Esposito K. Glucose, cholesterol, and blood pressure: is lower always better for type 2 diabetes? *Endocrine* 2016; **54**: 32-37 [PMID: 27220940 DOI: 10.1007/s12020-016-0981-y]

18 **Anjana RM**, Shanthi Rani CS, Deepa M, Pradeepa R, Sudha V, Divya Nair H, Lakshmipriya N, Subhashini S, Binu VS, Unnikrishnan R, Mohan V. Incidence of Diabetes and Prediabetes and Predictors of Progression Among Asian Indians: 10-Year Follow-up of the Chennai Urban Rural Epidemiology Study (CURES). *Diabetes Care* 2015; **38**: 1441-1448 [PMID: 25906786 DOI: 10.2337/dc14-2814]

19 **Mani P**, Ren HY, Neeland IJ, McGuire DK, Ayers CR, Khera A, Rohatgi A. The association between HDL particle concentration and incident metabolic syndrome in the multi-ethnic Dallas Heart Study. *Diabetes Metab Syndr* 2016; : [PMID: 27993539 DOI: 10.1016/j.dsx.2016.12.028]

20 **Brugnara L**, Murillo S, Novials A, Rojo-Martínez G, Soriguer F, Goday A, Calle-Pascual A, Castaño L, Gaztambide S, Valdés S, Franch J, Castell C, Vendrell J, Casamitjana R, Bosch-Comas A, Bordiú E, Carmena R, Catalá M, Delgado E, Girbés J, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Pascual-Manich G, Serrano-Ríos M, Gomis R, Ortega E. Low Physical Activity and Its Association with Diabetes and Other Cardiovascular Risk Factors: A Nationwide, Population-Based Study. *PLoS One* 2016; **11**: e0160959 [PMID: 27532610 DOI: 10.1371/journal.pone.0160959]

21 **Rampal S**, Mahadeva S, Guallar E, Bulgiba A, Mohamed R, Rahmat R, Arif MT, Rampal L. Ethnic differences in the prevalence of metabolic syndrome: results from a multi-ethnic population-based survey in Malaysia. *PLoS One* 2012; **7**: e46365 [PMID: 23029497 DOI: 10.1371/journal.pone.0046365]

22 **Kaur R**, Matharoo K, Sharma R, Bhanwer AJ. C-reactive protein + 1059 G& gt; C polymorphism in type 2 diabetes and coronary artery disease patients. *Meta Gene* 2013; **1**: 82-92 [PMID: 25606378 DOI: 10.1016/j.mgene.2013.10.012]

23 **Narayan KM**. Type 2 Diabetes: Why We Are Winning the Battle but Losing the War? 2015 Kelly West Award Lecture. *Diabetes Care* 2016; **39**: 653-663 [PMID: 27208372 DOI: 10.2337/dc16-0205]

24 **Kanaya AM**, Wassel CL, Mathur D, Stewart A, Herrington D, Budoff MJ, Ranpura V, Liu K. Prevalence and correlates of diabetes in South asian indians in the United States: findings from the metabolic syndrome and atherosclerosis in South asians living in america study and the multi-ethnic study of atherosclerosis. *Metab Syndr Relat Disord* 2010; **8**: 157-164 [PMID: 19943798 DOI: 10.1089/met.2009.0062]

25 **Hanks LJ**, Pelham JH, Vaid S, Casazza K, Ashraf AP. Overweight adolescents with type 2 diabetes have significantly higher lipoprotein abnormalities than those with type 1 diabetes. *Diabetes Res Clin Pract* 2016; **115**: 83-89 [PMID: 27242127 DOI: 10.1016/j.diabres.2016.03.004]

26 **Yajnik CS**, Yudkin JS. The Y-Y paradox. *Lancet* 2004; **363**: 163 [PMID: 14726172 DOI: 10.1016/S0140-6736(03)15269-5]

27 **Patel SA**, Shivashankar R, Ali MK, Anjana RM, Deepa M, Kapoor D, Kondal D, Rautela G, Mohan V, Narayan KM, Kadir MM, Fatmi Z, Prabhakaran D, Tandon N; [CARRS Investigators](https://www.ncbi.nlm.nih.gov/pubmed/?term=CARRS%20Investigators%5BCorporate%20Author%5D). Is the "South Asian Phenotype" Unique to South Asians?: Comparing Cardiometabolic Risk Factors in the CARRS and NHANES Studies. *Glob Heart* 2016; **11**: 89-96.e3 [PMID: 27102026 DOI: 10.1016/j.gheart.2015.12.010]

28 **Wild SH**, Byrne CD. Evidence for fetal programming of obesity with a focus on putative mechanisms. *Nutr Res Rev* 2004; **17**: 153-162 [PMID: 19079923 DOI: 10.1079/NRR200487]

29 **Misra A**, Shrivastava U. Obesity and dyslipidemia in South Asians. *Nutrients* 2013; **5**: 2708-2733 [PMID: 23863826 DOI: 10.3390/nu5072708]

30 **Abate N**, Chandalia M, Satija P, Adams-Huet B, Grundy SM, Sandeep S, Radha V, Deepa R, Mohan V. ENPP1/PC-1 K121Q polymorphism and genetic susceptibility to type 2 diabetes. *Diabetes* 2005; **54**: 1207-1213 [PMID: 15793263]

31 **Tabassum R**, Mahajan A, Chauhan G, Dwivedi OP, Ghosh S, Tandon N, Bharadwaj D. Evaluation of DOK5 as a susceptibility gene for type 2 diabetes and obesity in North Indian population. *BMC Med Genet* 2010; **11**: 35 [PMID: 20187968 DOI: 10.1186/1471-2350-11-35]

32 **Bhatt SP**, Nigam P, Misra A, Guleria R, Luthra K, Jain SK, Qadar Pasha MA. Association of the Myostatin gene with obesity, abdominal obesity and low lean body mass and in non-diabetic Asian Indians in north India. *PLoS One* 2012; **7**: e40977 [PMID: 22916099 DOI: 10.1371/journal.pone.0040977]

33 **Tabassum R**, Jaiswal A, Chauhan G, Dwivedi OP, Ghosh S, Marwaha RK, Tandon N, Bharadwaj D. Genetic variant of AMD1 is associated with obesity in urban Indian children. *PLoS One* 2012; **7**: e33162 [PMID: 22496743 DOI: 10.1371/journal.pone.0033162]

34 **Bhatt SP**, Nigam P, Misra A, Guleria R, Luthra K, Pandey RM, Pasha MA. Association of peroxisome proliferator activated receptor-γ gene with non-alcoholic fatty liver disease in Asian Indians residing in north India. *Gene* 2013; **512**: 143-147 [PMID: 23031808 DOI: 10.1016/j.gene.2012.09.067]

35 **Keles N**, Aksu F, Aciksari G, Yilmaz Y, Demircioglu K, Kostek O, Cekin ME, Kalcik M, Caliskan M. Is triglyceride/HDL ratio a reliable screening test for assessment of atherosclerotic risk in patients with chronic inflammatory disease? *North Clin Istanb* 2016; **3**: 39-45 [PMID: 28058384]

36 **Gordon DJ**, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR, Bangdiwala S, Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* 1989; **79**: 8-15 [PMID: 2642759]

37 **Prabhakaran D**, Chaturvedi V, Shah P, Manhapra A, Jeemon P, Shah B, Reddy KS. Differences in the prevalence of metabolic syndrome in urban and rural India: a problem of urbanization. *Chronic Illn* 2007; **3**: 8-19 [PMID: 18072694]

38 **Snehalatha C**, Ramachandran A. Cardiovascular risk factors in the normoglycaemic Asian-Indian population--influence of urbanisation. *Diabetologia* 2009; **52**: 596-599 [PMID: 19205658 DOI: 10.1007/s00125-009-1279-x]

39 **Bhongir AV**, Nemani S, Reddy PS. Rural-urban epidemiologic transition of risk factors for coronary artery disease in college students of Hyderabad and nearby rural area--a pilot study. *J Assoc Physicians India* 2011; **59**: 222-226 [PMID: 21755758]

40 **Surana SP**, Shah DB, Gala K, Susheja S, Hoskote SS, Gill N, Joshi SR, Panikar V. Prevalence of metabolic syndrome in an urban Indian diabetic population using the NCEP ATP III guidelines. *J Assoc Physicians India* 2008; **56**: 865-868 [PMID: 19263684]

41 **Ray S**, Kulkarni B, Sreenivas A. Prevalence of prehypertension in young military adults & amp; its association with overweight & amp; dyslipidaemia. *Indian J Med Res* 2011; **134**: 162-167 [PMID: 21911967]

42 **Dhabriya R**, Agrawal M, Gupta R, Mohan I, Sharma KK. Cardiometabolic risk factors in the Agarwal business community in India: Jaipur Heart Watch-6. *Indian Heart J* 2015; **67**: 347-350 [PMID: 26304567 DOI: 10.1016/j.ihj.2015.03.011]

43 **Thomas A**, Ashcraft A. Type 2 Diabetes Risk among Asian Indians in the US: A Pilot Study. *Nurs Res Pract* 2013; **2013**: 492893 [PMID: 23970965 DOI: 10.1155/2013/492893]

44 **Ghai NR**, Jacobsen SJ, Van Den Eeden SK, Ahmed AT, Haque R, Rhoads GG, Quinn VP. A comparison of lifestyle and behavioral cardiovascular disease risk factors between Asian Indian and White non-Hispanic men. *Ethn Dis* 2012; **22**: 168-174 [PMID: 22764638]

45 **Enas EA**, Singh V, Munjal YP, Bhandari S, Yadave RD, Manchanda SC. Reducing the burden of coronary artery disease in India: challenges and opportunities. *Indian Heart J* 2008; **60**: 161-175 [PMID: 19218731]

**P- Reviewer:** Aggarwal A, Cheng TH, Cosmi E

**S- Editor:** Song XX **L- Editor:** **E- Editor:**

**Specialty type:** Endocrinology and metabolism

**Country of origin:** United States

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

**Table 1 Significant differences between male and females for individual components of the metabolic syndrome**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **% Male Meeting Criteria** | **% Female Meeting Criteria** | **Significance** |
| Elevated blood glucose: ≥ 100 mg/dL or previous diagnosis of diabetes | 71.77% | 59.69% | F (1971) = 15.64  *P* < 0.001 |
| Elevated blood pressure: ≥ 130/≥ 85 mmHg or previous diagnosis of hypertension | 38.32% | 31.45% | F (1836) = 4.16  *P* = 0.042 |
| Elevated triglycerides: ≥150 mg/dL | 48.65% | 33.49% | F (11011) = 23.65  *P* < 0.001 |
| Elevated Waist Circumference: ≥ 35.4 inches for males, ≥ 31.5 inches for females | 56.41% | 67.78% | F (11018) = 13.59  *P* < 0.001 |
| Low HDL: low HDL < 40 mg/dL in males, < 50 mg/dL in females or previous treatment for low HDL | 34.48% | 42.3% | F (1987) = 6.26  *P* = 0.012 |

HDL: High density lipoprotein.

**Table 2** **Specifically at participants with diagnosed or undiagnosed type 2 diabetes mellitus**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **% Males with diagnosed Diabetes who Meet the Criteria** | **% Female with diagnosed Diabetes who Meet the Criteria** | **Significance** |
| Elevated blood pressure: ≥ 130/≥ 85 mmHg or previous diagnosis of hypertension | 54.95% | 54.72% | F (1162) = 0.001  *P* = 0.977 |
| Elevated triglycerides: ≥ 150 mg/dL | 57.63% | 51.72% | F (1174) = 0.545  *P* = 0.462 |
| Elevated Waist Circumference: ≥ 35.4 inches for males, ≥ 31.5 inches for females | 80% | 80.7% | F (1175) = 0.012  *P* = 0.913 |
| Low HDL: low HDL < 40 mg/dL in males, < 50 mg/dL in females or previous treatment for low HDL | 39.32% | 60.71% | F (1171) = 7.185  *P* = 0.008 |

HDL: High density lipoprotein.

**Table 3 Significant factors associated with low high density lipoprotein in Asian Indian population**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables in the Equation | | | | | | | | | |
|  | | B | SE | Wald | df | Sig. | Exp (B) | 95%CI for EXP(B) | |
| Lower | Upper |
| Step 1a | Diab\_Category |  |  | .229 | 2 | .892 |  |  |  |
| Diab\_Category(1) | -0.089 | 0.341 | 0.068 | 1 | 0.795 | 0.915 | 0.469 | 1.787 |
| Diab\_Category(2) | 0.057 | 0.252 | 0.051 | 1 | 0.821 | 1.059 | 0.646 | 1.737 |
| Gender(1) | -0.294 | 0.236 | 1.562 | 1 | 0.211 | 0.745 | 0.470 | 1.182 |
| Age of respondent | 0.028 | 0.010 | 8.793 | 1 | 0.003 | 1.029 | 1.010 | 1.048 |
| Physicalact | 1.004 | 0.409 | 6.034 | 1 | 0.014 | 2.730 | 1.225 | 6.082 |
| Nutrition | 0.100 | 0.407 | 0.061 | 1 | 0.806 | 1.105 | 0.498 | 2.453 |
| TobaccoUse\_Rec(1) | -0.513 | 0.508 | 1.019 | 1 | 0.313 | 0.599 | 0.221 | 1.621 |
| FamHistory | 0.148 | 0.226 | 0.425 | 1 | 0.515 | 1.159 | 0.744 | 1.807 |
| Income\_Rec |  |  | 3.456 | 2 | 0.178 |  |  |  |
| Income\_Rec(1) | 0.451 | 0.305 | 2.180 | 1 | 0.140 | 1.570 | 0.863 | 2.857 |
| Income\_Rec(2) | 0.424 | 0.254 | 2.801 | 1 | 0.094 | 1.529 | 0.930 | 2.513 |
| Lifestyle | -0.389 | 0.258 | 2.268 | 1 | 0.132 | 0.678 | 0.408 | 1.124 |
| Knowledge of CVD risk | 0.099 | 0.067 | 2.191 | 1 | 0.139 | 1.104 | 0.968 | 1.259 |
| Knowledge of DM Risk | -0.230 | 0.097 | 5.652 | 1 | 0.017 | 0.795 | 0.658 | 0.960 |
| BMI\_Up | -0.077 | 0.030 | 6.560 | 1 | 0.010 | 0.926 | 0.873 | 0.982 |
| Constant | 2.182 | 1.194 | 3.338 | 1 | 0.068 | 8.864 |  |  |

aVariable(s) entered on step 1: Diab\_Category, gender, age of respondent, physicalact, nutrition, TobaccoUse\_Rec, FamHistory, Income\_Rec, Lifestyle, Knowledge of CVD risk, Knowledge of DM Risk, BMI\_Up.