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Original article

Metabolic cardiovascular risk factors worsen continuously across the spectrum of body mass index in Asian Indians

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KEYWORDS

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Metabolic syndrome
Obesity
Risk factors

ABSTRACT

Objectives: To determine relationship of body mass index (BMI) with multiple cardiovascular risk factors.
Methods: Population-based surveys were performed and 1893 subjects aged 20–59 years evaluated. Data were collected using anthropometry and fasting glucose and lipid estimation. Statistical analyses were performed using curve fit and logistic regression.
Results: Body mass index was correlated significantly (Rho, R^2) with weight (0.80, 0.64), waist (0.74, 0.55) and waist hip ratio (0.24, 0.06) ($P<0.05$). Linear relationship was observed with systolic blood pressure (SBP) (0.39, 0.15), diastolic blood pressure (DBP) (0.29, 0.08), fasting glucose (0.13, 0.02), cholesterol (0.10, 0.01), high-density lipoprotein cholesterol (HDL-c) (–0.16, 0.03), and triglycerides (0.12, 0.01). Significant trends of risk factors with each increasing BMI unit (χ^2 test, $P<0.001$) were observed for hypertension (HTN) (214.4), diabetes (29.5), metabolic syndrome (108.9), and low HDL-c (40.5), and weaker trends with hypercholesterolemia (20.6), and hypertriglyceridemia (9.6). There was exponential relationship of BMI with age- and sex-adjusted odds ratios for HTN, diabetes, and metabolic syndrome.
Conclusion: Metabolic cardiovascular risk factors continuously worsen with increasing BMI.

Introduction

Prospective Studies Collaboration has reported that there is a significant correlation of body mass index (BMI) with cardiovascular mortality.[1] In a meta-analysis of about a million Caucasian subjects, who were prospectively followed for at least 2 years, it was reported that there was a U-shaped correlation of all-cause mortality with BMI; increased mortality in lower BMI arm was due to respiratory and infectious diseases while the higher BMI was associated with greater cardiovascular mortality. It was also reported that there is a continuous gradient of cardiovascular mortality starting with BMI of 21 kg/m^2. Similar U-shaped curve has been reported in studies from USA, UK, and Korea.[2–13] The US National Cancer Institute prospectively studied 1.46 million Caucasian subjects and reported a J-shaped mortality curve with lowest deaths at BMI of 22.5–24.9 and highest at >30.0 kg/m^2.[6] Two prospective studies from India noted a reverse J-shaped curve with greatest all-cause mortality at BMI <18 kg/m^2.[7,8] For cardiovascular mortality the relationship was not clear.[7] A Korean study[11] reported a linear increase in cardiovascular mortality as BMI increased from 18.5 kg/m^2 to >30 kg/m^2 while the US cancer cohort study showed a J-shaped graph with the lowest mortality at BMI 20–22.4 kg/m^2 and highest at 40–49 kg/m^2.[6]

Relationship of metabolic cardiovascular risk factors with BMI has been studied in multiple populations in Europe, north America and Asia.[2,14,15] These studies reported a variable trend in multiple metabolic risk factors with increasing BMI. Continuous linear relationship of hypertension (HTN) with increasing BMI has been reported in all the studies[16] while variable results have been obtained with other cardiovascular risk factors such as diabetes and dyslipidaemia.

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Framingham Offspring study reported significant correlation of BMI with blood pressure (BP), glucose, cholesterol, and other lipids[17] while a similar study in Chinese populations showed correlation with HTN and dyslipidaemia and not with diabetes.[18]

Indian National Family Health Surveys reported a rapid increase in BMI and prevalence of obesity in the country.[19] Increasing urbanisation with associated dietary and physical activity transitions is fuelling the obesity epidemic in India.[20] Increased BMI has been shown to be associated with increased cardiovascular risks in urban Indian populations.[21] There is controversy regarding levels of BMI where cardiovascular risks increases in various low income countries.[22] Studies have reported that BMI $\geq 25\,kg/m^2$ is associated with increased cardiovascular risks while a few suggest that BMI $\geq 23\,kg/m^2$ should be used as a cut-off for defining overweight.[23] We performed cross-sectional studies in north India to identify prevalence of major cardiovascular risk factors.[25,26] To correlate BMI and with multiple metabolic cardiovascular risk factors we analysed data using regression-based statistical techniques.

Methods

A series of cross-sectional epidemiological studies have been performed to determine cardiovascular risk factors in urban populations in Jaipur and Delhi. These studies were approved by the Institutional Ethics Committee and supported financially by different organisations. In Jaipur Heart Watch (JHW) series,[26,27] we targeted men and women for complete socioeconomic, physical, and biochemical profiles in contrast to the others where biochemical measurements were obtained in random subjects. We conducted stratified cluster sampling on the Voters' lists in six locations representing an adult population of about 130,000 in Jaipur city in JHW-2[26] and two locations in JHW-3.[27] The studies were representative of local population as reported earlier.[27] In JHW-2, of the targeted population proportionate 960 men and 840 women, we evaluated 550 men (57.3%) and 573 women (68.2%) and in JHW-3, of the eligible 320 men and 280 women, we evaluated 226 (70.6%) and 232 (82.9%), respectively (overall response rate 62%). For the present analyses we included subjects 20–59 years of age (619 men, 661 women). In Delhi,[25] data were obtained from a study by systematic random sampling among a population of about 30,000. The overall response rate was 80.5% as reported earlier.[28] In brief, we collected information regarding demographic data, educational level, history of chronic illnesses such as coronary heart disease, HTN, diabetes, or high cholesterol levels, and smoking or tobacco intake. Income details were not inquired. Brief questions were asked to evaluate physical activity and diet but the results were considered inadequate and not included in the analyses. Physical examination was performed to assess height, weight, waist and hip circumference, and BP. Body mass index was calculated as weight (kg) divided by squared height (m). Waist hip ratio (WHR) was calculated. Fasting glucose was determined at a central laboratory using glucose peroxidase method and external quality control. Total cholesterol (TC) was measured using cholesterol oxidase-phenol 4-aminophenazone peroxidase method and high-density lipoprotein cholesterol (HDL-c) using an enzymatic method after precipitating non-HDL-c with a manganese-heparin substrate. Triglycerides were measured using the glycerol phosphate oxidase-peroxidase enzymatic method. Quality control measures were followed for estimation of TC, HDL-c and triglycerides (TG) while low-density lipoprotein cholesterol (LDL-c) was estimated using the Friedewald's formula.

Diagnostic criteria

We used the diagnostic criteria as advised by American College of Cardiology clinical data standards.[29] Smokers included subjects with present or past smoking. Isolated non-smoked tobacco use was also identified. Hypertension was diagnosed when the systolic BP (SBP) or diastolic BP (DBP) was $\geq 140/\geq 90$ mmHg on a repeated single day measurements or the individual was a known hypertensive. Dyslipidaemia was defined by the presence of high TC (≥ 200 mg/dL), high LDL-c (≥ 130 mg/dL), low HDL-c (<40 mg/dL), or high TG (≥ 150 mg/dL) according to National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) guidelines.[30] Diabetes was diagnosed when a subject provided history of previously diagnosed diabetes or the fasting blood glucose was ≥ 126 mg/dL. Metabolic syndrome was also defined according to the NCEP ATP III guidelines[30] and presence of any three of the five criteria (high waist circumference [WC] >100 cm men, >90 cm women; BP ≥ 130 mmHg systolic and/or ≥ 90 mmHg diastolic; fasting hyperglycaemia ≥ 110 mg/dL; low HDL-c <40 mg/dL men <50 mg/dL women; and high TG ≥ 150 mg/dL) were considered diagnostic.

Statistical analysis

Continuous variables are reported as mean $\pm$ 1 standard deviation and ordinal variables in percent. Prevalence rates are reported in percent. Age- and sex-adjustment of various continuous variables (BMI, BP, glucose, and lipids) was performed within the statistical programme (SPSS version 15.0, SPSS Inc, Chicago, USA) using analysis of covariance (ANCOVA). Direct method was used for age adjustment of prevalence rates with standard Indian million population.[31] Linear associations of BMI with continuous risk factor variables were calculated using Spearman's rho, linear regression, exponential regression and quadratic regression analysis within the statistical programme.[32] Graphics to plot scatter distribution of BMI with numerical variables and box-plot graphs for BMI categories and numerical variables have been produced using SPSS programme. Significance has been evaluated using ANOVA for trend. Trends in prevalence rates have been calculated using Mantel Haenzel χ^2. Age- and sex-adjusted odds ratios (OR) for risk factor prevalence at each BMI category were calculated using logistic regression analysis. P values <0.05 are considered significant.