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Original article

The obesity paradox in the distribution of dyslipidemia in obese versus non – obese patients of CAD in Gujarati population

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Abstract:

Background: Cardiovascular diseases (CVD) are the major cause of morbidity and mortality in developing countries. Risk factors for CVD like hypertension, diabetes, dyslipidemia and smoking contribute significantly to atherosclerosis and consequently to CVD. The aim of this study was to observe distribution of these risk factors in Gujarati coronary artery disease (CAD) patients over the entire spectrum of BMI and to look for existence of obesity paradox.

Methods: This randomized and cross-sectional study was done in September, 2010 on 818 subjects. Subjects of established CAD were evaluated by pretested proforma, physical examinations and, tests of lipid profiles, blood sugar levels.

Results: The proportion of hypertension, was significantly higher in >30 BMI group than BMI <25 and 25-30 group (p=<0.0001). Diabetes and dyslipidemia were non-significantly higher in BMI 25-30 than BMI <25 and >30 showing possible effect of obesity paradox. In females, effect of obesity paradox was found in high cholesterol content which was statistically significant (p=0.0465) and low HDL was highest in BMI with <25 than those with BMI with 25-30 and >30 (p=0.1341). The same effect was observed with LDL also but in a non-significant (p=0.6556) fashion. The results found in male population were similar to the females in case of high cholesterol and LDL. Though statistically insignificant the age related dyslipidemia distribution also showed existence of obesity paradox.

Conclusion: In females, high cholesterol was more in BMI <25 than BMI 25-30 and >30 group. Same effect was found in males also but did not reach statistically significant level.

Key words: Obesity Paradox, Cardio-vascular diseases, Hypertension, Diabetes, Dyslipidemia

Introduction

Cardiovascular diseases (CVD) are the most common cause of death and disability in developed as well as developing countries. Almost all of the major coronary heart disease (CHD) risk factors, including lipid disorder, glucose abnormalities, diabetes mellitus (DM), hypertension (HTN), left ventricular hypertrophy, and physical inactivity, are all adversely affected by overweight and obesity. Low high-density lipoprotein cholesterol (HDL-C) imposes higher risk for coronary artery disease (CAD) in the general population independently of low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels[1].

Though overweight and obesity have adverse effects on CHD risk factors and CHD, numerous studies have addressed the "obesity paradox," suggesting once CV diseases are established, the overweight and obesity seem to have a better prognosis than do their leaner counterparts[2]. In spite of a marked increase in the CAD burden in Gujarati population, lacuna of research exists in the field of obesity paradox. Aim of the our study was to find out proportions and clinical profiles of CAD risk factors amongst thin Gujarati CAD patients compared to obese Gujarati CAD patients and to observe distribution of dyslipidemia (DLD) across the entire spectrum of body mass index (BMI) also to look for any possible cause of "obesity paradox".

Material and methods

Design and Data Collection

This was a cross sectional screening study for presence of CAD risk factors among Gujarati patients. Complete or unrestricted random selection of the patients was used to enrol the subjects. It was conducted in September 2010 at our institute, which is the only tertiary care Centre with superspeciality cardiology course in the state of Gujarat catering to population all across the state. The undiagnosed cases of cardiac problems were screened and randomly selected for confirmation of CAD. Confirmed cases who reported for evaluation were again selected randomly for the purpose of the study. However being Government funded institute all patients that reported to the hospital were assessed and evaluated but were excluded from the analysis if they were not the randomly selected case to avoid selection bias. Sample size of 818 adult patients with established CAD was determined with the help of research aid of sample size survey software (online calculator-specially designed for epidemiological studies). The study was approved by Institutional Ethics Committee (IEC) and written informed consent was obtained from all the patients. (Patients were enrolled according to Helsinki declaration of 1975, as revised in 2000) The project was handled by trained/qualified hospital doctor having expertise in the field, who were trained about the study protocol prior to the initiation of the study. Dyslipidemia risk and impaired blood sugar levels were determined as per National Cholesterol Education Program (NCEP) – Adult Treatment Panel (ATP) III guidelines and American Diabetes Association (ADA) respectively. Patients were screened and tested for the presence of HTN, DLD, DM and smoking. Age, sex, body mass index (BMI) and other relevant variables were also recorded at our institute. Three categories of BMI were designed according to the WHO standards[2].

Serum Lipid and Glucose Analysis

The sample analysis was carried by an automated clinical chemistry analyzer. Serum glucose was measured by oxygen rate method employing a Beckman oxygen electrode (glucose oxidase). Total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) concentrations were measured by International Federation of Clinical Chemistry (IFCC) approved enzymatic methods.

Definitions and Preferred Cut-off Values

Person was considered to be hypertensive if they have history of HTN followed by treatment of anti-hypertensive medications or their BP during the visit was exceeding 140 systolic or 90 diastolic on two different measurements.

Person was considered to be diabetic if they had known history of type I or type II diabetes or was on anti-diabetic medications including insulin or their fasting blood sugar was higher than 125 mg/dL or random blood sugar more than 200 mg/dL. Person was considered to have dyslipidemia if they have known history of DLD before or they were on anti-lipids medications or they had any one of the following criteria of lipid profile. (Total cholesterol >200 or Triglyceride >200 or LDL >130 or total lipids >400). Person was considered to be a smoker if he or she used to smoke cigarettes or any other form of smoked tobacco for more than 1 year.

Statistical Analysis

All collected data was analyzed by SPSS v 20. Quantitative data was expressed as mean plus-minus SD whereas qualitative data was expressed in percentage. Since all the data follows normal distribution, t-test, one way ANOVA and chi-square test had been used to calculate p-value. p-value, <0.05 was accepted as statistically significant.

Results

Results of the current study clearly indicates that proportion of hypertension was significantly (p<0.0001) higher in BMI >30 as compared to BMI 25 to 30 and <25, whereas dyslipidemia worsens in those with BMI >30 than those with BMI <25. Dyslipidemia and DM were insignificantly higher in BMI 25 to 30 group than BMI >30 group which may reflect possible obesity paradox (table 1). Gender comparison showed almost equal distribution of the risk factors of CVD in males and females. Smoking was significantly (p=0.0001) higher in males than females (table 1).

The distribution of dyslipidemia and lipid abnormalities in individuals with various BMIs has been shown in table 2. It is showing that low HDL was more in those with BMI >30 as compared to those with BMI <25 and 25-30. Proportion of low HDL was found to increase with the increase in BMI from <25 to >30 as expected obesity

Table 1: Prevalence of risk factors in various BMI and gender groups.

BMI & Risk factors				
	< 25 n=411 (%)	≥ 25-30 n= 310 (%)	≥ 30 n=97(%)	p-value
HT	**120 (29.2)**	**134 (43.2)**	**57 (58.8)**	**<0.0001**
DM	**45 (10.9)**	**41 (13.2)**	**10 (10.3)**	**0.5768**
DLD	**43 (10.5)**	**49 (15.8)**	**14 (14.4)**	**0.096**
SM	**17 (4.1)**	**12 (3.9)**	**3 (3.1)**	**0.8916**
Gender and Risk factors				
	Female n=334 (%)	Male n=484(%)		p- value
HT	**124 (37.1)**	**187(38.64)**		**0.7157**
DM	**39 (11.67)**	**57 (11.77)**		**0.9468**
DLD	**42 (12.6)**	**64 (13.2)**		**0.8686**
SM	**2 (0.6)**	**30 (6.2)**		**0.0001**

HT-Hypertension, DM- Diabetes Mellitus, DLD-Dyslipidemia, SM-Smoking, BMI-Body Mass Index

effect on dyslipidemia, But it was not statistically significant. However percentage of high LDL was found to reduce in BMI >30 group as compare to 25-30 group in a non-significant manner. In females, effect of obesity paradox was found in high cholesterol content which was statistically significant (p=0.0465). Low HDL was highest in BMI with <25 than those with BMI with 25-30 and >30 showing possible existence of obesity paradox (p=0.1341). The same effect was observed with LDL also but in a non-significant (p=0.6556) fashion. The results found in male population were similar to the females in case of high cholesterol and LDL as shown in table 2, however but it was statistically insignificant.

Though statistically insignificant the age related distribution of dyslipidemia was more in younger age group (20-39 years) with BMI of <25 than those with BMI >25

Table 2: Lipid profile of various BMI groups

	Lipid profile & BMI-All patients				Lipid profile & BMI-Female				Lipid profile & BMI-Male			
	<25, n=411	25-30, n=310	=30, n=97	p value	<25, n=162	25-30, n=108	=30, n=64	P value	<25: n=249	25-30, n=202	=30, n=33	p value
High Cholesterol	5 (1.2%)	2 (0.6%)	3(3.1%)	0.160	2 (1.2%)	0	3(4.7%)	0.0465	3(1.2%)	2(1.0%)	0	0.8106
Low HDL	61(14.8%)	53(17.1%)	21(21.6%)	0.250	27(16.7%)	9(8.3%)	10(15.6%)	0.1341	34(13.7%)	44(21.8%)	11(33.3%)	0.0062
High LDL	23(5.6%)	24(7.7%)	6(6.2)	0.507	10(6.2%)	4(3.7%)	3(4.7%)	0.6556	13(5.2%)	20(9.9%)	3(9.1%)	0.1581
High TG	9(2.2%)	9(2.9%)	4(4.1%	0.546	10(6.2%)	4(3.7%)	3(4.7%)	0.9610	5(2.0%)	6(3.0%)	2(6.1%)	0.3794
Presence of smoking	17(4.1%)	12(3.9%)	3(3.1%)	0.891	2(1.2%)	0	0	0.3437	15(6.0%)	12(5.9%)	3(9.1%)	0.7745

Table 3: Dyslipidemia distribution in various BMI and age group patients.

Dyslipidemia + BMI				
	< 25 n=43 (%)	≥ 25-30 n=50 (%)	≥ 30 n=13 (%)	p-value
<20	**0 (0)**	**0 (0)**	**0 (0)**	**<0.0001**
20-39	**5 (11.6)**	**3 (6)**	**0 (0)**	**0.3232**
40-59	**26 (60.5)**	**35 (70)**	**8 (61.5)**	**0.6043**
≥60	**12 (27.9)**	**12 (24)**	**5 (38.5)**	**0.5779**

In age group 40-59, the BMI 25-30 group patients were having higher proportion of dyslipidemia as compared to >30 BMI group. Moreover in ≥60 age group cases of dyslipidemia were higher in <25 BMI than 25-30 group showing possible existence of obesity paradox.

Discussion

Obesity is associated with cluster of metabolic complications, increasing the risk of hypertension, diabetes, dyslipidemia, all aggregate independently with BMI[3]. Dyslipidemia associated with obesity plays a major role in development of atherosclerosis and CVD in obese individuals. All components of dyslipidemia, including higher triglycerides, decreased HDL levels, and increased LDL particles, are found to be atherogenic[4]. Largest survey of the relationship of obesity on lipids is the Third National Health and Nutrition Examination Survey (NHANES) also shows that dyslipidemia is strongly associated with obesity as compared to non-obese patients, irrespective of age, sex, and race[5].

Previously only BMI was used as a screening tool for the risk assessment of metabolic syndrome. But several studies have shown that even normal weight subjects, those with a BMI <25 may have the presence of metabolic risk factors.

Numerous studies have addressed the "obesity paradox," suggests once CV diseases are established including CHD; the overweight and obesity seem to have a better prognosis than do their analogous. Even large meta-analyses of CHD and heart failure have demonstrated better event-free survival in patients with overweight and obesity compared with "normal"-weight patients. Galale et al have recently assessed 4.4 year mortality in more than 2300 patients who had peripheral artery disease and underwent major vascular surgery. Their follow-up showed powerful obesity paradox with progressive reductions in mortality in normal BMI, overweight, and obese groups compared with underweight patients[6].

Even though there is a higher prevalence of hypertension in obesity, recent data shows an obesity paradox. Uretsky, *et al.* [7] investigated effects of obesity on CV outcomes in more than 22000 treated hypertensive patients. During 2- year follow-up, mortality was 30% lower in overweight and obese patients, (despite less effective blood pressure control) compared with normal weight group. In aggregate, these studies suggest that although obesity may be a powerful risk factor for hypertension and left ventricular hypertrophy, obese hypertensive patients may paradoxically have a better prognosis, possibly because of having lower systemic vascular resistance and plasma renin activity compared with leaner hypertensive patients[8].

Although obesity paradox has been described in a number of studies of clinical populations over the last decade, in terms of better event free survival in overweight and obese individuals as compared to leaner counterpart once cardiovascular disease has been established [9,10,11].There are few studies assessing obesity paradox in prevalence of risk factors like dyslipidemia, hypertension and type II DM obese versus non-obese individuals in Guajarati population, our study described that proportion of CVD risk factors like hypertension and dyslipidemia increases significantly as BMI increases from <25 to >30, as expected. In females, percentage of lipid abnormalities (high cholesterol, low HDL and high LDL) was highly associated with low BMI group (<25) in contrast to high BMI group (25-30 & >30), where lesser proportion of lipid abnormalities were present. So possible obesity paradox exit in this study, in high lipid abnormality in relation to BMI. Dyslipidemia was also more distributed in low BMI individuals (<25) than those with high BMI (>25).

Part of explanation of the obesity paradox has been blaming on limitations of the BMI assessment of obesity, methods other than BMI (cardio respiratory function; metabolic equivalent, % body fat) may be better to detect obesity and predict increased cardiovascular risk[12].

Conclusion

The proportion of high cholesterol is more in those individuals with BMI >25 than BMI 25-30 and >30 suggesting possible obesity paradox, It is statistically significant in female (p = 0.0465) but not in male (p = 0.8106). Dyslipidemia is slightly more in lean and overweight population as compare to obese individuals, though it was statistically significant.

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