Original Article

Normal Weight Obesity: Role of apoB and Insulin Sensitivity in Predicting Future Cardiovascular Risk

Rukman M. Manapurath, Rujuta Hadaye, Barsha Gadapani

Department of Community Medicine, SETH GSMC and KEM Hospital, Mumbai, Maharashtra, India

Abstract

Background: According to NFHS-4 survey, obesity has doubled in India. BMI cannot differentiate body fat from lean mass. Normal weight obesity was defined to distinguish people with normal BMI and increased body fat percentage (BF%). In contrast to conventional atherogenic prediction, Apolipoprotein B level is elevated before LDL cholesterol. Adiposity is also known for causing insulin resistance. Hence this study is an attempt to find the correlation of apo B and Insulin sensitivity in predicting future cardiovascular risk among normal weight obese. To study the role of apoB and insulin resistance in predicting cardio vascular risk. **Methods:** 269 participants of age group 18-24 in a medical teaching institute were selected for the first phase of the study through systematic random sampling. BF% was calculated with Harpenden skinfold callipers using Jackson Pollock's method. Second phase of the study involved biochemical investigation of 30 NWO participants. ApoB level and insulin sensitivity using HOMA model was estimated. Spearman correlations and simple linear regression were used. Analysis done using SPSSv16. **Results:** Male and Females were 56.4% and 43.6%, respectively. Out of 269, 44 were found to be having NWO. Hence Prevalence was 16.4%.There is a positive correlation found between apoB and insulin resistance with increasing body fat percentage. **Conclusions:** Elevated levels of apo B and insulin resistance are seen in NWO individuals as the BF% increases. NWO should be diagnosed early and thus apoB and insulin resistance can be screened for cardio vascular risk prediction.

Keywords: *Adiposity, atherogenicity, body fat percentage, cardiovascular risk, diabetes, lean mass, insulin sensitivity*

Introduction

There is a growing body of literature that recognizes the importance of obesity in the development of chronic diseases. According to National Family Health Survey-4, obesity has doubled in India.[1] Conventionally, we rely on body mass index (BMI) for diagnosing obesity. But unfortunately BMI cannot differentiate lean mass from body fat and hence concept of normal weight obesity (NWO) was defined.

NWO as per Lohman's criteria was 17.6% cut off for males and 33.1% cut off for females.[2] A large cohort study in middle income country shows that there is increased risk of metabolic syndrome in normal weight obese individuals as they have increased adiposity.[3] Currently atherogenic risk is predicted based on lipid profile, which consists of Very Low Density Lipoprotein (VLDL), Intermediate Density Lipoprotein (IDL), Low Density Lipoprotein (LDL), and lipoprotein (a) [Lp (a)].[4] Lp (a) contains apo B which are retained in the arterial wall, proposed to be the causative factor of atherosclerotic changes.[5] Lp (a) particles contain apo B100 whereas another Lp chylomicrons contain apo B48. Plasma apo B is calculated as the sum of these two.[6] Multiple western epidemiological studies show apo B as a better predictor of cardio vascular risk than LDL.[7] Level of apo B at young age strongly correlates with middle age coronary artery calcification (CAC) which is a major adverse cardio vascular event.[8,9] Total number of adipocytes in the body is constant and is determined at adolescent age. NWO in young adults proved to be a risk factor for cardio vascular complications in later life. But few researches have tried to find the role of apo lipoproteins and insulin resistance in NWO. Systematic reviews from middle and low income countries show that young adult age group particularly 18–25 are more prone

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Address for correspondence:
Dr. Rujuta Hadaye, Department of Community Medicine, SETH GSMC and KEM Hospital, Mumbai - 400 012, Maharashtra, India.
E-mail: rujutahadaye@gmail.com

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for obesity and its related complications due to the changes in the lifestyle while transition from adolescent to adult.[3]

Apo lipoprotein B (apoB) can be a surrogate marker for lipid profile status for predicting risk as it appears in blood before elevation of other lipid markers.[10] Increasing insulin sensitivity by weight reduction is one of the most important step in management of impaired glucose tolerant and recently detected type 2 diabetes mellitus. Hence insulin sensitivity testing for those with excess adiposity may help screening diabetes at early stage. Markers which can identify development of cardio vascular risk and diabetes at early age based on adiposity should be included in routine screening for healthy individuals, since it can cut down the cost of healthcare expenses in future. This concept is very essential in a developing country like India where health care infrastructure is expanding enormously. Corresponding data from these areas are required to make policy regarding such implementation. Also, there are increasing evidences about higher incidence of obesity among health care providers.[11]

Aims

To study the relation of apoB and insulin sensitivity in normal weight obese individuals of young adult population.

Methods

After obtaining the ethical clearance, this descriptive cross sectional study was conducted in a medical college with a tertiary care hospital in Mumbai. This institution has 900 undergraduate students and those between the age group of 18–24 years were selected. There were no exclusion criteria for the study. There were two phases of the study. First phase of sample selection was based on systematic random sampling method. Sample size = $Z^2pqN/[e^2(N-1)+Z^2pq$, confidence interval (C.I) 95%, *P* 50%. The sample size estimated was 269, using the formula. Second phase of the study was based on estimated prevalence of 10% NWO among young adults and the value approximately taken as 30. Out of 44 normal weight obese participants after first phase of the study, 15 males and 15 females were selected by simple random method for second phase. This phase includes biochemical investigations like fasting lipid profile, fasting blood sugar, apoB, and insulin sensitivity. The study period was for one year from Sep 2017 to May 2018. Sampling interval "three" was calculated by dividing total number of students by estimated sample size.

Body caliper method was found to be a reliable and valid instrument for body composition assessment when compared to other standard techniques. Harpenden skin fold caliper is a commonly used caliper for epidemiological purposes for measuring body fat (accuracy 99%).[12] Nephelometric method was used for apoB estimation and cut off taken as 130mg/dl as per laboratory reference.[7] A fully automated chemi luminescent immune assay was used for estimating fasting insulin. Insulin resistance was measured as per equation, Homeostatic Model Assessment of Insulin Resistance (HOMA –IR) = fasting glucose*fasting insulin and cut off decided at 2.5 as per Indian standards to early detection of metabolic syndrome.[13]

All responses were tabulated using Microsoft Excel software. Spearman correlation coefficient was used to demonstrate the correlation of apoB and insulin sensitivity with increasing adiposity. A simple linear regression was used to predict the values of one variable based on the other. Scatter Plot diagram was used for showing correlation of variables. Data were analyzed using SPSS software 16.0 version.

Results

The first phase of the study includes 269 participants of which 56.4% were males and 43.6% females. The overall prevalence of NWO was 16.4%. The prevalence among males was 11.1% and that of females was 22.4%.

The second phase of the study enrolled 30 out of 44 participants from the first phase who were normal weight obese and was subjected to biochemical analysis. 15 out of 16 NWO males and 15 out of 28 NWO females were selected by simple random method to make the number 30. Table 1 shows the parameters under study for the study sample.

Correlation of apoB and insulin resistance with Body Fat (BF) percentage

Spearman's rank order correlation between BF percentage and apo-lipoprotein B value shows statistically significant, strong positive correlation between BF percentage and apoB level in blood in young adult males, rs = 0.693, $P < 0.005$. For females, there was a statistically significant, strong positive correlation between BF percentage and apoB levels; rs = 0.702, $P < 0.005$.

For insulin resistance in males, there was a statistically significant, strong positive correlation between BF%, and Insulin resistance; rs = 0.723, $P < 0.005$. For females, the correlation was weakly positive between BF% and insulin resistance; rs = 0.13, but statistically not significant (*P* value = 0.637). Figure 1 shows the scatter plot of apoB and insulin resistance with body fat percentage.

A simple linear regression was run to understand the effect of BF percentage in predicting apoB values and insulin sensitivity. For males, BF% accounted for 63.1%

Table 1:Characteristics of the study sample in second phase

Parameters	Males (*n*=15)	Females (*n*=15)
Age	21.26 (1.22)	23.7 (1.73)
BMI	22.8 (1.5)	23.2 (1.4)
Estimated BF%	21.44 (2.14)	34.94 (0.77)
apoB	152.3 (25.6)	146.8 (14.5)
Insulin sensitivity	1.68 (0.42)	1.95 (0.33)

Standard deviation of the parameters are given in brackets

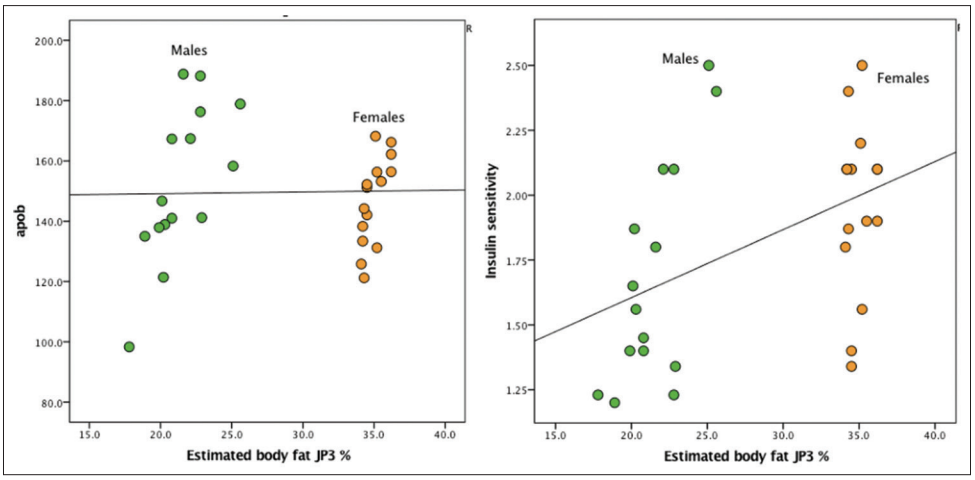

Figure 1: The scatter plot diagram showing the relation of apoB and insulin resistance with body fat percentage (BF%)

of the variation in unit change of apoB level with adjusted R2 = 63.1%, a large size effect according to Cohen (1988) and model being statistically significant ($P < 0.005$). This for females also turned out to be significant with adjusted $R^2 = 54.0$, P value <0.05. Among males, BF% accounted for 69.1% of the variation in unit change of Insulin sensitivity level with adjusted R2 = 69.1%, a large size effect. ($P < 0.005$). For females, BF% accounted for 67.5% of the variation in unit change of Insulin sensitivity level with adjusted R2 = 67.5%, a large size effect ($P < 0.005$).

Discussion

As per BMI, the study group consists of normal weight people with less anticipated fat related complications. But their BF% is higher than normal cut off. This study validates a strong association of apoB and insulin sensitivity with BF percentage.

Role of apoB

ApoB is a type of protein component of lipids which is involved in transport and distribution of lipoproteins. apoB is part of LDL, IDL, and VLDL and also helps in absorption of cholesterol. High level of apoB causes formation of atheroma in arterial walls eventually causing cardiovascular diseases. Traditionally LDL was used as marker for predicting cardiovascular (CV) risk. But meta-analysis have found apoB is the most potent predictor of CV risk in comparison with LDL.[14] Walldius *et al*. in the AMORIS study has also shown that elevated apoB is a better predictor of cardiovascular mortality in younger population.[15]

A graphical plot of BF% with apoB values shows a positive slope as shown in the graph. If we see the trend of apoB values and BF% of males, there is a strong positive correlation between these values. Among females also the correlation between apoB and BF % was strong. This implies that the value of adiposity increases when level of apoB increases, even though within normal range. Apo B has relatively better predictive capacity when added to central adipose measurements.[8] Visceral adiposity seems to have some association with apo B levels. Data from larger cross sectional studies says that apo B level normalizes once visceral fat is reduced.[10] Cost for estimating apoB can be reduced if it can be used routinely in practice.

Role of Insulin sensitivity

Existing literature suggests that there is marked insulin resistance for obese individuals. This is primarily due to altered lipid metabolism by subcutaneous adipose tissue (SAT) which is a regulator of whole body insulin sensitivity.[16] Adding to the literature, insulin resistance was inversely proportional to body fat percentage for males. For females the association was weakly positive even though correlation was not significant. It is also explained that normally insulin decreases apo B secretion, but as there is altered insulin sensitivity in excess adiposity apoB level also can be increased.[6] Interestingly this is the first study to the authors knowledge which has analyzed insulin resistance among normal weight obese individuals in Asian region.

Methodological advances of using apoB over LDL

In contrary to the popular belief that LDL screening can be beneficial for cardiovascular risk prediction, for those with insulin resistance or elevated triglycerides, this may not be accurate.[7] Hence apoB should be recommended for those with excess adiposity. There is WHO-IFCC 1990 international standards for apoB, unlike LDL values and also no fasting sample is required for apoB which makes it ideal for mass screening.[17]

Conclusions

ApoB was found to be positively correlated strongly with increasing BF percentage both in men and woman whereas insulin sensitivity has been found to be negatively associated with increasing adiposity. Both these markers are known to predict cardiovascular risk in later part of life, if

not intervened at the right time. Cut off for BF percentage to be determined by conducting larger studies.

Limitations

The study was conducted among students of a tertiary care institute which may not depict real scenario of the population. Another limitation of the study is the smaller sample size.

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Conflicts of interest

There are no conflicts of interest.

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