DOI: 10.21276/aimdr.2019.5.2.ME14

Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Relationship between Left Ventricular Mass Index and Insulin Resistance in Obese Subjects.

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Received: January 2019
Accepted: January 2019

ABSTRACT

Background: Obesity is an underestimated condition of clinical and public health importance across the world. Obesity has been associated with Left ventricular hypertrophy and insulin resistance, both of which are associated with cardiovascular morbidity and mortality. The aim of present study to determine relationship between left ventricular mass index and Insulin resistance in obese subjects. **Methods:** The present study is a observational study conducted in Guru Nanak Dev Hospital attached to Govt. Medical college Amritsar. Total 50 normotensive nondiabetic obese subjects of both genders were included in the study. **Results:** There was strong positive correlation of Left Ventricular Mass Index (LVMI) with HOMA-IR. Pearson's correlation coefficient (r) = 0.298 and P value was < 0.05. Left ventricular hypertrophy was present in 38% and 70% of obese subjects when left ventricular mass was indexed to body surface area and height respectively. **Conclusion:** The present study concludes that left ventricular mass index is strongly related with insulin resistance in normotensive nondiabetic obese subjects. So their earlier detection will reduce cardiovascular morbidity and mortality.

Keywords: LVMI: Left ventricular mass indexed to body surface area, HOMA-IR: Homeostatic Model Assesment Insulin resistance, Obesity.

INTRODUCTION

Obesity is a substantial public health crisis internationally. Its prevalence increasing rapidly in numerous industrialized nations. WHO define obesity as medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health.[1] Obesity increases the likelihood of various diseases particularly cardiovascular diseases, metabolic syndrome, Type 2 diabetes mellitus, obstructive sleep apnea, certain types of cancer, osteoarthritis and depression.[2] Obesity is associated with increased left ventricular mass, a significant independent predictor of cardiovascular morbidity and mortality. Duration of obesity is correlated well with Left Ventricular Hypertrophy.[3] A study done by Vetta F et al (1998), found an increased left ventricular mass in obese subjects.[4] In another study conducted by Rider OJ et al (2009), it was found that Obesity was associated with significantly increased left ventricular mass.[5] Obesity is also a most common cause of insulin resistance. It is associated with decreased number of insulin receptors and with post receptor failure to activate tyrosine kinase.[6] Insulin resistance and hyperinsulinemia may directly promote myocardial hypertrophy through the insulin-like growth factor-1 receptors (IGF-1).[7] In cross-sectional study done by Lim SM et al (2015), findings suggested that obesity indices are positively associated with insulin resistance in apparently healthy adolescents.[8] Another study done by Juneja A et al (2017) showed an overall prevalence of raised homeostatic model assessment of insulin resistance (HOMA-IR) in otherwise healthy young obese subjects.[9]

Few studies have determined the independent relationship between insulin resistnace and Left Ventricular Mass. However it has not been completely proven that Insulin Resistance is an independent indicator of the LVM increase. So the aim of present study was To assess the relationship between left ventricular mass index and Insulin resistance in normotensive and nondiabetics obese subjects.

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MATERIALS AND METHODS

The study is an observational study, conducted on 50 obese subjects with BMI > 29.9 Kg/m2 attending medical OPD or admitted in ward of Guru Nanak Dev Hospital, attached to Govt. Medical College Amritsar anf fulfilling inclusion and exclusion criteria of the study. Obese subjects were of age group of 25-60 years. 25 of them were males and 25 were females. These obese subjects were nondiabetic and normotensive. Patient's having ischemic heart disease, congenital heart disease, valvular heart disease, pulmonary embolism, Hypertension, Hypothyroidism, Diabetes Mellitus and patient's on chemotherapy were excluded from study. Smoker, patients of Gestational diabetes and patients not giving informed consent were also excluded from the study.

Weight measurements were made with thin clothing and without shoes with standard weighing machine. Height measurements were made bare foot. BMI was calculated after measuring their weight in kg and height in meters by Quetlet Index i.e. BMI= Weight in kg/Height in m.2 All patients with BMI (Kg/m2) between 0-18.5 were underweight, 18.5-24.9 healthy weight, 25- 29.9 overweight, 30-34.9 class I obesity, 35- 39.9 class II obesity and >40 class III obesity.[10,11]

Fasting Blood Sugar (FBS) and Fasting serum insulin levels were done after after keeeping the patient fasting for a minimal period of 8 hours. A Quantitative in vitro diagnostic measurement of fasting serum insulin was done by insulin ELISA kit EIA-2935, an enzyme immunoassay. This is a solid phase enzyme-linked immunosorbant assay (ELISA) based on sandwich principle.The test was performed with the help of automated microplate ELISA and microbiology Reader Erba LisaScan EM. Reading of absorbance (OD) is taken at 450+10 nm, with normal range of 2uIU/ml - 25uIU/ml. In each subject Insulin Resistance (IR) was measured by Homeostatic model of assessment-Estimated insulin resistance (HOMA-IR) Score. Normal range is 3.3 - 6.1 mmol/L. HOMA-IR Score is calculated with the formula of ''fasting plasma glucose (mmol/L) fasting serum insulin (mU/L) divided by 22.59".[12]

Echocardiography was done in all patients. Measurement of interventricular septal wall thickness (IVSD), Left Ventricular end diastolic dimension (LVEDD) and posterior wall thickness (PWTD) in diastole were recorded in accordance with the American society of Echocardiography recommendations using M- modefrom parasternal long axis view by with 2.5 mega hz probe in left lateral decubitus position. The left ventricular mass was calculated on Phillip i E33 machine using Devereux formula and indexed to body surface area to obtain left ventricular mass index(LVMI).[13] In addition, LV mass was indexed for height 2.7 (g/m2), to give more stringent allowance for body size. LVH is defined as LV mass indexed for body surface area ≥116 g/m2for men and ≥ 96 g/m2 in women or LV mass indexed for height 2.7 ≥ 49 g/m2.7 in men and ≥ 45 g/m2.7 in women.

The data from present data was systematically collected, compiled and statistically analyzed using software SPSS version 17.0 to draw relevant conclusions. Mean ± SD was obtained in all parameters. Chi – square test, students t- test and Pearson's correlation coefficient was used for comparing catagorical variables where ever appropriate. P value less than 0.05 was considered significant (P< 0.05) and p value less than 0.001 was considered highly significant (<0.001).

RESULTS

Out of total of 50 normotensive nondiabetic obese subjects 50% were male and 50% were females. Mean age ± standard deviation (SD) was 35.46±5.78 years (range: 25 to 60 years). [Table 1] summarizes the general characteristics of our patients.[Table 2] shows the distribution of patients by age and sex.

Table 1: General statistics for the study group

Variables	Mean ± SD
Age (in years)	35.46 ± 5.78
BMI (kg/m2)	35.90 ± 3.78
WC (in cm)	127.30 ± 19.73
SBP (in mm of Hg)	113.32 ± 8.76
DBP(in mm of Hg)	77.44 ± 3.59
TC (mg/dl)	193.66 ± 2.70
TG (mg/dl)	144.06 ± 2.51
HDL (mg/dl)	39.54 ± 2.06
LVMI (g/m2)	104.38 ± 10.67
LVM Indexed ht 2.7 (g/m2.7)	56.06 ± 7.53
FBS (mmol/L)	5.23 ± 0.19
Fasting serum Insulin (uIU/ml)	25.64 ± 3.54
HOMA-IR (mmol/L)	6.94 ± 7.56

Table 2: Gender wise Distribution of study group.

Sex	No. of Cases	Percentage (%)
Male	25	50.0
Female	25	50.0
Total	50	100.00

Table 3: Mean LVMI and LVM/H2.7 according to BMI (kg/m2).

Variable	30-34.9 (Class I obesity)	35-39.9 (Class II obesity)	>40 (Class III obesity)	P value
LVMI g/m2	101.16±10.2	105.1±2.28	109.38±10.5	0.128
LVM/H2.7g/m2.7	49.7±5.95	57.9±4.68	64.86±2.55	< 0.001

(LVMI: Left Ventricular mass indexed to body surface area; LVM/H2.7 : Left ventricular mass indexed to Height$^{2.7}$)

Table 4: Mean HOMA-IR according to BMI (kg/m2).

Variable	30-34.9 Class I obesity	35-39.9 Class II obesity	>40 Class III obesity	P value
HOMA-IR (mmol/L)	5.1±0.53	6.21±0.28	6.77±0.37	< 0.001

(Normal range : 3.3-6.1mmol/L; HOMA-IR: Homeostatic model of assessment insulin resistance)

Above mentioned table shows that Mean LVMI was 101.16±10.2, 105.1±2.28 and 109.38±10.5 g/m2 for Class I, Class II and Class III obesity respectively. Mean LVM/$H^{2.7}$ was 49.7±5.95, 57.9± 4.68 and 64.86±2.55 g/$m^{2.7}$ for Class I, Class II, and Class III obesity respectively. This suggested that with increase in degree of obesity there was increase in LVMI and LVM/$H^{2.7}$. The difference in mean value of LVM/$H^{2.7}$ in three classes of obesity was statistically significant (P < 0.001). But P value was not significant for mean LVMI.

Above mentioned table show that mean HOMA-IR was 5.1±0.53, 6.21±0.28 and 6.77±0.37 mmol/L for Class I, Class II and Class III obesity respectively. This suggested that with increase in degree of obesity there was increase in HOMA-IR value, with p value < 0.001 showing statistical significance.

Table 5: Prevalence of LVH in study group

Variable	Normal n (percentage)	LVH n (percentage)	Total
LVMI	31 (62%)	19 (38%)	50
LVM/$H^{2.7}$	15 (30%)	35(70%)	50

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[Normal range of LVMI : 43-95 g/m2 (Female) and 49-115 g/m2 (Male)]

[Normal range of LVM/H2.7: upto 44g/$m^{2.7}$ (Female) and upto 48g/$m^{2.7}$ (Male)]

Above mentioned table shows that there are 38% (n=19) of obese subjects out of total 50 that had LVH when LVM was indexed to body surface area I.e. LVMI (LVH in g/m2) and 70% (n=35) out of 50 that had LVH when LVM was indexed to height$^{2.7}$ i.e. LVM/$H^{2.7}$ (LVH in g/$m^{2.7}$).

Table 6: Correlation between LVMI (g/m2) and HOMA-IR by using Pearson's correlation coefficient

Variable	Pearson's correlation (r)	P value
Correlation b/w LVMI and HOMA-IR	0.298	0.035

Above mentioned table shows that There was significant positive correlation r= 0.298 (p < 0.05) between LVMI and HOMA-IR. Thus, with increase in LVMI, IR was also observed to be increased.

Table 7: Correlation between LVM/H2.7 (g/m2.7) and HOMA-IR by using Pearson's correlation coefficient

Variable	Pearson's correlation (r)	P value
Correlation between LVM/H2.7 and IR	0.705	< 0.001

Above mentioned table shows that there was significant positive correlation r= 0.705 (p < 0.001) between LVM/$H^{2.7}$ and IR. Thus, with increase in LVM/$H^{2.7}$, IR was also observed to be increased.

DISCUSSION

Obesity is becoming a global epidemic and the prevalence is increasing not only in the developed countries but also in developing countries. The main adverse consequences are cardiovascular diseases, Type 2 DM and several cancers. Left ventricular hypertrophy (LVH) is a cardiovascular consequence of obesity and it is an independent risk factor for stroke, myocardial infarction and sudden death. It is therefore necessary to know to what extent obesity is responsible for the development of LVH and what measures of obesity are implicated.

In present study it was found that with increase in degree of obesity there was increase in LVMI and LVM/$H^{2.7}$. This result was comparable to study conducted by Okpara IC et al (2009) in which there was strong correlation of LVM/H2 was noticed with class II and class III obesity When the subjects were divided according to BMI subgroups. Also Progressive increases in BMI was associated with progressive increases in the LVMI.[14]

In present study we found that LVH was present in 38% of total obese subjects when LVM was indexed to body surface area (BSA) for calculating LVMI(g/m2), whereas 70% of study population had LVH when LVM was indexed to height$^{2.7}$ ie. LVM/$H^{2.7}$ (g/m2.7). The prevalence of LVH (g/m2) was 41% in obesity group in study by Nkum BC et al (2014) and LVH (g/m2.7) was present in 74% of study population in study by Antonini-Canterin F et al (2018). The resuts were comparable to our study. The difference in prevalance of LVH by these different allometric indexation suggested that LVM indexation for BSA underestimated occurance of LVH in comparison to LVM/$H^{2.7}$. Thus LVM indexed to height$^{2.7}$ was a better for predicting LVH in obese subjects. This was in accordance with study conducted by de Simone G (1994).[15-17] Present study showed that there was significant positive linear correlation between LVMI and HOMA-IR. Pearson's correlation coefficient (r) = 0.298 and P value was < 0.05. Also there was significant positive linear correlation of LVM/H2.7 with HOMA-IR. Pearson's Correlation coefficient (r) was 0.705 and P value was <0.001. This suggested that with increase in LVMI, HOMA-IR was also observed to be increased and vice versa. Simlar result was observed in studies conducted by Altinok R et al (2016) where there was a significant correlation between LVMI and HOMA-IR (correlation coefficient ie r = 0.231 and P value = 0.012 ie. < 0.05) and they reported that left ventricular hypertrophy is induced by insulin resistance and high insulin level.[15] Other studies conducted by Rashid MA et al and Shah RV et al (MESA study) also showed positive correlation of LVMI with HOMA-IR. MESA study reported that insulin resistance causes concencenteric LVH in study population.[16,17] In a study of 40, otherwise healthy, non-diabetic, normotensive obese subjects Sasson et al demonstrated that IR was strongly associated with LVH and that this association was independent of blood pressure and body mass index

(BMI).[18] Lind et al., found LVH to be closely associated with IR and in multiple regression analysis IR accounted for 47% of the variability of left ventricular Mass.[19] The study conducted by Bulut C et al (2016) and Nkum et al (2014) reported that there is no correlation between HOMA-IR and LVMI.[20,12]

There are few limitations to present study. First, it was a small observational study. Our results reflect only nondiabetic, normotensive obese subjects and can not be generalized to all obese people. Second, duration of obesity and biochemical markers of endothelial damage that could influence LVMI were not examined in this study.

CONCLUSION

Left ventricular hypertrophy (LVH) and insulin resistance (IR) are both strong adverse factors for cardiovascular disease. The coexistence of LVH and IR is a clinical finding, which must be taken seriously, even in the absence of blood pressure levels above the usual limits for initiating drug therapy because it is a predictor of adverse risk for mortality and morbidity. LVH can no longer be viewed as a benign adapation, but must be considered a significant risk factor for the development of coronary insufficiecy, myocardial infarction, rhythm disturbance, congestive heart failure and sudden death. Routine follow up examination and intiating therapy before an increase in left ventricular wall thickness and before cardiac dysfunction may help to improve cardiovascular complications.

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How to cite this article: Chander R, Charan S, Kaur I, Bal BS, Salwan S, Gujjar A, Singh H, Sharma P, Bhateja A, Kathait A, Sondhi P. Relationship between Left Ventricular Mass Index and Insulin Resistance in Obese Subjects. Ann. Int. Med. Den. Res. 2019; 5(2):ME70-ME73.

Source of Support: Nil, **Conflict of Interest:** None declared