ORIGINAL ARTICLE

Association of central obesity with risk factors for cardiovascular disease in North Indian population: A case - control study

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Abstract

Background: Central obesity is a leading cause of insulin resistance, type 2 diabetes mellitus, dyslipidemia, and Cardiovascular Disease (CVD). Central obesity may act as an independent predictor for CVD. *Aim and Objectives:* To study the correlation of central obesity among obese patients with the risk factors for CVD. *Material and Methods:* In this case-control study, 50 non-obese and 50 obese subjects aged between 30-70 years were enrolled. Biochemical parameters: Fasting Blood Sugar (FBS), Glycated Hemoglobin (HbA1c), Total Cholesterol (TC), Triglyceride (TG), High-Density Lipoprotein-Cholesterol (HDL-C) and Low-Density Lipoprotein-Cholesterol (LDL-C) were estimated along with Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Body Mass Index (BMI) and Waist Circumference (WC). Value of p less than 0.05 was considered statistically significant. *Results:* Mean of FBS, HbA1c, TC, TG, LDL-C, SBP, DBP, BMI, and WC were significantly raised in obese compared to non-obese ($p<0.01$). However, the mean of HDL-C was significantly low in obese compared to non-obese ($p<0.01$). A significant positive correlation was found between age and WC ($r=0.426$, $p<0.01$), TC and TG ($r=0.628$, $p<0.01$), TC and LDL-C ($r=0.934$, $p<0.01$), TG and LDL-C ($r=0.647$, $p<0.01$) among obese. However, a significant negative correlation was found between TC and HDL-C ($r=-0.453$, $p<0.01$), TG and HDL-C ($r=-0.323$, $p<0.05$), and HDL-C and LDL-C ($r=-0.510$, $p<0.01$) among obese. Linear regression analysis model was found significant. *Conclusion:* Result showed that WC is an independent predictive marker for CVD. Further study is needed in larger sample to strengthen the hypothesis.

Keywords: Body Mass Index, Cardiovascular Disease, Diastolic Blood Pressure, Fasting Blood Sugar, Systolic Blood Pressure, Waist Circumference

Introduction

Obesity is considered as a multifactorial disease which is characterized by excess adiposity, and found to be associated with increased risk of cardio-metabolic diseases [1]. Type 2 Diabetes Mellitus (T2DM) which may or may not be associated with obesity, at the same time shares many risk factors with other non-communicable diseases that may include age, physical inactivity, Waist

Circumference (WC), insulin resistance, dyslipidemia and high blood pressure [2]. When compared to developed countries, it has been found that lack of exercise is a major risk factor for obesity in developing countries e.g. Indians' lifestyle, diet and exercise habits have undergone a sea change as a result of the economic and nutritional transition [3].

"Asian Indian Phenotype" due to greater abdominal adiposity, higher WC, and lower Body Mass Index (BMI), makes them more prone to diabetes and premature Coronary Artery Diseases (CADs) [4]. The study by Unnikrishnan *et al.* (2018) suggested that the epidemic of T2DM is also spreading in rural areas of South Asia. It is also reported that the risk of atherosclerotic Cardiovascular Disease (CVD) in India is greater in newly diagnosed T2DM. This study further supported an easy to use and cost-effective screening tool to screen T2DM and its complications at very early stage so that early detection and management is possible [5]. World Health Organization (WHO) on the basis of global estimation reported that nearly 13% of world's population (adult) which included 11% of men and 15% of women were obese in 2014 [6]. Pradeepa *et al.* (2021) in their study suggested that the increasing burden of T2DM is due to the high prevalence of overweight/obesity in India [7]. The epidemiological survey used BMI, WC and Waist-to-Hip Ratio (WHR) where BMI was used as a measure of general obesity while WC and WHR were used as measures of central/abdominal obesity [8]. A multi-regional Indian study reported that the prevalence of general obesity, abdominal obesity, and combined obesity were significantly higher among urban population as compared to rural population, and the study noted that the prevalence of abdominal obesity was higher than general obesity [9].

Eaton *et al.* (2017) reported that a high proportion of fat to muscle will result in increase in circulation of free fatty acids which would require greater insulin secretion for control of glucose metabolism. Hyper-insulinaemia de-sensitises insulin-sensitive tissues, which results in predisposing the individuals to T2DM [10]. It was seen in previous studies that Metabolic Syndrome (MetS) was also associated in developing CVD and the population-attributable fraction of MetS for CVD, T2DM, and all-cause of mortality was found to be 12–17%, 30–52%, and 6–7%, respectively [11].

The increasing prevalence of abdominal obesity may be the main cause of increasing incidence of CVD and CVD-associated mortality in India. A person who resides in rural area constitute 'vulnerable population' for developing CAD which may have poorer outcomes due to unhealthy habits and lack of immediate health care services [12]. In this study, we aimed to investigate the correlation and association of central obesity with the risk factors of CVD.

Material and Methods

In this case-control study, 100 subjects of which 50 non-obese with 23 (46%) females and 27 (54%) males, and 50 obese with 29 (58%) females and 21 (42%) males, in the age group of 30-70 years, were enrolled after taking proper case history and medical history based on inclusion/exclusion criteria. This study was approved by the Institutional Research Committee (IRC) and Institutional Ethics Committee (IEC) and followed the ethical standards of 1964 Helsinki declaration and its later

amendments or comparable ethical standards. Written informed consent was taken from each study subject.

The study was done in the Departments of Medicine, Biochemistry, and Basic Medical Sciences IIMSR, Lucknow. Duration of the study was 6 months. Two groups: non-obese and obese were differentiated on the basis of WC (measure of central/abdominal obesity) and BMI of the subjects. Obesity was defined when BMI ⩾ 25 kg/m^2 and abdominal obesity when WC for men was ⩾ 90 cm and for women was ⩾ 80 cm [8].

Inclusion criteria: Obese subjects aged in between 30-70 years, WC ⩾ 90cm for men and ⩾ 80 cm for women, with raised Fasting Blood Sugar (FBS) and HbA1c levels were included. Non-obese subjects aged in between 30-70 years, WC < 90 cm for men and < 80 cm for women with normal FBS and HbA1c levels were placed in non-obese group.

Exclusion criteria: Subjects having hypothyroidism and pregnancy.

Body Mass Index (BMI): Digital weighing machine and stadiometer were used for measuring the weight in kg and height in meters respectively of all the subjects. For BMI, we used the formula - (BMI = weight in kilogram/ [height in meters]^2). BMI interpretations were: Underweight BMI<18.5 kg/m^2; normal weight BMI = 18.5–22.9 kg/m^2; overweight BMI > 23–24.9 kg/m^2; and obese, ⩾25 kg/m^2 [8].

Waist Circumference (WC): Measurement of the waist circumference was done in the standing position by placing a plastic tape horizontally midway between 12th rib and iliac crest on the mid-axillary line [13]. The mean value of the measurement was recorded after repeating the measurements twice.

Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured and recorded using sphygmomanometer.

Fasting blood sugar was estimated by using commercially available kits-ERBA, by GOD-POD method [14] on Erba chem7. HbA1c was estimated by D10 HPLC based HbA1c analyser (Bio-Rad).

Lipid profile was also done using commercially available kits (ERBA) on semi auto analyser Erba chem7. All the data analyses were done using the software IBM SPSS version 20.0 (Armonk, NY, USA).

Diagnostic criteria of diabetes for the enrolled subjects was as follows: According to the guidelines of American Diabetes Association (ADA), HbA1c is considered as normal if < 5.7%; pre-diabetes if 5.7–6.4% and diabetes if ⩾ 6.5%. T2DM was defined based on HbA1c ⩾ 6.5% [15]. On the basis of FBS, if FBS level was ⩾ 126 mg/dl subjects were enrolled as T2DM patient [16].

Dyslipidemia was diagnosed as per the recommended values of components of lipid profile from the National Cholesterol Education Programme (NCEP), Adult Treatment Panel III (ATP III) guidelines: Total Cholesterol (TC) < 200 mg/dl was considered 'desirable' and > 200 mg/dl was considered 'hypercholesterolemia'. High Density Lipoprotein-Cholesterol (HDL-C) values less than 40 mg/dl were considered 'low'. Triglyceride (TG) > 150 mg/dl was considered as 'hypertriglyceridemia' [17]. Hypertension was diagnosed using the Joint National Committee (JNC) VIII criteria with systolic BP ⩾ 140 mmHg and/or diastolic ⩾ 90 mmHg [18].

Data were compared between the two groups by using Analysis of Variance (ANOVA) or unpaired t-test. Values were represented as Mean ± Standard Deviation (SD). Pearson correlation coefficient was calculated among obese. Regression analysis was performed. Value of $p < 0.05$ was considered as statistically significant for all data analysed.

Results

Demographic details of study subjects i.e. gender and age distribution has been shown in Table 1. Out of the total 100 subjects enrolled for the study, 52 (52%) were females and 48 (48%) were males. When age distribution was seen, it was found that 35 (35%) were in between 30-40 years, 29 (29%) were in between 41-50 years, 26 (26%) in between 51-60 years and 10 (10%) were in between 61-70 years of age. This shows that maximum subjects were in the age group of 30-40 years. It was reported that 50 (50%) were obese, 50 (50%) were T2DM, 17 (17%) found to have dyslipidemia and 19 (19%) subjects were reported as hypertensive.

It was observed that mean FBS, HbA1c, TC, TG, Low-density Lipoprotein-Cholesterol (LDL-C), SBP, DBP, BMI, and WC were significantly raised in obese as compared to non-obese ($p<0.01$). However, mean HDL-C was found significantly low in obese as compared to non-obese ($p<0.01$), shown in Table 2. A significant positive correlation was found between age and WC ($r= 0.426$, $p<0.01$). In between FBS and HbA1c, significant positive co-relation was observed ($r= 0.325$, $p< 0.05$). TC and TG levels were also significantly correlated ($r= 0.628$, $p< 0.01$). There was significant positive correlation in between TC and HDL-C ($r= -0.453$, $p< 0.01$) as well as TC and LDL-C ($r= 0.934$, $p< 0.01$). A significant correlation was also observed in between TG and HDL-C ($r= -0.323$, $p< 0.05$), TG and LDL-C ($r= 0.647$, $p< 0.01$) and HDL-C and LDL-C ($r= -0.510$, $p< 0.01$). It was observed that SBP and DBP were also significantly co-related ($r= 0.765$, $p< 0.01$). Co-relation among the clinical parameters is shown in Table 3. Linear multivariate regression analysis was done to investigate whether age, FBS, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, and BMI have significant association with WC or not. A hypothesis was designed as if there was significant association of FBS, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, and BMI with WC. The dependent variable WC was regressed on predicting variables age, FBS, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, and BMI to test the hypothesis. It was found that the **age** having ($F (10, 39) = 2.254$, $p< 0.05$), and **HDL-C** ($F (10, 39) = 2.254$, $p<0.05$) significantly associated with WC, which indicates that the age ($beta=0.194$, $p<0.05$) and HDL-C ($beta=-0.532$, $p<0.05$) were associated in promoting CVDs. These results clearly direct the positive affect of age and HDL-C on CVD. Moreover, the overall model was statistically significant ($p<0.034$) and $\mathbf{r^2 = 0.366}$ depicts that the model explains **36.6% of the variance in WC** and the (F value = 2.254). Linear regression analysis model was found fit and strongly supported the hypothesis that WC was an independent predictive marker of risk factors for CVD, shown in Table 4 and represented in figure 1, 2 & 3.

Table 1: Demographic characteristics of non-obese and obese

Variable		Non-obese N (%)	Obese N (%)
Gender	**Female**	23 (46%)	29 (58%)
	Male	27 (54%)	21 (42%)
Age (years)	**30-40**	17 (34%)	18 (36%)
	41-50	15 (30%)	14 (28%)
	51-60	13 (26%)	13 (26%)
	61-70	05 (10%)	05 (10%)
Subjects	**Obese**	00 (00%)	50 (50%)
	Diabetes	00 (00%)	50 (50%)
	Dyslipidemia	00 (00%)	17 (34%)
	Hypertension	00 (00%)	19 (38%)
	Mets	00 (00%)	17 (34%)

Table 2: Clinical characteristics of non-obese and obese

Parameters	Non-obese (N=50) Mean ± SD	Obese (N=50) Mean ± SD	*p*
Age (years)	44.9 ± 10.4	49.5 ± 11.1	0.36
FBS (mg/dl)	98.8 ± 11.2	170.4 ± 43.0	0.001**
HbA1c (%)	4.9 ± 0.3	8.0 ± 1.1	0.001**
TC (mg/dl)	176.3 ± 40.1	215.9 ± 46.5	0.001**
TG (mg/dl)	108.0 ± 36.2	158.6 ± 56.2	0.001**
HDL-C (mg/dl)	44.9 ± 3.7	39.9 ± 3.9	0.001**
LDL-C (mg/dl)	73.9 ± 29.4	142.0 ± 45.9	0.001**
SBP (mm of Hg)	131.8 ± 5.8	145.3 ± 11.4	0.001**
DBP (mm of Hg)	82.2 ± 4.9	87.8 ± 7.9	0.001**
BMI (kg/m^2)	22.9 ± 1.9	23.9 ± 1.9	0.013*
WC (cm)	76.7 ± 7.7	95.1 ± 5.5	0.001**

***Statistical significant at 0.01 level (2-tailed), p<0.01*
**Statistical significant at 0.05 level (2-tailed), p<0.05*
FBS: Fasting blood sugar, HbA1c: glaciated haemoglobin, TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist circumference

Table 3: Correlations among the clinical parameters of obese

	Age	FBS	HbA1C	TC	TG	HDL-C	LDL-C	SBP	DBP	BMI	WC
Age (years)	1	0.246	0.062	0.094	0.140	-0.065	0.124	0.038	0.158	0.196	**0.426****
FBS (mg/dl)	-	1	**0.325***	0.093	0.072	0.093	0.143	0.102	-0.122	-0.046	0.099
HbA1C (%)	-	-	1	0.057	-0.136	0.075	0.100	-0.243	-0.189	0.230	0.045
TC (mg/dl)	-	-	-	1	**0.628****	**-0.453****	**0.934****	0.119	0.149	-0.134	-0.143
TG (mg/dl)	-	-	-	-	1	**-0.323***	**0.647****	0.227	0.271	-0.190	-0.041
HDL-C (mg/dl)	-	-	-	-	-	1	**-0.510****	0.038	0.072	0.121	-0.196
LDL-C (mg/dl)	-	-	-	-	-	-	1	0.170	0.163	-0.152	-0.062
SBP (mm of Hg)	-	-	-	-	-	-	-	1	**0.765****	0.055	0.166
DBP (mm of Hg)	-	-	-	-	-	-	-	-	1	0.071	0.210
BMI (kg/m^2)	-	-	-	-	-	-	-	-	-	1	0.107
WC (cm)	-	-	-	-	-	-	-	-	-	-	1

***. Correlation is significant at the 0.01 level (2-tailed).*
**. Correlation is significant at the 0.05 level (2-tailed).*
FBS: Fasting blood sugar, HbA1C: Glycated haemoglobin, TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist circumference.

Table 4: Linear regression analysis among obese

Variables	Beta coefficient β (unstandardized)	t	p	95.0% Confidence interval for unstandardized β coefficient	
				Lower bound	Upper bound
Age (years)	0.194	2.677	**<0.05**	0.048	0.341
FBS (mg/dl)	0.007	0.353	-	-0.035	0.050
HbA1c (%)	0.505	0.663	-	-1.037	2.048
TC (mg/dl)	-0.052	-1.181	-	-0.142	0.037
TG (mg/dl)	-0.006	-0.341	-	-0.042	0.030
HDL-C (mg/dl)	-0.532	-2.399	**<0.05**	-0.981	-0.084
LDL-C (mg/dl)	0.009	0.185	-	-0.091	0.109
SBP (mm of Hg)	0.036	0.315	-	-0.192	0.263
DBP (mm of Hg)	0.153	0.953	-	-0.171	0.476
BMI (kg/m^2)	-0.067	-0.162	-	-0.905	0.770

***. Correlation is significant at the 0.01 level (2-tailed).*
**. Correlation is significant at the 0.05 level (2-tailed).*
FBS: Fasting blood sugar, HbA1C: Glycated haemoglobin, TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index

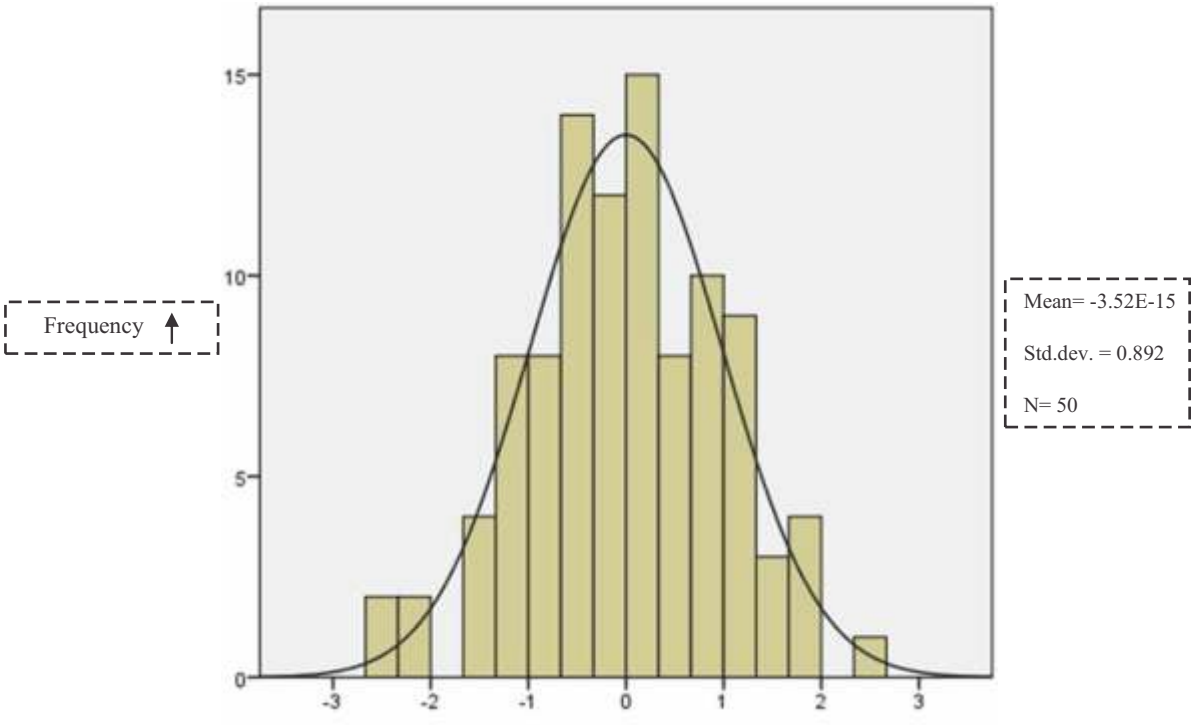

Figure 1: Histogram – Waist circumference as a dependable marker

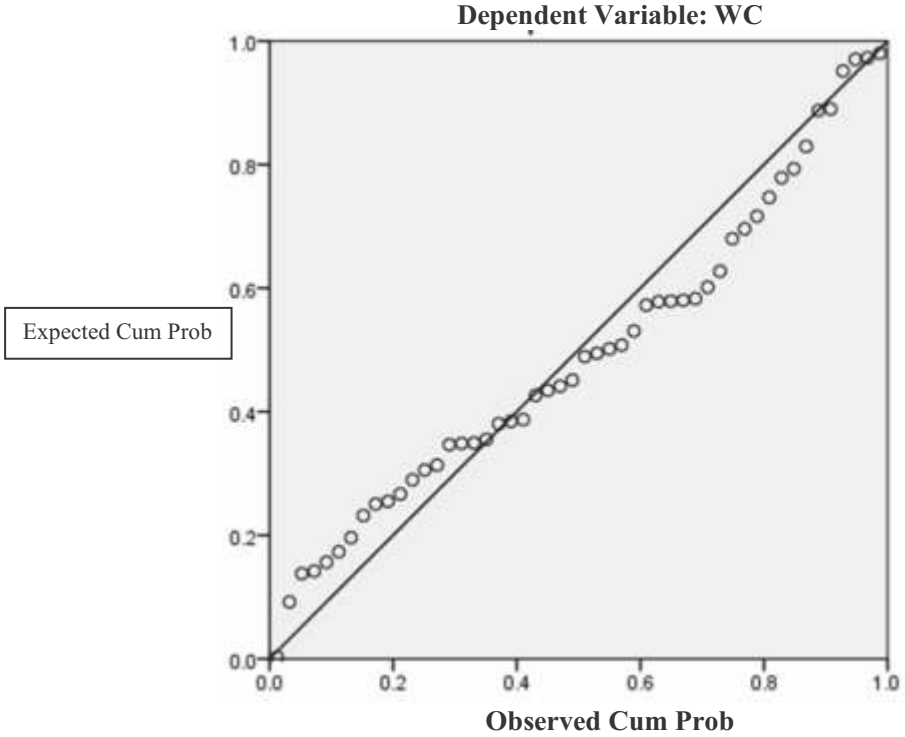

Figure 2: Normal P-P Plot of Regression Standardized Residual

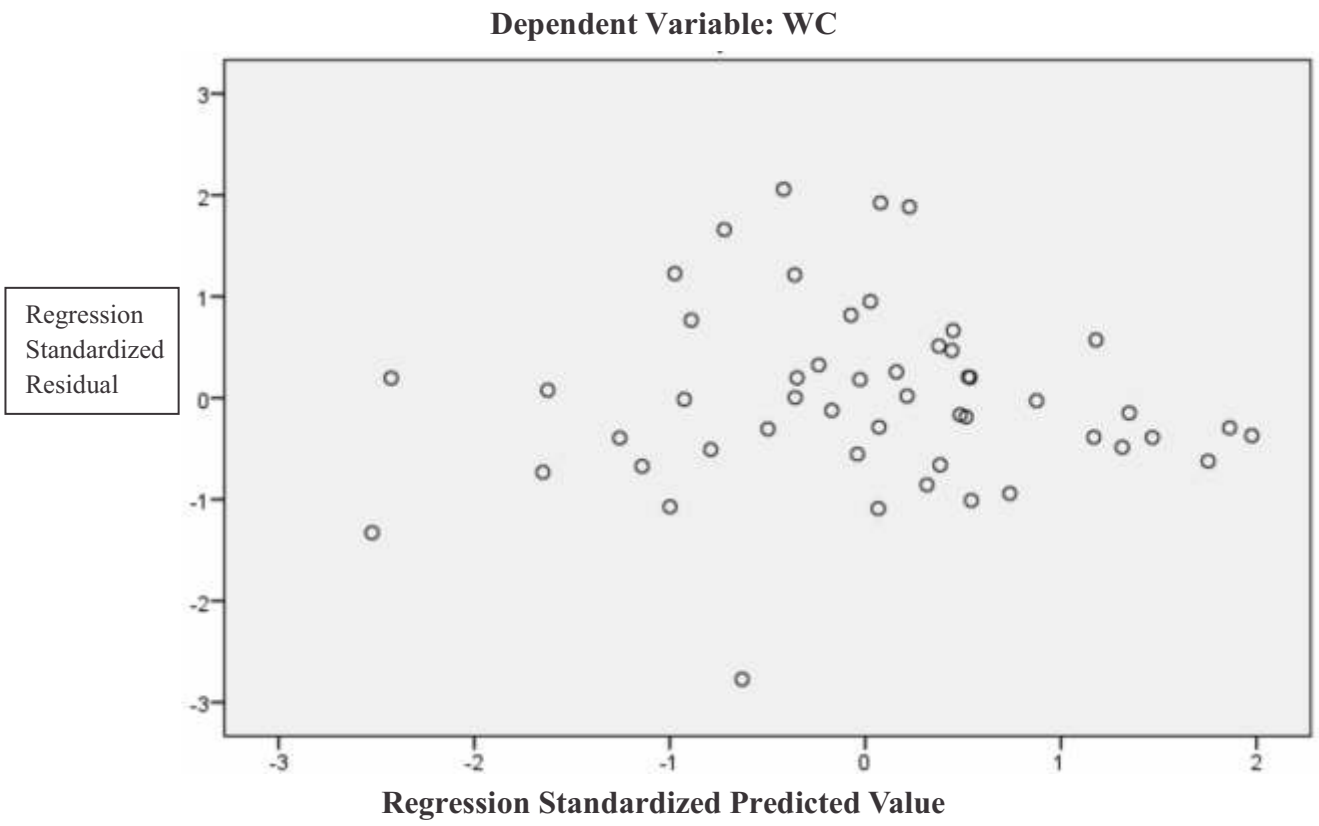

Figure 3: Scatterplot

Discussion

Obesity along with resistance in insulin participates in the progression of the cardio-metabolic risk factors which include impaired fasting glucose levels, hypertension, central obesity, and derangement in lipid profile i.e. dyslipidemia [19]. It is considered that obesity is participating as chief cause for MetS, T2DM, and CVD. Mohan *et al.* (2006) in Chennai Urban Population Study (CUPS) - a follow up study showed that the overall mortality rates in diabetic groups when compared to non-diabetic group was 3 times high and that was due to CVD and renal disease in diabetic subjects. This showed that T2DM was associated with CVD and which was associated with MetS and obesity [20]. Khan *et al.* (2022) in their study showed that association between the risk factor for CVDs and high saturated and trans-fatty acids in diet, obesity, sedentary lifestyle, and genetic predisposition may lead to atherosclerosis. Reduced level of HDL-C also contributes as an alarming risk factor [21]. In this present study - the value of all the clinical parameters i.e. FBS, HbA1c, lipid profile, SBP, DBP in obese group were significantly raised ($p<0.001$) when compared to controls (non -obese group). This result showed that obese patients are at greater risk for developing CVD in future. Mohan *et al.* (2007) advocated that Asian Indians have a unique phenotype that shows specific biochemical, physical and clinical characteristics. The Madras Diabetes Research Foundation-Indian Diabetes Risk Score (MDRF-IDRS) study

conducted by Mohan *et al.* (2005) revealed that the person having an MDRF-IDRS score ($\geqslant$ 60) are at high risk for T2DM and its complications. MDRF-IDRS score was calculated by using parameters (age, WC, physical activity, and family history of T2DM). WC is associated with the degree of obesity and the physical activity is connected with CVDs [22, 8, 23]. In this present study, age was significantly correlated with WC and demographic characteristics of subjects showed that those between 30-40 years were at higher risk indicating obesity was also related with age which may lead to MetS and CVD in future. Greater WC even in individuals with normal weight may indicate higher risk for CVD because WC is an indicator of abdominal body fat which is associated with cardio-metabolic diseases and may be a predictor of mortality [24]. According to Powell-wiley *et al.* (2021), WC is considered for measuring the abdominal obesity and abdominal obesity is a direct risk factor for CVDs, independent of BMI [25]. Khan *et al.* (2016) found a significant difference in BMI, WC, and WHR in between cases and controls and advocated that central obesity and high BMI were linked to increased risk factors for T2DM [26]. In our present study, when all parameters among the obese were regressed by making WC as dependable and predictive marker, it was seen that among all the independent variables, age and HDL-C were significantly dependent on WC. This indicates that variation in the investigative value of HDL-C depends on WC. WC is an indicator of obesity, hence an obese patient is at higher risk of CVD due to decrease in HDL-C as the age progresses. Malik *et al.* (2022) further reported that regular drinking of sugar-sweetened beverages are responsible for weight gain and also for increasing the risk for abdominal obesity, T2DM, CVD in high to low-income countries [27]. Anjana *et al.* (2022) reported in a study of the Indian Council of Medical Research (ICMR)-India Diabetes (INDIAB) study in India, that positive response of ABC targets i.e. {good control of blood glucose (A), blood pressure (B) and (C) LDL-C} was recorded in self-reported diabetes groups. It was also suggested through the study that education and awareness regarding diabetes can be a better way to achieve ABC targets among Indian population [28]. Ebong *et al.* (2022) in their study suggests that maintenance of a healthy body weight and WC may be protective against developing future increasing risk of heart failure, especially for women with late menopause [29]. This indicates that WC at menopausal age may be an indicator of CVD. Ueno *et al.* (2022) in an analysis of health check-up which was nationwide, demonstrated that normal weight central obesity was associated with higher risk of developing heart failure and atrial fibrillation when compared with normal-weight without central obesity [30].

Conclusion

Demographic study reveals that maximum subjects were in between the age of 30-40 years. Results indicated that person in between 30-40 years of age having T2DM, dyslipidemia, hypertension, with central/abdominal obesity will be at higher risk for developing CVD in future. It was further indicated abdominal obesity increases the risk of development of CVD in later stages of life. Linear regression analysis model was found fit and significant that strongly supports the hypothesis that WC is an independent predictive marker of risk factors for CVD. Further study is needed in larger sample to strengthen the hypothesis.

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