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Correlation of visceral obesity with fasting serum insulin and triglyceride levels in metabolic syndrome.

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List of Abbreviations:

1) FBS - Fasting blood sugar
2) TC - Total cholesterol
3) HDL-C - High density lipoprotein cholesterol
4) LDL-C - Low density lipoprotein cholesterol
5) TGL / TGs - Triglycerides
6) VLDL - Very low-density lipoprotein
7) LAP - Lipid accumulation product
8) CAD - coronary artery disease
9) CVD - cardiovascular disease
10) CHD - coronary heart disease
11) APO(a) - Apolipoprotein(a)
12) APO(B) - Apolipoprotein(B)
13) IDF - International diabetes federation
14) NCEP: ATP III - National cholesterol education program: Adult treatment panel
15) BMI - Body mass index
16) NEFA - Non esterified fatty acids
17) HPL - Hormone sensitive lipase
18) FFA - Free fatty acids
19) LPL - Lipoprotein lipase
20) ASCVD - Atherosclerotic cardiovascular disease
21) CRP - C-reactive protein
22) hs - CRP - High sensitivity c reactive protein
23) WC - Waist circumference
24) MetS / MS - Metabolic syndrome
25) IL-6 - Interleukin 6
26) TNF - Tumor necrosis factor

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27) VAT - Visceral adipose tissue
28) IRS - Insulin receptor substrate
29) PCOS - polycystic ovarian syndrome
30) ROS - Reactive oxygen species
31) NADPH - Nicotinamide dinucleotide phosphate
32) VFA - Visceral fat area
33) WHR - Waist to hip ratio
34) NASH – Non-alcoholic steato-hepatitis
35) NAFLD – Non-alcoholic fatty liver disease
36) OSA - Obstructive sleep apnea
37) DPP - Diabetes prevention program
38) AHA - American heart association.
39) IFG - Impaired fasting glucose
40) IGT - Impaired glucose tolerance

Abstract

Background: The Metabolic syndrome is a cluster of interrelated metabolic abnormalities that directly promote the development of atherosclerotic cardiovascular disease. Dyslipidemia and insulin resistance play a key role in the development of metabolic syndrome. The present study was conducted to correlate insulin resistance and hypertriglyceridemia with visceral obesity in patients with Metabolic syndrome.

Methods: A cross-sectional observational study was conducted to correlate insulin resistance and hypertriglyceridemia with visceral obesity in patients with Metabolic syndrome over a period of 18 months between January 2020 to June 2021. Detailed history and clinical examination along with waist circumference, a marker of visceral obesity was determined, and following investigations were done such as fasting glucose, fasting insulin, fasting triglyceride, and high-density lipoprotein levels. Descriptive statistics were performed for the categorical data and continuous data then it was represented in the form of frequencies, percentages, mean and standard deviation. Pearson's correlation was performed between the continuous variables: Waist circumference and Triglyceride levels; Waist circumference and Insulin levels.

Results: There was a positive correlation between the waist circumference and the triglyceride levels. That is, as the waist circumference increases, the triglyceride levels also increase. (Pearson's correlation of 0.436, P value of 0.001, indicating a statistical significance at 0.01 level). Also, there was a positive correlation between the waist circumference and the insulin levels. That is, as the waist circumference increases, the insulin levels also increase. (Pearson's correlation of 0.704, P value of 0.001, indicating a statistical significance at 0.01 level.

Conclusion: Waist circumference, a significant surrogate marker for visceral obesity is an important determinant of metabolic syndrome and increased waist circumference is directly related to increase in serum triglyceride levels and serum insulin levels which determines the degree of insulin resistance.

Keywords: Waist circumference**,** Metabolic syndrome, Hypertriglyceridemia, Insulin resistance.

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Introduction: The metabolic syndrome, also referred to as Syndrome X or insulin resistance syndrome, is a group of metabolic disorders that increases the risk of cardiovascular disease (CVD) and diabetes. Since the World Health Organization first defined the metabolic syndrome in 1998, the criteria have evolved to reflect increased clinical evidence and analysis by several consensus forums and professional groups. Central obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL) cholesterol, hyperglycaemia, and hypertension are all symptoms of the metabolic syndrome [1]. There is indeed a relation between all the metabolic syndrome components and insulin resistance [2].

After various investigations, investigators have used National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) definition and reported the prevalence of the Metabolic syndrome [3]. The global burden of metabolic syndrome was estimated to be around 20–25% [4] and in India the prevalence of this syndrome varies from region to region, and it is about 30% [5]. Most people with metabolic syndrome live in South Asia, and the prevalence of metabolic syndrome varies depending on where you live. According to recent data, metabolic syndrome affects approximately 33% of the urban population in India's large cities. And many of the risk factors that contribute to metabolic syndrome are frequent among Indians [6]. Increasing prevalence of Metabolic syndrome is being recognised as an important risk factor for cardiovascular disease [7]. Metabolic syndrome doubles the risk of death from myocardial infarction and triples the risk of developing myocardial infarction or stroke when compared to people without Metabolic syndrome [8]. They also have five times increased risk of developing type 2 diabetes mellitus (if not already present) [9]. Visceral Obesity has been consistently found in patients with insulin resistance syndrome. Epidemiological and pathophysiological data indicate visceral obesity as main factor in the occurrence of all the components of Metabolic syndrome. Some authors have proposed that visceral obesity and Metabolic syndrome may be considered as two faces of the same coin [10].

Waist circumference (WC) is considered as a surrogate marker of visceral obesity [11] and single value of waist circumference can be considered as strong correlate of visceral obesity [12]. In 2005, Kahn-43 proposed “lipid accumulation product” (LAP) a simple indicator of combining WC and triglycerides (TG) to reflect lipid overaccumulation, especially Visceral adipose tissue (VAT) depot i.e., LAP = [WC (cm)-65] × TG [mmol/L] for men and [WC (cm)-58] × TG [mmol/L] for women [13].

Roriz et al. demonstrated that LAP is an accurate indicator in visceral obesity discrimination among the general adult population [14]. Insulin resistance has the key role in pathophysiology of metabolic syndrome. It has originally been stated by Berson and Yalow as state of body, tissue, or system in which higher than normal amounts of insulin are required to elicit an effective normal response. Fasting insulin used as surrogate marker of insulin resistance, as it is found that Fasting insulin levels correlate with insulin resistance [15]. Fasting hyperinsulinemia has been shown to be associated with Clustering of cardiovascular risk factors like dyslipidaemia, raised blood pressure and endothelial dysfunction.

Different levels of Fasting insulin have been found in different ethics; South Asian population had higher level of fasting insulin as compared to population of European region [16].

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Monitoring of fasting insulin levels and fasting insulin level trends is useful to identify insulin resistance. Hypertriglyceridemia commonly occurs along with other components of the metabolic syndrome [17]. An elevated triglyceride is frequently the most available laboratory marker to uncover the coexistence of multiple risk factors, including nonlipid risk factors, such as hypertension [18], elevated plasma glucose, and a prothrombotic state [19]. There are various studies which have demonstrated the correlation between Visceral obesity, fasting serum insulin levels and triglycerides levels, but there is limited data on the same among Indian population. In this study we have demonstrated the correlation of visceral obesity with fasting serum insulin levels and serum triglyceride levels.

Methods: This cross-sectional observational study was conducted between January 2020 and June 2021 over a period of 18 months at a tertiary care hospital, Bangalore, India. Patients visiting the General Medicine outpatient department and Diabetic clinic and in-patients from the wards are taken up for the study after satisfying the inclusion criteria. Purposive sampling method was used for selection of the patients. A total of 100 patients were enrolled after satisfying the inclusion criteria and written informed consent have been obtained. Inclusion criteria: 1) Central obesity: Waist Circumference ≥90 cm in men and ≥80 cm in women, 2) Hypertriglyceridemia: ≥150 mg/dl (1.695 mmol/l), 3) Low HDL-Cholesterol levels: <40 mg/dl in men and <50 mg/dl in women, 4) High blood pressure (BP): systolic more than 130 and diastolic more than 85 mmHg, 5) High fasting glucose: more than 110 mg/dl in previously diagnosed type 2 diabetes mellitus, 6) Patient should satisfy at least three out of these five criteria according to National cholesterol education panel and adult treatment panel 3. Exclusion criteria: 1) Lipodystrophy in association with HIV, 2) Type 1 diabetes patients, 3) Patients on insulin therapy, 4) Patients not willing to give consent.

Methodology: After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Prior to consent, the participants were informed that refusal to participate in the study will not affect further management. Thorough history and clinical examination including waist circumference as a surrogate marker of visceral obesity was done along with following Investigations: such as fasting glucose levels, fasting serum insulin levels, fasting triglyceride (TG) levels, high-density lipoprotein (HDL) levels were measured using standard biochemical assay. Waist circumference is considered as a surrogate marker of visceral obesity [11] and single value of waist circumference can be considered as strong correlate of visceral obesity [12], direct methods of measuring visceral obesity are time consuming and costlier hence for feasibility waist circumference was measured.

Statistical Analysis: After data collection, the data was entered in the MS Excel sheet. Then the data was transferred to IBM Statistical Software for Social Science (SPSS) Software version 21.0.

P value of Kolmogorov Smirnov test was above 0.05, indicating that the data is normally distributed. Descriptive statistics was performed for the categorical data and continuous data then it was represented in the form of frequencies, percentages, mean and standard deviation. Pearson's correlation was performed between the continuous variables: Waist circumference and Triglyceride levels; Waist circumference and Insulin levels. The data analysis has been exhibited in the table and graph format.

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Results: The clinical characteristics of the study population with biochemistry parameters are presented in Table 1. Out of 100, about 29 amongst the study population had waist circumference between 101 to 110 cm. 5 of them had waist circumference between 81 to 90 cm and 2 of them had waist circumference between 141 to 150 cm. Maximum percentage of study population, that is 70% had serum triglyceride levels between 200 to 499 mg/dl. Only 1 individual had triglyceride levels less than 150 mg/dl. and 6 % of the population had triglyceride levels more than 500 mg/dl.

About 98% had the HDL levels lesser than or equal to 40 mg/dl and only 2% had HDL levels more than or equal to 41 mg/dl. Highest percentage among the study population i.e., 49 of them had fasting blood sugar levels between 151 to 200 mg/dl, and only 1 individual had fasting blood sugar levels more than or equal to 301 mg/dl. Majority of individuals, about 70% had fasting serum insulin levels between 2.6 to 24.9 µIU/ml. and about 30% of the study population has fasting serum insulin levels more than 25 µIU/ml. None of them had fasting serum insulin levels lesser than or equal to 2.5 µIU/ml.

Table 1: Baseline characteristics of study population.

Baseline characteristics	N	Minimum	Maximum	Mean	Std. Deviation
Age (in years)	100	31	81	55.44	11.92
DM Duration (in years)	100	0 (newly detected)	21	7.04	5.22
HTN Duration (in years)	100	0 (newly detected)	22	7.80	5.90
Waist Circumference (in cm)	100	84	145	113.11	13.52
SBP	100	130	180	153.00	10.81
DBP	100	80	110	90.75	6.32
TGL	100	140	841	285.83	116.94
HDL	100	8	45	28.35	7.36
FBS	100	113	306	166.31	33.48
Insulin	100	3.60	30.90	18.75	8.11

[DM-Diabetes mellitus, HTN-Hypertension, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, TGL-Triglyceride level, HDL-High density lipoprotein, FBS-Fasting blood sugar]

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Table 2 and figure 1 illustrates the Pearson's correlation between the waist circumference and the triglyceride levels. The results show that there is a positive correlation of 0.436 between them. That is, as the waist circumference increases, the triglyceride levels also increase. The P value is 0.001, indicating a statistical significance at 0.01 level. Table 3 and figure 2 illustrates the Pearson's correlation between the waist circumference and the insulin levels. The results show that there is a positive correlation of 0.704 between them. That is, as the waist circumference increases, the insulin levels also increase. The P value is 0.001, indicating a statistical significance at 0.01 level.

Table 2: Correlation between Waist circumference and Triglyceride levels.

Statistical test			**Waist circumference (in cm)**	**Triglyceride level**
Pearson's Correlation	**Waist circumference (in cm)**	Correlation Coefficient	1	0.436**
		Sig (1-tailed)		0.000
		N	100	100
	Triglyceride level	Correlation Coefficient	0.436**	1.000
		Sig (1-tailed)	0.000	
		N	100	100

[**Correlation is significant at the 0.01 level (1-tailed)]

Table 3: Correlation between Waist circumference and Fasting insulin levels. (Visceral obesity and Diabetes)

Statistical test			**Waist circumference (in cm)**	**Insulin**
Pearson's Correlation	**Waist circumference (in cm)**	Correlation Coefficient	1	0.704**
		Sig (1-tailed)		0.000
		N	100	100
	Fasting Insulin level	Correlation Coefficient	0.704**	1.000
		Sig (1-tailed)	0.000	
		N	100	100

[**Correlation is significant at the 0.01 level (1-tailed)]

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Figure 1: Correlation between Waist circumference (in cm) and Triglycerides levels (TGL).

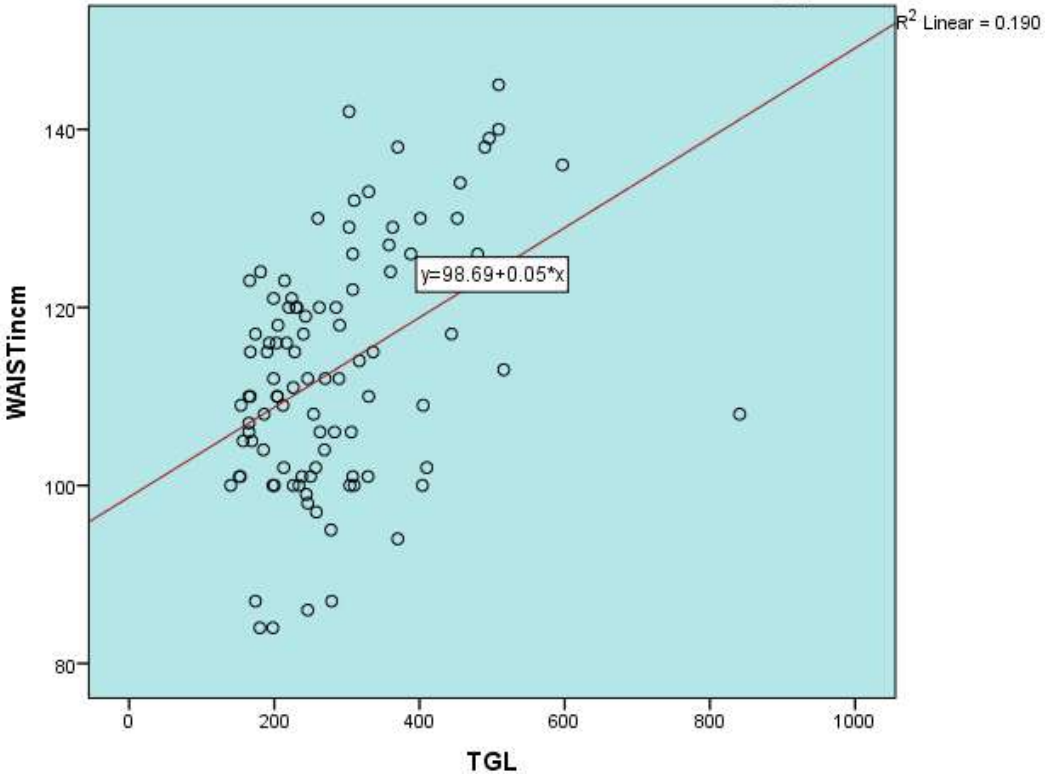
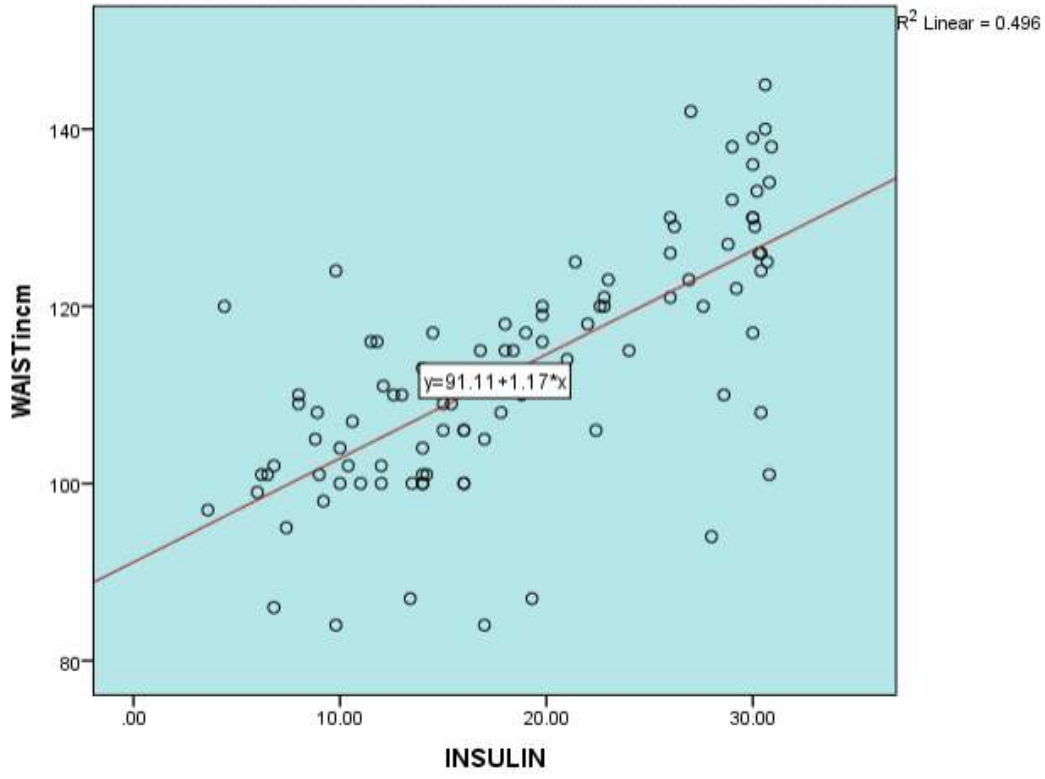


Figure 2: Correlation between Waist circumference (in cm) and Fasting insulin levels.



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Discussion: Visceral obesity is closely linked to insulin resistance and is currently regarded as a principal component of the metabolic syndrome. Waist circumference (WC) has been proposed as surrogate markers to estimate visceral adiposity [11] and single value of waist circumference can be considered as strong correlate of visceral obesity [12]. **Seidell et al**. observed positive associations between WC, insulin, and triglyceride concentrations [20]. The variables included in the study are age, gender, waist circumference, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Serum Triglyceride levels (TGL), High Density Lipoprotein Cholesterol (HDL), Fasting Blood Sugar Levels (FBS) and Fasting Serum Insulin levels.

Out of 100 subjects studied 36 were females and 64 were males. However, there are many studies that show a higher female prevalence of Metabolic syndrome. But as this study has a higher percent of male sample subjects than female subjects, a male preponderance of metabolic syndrome was noted. The age ranged from 31 years to 81 years. Majority of the patients were in age group between 51 to 70 years of age and the mean age of the study population was 55.44 ± 11.92 years of age. There was only one subject in the age group of 81-90 years and 6 subjects in the age group of 71-80 years. This shows the prevalence of metabolic syndrome is higher in older age group which is supported by the following studies: **Fabiola MS Adam et al**. conducted a study in which mean age was 50.09 ± 9.42 years [2]. The mean waist circumference was 109.50 ± 15.50 in females and 115.14 ± 11.91 in males. The studies conducted by **Ford et al**. and **Stevens et al**. concluded that WC is larger in males compared with females and larger in older adults compared with younger adults up to the age of 70 [21,22]. In a study by **Maria Kampoti et al**. it was 105 ± 9 cm in females and 108 ± 11 cm in males [23] and by **Fared F et al**. it was 108.5 ± 10.5 cm in females and 104.5 ± 13.2 cm in males [24]. In another study by **Fabiola MS Adam et al**. the mean waist circumference among patients with Metabolic syndrome was 98.41 ± 5.32 cm.

In the present study mean Systolic Blood Pressure among patients with Metabolic syndrome was 153 ± 10.81 mmHg and diastolic BP was 90.75 ± 6.32 mmHg. Hypertension is one of the components of metabolic syndrome hence all the 100 patients recruited were hypertensive. In the study conducted by **Fabiola MS Adam et al**. the mean Systolic Blood Pressure in Metabolic syndrome was 158.10 ± 10.55 mmHg and mean diastolic BP was 84.5 ± 10.32 mmHg. In the study by **Maria Kampoti et al**. the mean systolic Blood Pressure in Metabolic syndrome was 134 ±19 mm Hg and mean diastolic blood pressure was 79 ± 11 mm Hg. Our study showed that 86 patients were known diabetic (86%) and 14 were newly detected cases of Diabetes Mellites (14%). The mean FBS value in present study was 166.31 ± 33.48mg/dl. Other similar studies showed that the mean FBS value to be higher than the current study. In a study by **Fabiola MS Adam et al**. it was 219.22 ± 62.23 mg/dl and by **Fared F et al**. it was 187 ± 67.2 mg/dl. The mean serum Triglyceride level among cases was 285.83 ± 116.94 mg/dl. **Fabiola MS Adam et al**. showed a higher score of 311.79 ± 86.92 mg/dl. Whereas **Maria Kampoti et al**. and **Fared F et al**. showed a much lower value than the current study of 164 ± 90 mg/dl and 176.9 ± 38.4 mg/dl respectively. **Maria Kampoti et al**. also concluded that serum triglycerides had the highest predictive ability for Metabolic syndrome. In this study the mean serum HDL among cases was 28.35 ± 7.36 mg. Almost similar value of 33.12 ± 6.38 mg/dl was seen in a study by **Fabiola MS Adam et al**. Much higher value of 50 ± 11 mg/dl and 50.2 ± 22.3 mg/dl was seen in studies by **Maria Kampoti et al**. and **Fared F et al**. respectively. A serum HDL lower than 50 mg/dl in females with diabetes (HDL criterion fulfilled) predicted the presence of the whole syndrome with a specificity of 92%. In the present study mean fasting serum insulin levels value

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among study group was 18.75 ± 8.11 uIU/ml. In the study by **Fabiola MS Adam et al**. the mean fasting serum insulin level was 15.68 ± 7.85 uIU/ml. Other studies by **Tabata et al**. and **Nilsson et al**. also found to have higher levels of fasting serum insulin levels which signifies that insulin resistance is important factor in metabolic syndrome [25,26]. In the present study mean fasting serum insulin levels value among study group was 18.75 ± 8.11 uIU/ml. In the study by **Fabiola MS Adam et al**, the mean fasting serum insulin level was 15.68 ± 7.85 uIU/ml. Other studies by **Tabata et al**. and **Nilsson et al**. also found to have higher levels of fasting serum insulin levels which signifies that insulin resistance is important factor in metabolic syndrome.

The current study demonstrated a statistical significance, linear positive correlation of 0.436 (Pearson's correlation coefficient) between the waist circumference and the triglyceride levels. That is, the study demonstrated that in a person with raised waist circumference, the triglyceride levels are also raised. **Mostaza et al**. found that patients with primary hypertriglyceridemia have an elevated turnover rate of non-esterified fatty acids; this elevation occurred independently of body fat content and abdominal obesity [27]. This elevation suggests that patients with primary hypertriglyceridemia have insulin resistance at the level of adipose tissue. Similar results were observed in studies conducted by **Fared F et al**. another study by **Raj et al**. showed same results that greater the waist circumference greater is the serum triglyceride level [28], similarly study conducted by **huang et al**. demonstrated the positive association between serum TGs level and visceral fat amount [29].

The other parameter, insulin levels also demonstrated a statistical significance, linear positive correlation of 0.704 (Pearson's correlation coefficient) with the waist circumference. That is, it showed that as the waist circumference increases, the insulin levels also increase. Similar results were observed in the other studies conducted by **Fared F et al, Göran Nilsson, Shinji Tabata and Fabiola MS Adam**. Insulin resistance is positively associated with the degree of visceral obesity in middle-aged and elderly individuals [30,31]. A close relation between waist circumference, visceral obesity and insulin resistance has been demonstrated using determination of the magnitude of visceral adipose tissue by computer tomography and magnetic resonance imaging in combination with measuring insulin resistance directly by the euglycemic–hyper insulinemic clamp technique. In current study we demonstrated the correlation between waist circumference and fasting serum insulin levels.

Conclusion: Waist circumference is an important determinant of metabolic syndrome and its correlation with visceral obesity has been demonstrated in various studies. From the above-mentioned results and discussion, we can conclude that the increased waist circumference is directly related to increase in serum insulin levels which signifies insulin resistance and serum triglyceride levels. The prevalence of diabetes and hypertension is very high in population with metabolic syndrome and the older age group with slight male predominance.

Declarations:

Ethics approval and consent to participate:
Our case report has been approved by the Institutional Ethics Committee and the consent to participation has been obtained.

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Consent for publication:
Consent for his/her data, other clinical information consent for publication/reporting in the journal has been obtained for our study. The patient and his/her attenders understand that their names and initials will not be published, and due efforts will be made to conceal their identity.
We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Availability of data and materials:
The data that support the findings of this study are available from the corresponding author upon reasonable request. Data sharing is not applicable to this article as no new data was created or analyzed in this study.

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Conflict of interests:
There are no financial or non-financial competing interests among the authors.

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