ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 2, April - 2023, Page No. : 01 - 09

Correlation between Fasting Insulin level and Metabolic Syndrome Diagnostic components among non-diabetics - A Cross Sectional study

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How to citation this article: Dr. Baby Sruthi S. D, Dr. Jimnaz P. A, Dr. Alavi K. P, "Correlation between Fasting Insulin level and Metabolic Syndrome Diagnostic components among non-diabetics- A Cross Sectional study", IJMACR- April - 2023, Volume – 6, Issue - 2, P. No. 01 – 09.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Aims and Objectives: To find out the relationship between high Fasting Insulin (FI) levels and metabolic syndrome diagnostic components (Mets-DCs) in non-diabetics.

Materials and Methods: A Hospital based cross sectional Study was conducted among the patients of age group 25 years and above, satisfying the criteria of metabolic syndrome, who are non-diabetic, attended MES medical college during the period from 1st January 2021 to 31st December 2021. Sample size required was 53.For those with an elevated SBP/DBP and high WC, a detailed clinical history, physical examination were carried out .FLP and FPG tests were done and then FI was done for those satisfying the criteria MetS.FI levels, Fasting lipid profile and fasting glucose were checked by blood sampling Data are entered into MS excel and analysis done using SSPS® software version 25.

Results: A total of 53 participants were included in the final analysis as per ATPIII (2002) Asian diagnostic criteria for Met S. The median age of the study population was 39 and patients were classified accordingly. Out of this 62.3% were female and37.7%weremale.Systolic and diastolic Blood Pressure was negatively correlated with FI (r=-0.008 and -0.046) and the correlation was not significant with a P value >0.05.HDL and TG was positively correlated with FI but the correlation was non significant. Waist circumference (r= 0.273, P value = 0.048) and FPG (r=0.287,P value = 0.037) was positively correlated with FI and the Correlation was statistically significant.

Conclusion: As we included participants satisfying metabolic syndrome criteria and analyzed their FI

levels, majority were falling under the high insulin group. The high FI group had increased levels of FPG, which is statistically significant ($p<0.05$). Hence there may be increased incidence of T2D Min the high insulin group in future.

Keywords: Metabolic syndrome, metabolic syndrome diagnostic components, Fasting insulin.

Introduction

Globally, the prevalence of the metabolic syndrome (MetS), syndrome X, and insulin resistance syndrome is rising. It is a pathogenic condition, according to WHO, that is characterised by central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension 1-2. Overweight/obesity, a sedentary lifestyle, genetics, and ageing are risk factors. Insulin resistance is the most widely recognised theory to explain the pathogenesis of MetS.[3] Individuals experience postprandial hyperinsulinemia, fasting hyperinsulinemia, and then hyperglycemia before the formation of insulin resistance.4Fasting insulin (FI) levels, which signify insulin resistance, have been linked to the prevalence of MetS, according to certain studies.5-6 45% to 50% of the daily insulin needs are met by basal insulin, and FI is roughly equivalent to basal insulin.7 Increased FI levels have been demonstrated to be able to forecast the occurrence of MetS in the future. 8-9 A high FI warns the doctor about the prevalence of metabolic disorders and cardiovascular risks since insulin resistance is the basis of MetS and because FI symbolises insulin resistance.10 MetS increases the chance of developing CVD, T2DM, and other non-communicable diseases (NCDs), such as polycystic ovary syndrome, hyperuricemia, non-alcoholic fatty liver disease, and obstructive sleep apnea.. Almost every community on earth has some kind of diabetes, impaired glucose tolerance (IGT), or impaired fasting glucose (IFG), and epidemiological data indicates that the burden of diabetes is likely to rise worldwide without effective prevention and control measures.15-16 Diabetes is discovered in a significant portion of MES patients (both inpatients and outpatients), and the majority of these patients are obese. It is discovered that diabetes mellitus is a typical metabolic condition that manifests as a side effect of Mets. It has diverse aetiologies and is defined by chronic hyperglycemia and abnormalities in protein, lipid, and carbohydrate metabolism brought on by deficiencies in insulin secretion or action, or both. The retinopathy, nephropathy, and neuropathy development of diabetes are some of the long-term relatively specific complications. Diabetes also increases the risk of cardiovascular, peripheral arterial, and cerebral diseases[6].

Insulin resistance syndrome, syndrome X, and the metabolic syndrome are terminology used to characterise metabolic derangements that include central obesity, insulin resistance, hypertension, dyslipidemia, IGT/IFG, and increase the risk of T2 DM and cardiovascular disease.17In this age of urbanisation and sedentary lifestyles, individuals consume excessive amounts of energy.As a result, obesity is on the rise and the clinical and public health burden of metabolic syndrome (MetS) is significant and expanding. Over the next five to ten years, patients with the MetS have a five-fold increased risk of developing type 2 diabetes (T2DM), a two-fold increased risk of cardiovascular disease (CVD), a three- to four-fold increased risk of myocardial infarction (MI), and a two- to four-fold increased risk of stroke.18 The Third Report of the Adult Treatment Panel (ATP III) of the National Cholesterol Education Programme Expert

Panel (NCEP) on 2002 Asian diagnostic criteria defines MetS. MetS is defined by three out of five or more (MetS-DCs).[19]

1. Having an anti-hypertensive medication prescription or having a systolic blood pressure (SBP) less than 130 mmHg and/or a diastolic blood pressure (DBP) less than 85 mmHg.
2. Treatment for dyslipidemia or a decrease in the level of HDL-C in the blood (40 mg/dL in men and 50 mg/dL in women).
3. A TG concentration of less than 150 mg/dL or treatment for hypertriglyceridemia.
4. Hyperglycemia, defined as fasting plasma glucose greater than 100 mg/dl.
5. Men's waist circumference (WC) of ≥90 cm or women's WC of ≥80 cm.

The pathophysiological condition known as insulin resistance is characterized by a normal insulin concentration that is unable to fulfil a normal insulin response in peripheral target tissues such adipose, muscle, and liver. To combat the hyperglycemia in this situation, the pancreatic beta cell secretes more insulin. Although it may also result in an excess of insulin activity in some typically sensitive tissues, hyperinsulinemia can compensate for insulin resistance to some of the physiologic effects of insulin.The clinical symptoms of MetS33 are caused by this accentuation of some insulin actions and a resistance to other insulin effects. Hyperglycemia and overt T2DM result from the pancreatic beta cells' inability to produce enough insulin over time to address the growing tissue insulin resistance.[20]

There aren't many studies on the connection between FI levels and MetS. In order to prevent its repercussions, such as T2DM and CVD, this study intends to shed light on the association between high FI levels and MetS Diagnostic components in non-diabetics. It does this by recommending a weight reduction diet, an exercise regimen, and behavioural changes.

Methodology

Ethicalclearance

Patients provided written informed consent. The patient's privacy and confidentiality were upheld during the entire study. The information was only accessible to the investigator and the guide. Ethical approval was obtained from institutional ethics committee (IEC/MES/14/2020).

Study design

This Hospital based cross sectional study was conducted among Patients attending General medicine OPD and admitted in ward in MES Medical College hospital, Perinthalmanna. All patients with metabolic syndrome attended general medicine outpatient department to f MES Medical College and admitted in ward during the period of study satisfying inclusion criteria were recruited. For the study, the definition of MetS was taken as per the Third Report of the National Cholesterol Education Programme Expert Panel(NCEP)on Adult ≥Treatment Panel (ATP III) 2002 Asian diagnostic criteria[19].MetS is defined by at least three of five (MetS-DCs)

1. Having an anti-hypertensive medication prescription or having a systolic blood pressure (SBP) less than 130 mmHg and/or a diastolic blood pressure (DBP) less than 85 mmHg.
2. Treatment for dyslipidemia or a decrease in serum HDL-C content, which should be greater than +40 mg/dL in men and 50 mg/dL in women.
3. A TG concentration of less than 150 mg/dL or treatment for hypertriglyceridemia.

4. Hyperglycemia, defined as fasting plasma glucose greater than 100 mg/dL;

5. Men's waist circumference (WC) of ≥90 cm or women's WC of ≥80 cm.The American Diabetes Association's Diabetes Care 202015 Standards were applied to the current investigation. Plasma glucose criteria, such as the fasting plasma glucose (FPG) value or the 2-hour plasma glucose (2-h PG) value during a 75-gram oral glucose tolerance test (OGTT), or A1C criteria may be used to diagnose diabetes.

Criteria for the diagnosis of diabetes

126 mg/dL (7.0 mmol/L) of FPG. No calorie intake for at least 8 hours is considered to be fasting

OR

On an oral glucose tolerance test, the 2-h PG was below 200 mg/dL (11.1 mmol/L) (OGTT). The test should be carried out in accordance with the WHO's instructions, using a glucose load that is equal to 75 g of anhydrous glucose dissolved in water. OR 6.5% A1C (48 mmol/mol). A technique that is NGSP (National glycohemoglobin standardization programme) certified and standardized to the DCCT (Diabetes control and complications trial) assay should be used to conduct the test in a lab. OR A random plasma glucose level of less than 200 mg/dL (11.1 mmol/L) in a patient with the typical signs and symptoms of hyperglycemia or hyperglycemic crises. Those Patients with MetS were included based on Third Report of the National Cholesterol Education Programme Expert Panel (NCEP) on Adult Treatment Panel (ATP III) 2002 Asian diagnostic criteria19.Participants with a FPG. According to a previous study16, estimation of sample size is done using Pearson correlation coefficient, Estimated correlation coefficient (ϒ) = 0.38

$$\text{Sample size, } (n) = \left[\frac{Z(1-a/2)+Z(1-\beta)}{\frac{1}{2}\log_e\frac{1+y}{1-Y}}\right]+3$$

Alpha (α) = 0.05

Beta (β) = 0.2

Minimum sample size required=53

Sampling technique Convenient

Sampling Period of study January 1st 2021 to December 31st 2021.

Data collection All persons 25 years of age and older who visited the medicine OPD had their blood pressure checked and their waist circumference assessed. In an upright position, the waist circumference (WC) was measured in the horizontal plane halfway between the iliac crest and the inferior border of the lowest rib. After five minutes of rest, blood pressure (SBP) and diastolic blood pressure (DBP) were tested at least twice while seated. A thorough clinical history, physical examination, and written informed consent were obtained from patients who had high WC, raised SBP/DBP, and both. For those who met the MetS criteria, FLP and FPG tests were conducted before FI. After a 10-hour overnight fast, FI levels, a fasting lipid profile, and a fasting glucose level were assessed by blood samples. After an overnight fast, 2 cc of serum from 1 serum separating tube was chilled or frozen. To calculate fasting insulin levels, chemiluminescent micro particle immunoassay was used.

Statistical analysis

Data was collected in a preformed questionnaire and entered in Microsoft excel. Descriptive statistics giving Frequency and percentage were calculated .Pearson's correlation was performed for each of the MetS-DC in

relation to FI levels using SPSS software of version V26. P value of ≤0.05 was taken as significant.

Results

Out of total number of patients, 62 % were female and 38% male population(Figure 1).The median age of the patients were 39. Hence, the patients were classifiedaccording to median age.52.8% patients belonged to age group <=39 and 47.2 % above 39 age group.

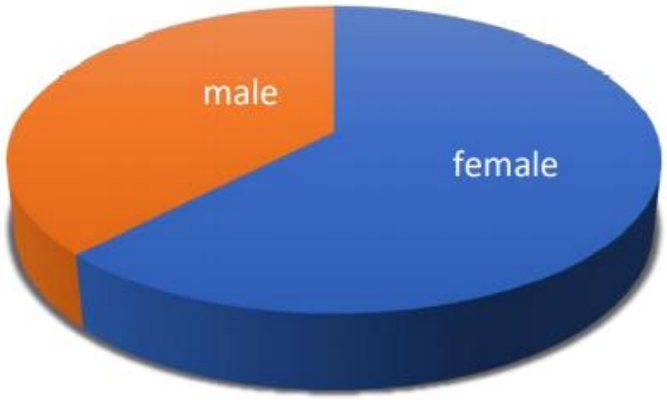

Figure 1: Gender distribution of the study participants

Table 1: BMI status of study participants

BMI	Frequency	Percent
Overweight	5	9.4
Obese1	27	50.9
Obese2	21	39.6
Total	53	100.0

Table 2: Classification of systolic Blood Pressure

SBP	Frequency	Percent
Normal	28	52.8
Prehypertension	20	37.7
Stage 1 hypertension	5	9.4
Total	53	100.0

Table 3 : Classification of Diastolic Blood Pressure

Diastolic blood pressure	Frequency	Percent
Normal	33	62.3
Prehypertension	9	17.0
Stage 1 hypertension	11	20.8
Total	53	100.0

Table 4: Correlation of Fasting Insulin values with Mets –Diagnostic components

Mets-diagnostic components	Correlation Coefficient	P-value
Waist circumference	0.273	0.048
SBP	-0.008	0.955
DBP	-0.046	0.743
FPG	0.287	0.037
TG	0.017	0.901
HDL	0.015	0.916

Test Applied : Pearson Correlation test — P value <0.0 statistically significant

Systolic and diastolic Blood Pressure was negatively correlated with FI (r=-0.008 and -0.046) and the correlation was not significant with a P value >0.05.HDL and TG was positively correlated with FI but the correlation was non significant. Waist circumference (r= 0.273, P value = 0.048) and FPG (r=0.287,P value = 0.037) was positively correlated with FI and the Correlation was statistically significant.

Discussion

The ATP III 2002 recommendations describe metabolic syndrome as the presence of at least three out of the five Mets-DCs, which is a major global health concern. Diabetes mellitus is a serious Health complication that is spreading at an alarming rate worldwide. Therefore, it is imperative that the general public be screened for MetS and that essential lifestyle changes be made to stop its consequences, such as T2DM, CVA, CVD, and POVD. In this investigation, we used a technique that has been used in other studies: serum Fasting Insulin Levels. 23-25 We made an effort to determine the connection between metabolic syndrome and high fasting insulin

levels, as well as the association between fasting insulin and each Mets-DC. It is still unclear whether metabolic syndrome or insulin resistance is to blame. However, it is evident that FI serves as a stand-in for insulin resistance. 21-22 The current study is a hospital based study, a total of 53 subjects were included in thefinal analysis who satisfy the criteria for MetS as per the NCEP on ATP III 2002 Asian diagnostic criteria19.The median age of the study population is 39 and patientswere classified accordingly. Out of this 62.3% were female and 37.7% were male. This correlated with the demographics of study by Yun hung chen etal 23which had amean age of 63.91, 34.6% were male and 65.4% were female. The median fasting insulin (FI) value was 13.1 in males and 14 in females, with no discernible gender differences in the distribution of fasting insulin values (p=0.956). 90% of men and 78.8% of women belonged to high fasting insulin groups. There was no statistically significant difference in age or gender between the middle and high insulin groups, as there had been in the earlier trial by Yung hang Chen et al.The mean age in each group was 41.9, 42, 40.7, 40.7 in a related Korean follow-up study24 where individuals were separated into insulin quartiles, although the proportion of men was high at 75, 74, 73, and 74, respectively. A 28% prevalence of metabolic syndrome was found in the study by Yung hang Chen et al.,23 which was done among non-diabetic middle-aged and elderly people after splitting them into 3 tertiles of fasting insulin. According to that study, as FI levels rose, so did the proportion of metabolic syndrome and its diagnostic elements. We compared the association between fasting insulin levels and each of the diagnostic criteria for the metabolic syndrome as well as MetS, just like in the study by Yung hang Chen et al.We considered physical activity, eating patterns, S. creatinine levels, and hepatic transaminases levels as well as waist circumference, Systolic and Diastolic blood pressures, HDL cholesterol levels, Triglyceride levels, and Fasting plasma glucose values in the diagnostic criteria. Middle range (4.9–7.8) and high range (>=7.9) fasting insulin levels are separated into these two categories. Age, BMI, WC, HC, SBP, DBP, TC, LDL, TG, HDL, SGOT, and SGPT levels did not differ statistically significantly between intermediate and high insulin levels, but FPG did (0.001) There were variations in the study by yung hang Chen et al. regarding WC, SBP, HDL-C, and TG. In contrast, in our investigation, we only found a link between FPG and WC.

Because FI also varies by ethnicity, there are no established reference levels for it in the literature. The study's participants were all of the same ethnicity. Based on their FI levels, we separated individuals into two groups: those with moderate levels (4.9–7.8) and those with high levels (> 7.9U/ml). In the study by Yung hang Chen et al., it was in the range of (1.57-16.32)U/ml, and their cutoff value was >7.35U/ml. It was discovered that FI >9 U/ml/42 was present in 80% of the prediabetic. A positive co-relation was seen for Waist circumference, FPG with FI with p-values0.048, 0.037 respectively. In study by Yung chen etal where FI was positively correlated with SBP, WC, FPG and TG, and negatively correlated with HDL-C.

Co-relation between FI levels and Mets-DCs

variables	Present study		Yung hung study	
	Correlation coefficient	P value	Correlation Coefficient	P value
WC	0.273	0.048	0.44	<0.001
SBP	-0.008	0.955	0.22	<0.001
DBP	-0.046	0.743	0.10	0.07
FPG	0.287	0.037	0.39	<0.001
TG	0.287	0.901	0.37	<0.001
HDL	0.015	0.916	−0.37	<0.001

In the study by Yung Hung etal, proportion of MetS and each of Mets-DC were increasing with levels of FI. The proportion of people in the korean follow-up study24 who had MetS likewise increased as the quartile of FI increased. From the first to the fourth quartile of FI, there was a rise in the percentage of people who developed DM. We included participants in our study who met the MetS requirements. 53 people met three or more of the requirements for MetS.HbA1c and insulin levels were linked to MetS criteria and insulin resistance in Gabriela et al. 25study of aragon workers. High fasting glucose and insulin resistance were linked to high HbA1c levels in MetS individuals, while high FI also increased waist circumference.

Comparison of relationship between Fasting insulin levels with each of the metabolic syndrome diagnostic criteria

	Present study		Yung hung	Et al study
Insulin levels (µU/ml)	Middle insulin (4.9–7.8)	High insulin >=7.9	Middle insulin (4.9–7.8)	High insulin >=7.9
Waist circumference (WC) (cm)	96.00(91.50,107.50)	100.50(96.00,113.50)	83.78 ±8.63	89.51 ±9.65
SBP(mmHg)	130(120,130)	120(120,130)	129.52 ±14.51	134.13 ±16.20
DBP(mmHg)	80(80,85)	80(78,88)	76.92 ±10.03	78.79 ±10.60
FPG(mg/dL)	94(90,98.50)	105(100.25,109)	89.18 ±8.52	93.05 ±10.60
TG(mg/dL)	121(99.50,165.50)	128(110.75,159)	111.04 ±49.83	147.05 ±72.48
HDL(mg/dL)	47(40.50,48.50)	45(40,50)	55.59 ±13.17	50.28 ±11.94

It was found that FI and hs-CRP levels rise as the number of MetS-DC increases in the study by Fabiola et al. 26on obese adults with a 68% prevalence of MetS. In our study, 13 patients had more than three MetS-DCs, and 40 persons had three MetS-DCs. No association between MetS-DC and FI levels was discovered. When patients who met the criteria for MetS were included in our study, 84.90% had high FI levels. DM and CVD are

risk factors for FI. In order to benefit the general public in the early phases of insulin resistance, more research on this topic should thus be promoted. One of the study's strengths is Because participants came from the same ethnic group and environment, confounders were reduced. Anthropometric measurements were taken using standardised lab procedures, and we The influence of anti-diabetic medicines on FI was excluded because the diabetic group was excluded. The following were some of the study's flaws: Participants came from a nearby community, and the sample size was modest. As a result, conclusions cannot be extrapolated to other ethnic groups. Due to the greater participation of women than men in our study, there might be a selection bias. With regard to insulin assays and various ethnic groups, the FI cut-off value differs. Hence we recommend more studies with large sample size and prospective cohort type are needed. Whether lifestyle modifications could revert MetS in high FI group requires further studies to elaborate.

Conclusion

There is a positive co-relation of Fasting Insulin with waist circumference, BMI, FPG. In the middle (4.9 to 7.8) and high (≥7.9) fasting Insulin level groups, FPG was found to be more in the high FI group.

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