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STUDY OF INSULIN RESISTANCE IN METABOLIC SYNDROME AND CORRELATION WITH HOMA-IR

Medicine

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ABSTRACT

Objective: This study was done to study Insulin Resistance In Metabolic Syndrome and to asses Fasting Plasma Insulin, S. Ferritin, A1C, Fasting Lipid Profile In Metabolic Syndrome And Their Correlation With HOMA-IR. **Method:** This study was an observational cross-sectional study. Patients of Metabolic Syndrome aged ≥18 years diagnosed by suggestive symptoms and confirmed by physical examination and laboratory investigations (as per ATP III Criteria)were selected randomly from outpatient clinic/ indoor general medicine SRNH, Prayagraj. Sex and age matched healthy individuals were taken as controls. Baseline investigations were done for enrolled patients, which included:Fasting blood glucose, waist circumference, Blood Pressure, Fasting lipid profile, Serum Urea and Creatinine. **Result:** Total study population was 100 of which cases were 50 and controls were 50. In cases with metabolic syndrome there were 31(62%) males and 19(38%) females. Mean age of cases was 46.9 ± 7.25 year and controls was 47.08 ± 8.94 year. The mean HDL, TC, TG in case group was 38.35±4.70 mg/dl,252. 47±33.37mg/dl, 237.75±24.91mg/dl respectively and in control group was 58.94±8.78mg/dl,132.23±22.12mg/dl, 142.94±14.92mg/dl respectively and the difference was statistically significant (p<0.05). The mean S. Ferritin in case group was 199.9±22.05 ng/ml and in control group was 79.6±22.7 ng/ml and the difference was statistically significant (p <0.005). The mean S. Ferritin was higher in cases as compared to controls. The mean S. Fasting plasma insulin in case group was 24.57±6.99µIU/ml and in control group was 4.41±1.88µIU/ml and the difference was statistically significant (p <0.05). The mean S. Fasting plasma insulin was higher in cases as compared to controls. The mean HOMA-IR in case group was 6.29±0.75mg-µIU/ml and in control group was 1.183±0.52mg-µIU/ml and the difference was statistically significant (p <0.05).The mean HOMA-IR was higher in cases as compared to controls. **Conclusion:** The results showed prevalence of metabolic syndrome to be higher in males as compared to females. The results of this study show TG/HDL and TC/HDL ratios serve as an easily available and economic marker for identifying insulin resistance in metabolic syndrome patients. Metabolic syndrome is associated with significantly increased serum ferritin level. HbA1c is more readily available than fasting insulin estimation and outperforms FPG/PPPG in terms of association with risk factors and cardiovascular risk. The combination of these evaluated markers may identify a group of patients with a more marked risk for insulin resistance and cardiovascular disease risk.

KEYWORDS

HOMA-IR, Metabolic syndrome, Fasting Insulin, Insulin Resistance

INTRODUCTION

Metabolic syndrome is characteristically defined as a clustering condition of cardiovascular risk factors including hyperglycemia, dyslipidemia, hypertension, and central obesity[1]. Its occurrence is strongly associated with increased risk in the development of type 2 diabetes mellitus and cardiovascular disease.[2]

ATP III considered the "obesity epidemic" as mainly responsible for the rising prevalence of metabolic syndrome. Obesity contributes to hypertension, high serum cholesterol, low HDL cholesterol, and hyperglycemia, and it otherwise associates with higher CVD risk. Many of its features are associated with insulin resistance.

It is estimated that around 20-25 percent of the world's adult population have the metabolic syndrome and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.[3]

IFG and IGT represent intermediate states of abnormal glucose regulation that exist between normal glucose homeostasis and diabetes. The transition from the early metabolic abnormalities that precede diabetes, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), to diabetes may take many years, however, current estimates indicate that most individuals (perhaps up to 70%) with these pre-diabetic states eventually develop diabetes.[4]

Currently, there are several direct and indirect methods to assess insulin resistance. One of the most widely used validation measures for IR is the Homeostasis Model Assessment−Insulin Resistance (HOMA−IR) index.

Other possible indicators are the lipid ratios such as TG/HDL and TC/HDL ratios. These ratios are reliable marker for estimating the insulin resistance. Insulin resistance and dyslipidemia leads to increased secretion of triglyceride and decreased HDL cholesterol and increased concentration of small dense LDL–cholesterol particles[5] Hence, the TG/HDL and TC/HDL cholesterol ratios are strong correlate of insulin resistance and type 2 diabetes mellitus.

Some studies demonstrate the strong associations between ferritin concentrations, obesity and inflammation, that contribute to the development of type II diabetes. It is well known that metabolic syndrome is a major risk factor for development of type 2 diabetes, it is now necessary to establish the link between the serum ferritin levels and risk of type 2 diabetes. Most of the previous studies have evaluated only the individual components of metabolic syndrome with serum ferritin levels rather than the clustered condition of metabolic syndrome per se unlike this present study[6].

AIMS AND OBJECTIVES-

The aim of present study was to evaluate Insulin Resistance in Metabolic Syndrome and to study Levels of Fasting Plasma Insulin, S. Ferritin, A1C, Fasting Lipid Profile In Metabolic Syndrome And Their Correlation With HOMA-IR.

MATERIALS AND METHODS

Study Design

Patients of Metabolic Syndrome diagnosed by suggestive symptoms and confirmed by physical examination and laboratory investigations (as per ATP III Criteria)were selected randomly from outpatient clinic/ indoor general medicine SRNH, Prayagraj**.** Sex and age matched healthy individuals were taken as controls.

Exclusion Criteria-

- Patients with history of coronary heart disease and/or carotid or peripheral vascular disease
- Chronic kidney disease patients
- Liver disease
- Patient on Lipid-lowering therapy (statins, ezetimibe, fibrates, nicotinic acid and omega-3)

- Pregnancy
- Causes of Hyperferritinemia (Inflamamtion, infection, chronic Iron overload etc.)

METHODOLOGY-

After obtaining written informed consent, patient qualifying inclusion criteria were included in the study. Demographic data was recorded and subjects were interviewed about medical history, education, family medical history, and intake of medications. Patients were undergone a morning fasting glucose estimation (after 8 hours of fasting at least) and fasting lipid profile, fasting Insulin levels. Serial blood pressure measurements was recorded.(after 10 minute of rest in sitting position and mean of 3 measurement with 2 minute interval). Waist circumference (measure at midway between lower thoracic bony cage and brim of iliac crest) was noted.

RESULT

Total study population was 100 of which cases were 50 and controls were 50. In cases with metabolic syndrome there were 31(62%) males and 19(38%) females. The percentage of males in the cases with metabolic syndrome was higher, 62% as compared with females 38%.Mean age of cases was 46.9 ± 7.25 year and controls was 47.08 ± 8.94 year. The mean systolic blood pressure in case group was 158.32±13.70mmHg and in control group was 127.92±14.47mmHg and the mean diastolic blood pressure in case group was 89.92±6.68 and in control group was 77.88±6.70 the difference was statistically significant (p <0.05). The mean systolic blood pressure and the mean diastolic blood pressure was higher in cases as compare to controls.

The mean HDL,TC,TG in case group was 38.35±4.70 mg/dl, 252.47±33.37mg/dl, 237.75±24.91mg/dl respectively and in control group was 58.94±8.78mg/dl, 132.23±22.12mg/dl, 142.94± 14.92mg/dl respectively and the difference was statistically significant (p <0.05). The mean TG,TC, was higher in cases as compared to controls, and the mean HDL was higher in controls as compared to cases. The mean S.ferritin in case group was 199.9±22.05 ng/ml and in control group was 79.6±22.7 ng/ml and the difference was statistically significant (p <0.005). The mean S.ferritin was higher in cases as compared to controls.

The mean S. fasting plasma insulin in case group was 24.57±6.99µIU/ml and in control group was 4.41±1.88µIU/ml and the difference was statistically significant (p <0.05).The mean S.fasting plasma insulin was higher in cases as compared to controls.n The mean HOMA-IR in case group was 6.29±0.75mg-µIU/mland in control group was 1.183±0.52mg-µIU/ml and the difference was statistically significant (p <0.05).The mean HOMA-IR was higher in cases as compared to controls.

Table 1- Comparison Between S. Ferritin In Cases And Controls

PARAMETERS	CASES (n=50)	CONTROLS (n=50)	p-value
S.FERRITIN (ng/ml) mean ±SD	199.91±22.05	79.6±22.7	<0.05 (Significant)

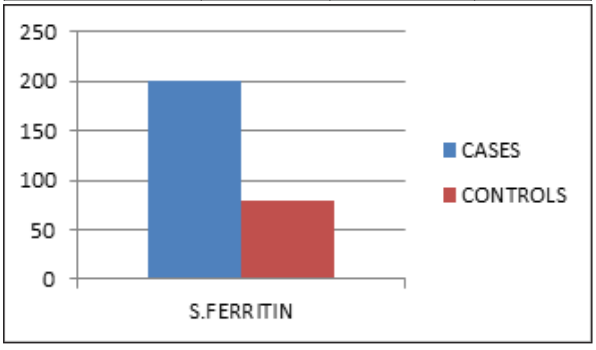

Fig.1- Comparison Between S.ferritin In Cases And Controls

Table 2- Comparison Of HOMA-IR In Cases And Controls

PARAMETER	CASES (n=50)	CONTROLS (n=50)	p-value
HOMA-IR (mg-µIU/ml)) mean ±SD	6.29±0.75	1.183±0.52	<0.05 (Significant)

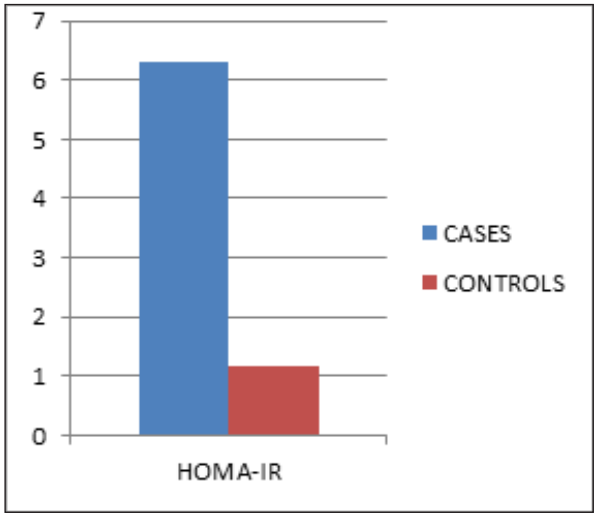

Fig.2- Comparison Of HOMA-IR IN Cases And Controls

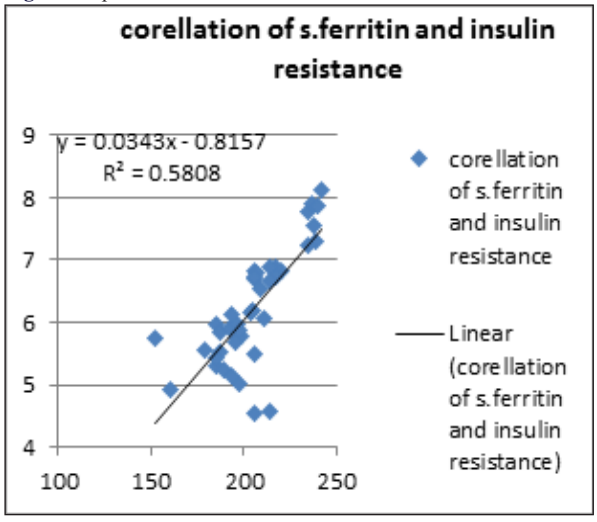

Fig 3. Scatter Diagram Showing Correlation Between S.ferritin And Insulin Resistance

Scatter diagram shows positive linear correlation between s.ferritin and Insulin resistence with R^2 value of 0.580.

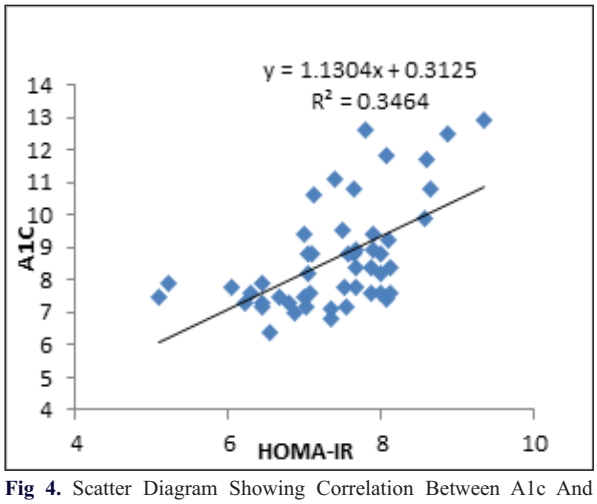

Fig 4. Scatter Diagram Showing Correlation Between A1c And HOMA-IR

Scatter diagram showing positive linear correlation A1c and HOMA-IR with R^2 value of 0.346.

DISCUSSION

The present study was designed to explore the association of fasting

plasma insulin, serum ferritin, A1C, fasting lipid profile levels with metabolic syndrome and their correlation with insulin resistance (HOMA-IR). Total study population was 100 of which cases were 50 and controls were 50. In cases with metabolic syndrome there were 19 females and 31 were males. The percentage of males in the cases with metabolic syndrome was higher, 62% as compared with females 38%. The difference of mean systolic blood pressure and mean diastolic blood pressure of cases was higher than controls in present study. The difference was statistically significant(p-value <0.05). In the present study, we have considered patients with systolic BP >130 and diastolic BP > 85 mmHg for metabolic syndrome under NCEP-ATP IIIcriteria.
Mean HOMA-IR value was 5.5 for systolic BP 131-150 mmHg, 7.3 for systolic BP 151-174 mmHg, and 8.4 for systolic BP 175- 200 mmHg. Difference in HOMA–IR of these groups was statistically significant (p <0.05). Thus, as systolic blood pressure increases, HOMA-IR shows positive correlatiion. Diastolic BP also showed similar pattern in our study group. HOMA-IR being 4.6- 5.3 for diastolic BP 85-90 mmHg, 91-95 mmHg and 5.7- 8.2 for diastolic BP 96-100 mmHg, > 100 mmHg respectively. Thus, as diastolic blood pressure increases, HOMA-IR shows positive correlation. Difference in HOMA-IR of these groups was statistically significant (p <0.05). Choudhary et al, 2012[7] studied correlation between Hypertension with Insulin Resistance (HOMA-IR) in patients with metabolic syndrome. In their study, they have done a cross-sectional study of patients who fulfilled NCEP-ATPIII criteria of metabolic syndrome. These findings are similar to our present study, hence higher systolic and diastolic blood pressure have positive correlation with HOMA-IR in cases with metabolic syndrome.

In present study, we have studied the correlation of A1c with HOMA-IR. For patients with mean A1c 8.9% and mean A1c 11.6%, mean HOMA-IR was 7.3 and 8.4 respectively. The difference between these groups was statistically significant (p <0.05). In present study also it was seen that mean HOMA-IR increases with increase in A1c. Gabriela Saravia et al[8] studied on Glycated Hemoglobin, Fasting Insulin and the metabolic syndrome in Males. They used baseline data from 3200 non-diabetic male participants in the Aragon Workers' Health Study. They conducted analysis to estimate age-adjusted odds ratios (ORs) across quartiles of HbA1c and insulin. Fasting glucose and Homeostatic model assessment – Insulin Resistance were used as reference. They report the uppermost-to-lowest quartile ORs (95%CI). Mean age (SD) was 48.5 (8.8) years and 23% of participants had metabolic syndrome. The findings of our study match the above mentioned and prove relevance of HbA1c and FBG ,PPBG measurement in metabolic syndrome.

In the present study the value of mean HDL in cases was 38.35±4.70 mg/dl and in controls was 58.94±8.78 mg/dl. The mean HDL in cases was lower than controls which was statically significant (p-value=<0.05). In our study the value of mean TC in cases was 252.49±33.37 mg/dl and in controls was 132.23±22.12 mg/dl. The mean TC in cases was higher than controls which was statistically significant(p-value=<0.05). In the present study the value of mean TG in cases was 237.75±24.91mg/dl and in controls was 142.94±14.92 mg/dl. The mean TG in cases was higher than controls which was statistically significant (p-value=<0.05).

In our study, we have studied the correlation of HDL with HOMA-IR. For patients with mean HDL 30.78 mg/dl and mean HDL 38..65 mg/dl , Mean HOMA-IR was 6.7 and 8.4 respectively. The difference between these groups was statistically significant (p <0.05).In our study, it was seen that mean HOMA-IR increases with decrease in HDL. In our study, we have studied the correlation of TC with HOMA-IR. For patient with mean TC 232.64 mg/dl and mean TC 285.56 mg/dl the mean HOMA-IR was 7.4 and 8.6 respectively. The difference between these groups was Statistically significant (p<0.05). In present study, it was seen that mean HOMA-IR increases with increase in TC. In present study, we have studied the correlation of TG with HOMA-IR. For patients with mean TG 226.67 mg/dl and mean 262.45 mg/dl, mean HOMA-IR was 7.3and 8.4 respectively. The difference between these groups was statistically significant (p <0.05). In our study, it was seen that mean HOMA-IR increases with increase in TG. Our study is in accordance to Salzar et al. (2013) [9] and Teodoro Marotta et al[10] who demonstrated positive correlation between TG/HDL ratios and insulinresistance, confirming that the TG/HDL ratio predicts insulin resistance in metabolic syndrome. But an independent study by stated that Anne E Sumner et al[11] TG/HDL ratio fails to predict Insulin resistance in African American women. These findings are significant from our study because of ethenic variations.
In our study, we have studied the correlation of FASTING PLAMA INSULIN with HOMA-IR. For patients with mean FASTING PLASMA INSULIN 18.43µIU/ml and mean FASTING PLASMA INSULIN 25.65 µIU/ml , mean HOMA-IR was 6.7 and 8.4 respectively. In our study, it was seen that mean HOMA-IR increases with increase in fasting plasma insulin which was statistically significant (p <0.05).

In our study, we have studied the correlation of S.FERRITIN with HOMA-IR. For patient with mean S.FERRITIN 163.43ng/ml and mean S.FERRITIN 220.45ng/ml the mean HOMA-IR was 7.4 and 8.6 respectively. In our study, it was seen that mean HOMA-IR increases with increase in S.FERRITIN which was Statistically significant(p<0.05). Sally Christina et al [12] have studied Association Between Serum Ferritin Levels and Insulin Resistance in Nondiabetic Brazilians. Previous studies have pointed to a relation between high serum levels of ferritin and insulin resistance. The study was done to analyze the association between the serum concentrations of ferritin and resistance to insulin, and metabolism of glucose, in nondiabetic persons There was a statistically significant association between prediabetes and insulin resistance and raised levels of ferritin. Thus increase levels of S.ferritin and positive correlation with HOMA-IR in metabolic syndrome as shown by our study is similar to previous study. In this study correlation between S.ferritin, S.fasting plasma insulin and HOMA-IR is very significant in metabolic syndromes.

CONCLUSION:

The results showed prevalence of metabolic syndrome to be higher in males as compared to females. One of the most widely used validation measures for IR in case of metabolic syndrome is the HOMA-IR index, which uses the determination of fasting insulin and glucose. This is cumbersome and costly investigation. Hence for daily clinical practice, it is necessary to use other easily applied measurements in the general population. Therefore the results of this study show TG/HDL and TC/HDL ratios serve as an easily available and economic marker for identifying insulin resistance in metabolic syndrome patients. The combination of these evaluated markers may identify a group of patients with a more marked risk for insulin resistance and cardiovascular disease risk. From the findings of our study we can conclude that metabolic syndrome is associated with significantly increased serum ferritin. Increased serum ferritin levels may be one of the key elements that progresses the journey of metabolic syndrome to Type II DM and other cardio metabolic derangements. HbA1c is more readily available than fasting insulin estimation and outperforms FPG/PPPG in terms of association with risk factors, clusters and cardiovascular risk.

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