COMPARISON OF INSULIN RESISTANCE WITH THE SEVERITY OF METABOLIC SYNDROME

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ABSTRACT

Objective: Insulin resistance (IR) means a reduced ability of insulin to stimulate glucose utilization. IR is related to cardiovascular disease (CVD) risk as the IR forms the basis for atherogenesis and acts as a major risk factor for atherosclerotic CVD.

Methods: Total of 195 participants were recruited divided into three groups based on the presence of metabolic abnormalities as control Group I (with <3 components of metabolic syndrome [MS]), MS group as Group II (with any 3 components of MS), and severe MS as Group III (with more than three components of MS).

Results: Results showed that fasting blood sugar (FBS) and glycated hemoglobin showed a significant difference between the groups (p<0.001), whereas fasting insulin and IR were higher in severe MS which showed statistically significant difference (p<0.001) in comparison with control and MS group.

Conclusion: IR is one of the principal factors for the development of MS and further threw light that the increase in the IR level proportionately increases the severity of MS.

Keywords: Cardiovascular disease, Insulin resistance, Metabolic syndrome.

INTRODUCTION

IR means a reduced ability of insulin to stimulate glucose utilization [1]. In most cases, reflex compensatory hyperinsulinemia is seen in IR due to increased secretion of insulin from the beta-cells of the pancreas to maintain euglycemia [2]. IR is related to cardiovascular disease (CVD) risk as the IR forms the basis for atherogenesis and acts as a major risk factor for atherosclerotic CVD [3,4]. Increased levels of circulating free fatty acids resulted from adipose tissue form a connection between obesity and IR, and obesity forms the most important factor for insulin resistance (IR) [5,6]. Furthermore, Reaven, in 1988, proposed the concept of syndrome X to explain the clustering of metabolic syndrome (MS) components with IR as the common denominator [7]. MS is a constellation of diseases caused by several interconnected cardiometabolic risk factors such as hypertension, obesity, hyperglycemia, and dyslipidemia [8]. Other comorbid conditions associated with MS include vascular dysregulation, pro-inflammatory state, pro-thrombotic state, hyperuricemia, non-alcoholic fatty liver disease, erectile dysfunction in males, and polycystic ovarian syndrome in females. MS prevalence is increasing in Asia due to increased stress, less physical activity, high consumption of fast food, and changes in daily lifestyle [9].

Since obesity and diabetes are reaching epidemic proportions, understanding the role of IR and its development is gaining importance as the foremost factor of medical research. Hence, this study is designed to compare the level of IR with different degrees of MS. Homeostatic model assessment-IR (HOMA-IR) is regarded as a reliable tool to evaluate IR in individuals with or without glucose intolerance [10]. Research on the comparison of IR with the severity of MS is not yet elucidated. In this study, the HOMA-IR was used as an IR index and compared the index value with the severity of the MS. Hence, the present study was aimed to compare IR in different groups of MS based on the severity.

METHODS

The study commenced after getting approval from the Institutional Human Ethical Committee (IHEC), IHEC No. 005/12/2014/IEC/SU Saveetha University. The data collected from the participants after giving a detailed explanation about the procedure of the study and their cooperation and willingness were obtained with written informed consent. Blood sample collected after overnight fast from all patients was used to study fasting blood sugar (FBS) in mg/dL, postprandial blood sugar (PPBS; mg/dL), glycated hemoglobin (HbA$_1$C), and % fasting insulin (mU/L) by the standard laboratory technique, and then, IR was calculated. The IR was calculated by HOMA-IR as fasting blood glucose multiplied by fasting insulin and divided by 22.5. Fasting glucose is in mmol/L and fasting insulin is in mU/L [11].

Statistical analysis

All the data were expressed as mean±standard error. The mean was analyzed by a one-way analysis of variance with multiple comparison test of Student Newman–Keuls test. Statistical analysis, as well as plotting of graphs, was carried out using Sigma Plot 13.0 (Systat Software, USA). Statistical significance was considered if p<0.05.

RESULTS

In the present study (Table 1), the values of FBS in the different groups of the participants are as follows: Control 123.01 mg/dl, MS 136.89 mg/dl, and severe MS 141.10 mg/dl. Observations showed significant difference (p=0.004) of FBS among the groups and in severe MS and MS, the FBS values were more in comparison with that of the control group, whereas the mean values of PPBS (control=175.87 mg/dl, MS=191.13 mg/dl, and severe MS=193.55 mg/dl) recorded from the subjects did not show a significant difference (p=0.064) among themselves. However, the mean values of HbA$_1$C obtained in control 4.69%, in MS 5.84% and severe MS 7.69% were found to be significant (F=146.489, p<0.001) among all groups.

Table 1: Comparison of FBS, PPBS, and HbA$_1$C in control, MS, and severe MS

Parameters	Control Group I	MS Group II	Severe MS Group III	Statistical information	
				F-value	p-value
FBS (mg/dl)	123.0±3.8	136.8±4.6	141.1±3.3	F=5.701	p=0.004*
PPBS (mg/dl)	175.8±6.8	191.1±5.4	193.5±4.6	F=2.788	p=0.064
HbA$_1$C (%)	4.6±0.1	5.8±0.1	7.6 ± 0.1	F=146.48	p<0.001*

Values expressed as mean±SE. (n=195, 65 in each group), *Significant. FBS: fasting blood sugar. HbA$_1$C: Glycated hemoglobin, SE: Standard error

The result of the fasting insulin level and IR of the present study is presented in Fig. 1. It showed that the mean value of fasting insulin of the groups was 12.4 mU/L in control, 13.0 mU/L in MS, and 16.1 mU/L in severe MS group. Observations indicated that fasting insulin values of the different groups were significantly varied (F=7.768, p<0.001). Fasting insulin level was more in severe MS group in comparison with that of control and MS groups. However, there was no significant difference observed in the fasting insulin level between control and MS group. Furthermore, the insulin resistance value was higher in severe MS group (5.4), which showed statistically significant difference when compared with that of control and MS group (F=10.574, p<0.001).

DISCUSSION

In the present study, FBS, PPBS, HbA$_1$C, fasting insulin, and IR were recorded in all participants. These parameters were compared between the groups divided based on the severity of the MS as control, MS, and severe MS groups. The result of the present study (Table 1) showed that there was a significant difference in FBS and HbA$_1$C values in severe MS when compared with that of MS and control group which was in agreement with the reports published recently [9,12]. Similarly, the present study result also showed that the value of fasting insulin and IR were higher in severe MS group, which was statistically significant when compared with that of control and MS groups. These results of the present study are in concordance with the work that showed a significant difference in fasting insulin and IR in the MS group when compared with that of non-MS group [12].

Elevated levels of fasting glucose are an important MS component, but neither impaired fasting glucose (IFG) nor diabetes is an absolute criterion. IR is the obvious factor in the genesis of IFG, impaired glucose tolerance (IGT), and type 2 diabetes [13]. Insulin is a peptide hormone secreted from the islets of pancreatic beta-cells which facilitate glucose absorption in most of the tissues. In the case of IR, body cells will have reduced sensitivity to insulin and thereby having resistance to insulin activity. When the cells are not able to absorb glucose, it remains in the blood resulting in hyperglycemia and compensatory hyperinsulinemia [14]. The hyperinsulinemia is very common in IR individuals due to increased secretion of insulin from the pancreatic beta-cells to maintain euglycemia [2]. Further, IR individuals develop IFG, IGT, and type2 diabetes [13].

The principal cause for the development of IR may be due to an imbalance in lipid metabolism. It is well known that obesity reduces the insulin receptor level in tissues and thereby causes IR. The IR usually associated with obesity due to excess adipose tissues in obese individuals which release non-esterified fatty acids in excess that could lead to IR [15]. During IR, free fatty acid flux is increased from the liver, which promotes the production of very-low-density lipoprotein (VLDL) from the liver. The peripheral uptake of triglycerides from VLDL is decreased because the activity of lipoprotein lipase is dependent on insulin, and it is impaired by IR. FFA itself decreases insulin sensitivity in muscle by inhibiting insulin-mediated glucose uptake [16]. The resultant hyperglycemia further increases lipid synthesis leading to hypertriglyceridemia of IR [2]. With the result, cholesterol associated with high-density lipoprotein is decreased, and simultaneous increases in low-density lipoprotein cholesterol [17]. IGT and IFG are the powerful predictors of future diabetes [18], and CVD risk increases with the progression of glucose intolerance [19]. According to a prospective
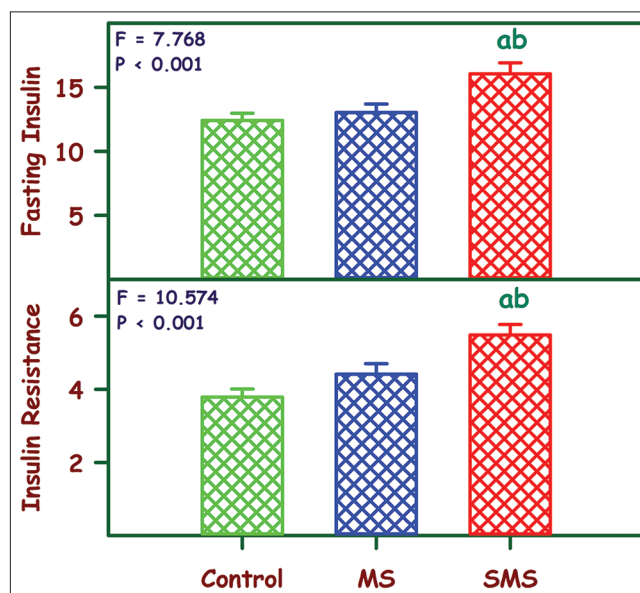
Fig. 1: The fasting insulin (FI; mU/L) and insulin resistance (IR) in control, MS (MS) and severe MS (SMS). [a]Significantly different from control. [b]Significantly different from MS

population-based study, IGT and type2 diabetes were independent predictors of advanced carotid atherosclerosis [20]. Furthermore, inflammatory markers get elevated not only due to obesity but also MS [21]. The result from the prospective study has shown that hyperglycemia and diabetes were the predictors of CVD mortality and all-cause mortality [22].

MS is a group of metabolic abnormalities that increase CVD risk. The underlying mechanism for the cause of CVD due to IR though not fully understood, the possible mechanisms include the role of IR in the development of endothelial dysfunction, inflammation, sympathetic hyperactivity and proliferation of vascular smooth muscles, and increased FFA levels and diabetes. This is supported by the available report which states that IR leads to CVD through hypertension, an increase in waist circumference, and dyslipidemia [23]. Moreover, as the insulin increases renal tubular reabsorption of sodium, both sodium and water reabsorption increased in the kidney during hyperinsulinemia, and the resultant increase in blood volume elevates BP [24].

CONCLUSION

Thus, this study supports that IR as one of the principal factors for the development of MS and further threw light that the increase in IR level proportionately increases the severity of MS.

AUTHORS' CONTRIBUTIONS

All the authors contributed to the preparation of the final manuscript.

CONFLICTS OF INTEREST

None declared.

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