Research Article

Study of insulin status in metabolic syndrome in correlation with presence of other risk factors

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ABSTRACT

Background: The metabolic syndrome or insulin resistance syndrome is widely prevalent and multifactorial disorder. The majority of persons with metabolic syndrome have insulin resistance. Insulin resistance and / or associated hyperinsulinemia are believed to be the direct cause of other metabolic syndrome risk factors. The present work is being done to assess the insulin status and to assess the correlation between insulin status and other component of metabolic syndrome.
Methods: The present work is being carried out in 112 cases of metabolic syndrome, defined as per modified NCEP ATP III (MS-4) criteria. Serum insulin of all cases was measured by chemiluminescent microparticle immunoassay (CMIA) technique.
Results: It was observed that 62% of the patients of metabolic syndrome had elevated serum insulin level (Hyperinsulinemia). Hyperinsulinemia was found to be significantly associated with diastolic hypertension and HDL in males. A high association was also noted with BMI. Insulin resistance (HOMA-IR >2.50) was significantly associated with waist circumference in males (p value<0.05).
Conclusions: It was observed that metabolic syndrome is associated with elevated serum insulin levels and each component of metabolic syndrome, both biochemical as well as clinical, is associated with hyper-insulinemia and this reflects the presence of insulin resistance in subjects of study.

Keywords: Insulin, Metabolic syndrome, Diabetes, Hypertension

INTRODUCTION

The metabolic syndrome (MS) is a constellation of risk factors of metabolic origin that are accompanied by increased risk for cardiovascular disease and type 2 diabetes. It is basically a constellation of central obesity, dyslipidemia (hypertriglyceridemia and low HDL) hypertension, and impaired glucose tolerance.[1,2]

Recent studies in India shows that about one third of urban population in major cities has metabolic syndrome.[3] The majority of persons with metabolic syndrome have insulin resistance. Insulin resistance and/or associated hyperinsulinemia are believed to be the direct cause of other metabolic syndrome risk factors.[4]

Insulin resistance is usually caused by a defect in insulin action within target organs and tissues that result in compensatory hyperinsulinemia.[5] It has been proved that insulin resistance and hyperinsulinemia are closely linked.[6] Although hyperinsulinemia may compensate for insulin resistance to some biological actions of insulin,

i.e., maintenance of normoglycemia in some tissues, it may cause over expression of insulin activity in normally sensitive tissues. This accentuation of some insulin actions coupled with resistance to other actions of insulin results in the clinical manifestations of metabolic syndrome.[7]

Hyperinsulinemia promotes sodium reabsorption and activates sympathetic system causing hypertension. Hyperinsulinemia have additional effects on growth and development as well as on carbohydrate, protein and lipid metabolism which might promote atherosclerosis.[8]

Chronic high levels of insulin secretion will eventually exhaust the beta cells of the pancreas, increasing the likelihood of a functional deficit of these tissues, resulting in adult onset diabetes mellitus. The present work is being done to determine the level of insulin in patient of MS and to find out an association between hyperinsulinemia and other risk factors.

METHODS

The study was conducted (with Institutional Ethical Committee approval) in 112 cases of MS with age group of 18-60 year. Subjects were selected from the patients coming for routine health checkup or blood sugar check up to the department of biochemistry, RIMS, Ranchi, India. MS was diagnosed as per modified NCEP ATP III (MS-4) criteria.[9]

Metabolic syndrome is considered to be present if three or more defining criteria are detected. Waist circumference >90 cm for men and >80 cm for women; Serum Triglyceride >150mg/dl; HDL Cholesterol <40 mg/dl in men and <50 mg/dl in women or treatment for low HDL; Blood pressure >130/85 mm Hg or treatment for high blood pressure; Serum fasting glucose >100 mg/dl; BMI ≥ 23Kg/m².

A fasting blood sample from these patients was collected for measurement of glucose and lipid profile. Anthropometric measurements were done and a life style questionnaire was filled up. The patients diagnosed to be having MS were selected as per MS-4 criteria and their blood sample was taken for insulin estimation.

Fasting plasma sugar and lipid profile were analyzed in an automated analyzer (Beckman Coulter Au480). Insulin was measured by a chemiluminescent immunometric auto analyzer (ABBOTT i1000 SR). All the samples were analyzed on the same day or kept at -20 0C to be analyzed within next two days. Statistical analysis was performed using SPSS software version 20.0.

A p value <0.05 was considered statistically significant. Hyperinsulinemia was defined as fasting serum insulin >9.5µIU/ml. Insulin resistance (insulin x glucose/405) was calculated from fasting values using the homeostasis model assessment as an index of insulin resistance,

HOMA-IR index10. HOMA >2.50 was considered as cut off for insulin resistance.

RESULTS

Hyperinsulinemia was present in 62% of the MS patients. Hyperinsulinemia was found to be significantly associated with diastolic hypertension and HDL in males (p value <0.05). A high association was also noted with BMI. Insulin resistance (HOMA >2.50) was significantly associated with waist circumference in males (p value <0.05).

DISCUSSION

Metabolic Syndrome is a cluster of risk factors such as abdominal obesity, dyslipidemia, insulin resistance, impaired fasting glucose and raised blood pressure. Additionally, Metabolic Syndrome increases the risk of developing diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, stroke and a number of other disorders.

Insulin resistance and/or associated hyperinsulinemia is fundamental to development of other metabolic syndrome risk factors. In the present study, we observed 62% of the patients of MS had hyperinsulinemia. This is consistent with the studies of Fernando et al wherein 44 patients out of 76 individuals had high fasting and 2-hour serum insulin level in year 2003.[11] The similar result was also obtained by Kawada et al in Japan.[12]

Insulin resistance results in compensatory hyperinsulinemia. We found that 52% of the study subjects had high HOMA-IR value which indicates about insulin resistance.

95% of the cases with poor insulin sensitivity (high HOMA-IR) had hyperinsulinemia. This is in line with the study on young adults in urban south India by R. Hemlata et al.[13]

Hyperinsulinemia is associated with other risk factors of MS. Hyperinsulinemia, by producing more catecholamine and increasing sodium reabsorption in kidney, has a role in development of hypertension. In this work, we observed a significant association between hyperinsulinemia and diastolic hypertension (p value <0.05). This observation is very similar to the result obtained in the study done by Reavan on role of insulin resistance.[14]

In present study, a significant correlation between hyperinsulinemia and HDL in male was noted (p value <0.05). In a study, Mitchell BD et al reported that fasting insulin at baseline correlated positively with 8 year changes in triglyceride level and negatively with change in HDL-C level.[15] These results substantiate the hypothesis that in non-diabetic individuals, insulin has a direct regulatory effect on triglycerides and HDL-C

levels. Obesity is the most important factor associated with insulin resistance.

Study found a high association between hyperinsulinemia and BMI. 65.6% of the cases with BMI >23Kg/m^2 had

hyperinsulinemia. In the study done by Reeta et al [16] it was shown that with increase in BMI the insulin resistance increases. In the present study we observed a significant correlation between HOMA-IR and waist circumference in male (p value <0.05).

Table 1: Correlation of variable with hyperinsulinemia and HOMA-IR.

Variable	Criteria	Hyperinsulinemia (FSI <9.5µIU/ml)		HOMA-IR	
		No N=43 (38.4%)	Yes N=69 (61.6%)	<2.5 N=54(48.2%)	>2.5 N=58 (51.8%)
Age (years)	20-29	7 (38.9%)	11 (61.1%)	8 (44.4%)	10 (55.6)
	30-39	17 (32.7%)	35 (67.3%)	23 (44.2%)	29 (55.8%)
	40-49	12 (37.5%)	20 (62.5%)	15 (46.9%)	17 (53.1%)
	50-59	7 (70%)	3 (30%)	8 (80.0%)	2 (20.0%)
BMI (Kg/m^2)	<23	11 (57.9%)	8 (42.1%) **	11 (57.9%)	8 (42.1%)
	>23	32 (34.4%)	61 (65.6%) **	43 (46.2%)	50 (53.8%)
WC -Male (Cm)	<90	10 (28.6%)	25 (71.4%)	20 (57.1%)	15 (42.9%)*
	≥90	7 (30.4%)	16 (69.6%)	7 (30.4%)	16 (69.6%)*
WC -Female (Cm)	<80	1 (33.3%)	2 (66.7%)	1 (33.3%)	2 (66.7%)
	≥80	25 (49.0%)	26 (51%)	26 (51.0%)	25 (49.0)
SBP (mm of Hg)	<130	17 (38.6%)	27 (61.4%)	19 (43.2%)	25 (56.8%)
	≥130	26 (38.2%)	42 (61.8%)	35 (51.5%)	33 (48.5%)
DBP (mm of Hg)	<85	21 (50.0%)	21 (50.0%)*	24 (57.1%)	18 (42.9%)
	≥85	22 (31.4%)	48 (68.6%)*	30 (42.9%)	40 (57.1%)
FPG (mg/dl)	<100	10 (28.6%)	25 (71.4%)	2 (2.8%)	69 (97.2%)
	≥100	33 (42.9%)	44 (57.1%)	28 (36.4%)	49 (63.6%)
TG (mg/dl)	<150	11 (42.3%)	15 (57.7%)	10 (38.5%)	16 (61.5%)
	≥150	32 (37.2%)	54 (62.8%)	42 (48.8%)	44 (51.2%)
HDL-Male (mg/dl)	≥40	7 (50.0%)	7 (50.0%)*	7 (50.0%)	7 (50.0%)
	<40	10 (22.7%)	34(77.3)*	20 (45.5%)	24 (54.5%)
HDL-Female (mg/dl)	≥50	4 (66.7%)	2 (33.3%)	3 (50.0%)	3 (50.0%)
	<50	22 (45.8%)	26 (54.2%)	24 (50.0%)	24 (50.0%)

N =number of patients, FSI= Fasting Serum Insulin, BMI=Body Mass Index, WC= Waist Circumference, SBP=Systolic Blood Pressure, DBP= Diastolic Blood Pressure, FPG= Fasting Plasma Glucose, TG= Triglyceride, HDL=High Density Lipoprotein**. * P<0.050, **P=0.055.**

This finding is supported by two studies which used only waist circumference to determine insulin resistance. Wahrenberg et al[17] used a sample of 2746 healthy adults and measured waist circumference and BMI and compared these measurements to the HOMA index. Using multivariate regression models to assess the predictive power of the variable, waist circumference was the strongest regressor of the covariates. In a study, Steele et al found that Insulin resistance was strongly associated with waist, subscapular skin fold and BMI measurements.[18] In a linear regression analysis with BMI included as a covariate to waist circumference, BMI did not improve the correlation with insulin resistance, suggesting that BMI does not provide additional useful information on top of waist circumference in predicting insulin resistance.

Hyperinsulinemia is indeed an indicator of insulin resistance and this has a predictive value for development

of metabolic syndrome and also can be an important component of metabolic syndrome. A routine assay of serum insulin levels in patients with metabolic syndrome may be considered, however presently serum insulin levels are not included in the criteria to diagnose metabolic syndrome.

CONCLUSION

It was observed that each component of metabolic syndrome, both biochemical as well as clinical, was associated with hyperinsulinemia and this reflects the presence of insulin resistance in subjects of study.

The clinical evidence includes high blood pressure, increased waist circumference and presence of other clinical sign of insulin resistance. But a biochemical evaluation of insulin resistance was targeted in this study by measurement of serum insulin level.

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