Original Research Article

Insulin resistance and its associated comorbidities in young individuals: a HOMA study

Irfan Ahamed H. B.[1]*, Bilal Bin Abdullah[2], Mohammed Ismail[2], Syed Aman Jagirdar[2]

[1]Department of Internal Medicine, [2]Department of Medicine, Al-Ameen Medical College, Bijapur, Karnataka, India

*Correspondence:
Dr. Irfan Ahamed H.,
E-mail: drirfan28@gmail.com

ABSTRACT

Background: The strongest relationship between insulin resistance and cardiovascular risk factors is observed in middle-aged persons rather than in older individuals. Hence it is important to evaluate the young high risk individuals for insulin resistance and to study its significant co-morbidities. Therefore, the present study was designed to evaluate the high risk individuals for insulin resistance and co-morbidities in young individuals.

Methods: The body mass index and the waist-hip ratio of all the participants were measured. A 5 ml of fasting venous blood was collected from each patient and was used for the estimation of fasting blood glucose level, lipid profile, fasting insulin level and glycated hemoglobin using commercially available kit according to the manufacturer's guidelines. Subjects' full filling inclusion criteria and preliminary tests for insulin resistance are further evaluated with HOMA. The data obtained was represented as Mean±S.D and was analyzed for statistical significance using chi-square test and correlation of HOMA with study variables were performed using Pearson correlation test using SPSS Version 20. P - value less than 0.05 was considered the level of significance.

Results: In the present study we found that, non- diabetic group patients are having strong association with hypertension and insulin resistance. When the study variables in the recruited subjects were correlated with HOMA using Pearson correlation, showed a significant correlation with fasting blood sugar, glycated hemoglobin and hypertension in diabetic patients. In non-diabetic subjects fasting blood sugar and glycated hemoglobin was not correlated significantly. But, hypertension showed a significant correlation.

Conclusions: Insulin resistance was strongly associated with co-morbidities like hypertension, obesity, hyperlipidemia, hyperuricemia. High incidence and prevalence of insulin resistance was also seen in non-diabetic individuals.

Keywords: HOMA, Hypertension, Hyperlipidemia, Hyperuricemia, Obesity

INTRODUCTION

Prevalence rates of insulin resistance syndrome reported for white populations ranged from 3-16%; a rate of less than 2% was reported among Japanese populations.[1,2] Type-A insulin resistance typically occurs in younger patients, while type B insulin resistance occurs more often in older women. Women with polycystic ovary syndrome (PCOS) usually present in their mid-20s. Many rare disorders of insulin resistance present in early life such as leprechaunism during first year of life and lipodystrophic states between the ages 6-9 years until early puberty.

The strongest relationship between insulin resistance and cardiovascular risk factors is observed in middle-aged persons rather than in older individuals, although cardiovascular morbidity and mortality increase with age.

No more studies have been done in young aged less than 40 years. Despite the growing obesity epidemic and insulin resistance in children, no clear diagnostic criteria and surrogate markers have been identified. An international consensus group recommended against screening children for insulin resistance in children based on existing methodology and criteria.[3]

Insulin resistance syndrome is found in all races. The degree of clustering of the risk variables of the metabolic syndrome is generally considered to be higher among whites. However, prevalence rates of the various components of the metabolic syndrome tend to be higher among non-white populations.[4] Acanthosis nigricans, a common physical sign of insulin resistance syndrome, occurs in all ethnic groups, but the prevalence is higher in Hispanics and blacks than it is in whites.

In India, there is a rapidly escalating epidemic of insulin resistance syndrome such as diabetes and coronary heart disease. Contribution of genes and environment is under debate. Small size at birth coupled with subsequent obesity increases risk for insulin resistance syndrome in later life.[5] The tendency of Indians to have higher body fat and central adiposity compared with other races may be programmed in utero. The adipose tissue releases not only fatty acids but also a number of pro inflammatory cytokines, which increase insulin resistance and cause endothelial dysfunction. Crowding, infections, and environmental pollution in Indian cities may increase cardiovascular risk by stimulating fat cells. Prevention of diabetes and coronary heart disease in India will have to be approached throughout the life cycle.[6] Hence it is important to evaluate the young high risk individuals for insulin resistance and to study its significant co-morbidities. Therefore, the present study was designed to evaluate the high risk individuals for insulin resistance and co-morbidities in young individuals.

METHODS

In the present prospective study, the patients were recruited after their informed consent. The study was approved by the institutional ethical committee. Hundred patients, 50 non-diabetic patients and 50 patients with type 2 diabetes mellitus, attending diabetic OPD in a tertiary care Hospital at Bijapur, Karnataka, India belong to the age group of less than or equal to 40 years were recruited.

Patients with high risk group, with family history of diabetes mellitus and hypertension, obesity, hyperlipidemia, gestational diabetes and polycystic ovarian disease (PCOD) and age less than or equal to 40 years were included. Patients with age more than 40 years, hypothyroidism/ cushings syndrome and non obese type 2 diabetes were included.

All the recruited patients were subjected the anthropometric measurements like height, weight, waist circumference and hip circumference. The body mass index and the waist-hip ratio were calculated. A 5 ml of fasting venous blood was collected from each patient and was used for the estimation of fasting blood glucose level, lipid profile, fasting insulin level and glycated hemoglobin using commercially available kit according to the manufacturer's guidelines.

Subjects' full filling inclusion criteria and preliminary tests for insulin resistance are further evaluated with HOMA (homeostasis model assessment).

The data obtained was represented as Mean±SD and was analyzed for statistical significance between non-diabetic young individuals and diabetic patients using chi-square test by using SPSS Version 20. Correlation of HOMA with study variables were performed using Pearson correlation test. P value less than 0.05 was considered the level of significance.

RESULTS

In the present study, it was observed that, out of 27 positive HOMA patients in Diabetic group, 15 (55.56%) patients were having raised BMI levels and in 35 positive HOMA patients in non-diabetic group, 25 (71.4%) patients were having raised BMI levels. It is seen here that, non-diabetic high risk group patients are having strong association with obesity and insulin resistance (Table 1).

Table 1: Association of body mass index (kg/m^2) with homa in the recruited subjects.

BMI (kg/m^2)	HOMA		Total (n = 50)	P-value
	No	Yes		
Diabetic group				
Normal	8 (34.7%)	12 (44.44%)	20 (40%)	0.487 (Non-significant)
Raised	15 (65.3%)	15 (55.56%)	30 (60%)	
Non-diabetic group				
Normal	12 (80%)	10 (28.6%)	22 (44%)	0.001** (Highly significant)
Raised	3 (20%)	25 (71.4%)	28 (56%)	

Out of 27 positive HOMA patients in Diabetic group, 18 (66.67%) patients were having raised WHR and in 35 positive HOMA patients in non-diabetic group, 29 (82.86%) patients were having raised WHR.

It is seen here that, non-diabetic high risk group patients are having strong association with obesity and insulin resistance (Table 2).

Table 2: Association of waist hip ratio with HOMA in the recruited subjects.

Waist hip ratio	HOMA		Total (n = 50)	P-value
	No	Yes		
Diabetic group				
Normal	7 (30.4%)	9 (33.33%)	16 (32%)	0.827
Raised	16 (69.56%)	18 (66.67%)	34 (68%)	(Non-significant)
Non-diabetic group				
Normal	7 (46.6%)	6 (17.14%)	13 (26%)	1.000
Raised	8 (53.4%)	29 (82.86%)	37 (74%)	(Non-significant)

Table 3: Association of FBS levels with HOMA in the recruited subjects.

FBS	HOMA		Total (n = 50)	P value
	No	Yes		
Diabetic group				
Normal	4 (17.39%)	8 (29.62%)	12 (24%)	0.313
Raised	19 (82.61%)	19 (70.38%)	38 (76%)	(Non-significant)
Non-diabetic group				
Normal	13 (86.7%)	25 (71.4%)	38 (76%)	0.304
Raised	2 (13.3%)	10 (28.6%)	12 (24%)	(Non-significant)

Table 4: Association of HbA1c with HOMA in the recruited subjects.

HbA1c	HOMA		Total (n = 50)	P value
	No	Yes		
Diabetic group				
Normal	1 (4.34%)	3 (11.11%)	4 (8%)	0.614
Raised	22 (95.65%)	24 (88.88%)	46 (92%)	(Non-significant)
Non-diabetic group				
Normal	14 (93.3%)	35 (100%)	49 (98%)	0.300
Raised	1 (6.7%)	0 (0%)	1 (2%)	(Non-significant)

Table 5: Association of hypertension with HOMA in the recruited subjects.

HTN	HOMA		Total (n = 50)
	No	Yes	
Diabetic group			
Normal	10 (43.47%)	18 (66.66%)	28 (56%)
Raised	13 (56.53%)	9 (33.33)	22 (44%)
Non-diabetic group			
Normal	15 (100%)	9 (25.71%)	24 (48%)
Raised	0 (0%)	26 (74.29%)	26 (52%)

We also found that, out of 27 positive HOMA patients in diabetic group, 19 (70.38%) patients were having raised FBS levels and in 35 positive HOMA patients in non-diabetic group, 10 (28.6%) patients were having raised FBS levels.

It is seen here that, diabetic group patients are having strong association with Type 2 diabetes mellitus and insulin resistance (Table 3). Out of 27 positive HOMA patients in diabetic group, 24 (88.88%) patients were having raised HbA1C levels and in 35 positive HOMA

patients in non-diabetic group, 0 (0%) patients were having raised HbA1C levels. It is seen here that, diabetic

group patients are having strong association with Type 2 diabetes mellitus and insulin resistance (Table 4).

Table 6: Pearson correlation of HOMA with study variables in the recruited subjects. (n = 50).

	Diabetic group		Non-diabetic group	
	r value	P value	r value	P value
HOMA versus body mass index (kg/m^2)	0.160	0.914	0.350	0.013 NS
HOMA versus waist hip ratio	0.262	0.671	0.612	0.017 NS
HOMA versus fasting blood sugar	0.536	<0.001**	0.125	0.387 NS
HOMA versus total cholesterol	0.570	0.066	0.430	0.067 NS
HOMA versus triglyceride	0.554	0.012	0.435	0.027 NS
HOMA versus LDL	0.016	0.911	0.139	0.034 NS
HOMA versus HDL	0.309	0.029*	0.197	0.502 NS
HOMA versus HbA1c	0.384	0.006**	0.105	0.468 NS
HOMA versus hypertension	0.623	0.003**	0.581	<0.001**
HOMA versus uric acid	0.411	0.041	0.311	0.061 NS
HOMA versus insulin levels	0.211	0.092	0.413	0.071 NS

** =Highly significant, NS=Non-Significant

In the present study we found that, out of 27 positive HOMA patients in diabetic group, 9 (33.5%) patients were having hypertension and in 35 positive HOMA patients in non-diabetic group, 26 (74.29%) patients were having hypertension. It is seen here that, non- diabetic group patients are having strong association with hypertension and insulin resistance (Table 5).When the study variables in the recruited subjects were correlated with HOMA using Pearson correlation, showed a significant correlation with fasting blood sugar (p < 0.001), glycated hemoglobin (p = 0.006) and hypertension (p = 0.003) in diabetic patients. In non-diabetic subjects fasting blood sugar and glycated hemoglobin was not correlated significantly. But, hypertension showed a significant (p < 0.001) correlation. All other parameters studied were not shown any correlation with HOMA in both the study groups (Table 6).

DISCUSSION

In the present study, out of 27 positive HOMA patients in diabetic group, 9 (33.5%) patients are having hypertension and in 35 positive HOMA patients in non-diabetic group, 26 (74.29%) patients are having hypertension. We found that, correlation of hypertension with HOMA in diabetic patients as well as non-diabetic subjects was highly significant. The insulin resistance was also found to have strong association with HOMA in diabetes and hypertension. It was in agreement with the studies by Ferrani I et al, who reported > 80% hypertensive cases exhibit hyperinsulinaemia and Insulin resistance.[9] Reaven et al showed 41% were hyperinsulinemic.[10] From this, it is obvious that hypertension is insulin-resistant states, and their frequent occurrence in the individual is probably more than a chance association. An alternative explanation for the link between hypertension and insulin resistance is the

development of hyperinsulinemia. The normal beta-cell response to insulin resistance is to augment its secretion of insulin and individuals with essential hypertension, obesity and type 2 DM clearly have been shown to be hyperinsulinemic.

Present study, we observed a correlation of BMI and WHR with HOMA in Diabetic group of patients was not significant. But, non-diabetic group showed moderate correlation. Similar observations were made by other researchers. In a study by Bonora E et al, the prevalence of insulin resistance in overweight subjects (BMI>25 Kg/m2) with no metabolic abnormalities, was 42%. In another study by Mathur SK et al, the diabetic and non-diabetic subjects in the study were found to have higher W: H ratio, FFA and HOMA-R but there was no significant difference in their BMI.[9,10] Association of visceral obesity with increased free fatty acid flux and high insulin resistance is well known.[11] Obesity-associated insulin resistance is a major risk factor for type 2 diabetes and cardiovascular disease. It is important to know the mechanism and factors responsible for obesity induced insulin resistance. The present study also showed a significant correlation of FBS and HbA1C with HOMA in Diabetic group of patients. In non-diabetic group it was not significant. It is in agreement with the studies by Keigue et al who hypothesized that insulin resistance may be common in these people and that this may be the underlying mechanism leading to the predisposition to diabetes mellitus.[12] Reaven et al postulated that where there is resistance to insulin stimulated glucose uptake, deterioration of glucose tolerance can only be prevented if the beta cells are able to maintain increased insulin secretion.[8] If this state of hyperinsulinaemia cannot be maintained then loss of glucose tolerance would result, followed by overt diabetes mellitus. Thus a state of hyperinsulinaemia resulting from insulin resistance would be characteristic of individuals or groups at increased risk of diabetes.

The present study showed a significant correlation of total Cholesterol, triglyceride, HDL, levels with HOMA in Diabetic group of patient's non-diabetic group. But, there was no significant correlation of LDL levels with HOMA in both the groups. Laakso M et al and Garg A et al stated that insulin resistance has been hypothesized to play a major role in dyslipidemia in individuals with normal glucose tolerance, as well as in those with impaired glucose tolerance and type 2 diabetes.[13,14] In the studies done by Evans DJ et al and Krotkiewski M et al, it has been reported that lipid abnormalities like elevated triglycerides and LDL cholesterol and low levels of HDL cholesterol are likely to be seen in insulin resistance patients.[15,16]

It was also observed that, correlation of uric acid with HOMA in Diabetic group of patients and non-diabetic subjects was significant. Sung KC et al showed that, hyperuricemia is considered by some investigators to be a component of metabolic syndrome that reflects insulin resistance.[17] Enzo Bonora et al, it was shown that hyperuricemia is often accompanied by IR when it is associated with other metabolic disorders, but it is not an insulin-resistant state itself.[13,18] There is supporting evidence that uric acid may have a pathogenic role in metabolic syndrome. Hyperuricemia has been found to predict the development of both obesity and type 2 diabetes. Hyperuricemia is also commonly observed in metabolic syndrome, as well as in secondary insulin resistance syndromes such as that associated with gout, diuretic usage, or preeclampsia.[19]

CONCLUSION

High incidence and prevalence of insulin resistance was seen in young individuals. Insulin resistance showed a strong association with co-morbidities like hypertension, obesity, hyperlipidemia, hyperuricemia. High incidence and prevalence of insulin resistance was also seen in non-diabetic individuals.

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