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ORIGINAL ARTICLE RESEARCH

Assessment of the Standardized Reference Range for HOMA – IR among Apparently Normal Population of Ottappalam

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ABSTRACT

Aim: To determine the standardized reference range for HOMA – IR among apparently normal population of Ottappalam.

Methodology: 100 apparently normal subjects were selected and subjected to blood pressure measurement, Weight and height, BMI, Triglyceride, HDL and LDL cholesterol and HOMA – IR was calculated.

Results: Age group 20-25 years had 5%, 26-30 years had 80%, 31-35 years had 9%, 36-40 years had 3% and >40 years had 3% patients. The mean age was 28.78 years. Most of the subjects taken for the study were females – 62%. Most of the subjects were in the 18.5 – 22.9 kg/m^2 group (94%). Minimum value of HOMA – IR was 0.74 and maximum value was 5.38. Mean HOMA – IR for the apparently normal population of Ottappalam was calculated as 2.65. Range for HOMA – IR according to 95% confidence intervals was 2.46 to 2.84. HOMA – IR had a positive correlation with age, which means as age advances the insulin resistance also rises, p value for this observation being 0.023. HOMA – IR had a positive correlation with BMI, p value being <0.001. HOMA – IR had a positive correlation with both systolic and diastolic BP. Fasting plasma insulin levels had positive correlation with BMI, systolic and diastolic blood pressures.

Conclusion: The mean HOMA – IR is higher among Indian population than other population. HOMA – IR is directly related to risk factors of coronary artery disease. Early identification of individuals with high insulin resistance and timely and wise intervention can prevent many cases of type 2 diabetes mellitus and coronary artery disease.

Keywords: Insulin, HOMA- IR, BMI

INTRODUCTION

Prevalence of diabetes has been on the rise dramatically over the past 2 decades, from an estimated 30 million cases in 1985 to 285 million in 2010. International Diabetes Federation prediction is that 438 million individuals will have diabetes by the year 2030. Although the prevalence of both type 1 and type 2 diabetes is on the rise worldwide, it is type 2 diabetes which is rising much rapidly, presumably because of increasing obesity, reduction in the activity levels as countries become more industrialized and aging of the population.[1]

Insulin resistance and abnormal insulin secretion are the 2 central pillars to the development of type 2 diabetes. Though the primary defect is controversial, most studies support the view that insulin resistance precedes an insulin secretary defect.[1] Another non – communicable disease epidemic that is going on worldwide is that of coronary artery disease. CAD is the single most common cause of death in men and women and the economic burden of CAD on any country is tremendous. The WHO estimates that by the year 2020 the global number of deaths from CAD will have risen from 7.1 million in 2002 to 11.1 million.[2]

It is a well- established fact that there is a significant association between insulin resistance and CAD.[3] Gold standard for measurement of insulin resistance is the euglycemic clamp method.[4,5] Another method that has been widely used to estimate insulin resistance is the homeostasis model assessment – estimated insulin resistance (HOMA – IR), developed by Matthews et al.[6] Quantification of insulin resistance by HOMA – IR is more convenient. It is calculated by multiplying fasting plasma insulin by fasting plasma glucose then dividing by the constant 405. Many studies have addressed a standardized reference range for HOMA – IR among different populations.[7] But the non – availability of a standardized reference range for HOMA – IR among Indian population has limited its clinical and population application. To address to this issue this study was undertaken to determine the standardized reference range for HOMA – IR among apparently normal population of Ottappalam.

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MATERIAL AND METHODS

It was a cross – sectional study. 100 apparently normal subjects fulfilling the inclusion and exclusion criteria, and willing to be part of the study were enrolled.

Inclusion criteria was subjects with age 18 years and above. Exclusion criteria was subjects with family history of diabetes mellitus, hypertension or coronary artery disease in first degree relatives, subjects with a blood pressure more than 130/85 mm Hg. Subjects with a fasting blood sugar more than 100 mg/dl, subjects with a body mass index more than 22.9 kg/m^2, subjects who are on systemic steroids for any reason, subjects with an abnormal fasting lipid profile (total cholesterol more than 200 mg/dl or triglycerides more than 150 mg/dl or LDL cholesterol more than 100 mg/dl or HDL cholesterol less than 40 mg/dl), subjects with history of tobacco smoking, tobacco chewing and alcohol consumption and subjects fulfilling these criteria were selected for the study.

Parameters such as age, family history of diabetes mellitus, hypertension and coronary artery disease, history of tobacco smoking, tobacco chewing and alcohol consumption, and history of usage of systemic steroids was obtained by detailed history taking.

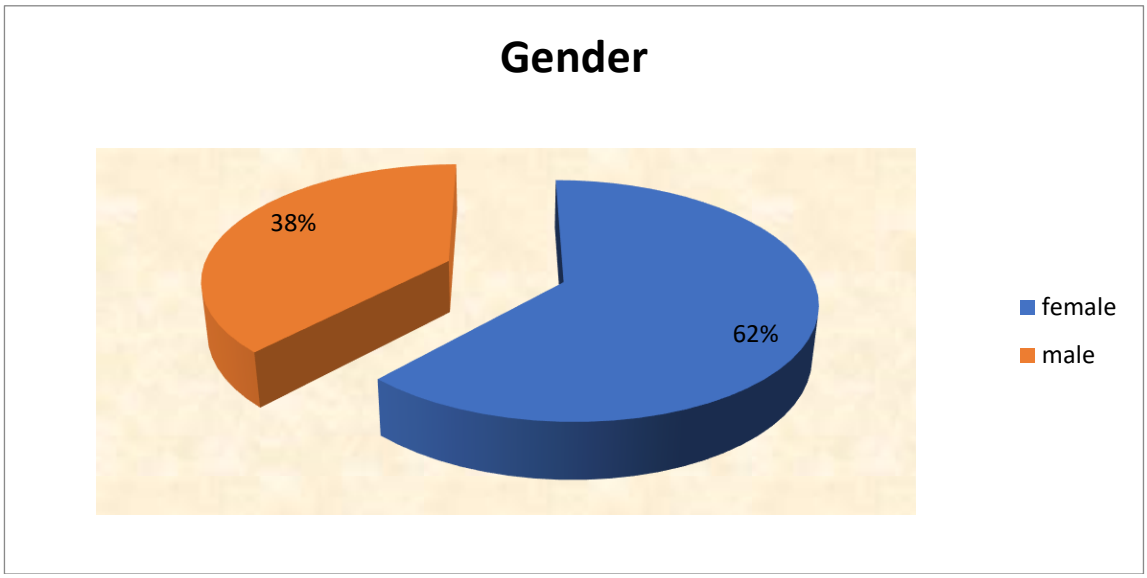
Blood pressure measurement was taken according to the recommendations of the American Heart Association guidelines. Weight and height were measured with the subjects wearing light clothing and without shoes on. BMI was calculated according to the formula BMI = weight in kgs/ (height in metres).^{2} Blood samples were collected after a 12 hour overnight fasting. Fasting blood sugar was determined by the oxidase - peroxidase method. Total cholesterol was measured by the cholesterol oxidase – peroxidase method. Triglyceride levels were assessed by glycerol phospho oxidase – peroxidise method. HDL and LDL cholesterol were measured by the direct enzymatic colorimetric assay. Fasting plasma insulin was determined by the electro chemiluminescence assay. HOMA – IR was calculated by the formula, HOMA – IR = fasting Glucose (mg/dl) x fasting plasma Insulin (µU/mL)/405. Collected data was analysed using SPSS (Statistical Package for the Social Sciences) version 11 for qualitative data. For statistical analysis chisquare test was used. For quantitative data student t test was used. P value of less than 0.05 was considered significant.

RESULTS

Table I Patients Distribution

Age group (years)	Percentage	P value
20-25	5%	0.02
26-30	80%	
31-35	9%	
36-40	3%	
>40	3%	

Age group 20-25 years had 5%, 26-30 years had 80%, 31-35 years had 9%, 36-40 years had 3% and >40 years had 3% patients. The mean age was 28.78 years. The difference was significant (P< 0.05) (Table I).



Graph I Gender distribution

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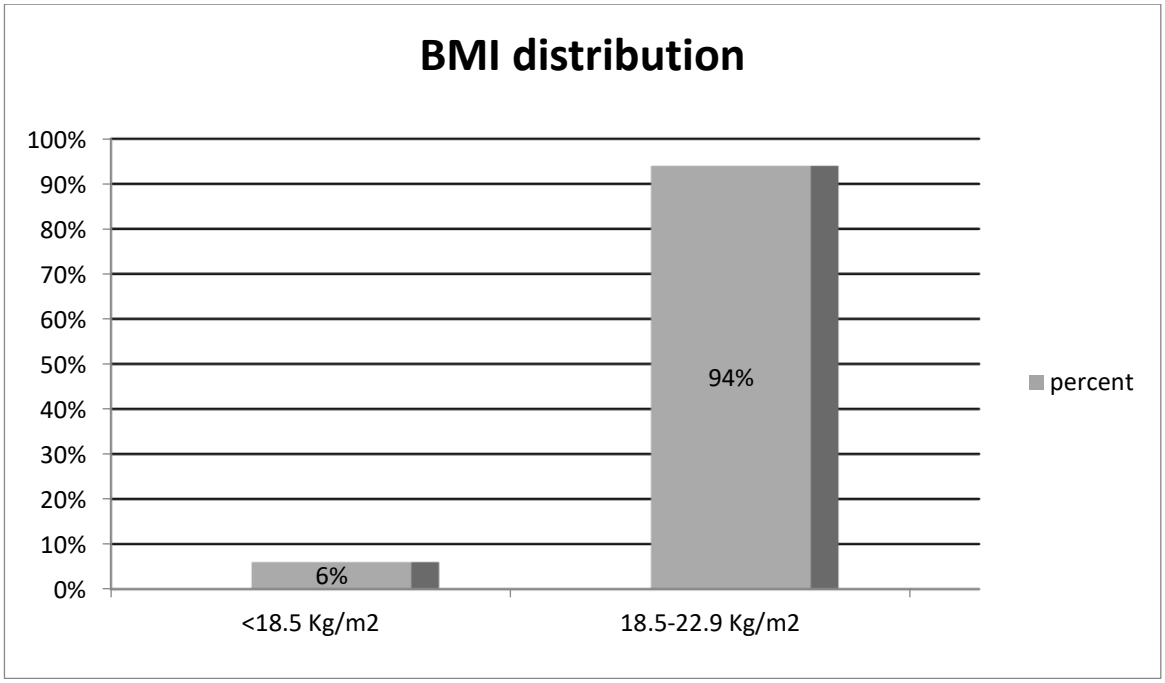
Most of the subjects taken for the study were females – 62% (Graph I).



Graph II Distribution of BMI

With regards to BMI, most of the subjects were in the 18.5 – 22.9 kg/m^2 group (94%) (Graph II).

Table II Description of each variable studied

Parameters	Mean	Std. Deviation	Maximum	Minimum
FBS (mg/dl)	86.96	5.79	99	70
FPI (µU/mL)	12.20	3.90	24.24	3.86
IR (HOMA)	2.65	.94	5.38	.74
BMI (kg/m2)	20.51	1.37	22.9	18.0
SBP (mm HG)	109.16	11.77	128	80
DBP (mm HG)	72.96	6.45	84	60

Minimum value of HOMA – IR was 0.74 and maximum value was 5.38. Mean HOMA – IR for the apparently normal population of Ottappalam was calculated as 2.65. Range for HOMA – IR according to 95% confidence intervals was 2.46 to 2.84 (Table II).

Table III Correlation of HOMA – IR with other factors

Parameters	R value	P value
Age	0.82	0.023
BMI	0.92	0.001
Blood pressure	0.75	0.001

HOMA – IR had a positive correlation with age, which means as age advances the insulin resistance also rises, p value for this observation being 0.023. HOMA – IR had a positive correlation with BMI, p value being <0.001. HOMA – IR had a positive correlation with both systolic and diastolic BP, p value being <0.001 (Table III).

Table IV Correlation of fasting plasma insulin with other factors

Parameters	R value	P value

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BMI	0.94	0.02
Blood pressure	0.67	0.001

Fasting plasma insulin levels had positive correlation with BMI, systolic and diastolic blood pressures, the p value being <0.001 (Table IV).

DISCUSSION

Insulin resistance is strongly related to several classic cardiovascular risk factors like hyperglycemia, obesity, hypertension and microalbuminuria. Insulin resistance in muscle and adipose tissue results in an increase in plasma insulin and free fatty acid concentration. These changes act on the liver to increase triglyceride synthesis and secretion, thereby initiating a series of metabolic events that result in a highly atherogenic lipoprotein profile: high triglyceride levels and low levels of high- density lipoprotein cholesterol; small, dense, low density lipoprotein particles; and accumulation of post prandial remnant lipoproteins.[8] These changes are each known to contribute to an increased risk of coronary artery disease. this study was undertaken to determine the standardized reference range for HOMA – IR among apparently normal population of Ottappalam.

Our results showed that age group 20-25 years had 5%, 26-30 years had 80%, 31-35 years had 9%, 36-40 years had 3% and >40 years had 3% patients. The mean age was 28.78 years. Most of the subjects taken for the study were females – 62%. Most of the subjects were in the 18.5 – 22.9 kg/m^2 group (94%).

HOMA – IR had a positive correlation with age, which means as age advances the insulin resistance also rises, p value for this observation being 0.023. HOMA – IR had a positive correlation with BMI, p value being <0.001. HOMA – IR had a positive correlation with both systolic and diastolic BP, p value being <0.001. The HOMA method developed by Matthews et al[6] was used in this study to quantify insulin resistance as it is simple and appropriate to our condition.

In this study, the mean HOMA – IR value was found to be 2.65 and 97 (97%) of the subjects demonstrated HOMA – IR values greater than 1. HOMA – IR score greater than 1 implies insulin sensitivity less than 100% and this could imply insulin resistance. Though a HOMA – IR score of 1 is considered ideal, a HOMA – IR value between 1.21 and 1.45 was reported for normal subjects by Matthews et al.[6] Bonora et al[9] found a mean HOMA – IR score of 2.06 ± 0.14 among 62 non – diabetic subjects, the mean BMI of that Italian population being 27.8 ± 0.7 and 16 of them being hypertensives. Esteghamati et al[10] studied 1276 non – diabetic, normotensive Iranian subjects and arrived at a HOMA – IR cut off at 1.847. Do HD et al[11] studied 738 Thai subjects with normal BMI and FBS and the HOMA – IR cut off obtained was 1.5548. Nakai Y et al[12] 161 healthy Japanese subjects and the HOMA – IR cut off was 1.749. Salgado AL et al[13] studied 88 non – diabetic subjects in Brazil and found that HOMA – IR cut off was 1.78. Hydrie et al[14] studied 227 Pakistani subjects who were normoglycemics and the HOMA – IR value obtained was 1.82. Ascaso et al[15] studied 65 subjects with normal glucose tolerance and normal fasting lipid profile from Spain and the cut-off point to define insulin resistance with HOMA was found to be 2.6.

Fasting plasma insulin levels had positive correlation with BMI, systolic and diastolic blood pressures. Sowjanya et al[16] studied 38 normal glucose tolerant non – metabolic syndrome subjects and the mean HOMA – IR was found to be 1.97.

Provided the finding that insulin resistance precedes type 2 diabetes mellitus by decades and insulin resistance is a fore runner of coronary artery disease, with the help of a reference range for HOMA – IR in an apparently normal population we can find out those individuals with high insulin resistance and intervene at an earlier stage in the form of weight loss and exercise. This may be the ray of hope in prevention of the epidemic of type 2 diabetes mellitus that is going on in India. Limitations of this study being cross sectional in nature, it can show statistical associations but not a cause and effect relationship. This study never correlated HOMA – IR values with lipid profile.

CONCLUSION

The results of the present study suggest that mean HOMA – IR is higher among Indian population than other population. HOMA – IR is directly related to risk factors of coronary artery disease. Early identification of individuals with high insulin resistance and timely and wise intervention can prevent many cases of type 2 diabetes mellitus and coronary artery disease.

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