Insulin Resistance: Detection By Fasting Insulin In North Indian Obese Adults

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Abstract: Background&objectives:Several studies have shown that obesity is closely related to Insulin resistance(IR). Insulin resistance has been suggested as a primary cause for metabolic syndrome. Identifying such individuals would help to prevent progression of comorbidities associated with IR. Hence present study was planned to assess the importance of Fasting Insulin(FI) as a measure of IR and to analyze its correlation with other indirect methods for the assessment of IR . Methods: Study was conducted in fifty obese and overweight subjects.Body Mass Index of all subjects was calculated . Blood glucose, and FI were assayed after twelve hours of fasting. Homeostasis model assessment (HOMA) and Quantitative insulin sensitivity check indices (QUICKI) were calculated. Results: Present study showed that 90% of subjects had IR by HOMA and QUICKI.Correlation of FI with HOMA and QUICKI was statistically significant ($P < 0.05$). FI test had significant sensitivity and specificity when compared with HOMA and QUICKI indices. Validity of FI was further analyzed by Cohen's kappa test and had good agreement ($\kappa = 0.67$). Conclusion: FI was sensitive and also specific as HOMA and QUICKI in assessment of IR in obese. Thus, FI can be used as a simple test and feasable tool to detect IR in obese subjects. [AnshuKhatri NJIRM 2016; 7(5):1-4]

Key Words: Fasting Insulin, HOMA Index, Obesity, QUICKI Index

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Introduction: The prevalence of overweight and obesity is increasing at an alarming rate worldwide.According to global health observatory data, worldwide, 39% of adults aged 18 years and over were overweight and 13% were obese in 2014[1].

Various studies have shown that obesity is associated with chronic diseases including diabetes, hypertension and metabolic syndrome which are the accompanying metabolic abnormalities of insulin resistance (IR)[2] .Insulin resistance is defined as a failure of target organs to respond normally to the action of insulin. Insulin resistance causes incomplete suppression of hepatic glucose output and impaired insulin-mediated glucose uptake in the periphery (skeletal muscle and adipose tissue), leading to increased insulin requirements.

Adipose tissue has traditionally been considered an energy storage organ, but over the last decade, a novel role of the adipose tissue as an endocrine organ has emerged. Various adipocytokines are released from adipose tissue and some of these adipocytokines have been implicated in the development of insulin resistance[3].The euglycaemic hyperinsulinaemic(EH) clamp technique is the 'gold-standard' method of measuring insulin resistance[4]but this method is expensive, time-consuming and cumbersome in clinical practice as well as for epidemiological researches. However, there are various indirect methods for the assessment of IR. These are Homeostasis Model Assessment (HOMA)[5] , Quantitative Insulin Sensitivity Check Index (QUICKI)[6], and McAuley index (McA)[7]. The homoeostasis model assessment and the quantitative insulin sensitivity check index have become the most widely used surrogate indices. Both are based on fasting plasma glucose and insulin values, and correlate well with the EHclamp[8].

It has been observed that Fasting Insulin(FI) is also accurate at predicting IR in normoglycaemic population similar to HOMA, insulin to glucose ratio and Bennet index[9].

As Insulin resistance contributes to the pathophysiology of type 2 diabetes mellitus and is closely associated with obesity, metabolic syndrome, and their cardiovascular complications[10] a simple test for early detection of insulin resistance is required. Measurement of Fasting Insulin could be used as a simple and rapid diagnostic test when compared to other indirect methods of diagnosing IR. Though Studies are there regarding comparison of fasting insulin with other indirect measures of insulin resistance indiabetic population[11] but data regarding this is sparse in North Indian obese Adults. Therefore present study was planned to evaluate the importance of fasting Insulin as a diagnostic test for insulin resistance by analyzing its correlation with HOMA and QUICKI methods.

Methods: The study was conducted in Department of Physiology in collaboration with Department of Medicine in King George's Medical College Lucknow, after taking permission from ethical committee of

institution. Fifty Obese and overweight males and females between age group of 20-40 years were enrolled for the study. Subjects were classified overweight and obese according to WHO criteria[12].Overweight is defined as BMI ≥25 and Obesity is defined as BMI ≥30 .Participants in the study were selected from volunteers and subjects who have recently enrolled themselves in various fitness centres but not yet have started the exercise regime. Informed consent was taken from all participants.After detailed medical history thorough Physical examination was carried out and routine haematological test, and ECG were done in order to rule out any disease. Subjects having diabetes, hypertension, any other chronic illness, smokers, alcoholics, pregnant, lactating and postmenopausal females and subjects who were engaged in heavy physical activity likewise sports persons and manual labourers were excluded from study. BMI of participants was calculated as: BMI=weight (kg)/height (m^2).

Assay: Blood samples were collected from all the subjects in the morning after 12 hours of fasting.Fasting blood glucose was measured using an automated glucose oxidase method. Sera that were separated, immediately after centrifugation were stored at -20^{0}C until the assay for Insulin was performed. Serum insulin was measured by Radio Immunoassay with polyethylene glycol separation method.

HOMA‑IR and QUICKI were calculated using the following equations[5,6]:

HOMA=insulin(µU/ml)×glucose(mmol/L)
/22.5

QUICKI =1/(log fasting insulin [µU/ml]+ log glucose [mg/dl])

Patients were considered as Insulin Resistant when; HOMA ≥ 2.6 and QUICKI ≤0.33. FI level ≥12 mU/L was considered as IR[11].

Statistical analysis : Data are expressed as means ± S.D. Correlation of Fasting Insulin was analyzed using Pearson's correlation coefficient. Sensitivity and Specificity of fasting insulin as a diagnostic test was compared with HOMA and QUICKI. P < 0.05 was considered to be statistically significant.

Results: Baseline characteristics of study population are shown in table 1.

Table 1.shows the mean values of age, BMI, Fasting blood sugar, Fasting Insulin, HOMA INDEX and QUICKI in males and females.

	Males(28)	Females(22)
Age(years)	28.64±5.60	29.54±5.30
BMI(kg/m^2)	30.57±1.95	29.68±2.88
Fasting glucose(mg/dl)	88.03±12.97	94.18±10.63
Fasting Insulin((µu/ml)	27.50±11.57	34.47±16.14
HOMA Index	5.68±2.12	7.77±3.39
QUICKI Index	0.29±0.02	0.30±0.03

Results of present study shows that 90 % subjects are Insulin resistant by HOMA and QUICKI. 82 % were found to be IR by fasting insulin. The cut‑off limit for considering a patient Insulin resistant were HOMA ≥2.6 and QUICKI ≤0.33 .

Out of subjects who were Insulin resistant by HOMA and QUICKI 91% were detected having IR by Fasting Insulin and 8.8 % subjects were not detected by fasting insulin. Correlation coefficient between FI and HOMA and QUICKI was analyzed. Results of present study showed that correlation between FI and HOMA ($r = 0.93$, $p < 0.05$) and QUICKI ($r = - 0.57$, $p < 0.05$) was statistically significant. We further analyzed the specificity and sensitivity of FI as a diagnostic test by comparing it with HOMA and QUICKI in this study. We found that FI test had 91% of sensitivity and 100% of specificity when compared to HOMA & QUICKI. Validity of FI as a diagnostic test of Insulin resistance was further analyzed by Cohen's kappa test. FI had a good agreement (k=0.67) when compared with HOMA as well as QUICKI (Table 2).

Table2:Sensitivity and Specificity of Fasting Insulin as a diagnostic test of IR in comparison to HOMA and QUICKI

	HOMA	QUICKI
Sensitivity	91%	91%
Specificity	100%	100%
Kappa	0.67	0.67
Agreement	good	good

Discussion: Obesity associated insulin resistance is a major risk factor for type 2 diabetes mellitus and

cardiovascular disease. Therefore a simple test for early detectionof IR is utmost requirement. Hence present study wasplanned to assess the diagnostic importance of fasting insulin in assessment of IR by analyzing its correlation with HOMA and QUICKI.

In the present study 90% of subjects were insulin resistant when detected by HOMA and QUICKI. Obesity is a well known risk factor for Insulin resistance.The high association between obesity and insulin resistance was recognized among both males and females, and it appeared across all ethnic groups[13].Studies are there showing correlation of various parameters of obesity with insulin resistance[14]. It has also been observed that reduction in weight is associated with increase in insulin sensitivity.A randomized control trial was held in western world by Robert Ross et al and it was shown that exercise is associated with reduction in weight and insulin resistance in women[15]. Decrease in IR improves glycaemic control and favourably modifies other components of Metabolic Syndrome[16].82% subjects were having IR by fasting Insulin. Subjects who were detected having IR by HOMA and QUICKI , 91% of them were detected by Fasting Insulin. 8.8% were not detected by Fasting Insulin.

On analyzing the correlation of fasting insulin with HOMA and QUICKI statistically significant correlation was observed in the present study (p=<0.05). This is in agreement with previous studies[11,17]elsewhere where statistically significant correlation of fasting Insulin with HOMA and QUICKI was observed in Diabetic patients and Obese and overweight subjects respectively.Sensitivity and specificity of fasting Insulin was compared with HOMA and QUICKI, and it was found to besignificant.Validity of fasting Insulin was further analyzed by Cohen's kappa test and it had good agreement.Thus present study suggested that fasting Insulin was sensitive and specific to HOMA and QUICKI in assessment of insulin resistance in overweight and obese. Hence FI can be used as a simple and feasable tool to detect IR in obese and overweight subjects.

Conclusion: Present study suggested that FI was sensitive and also specific as HOMA and QUICKI in assessment of IR in obese subjects. Thus, FI can be used as an easy and feasable test to detect IR in obese subjects.The future prediction of development of cardiovascular diseases and type 2 diabetes mellitus is mainly dependent on Insulin resistance which not only enhances the risk of above diseases but also development of metabolic syndrome. Hence a measure which can predict Insulin resistance can help in the prevention of not only diabetes mellitus but also decrease in cardiovascular morbities and mortalities.

As sample size in present study is small, therefore further studies involving large number of subjects are required so that fasting Insulin can be designated a specific diagnostic test for future modality.

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Conflict of interest: None

Funding: None

Cite this Article asAnshu k, Parshant c Fasting Insulin and Insulin Resistance in Obese. Natl J Integr Res Med 2016; 7(4): 1-4