

Correlation of insulin resistance by various methods with fasting insulin in obese

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ABSTRACT

Background: Several studies indicate that obesity is closely related to insulin resistance (IR). However, this relationship has not been adequately explored. **Aims:** This study aims to evaluate the prevalence of IR among obese using some indirect methods for assessment of IR. **Materials and Methods:** We analyzed the correlation of fasting insulin (FI) with body mass index. We examined 100 obese and overweight. Anthropometric measurements were done for all individuals. Blood lipids parameters, glucose, and insulin were assayed after a 10 h fast. The indices McAuley (McA), homeostasis model assessments (HOMA), quantitative insulin sensitivity check index (QUICKI) were used to assess IR. **Results:** In this study, the correlations of FI with McA, HOMA and QUICKI were significant ($P < 0.05$). FI test had significant sensitivity and specificity when compared with McA, HOMA and QUICKI indices. FI gives parallel results to the assessment of IR by other methods. Validity of FI was further analyzed by Cohen's kappa test and had a satisfactory agreement ($\kappa = 0.940$). **Conclusion:** Altogether, this study suggested that FI was sensitive and also specific as McA in assessment of IR in obese. Thus, FI can be used as an easy test to detect IR also in obese.

Key words: Body mass index, homeostasis model assessments, insulin resistance, McAuley, obesity, quantitative insulin sensitivity check index

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INTRODUCTION

The prevalence of overweight and obesity is rapidly increasing in developing as well as industrialized countries.^[1] Some studies from urban populations have shown that overweight and obesity are increasingly common.^[2,3] Several 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] IR is a state in which a given amount of insulin produces a subnormal biological response.^[4] Furthermore,

it is characterized by a decrease in the ability of insulin to stimulate the use of glucose by muscles and adipose tissue and to suppress hepatic glucose production and output.^[5] Furthermore, it accounts for a resistance to insulin action on protein and lipid metabolism as well as on vascular endothelial function and gene expression.^[6] Adipose tissue seems to play a key role in the pathogenesis of IR through several released metabolites, hormones, and adipocytokins that can affect different steps in insulin action.^[7] Adipocytes produce nonesterified fatty acids, which inhibit carbohydrate metabolism via substrate competition and impaired intracellular insulin signaling.^[7,8]

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The euglycemic insulin clamp^[9] and the intravenous glucose tolerance tests^[10] are gold standard methods for measurement of IR in research, but they are cumbersome in clinical practice and are difficult to perform in population-based research studies. Fasting insulin (FI)^[11] is accurate at predicting IR. In addition to these standard methods, there are various indirect methods for the assessment of IR. The homeostasis model assessments (HOMA)^[12] and the quantitative insulin sensitivity check index (QUICKI)^[13] indices are calculated using both the FI and fasting blood glucose levels while the

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McAuley index (McA)^[14] are calculated using FI and fasting triglyceride level. Measurement of the FI level has long been considered the most practical approach for the measurement of IR. It correlates well with IR. A considerable correlation has been found between FI levels and insulin action as measured by the clamp technique. A substantial overlap between IR and normal subjects is a constraint, as there is a lack of standardization of the insulin assay procedure. Nevertheless, with a reliable insulin assay, IR can be detected early, before clinical disease appears.^[15]

The aim of this study was to determine the prevalence and some determinants of the IR among obese patients. The correlation between the IR indices by FI with body mass index (BMI) to predict IR was also studied.

MATERIALS AND METHODS

Study population

The study was performed in Department of Biochemistry in collaboration with Department of Medicine in Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India.

Data were collected through exploration of questionnaires. Inclusion criteria for study participation included: Aged 30-70 years, diagnosed as having simple obesity through physical examination, with no concomitant diseases and without any pharmacological treatment; stable body weight (± 2 kg) for at least 3 months prior to study randomization without use of medication known or suspected to affect body weight or appetite; BMI from 23 kg/m² for overweight and BMI greater to 25 kg/m² for obese; no weight loss attempts through dietary intervention over the 3 months prior to trial randomization.

Excluded were patients with known endocrine particularly hypothyroidism, liver and kidney diseases.

Based on the above criteria, 100 consenting volunteers were selected to participate in this study. The study protocol was approved by the Institutional Ethical committee.

Anthropometric measurements

Height was measured with a locally manufactured wall mounted stadiometer, body weight was assessed using a weighing machine. BMI was calculated using the weight and height measurements. Waist circumference measurements to the nearest 0.1 cm were taken at the mid-point between the bottom rib and the hip bone.

Laboratory data

At baseline, in the morning after a 10 h overnight fast, venous blood was sampled for the measurement of the blood

glucose, total and high-density lipoprotein (HDL) cholesterol, triglycerides, and insulin. Blood glucose was measured by a glucose-oxidase method. Serum total cholesterol, HDL cholesterol, and triglycerides were assessed with standard enzymatic spectrophotometric techniques. Serum low-density lipoprotein cholesterol was calculated using Friedewald's equation, except when triglycerides exceeded 400 mg/dL. Serum insulin was determined using an enzyme-linked immunosorbent assay. The sensitivity of the assay was 1.5 μ U/ml and the variation coefficient inter-assay and intra-assay were 6.29 and 7.67%, respectively.

Data analysis

These indirect methods were used for the assessment of HOMA-IR, QUICKI, McA, FI. These were calculated using the following equations: HOMA = insulin (μ U/l) \times (glucose [mmol/L]/22.5); QUICKI = $1/(\log \text{insulin} + \log \text{glucose in mg/dL})$; McA = $\exp(2.63 - 0.28 \ln [\text{insulin in } \mu\text{U/L}] - 0.31 \ln [\text{triglycerides in mmol/L}])$. According to different indices, the following thresholds defined IR state among nondiabetic participants: McA ≤ 5.8 , HOMA ≥ 2.6 and QUICKI ≤ 0.339 . FI level $\geq 12 \mu\text{U/L}$ was considered as IR. All these indices were compared with FI to evaluate the sensitivity and specificity in predicting IR. Statistical analysis was performed using Statistical Package for Social Sciences (Softonic) Windows version 12.0. Descriptive analysis included the estimation of mean values and standard deviations (SD) for continuous variables. Categorical variables were compared by the Chi-square. $P < 0.05$ were considered to be statistically significant.

RESULTS

In the study population, 20% of patients were overweight and 80% obese aged 30–70 years old. Obese patient's anthropometric measurements were higher than in overweight. The mean fasting blood glucose was higher in obese participants. The average values of most of the parameters were relatively closed to the threshold of detection of IR in obese patients [Tables 1-3].

Prevalence of insulin resistance

About 80% of obese were IR considering McA. Of these, only 2% were not detected by FI. Furthermore, significant positive correlation was found between FI and BMI in study group ($P < 0.005$). Coefficient of correlation was +0.40. Mean \pm SD of FI and BMI was 25.9 ± 1.58 and 27.29 ± 8.64 , respectively.

Determinants of insulin resistance among obese subject

Positive correlation was found between FI and weight, BMI as well as with body fatness. IR by HOMA, McA and QUICKI

Table 1: Basic characteristics of obese patients

Characteristics	Mean±SEM
Age (years)	46±1.6
BMI (kg/m ²)	27.29±8.64
Total cholesterol (mg/dL)	248.2±7.6
Triglycerides (mg/dL)	158.0±6.1
HDL cholesterol (mg/dL)	57.5±1.6
LDL cholesterol (mg/dL)	158.2±7.6
Fasting blood glucose (mg/dL)	111.3±10.2
Fasting insulin (U/L)	25.9±1.58
McA index	5.04±1.19
HOMA index	8.32±3.79
QUICKI index	0.28±0.022

SEM: Standard error of mean; BMI: Body mass index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; McA: McAuley; HOMA: Homeostasis model assessments; QUICKI: Quantitative insulin sensitivity check index

Table 2: Basic characteristics of overweight patients

Characteristics	Mean±SEM
Age (years)	48±1.46
BMI (kg/m ²)	25.64±7.45
Total cholesterol (mg/dL)	192.8±6.5
Triglycerides (mg/dL)	147.23±5.78
HDL cholesterol (mg/dL)	48.38±2.1
LDL cholesterol (mg/dL)	153.18±6.5
Fasting blood glucose (mg/dL)	105.2±9.8
Fasting insulin (mU/L)	11.42±1.8
McA index	6.2±1.14
HOMA index	2.2±0.79
QUICKI index	0.342±0.031

SEM: Standard error of mean; BMI: Body mass index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; McA: McAuley; HOMA: Homeostasis model assessments; QUICKI: Quantitative insulin sensitivity check index

Table 3: Percentage of IR calculated by FI following age

Age	FI (%)
30-39 (n=18)	17 (22.6)
40-49 (n=56)	38 (46.6)
50-59 (n=12)	12 (14.6)
60+ (n=14)	13 (16)
Total (n=100)	80

FI: Fasting insulin; IR: Insulin resistance

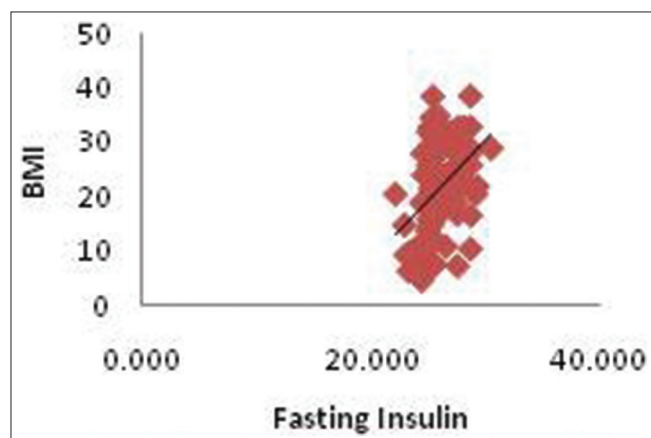


Figure 1: Correlation between insulin resistance by fasting insulin and body mass index

was found significant in study group. Mean \pm SD of McA, HOMA and QUICKI was 5.04 ± 1.19 , 8.32 ± 3.79 and 0.28 ± 0.022 , respectively. The cut-off limit for considering a patient IR of these measures were $McA \leq 5.8$, $HOMA \geq 2.6$ and $QUICKI \leq 0.33$ [Figures 1-3].

Out of the patients who were resistant by McA, 98% of them were resistant by FI and only 2% of them were unable to be detected by FI test. Out of the patients who had IR by HOMA and QUICKI indices, only 80% were detected having IR by FI test. About 20% of patients who were detected by HOMA and QUICKI were not detected by FI [Table 4].

DISCUSSION

In this study, results showed that 78% of the obese were IR by FI. Several researchers have shown the strong correlation between these indices and the method of reference clamp. According to the previous research, McA is the most accurate indirect method of detecting IR and when confronted with the results obtained by the minimal model approximation of the metabolism of glucose, the sensitivity and specificity of diagnosis were also higher by McA.^[14] It has been already found that FI test is accurate at predicting IR in normoglycemic population and in this study it has been proved that FI test in obese can significantly detect the IR similar to McA.^[16] Measurement of HOMA-IR had high sensitivity and specificity among children and adolescents for measuring IR and it is more reliable than QUICKI.^[17]

Similar results were obtained by Conwell et al.^[18] showing that significant negative correlation between HOMA-IR and sensitivity ($r = -0.89$, $r = -0.90$, and $r = -0.81$, $P < 0.01$) and a significant positive correlation between QUICKI and S ($r = 0.89$, $r = 0.90$, and $r = 0.81$, $P < 0.01$) at each time point. They suggested that HOMA-IR, QUICKI and FI correlate strongly with sensitivity assessed by the frequently sampled intravenous glucose tolerance test in obese children and

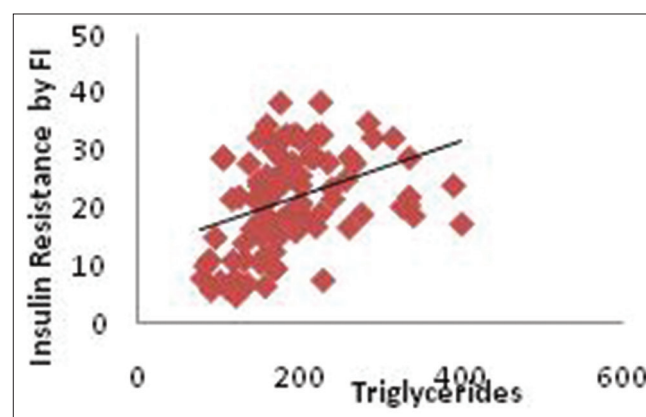


Figure 2: Correlation between insulin resistance by fasting insulin and triglycerides

Table 4: Sensitivity and specificity of FI as IR when compared to McA, HOMA and QUICKI

Parameters	True positive	False positive	True negative	False negative	n	Sensitivity (%)	Specificity (%)
HOMA	80	10	10	0	100	100.00	50.00
McA	78	0	20	2	100	97.50	100.000
QUICKI	80	10	10	0	100	100.00	50.00

FI: Fasting insulin; McA: McAuley; HOMA: Homeostasis model assessments; QUICKI: Quantitative insulin sensitivity check index; IR: Insulin resistance

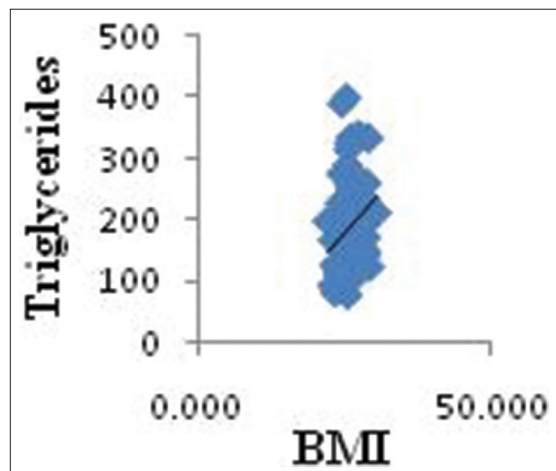


Figure 3: Correlation between triglycerides and body mass index

adolescents. Out of the patients who had IR by HOMA and QUICKI indices, only 80% were detected having IR by FI test. 20% of patients who were detected by HOMA and QUICKI were not detected by FI. This can be explained by limitations that were found with HOMA and QUICKI by other researchers. As HOMA is calculated from fasting glucose and FI and thereby reflects only hepatic insulin sensitivity.^[11] Results of the Miyazaki's group facilitate these findings by studying the composite IR, which includes both hepatic and peripheral resistance for the assessment of insulin sensitivity in diabetic patients.^[19]

Walker^[20] showed that obese patients have a lower tissue response to insulin than lean individuals. This suggests that obesity promotes the development of IR. Obese patients have decreased glucose-oxidation and increased lipid oxidation compared with lean individuals. These are hyperinsulinemic, but insulin sensitivity improves with weight loss in obese patients. Obesity has been strongly associated with IR in normoglycemic patients and in individuals with Type 2 diabetes.^[21] The association of obesity with IR is not only related to degree of obesity but also seems to be critically dependent on fat distribution. Thus, individuals with greater degrees of central adiposity develop this syndrome more frequently.^[22]

Weight loss is associated with a decrease in insulin concentration and an increase in insulin sensitivity in adults. An elevated HOMA-IR in both obese and overweight

children were found by Huguette *et al.*^[23] Significant elevated BMI in both obese and overweight children and adolescents than controls and these observations strongly suggest the association between adiposity and IR.^[24] This suggests that correction of excess body weight should have beneficial effects against the development of insulin resistance syndrome.

In this study, the correlations of FI with McA, HOMA and QUICKI were significant ($P < 0.05$). FI test had significant sensitivity and specificity when compared to McA, HOMA and QUICKI indices. FI gives parallel results to the assessment of IR by other methods. Validity of FI was further analyzed by Cohen's kappa test and had a satisfactory agreement ($\kappa = 0.940$). Altogether, this study suggested that FI was sensitive and also specific as McA in assessment of IR in obese. Thus, FI can be used as an easy test to detect IR also in obese.

CONCLUSION

This study suggested that FI was sensitive and also specific as McA in assessment of IR in obese. Thus, FI can be used as an easy test to detect IR also in obese.

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