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Determination of Optimal HOMA-IR Cut-off Value for Identifying Insulin Resistance in a Tertiary Care Hospital, Bangladesh

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Key words:
HOMA-IR, insulin resistance, metabolic syndrome, Bangladesh, cut-off value.

Abstract

Background: *Insulin resistance (IR) is a key predictor of metabolic syndrome and type 2 diabetes mellitus. HOMA-IR is widely used to assess IR, but cut-off values vary across populations. This study aimed to determine the optimal HOMA-IR cut-off for Bangladeshi adults.* ***Methods:*** *A cross-sectional analytical study was conducted on 1,250 adults from BSMMU outpatient department. Anthropometric measurements, blood pressure, fasting glucose, insulin, triglycerides, and HDL-C were measured. HOMA-IR was calculated using HOMA2 calculator. Optimal cut-off values were determined using percentile and metabolic syndrome criteria, and ROC curve analysis.* ***Results:*** *Median HOMA-IR was 1.6 (IQR: 1.1–2.3) for the total population, 1.5 for males and 1.7 for females. The 75th percentile was 2.2 overall, higher in females. ROC analysis using metabolic syndrome criteria yielded an optimal HOMA-IR cut-off of 1.4 for the total population (AUC: 0.641, p<0.001), with sex-specific cut-offs of 1.2 for males and 1.3 for females. Sensitivity and specificity were 70.3% and 49.5% for the total population, respectively.* ***Conclusion:*** *The HOMA-IR cut-off of 1.4 is recommended for detecting insulin resistance among Bangladeshi adults, with slightly lower thresholds for males and higher for females. These population-specific cut-offs may facilitate early identification of individuals at risk for metabolic syndrome and type 2 diabetes.*

Introduction

Insulin resistance (IR) is a metabolic condition characterized by reduced responsiveness of target tissues-primarily skeletal muscle, liver, and adipose tissue-to the action of insulin. This defect leads to decreased glucose uptake in peripheral tissues and increased hepatic glucose output, ultimately disrupting glucose homeostasis[1]. IR is a central feature in the pathogenesis of type 2 diabetes mellitus (T2DM), dyslipidemia, and cardiovascular disease, and is now recognized as a key pathophysiological link underlying metabolic syndrome [2,3].

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Accurate measurement of insulin resistance in large-scale population studies remains challenging because the reference method, the hyper-insulinemic–euglycemic clamp, although precise, is technically demanding, time-consuming, and unsuitable for routine clinical or epidemiological use[4]. To address this limitation, several surrogate indices have been developed, among which the homeostasis model assessment of insulin resistance (HOMA-IR) is the most widely used. HOMA-IR estimates insulin sensitivity from fasting plasma glucose and insulin concentrations and provides a practical, inexpensive, and reasonably reliable alternative for large-scale studies[5].

An updated version, HOMA2, was introduced to account for non-linear relationships between insulin and glucose and to adjust for assay variability, thereby improving accuracy over the original HOMA1 model[6]. Although both models are widely used, there remains no universal consensus on the threshold HOMA-IR value that defines insulin resistance. Reported cut-offs differ considerably across populations due to variations in genetic background, body composition, assay methodology, and statistical approach[7,8].

Studies from different regions illustrate this variability. Optimal HOMA-IR cut-off values have ranged from approximately 1.7–2.0 in East Asian populations, 2.5–2.7 in South American cohorts, and values exceeding 3.0 in some European studies[7,9,10]. In Bangladesh, limited data are available; one rural study reported a 75th-percentile HOMA-IR value of around 2.6. However, comprehensive evaluation using the improved HOMA2 model and larger, more representative samples is still lacking[11]. Given the rapidly increasing prevalence of obesity, metabolic syndrome, and T2DM in Bangladesh[12,13], establishing a reliable, population-specific HOMA-IR reference value is crucial for early identification of individuals at increased cardiometabolic risk.

Therefore, the present study aims to determine the optimal cut-off value of HOMA-IR using the HOMA2 model for defining insulin resistance in Bangladeshi adults and to assess its relationship with age, sex, and individual components of metabolic syndrome.

Methods:

A cross-sectional analytical study was conducted on 1,250 adult individuals attending the outpatient department of Bangabandhu Sheikh Mujib Medical University (BSMMU). Participants were stratified by age and sex. Written informed consent was obtained from all subjects. Body mass index (BMI) and waist circumference (WC) were measured using standard protocols. Blood pressure (BP) was recorded in a seated position using a sphygmomanometer. Fasting blood samples were collected under aseptic conditions. Serum glucose, insulin and lipid profile were analyzed at the Department of Biochemistry & Molecular Biology, BSMMU.Metabolic syndrome was defined as the presence of three or more of the following according to modified ATP III criteria:

a) HDL cholesterol < 40 mg/dl (male) and < 50mg/dl (females) or specific treatment for this lipid abnormality.

b) Blood pressure ≥130/85 mmHg or treatment for previously diagnosed hypertension.

c) Fasting plasma glucose ≥5.6 mmol/l or previously diagnosed type 2 diabetes.

d) Triglycerides ≥150 mg/dl or specific treatment for this lipid abnormality.

e) Waist circumference ≥ 90 cm for males and ≥80 cm for females, by World Health Organization- Asian Pacific region criteria.

HOMA-IR was calculated using the HOMA2 calculator. 49 patients sample were excluded because IR index can be calculated by HOMA calculator when fasting glucose is between 3-25 mmol/L and insulin level is between 2.9-57.6 μU/ml.

Collected data were checked, edited and processed with the help of the software Statistical Package for Social Sciences (SPSS) version 20.0. A *p* value < 0.05 was considered statistically significant. Data were presented as mean ± standard deviation (SD) or median/interquartile range. The cut-off values for insulin resistance was based on 50th percentile for healthy group. Sensitivity, specificity, positive and negative predictive value were calculated at different cut-off points of the HOMA-IR in relation to metabolic syndrome. The Youden index (max of sensitivity+specificity) was calculated to idntify the

cuttoff point. To determine the optimal cut-off value, the point on the ROC curve with maximum Youden index (sensitivity-(1-specificity)) was calculated. The whole analysis were performed seperately for gender-and age-specific and age-combined group to identify if the cut-off values of HOMA-IR differ across the groups.

Results:

The baseline characteristics of participants are summarized in Table I. The study included 649 male and 552 female participants with comparable mean ages (39.8 ± 12.1 vs. 39.6 ± 11.1 years). 19.3%). Metabolic syndrome was more frequent in females (56.5%) than in males (48.5%). The median HOMA-IR value was also higher in females (1.7) than in males (1.5), indicating greater insulin resistance among females.

Table I: anthropometric and clinical characteristics of study subjects

Parameter	Male (n = 649) Mean ± SD	Female(n = 552) Mean ± SD
Age(years)	39.8 ± 12.1	39.6 ±11.1
BMI(kg/m^2)	25.8 ± 3.9	27.5 ±5.7
WC(cm)	92.3 ± 9.2	92.8 ±10.6
DM	20% (n = 135)	21.9% (n = 121)
HTN	19.3% (n = 125)	21.4% (n = 118)
MetS	48.5%	56.5%
(frequency%)	(n = 315)	(n = 312)
HOMA-IR(IQR)	1.5(median)	1.7(median)

Table II shows the percentile distribution of HOMA–IR values with a gradual increase across both sexes, with females demonstrating slightly higher values than males at each percentile. The median (50th percentile) HOMA–IR value for the total population was 1.6, increasing to 4.2 at the 95th percentile, indicating a wide variability in insulin sensitivity among individuals.

Table II: Cut–off value of HOMA–IR determined by percentile criteria in adultBangladeshi population at different percentile

Population	HOMA – IR				
	50th	75th	85th	90th	95th
Total population n=1201	1.6	2.2	2.6	3.1	4.2
Malen= 649	1.5	2.1	2.6	3.1	4.1
Femalen=552	1.7	2.3	2.7	3.2	4.2

Table III and Figure 1 shows the optimal cut–off value of HOMA–IR for identifying insulin resistance among the adult population (n = 1201) in the study. It shows that, based on ROC curve analysis, the best cut – off value of HOMA–IR was 1.4. The area under the curve (AUC) was 0.641, indicating a moderate diagnostic accuracy of HOMA–IR in this group. The p value (<0.001) confirms that the association is statistically significant.

Table III: Optimal cut–off value of HOMA–IR (based on Youden index) determined by metabolic syndrome ATP III criteria

Population	Optimal cut–off value of HOMA- IR	AUC	p value
Total population n=1201	1.4	0.641	<0.001

AUC=Area under curve

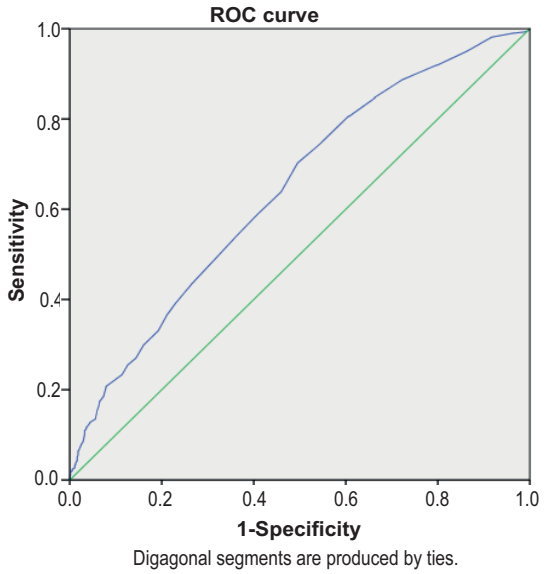

Figure-1: *ROC curve analysis of HOMA–IR determined by metabolic syndromecriteria*

Table IV and Figure 2 shows the optimal cut–off value of HOMA–IR for identifying insulin resistance among the total male(n = 649) and female (n = 552) population in the study. It shows that, based on ROC curve analysis, the best cut – off value of HOMA–IR was 1.2 for male and 1.3 for female.The area under the curve (AUC) was 0.630 and 0.654 respectively, indicating a moderate diagnostic accuracy of HOMA–IR in this group. The p value (<0.001) confirms that the association is statistically significant.

Table IV: *Optimal cut–off value of HOMA–IR (based on Youden index) determined by Metabolic syndrome ATP III criteria (according to sex)*

Population	Optimal cut–off value of HOMA- IR	AUC	p value
Total male populationn= 649	1.2	0.630	<0.001
Total female populationn=552	1.3	0.651	<0.001

AUC=Area under curve

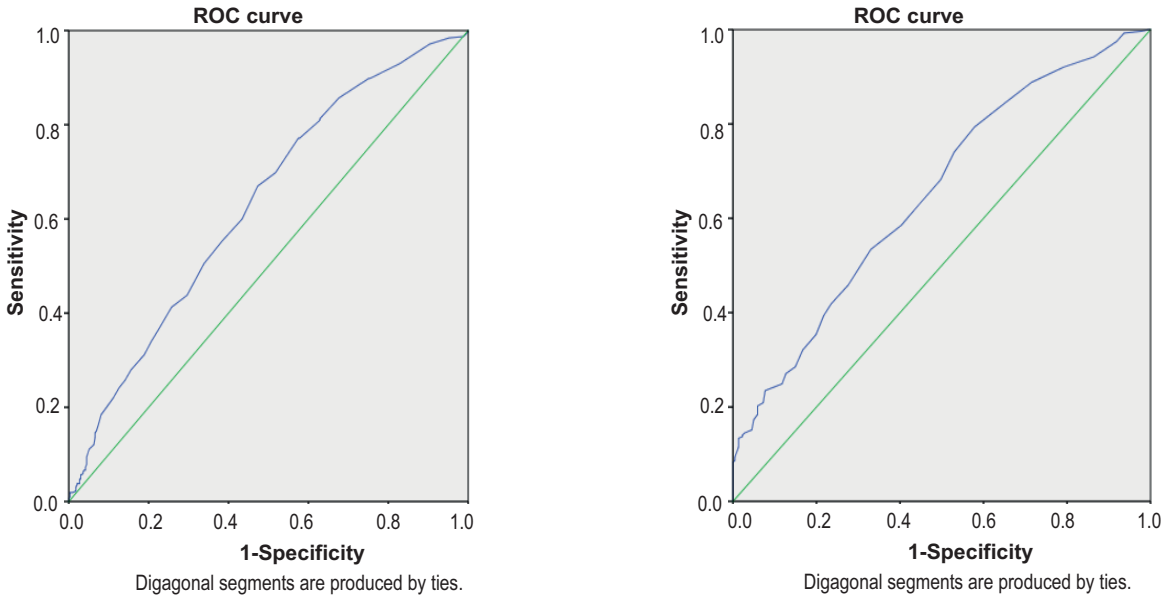

Figure-2: *ROC curve analysis of HOMA–IR determined by metabolic syndrome criteria in adult Bangladeshi male and female population*

Table V summarizes the diagnostic accuracy of a HOMA–IR cut–off value of 1.2 and 1.3 for identifying insulin resistance among male and female respectively. At HOMA–IR cut–off value of 1.2, the test demonstrated a sensitivity of 77.1% and specificity of 57.5% for detecting insulin resistance among males. The positive predictive value was 64.5%, and the negative predictive value was 71.5%. At HOMA–IR cut–off value of 1.3, the test demonstrated a sensitivity of 79.4% and specificity of 57.9% for detecting insulin resistance among females. The positive predictivevalue was 65.3%, and the negative predictive value was 73.8%,indicating that thesecut – off value offers a reasonable balance between identifying true positive and true negative cases, making it a suitable screening value for the studied population.

Table V Isummarizes the diagnostic accuracy at a HOMA–IR cut–off value of 1.4, common to both the metabolic syndrome criteria and the 50th percentile, the sensitivity and specificity for detecting insulin resistance in the adult Bangladeshi population were 70.3% and 49.5%, respectively. The PPV (58.2%) and NPV (62.5%) indicate a moderate diagnostic efficiency of this threshold when applied irrespective of age and sex.

Table V

Performance of HOMA–IR cut–off value (1.2) for identification of insulin resistance in adult Bangladeshi male population

Cut-off value	Sensitivity	Specificity	PPV	NPV
1.2	77.1%	57.5%	64.5%	71.5%
1.3	79.4%	57.9%	65.3%	73.8%

Table VI

Performance HOMA – IR cut – off value 1.4 (common to MetS criteria and P_{50}) fordiagnosis of insulin resistance in adult Bangladeshi population irrespective of age andsex

Cut- off value	Sensitivity	Specificity	PPV	NPV
1.4	70.3%	49.5%	58.2%	62.5%

Discussion:

This cross-sectional study among adults in Bangladesh attending the Bangabandhu Sheikh Mujib Medical University (BSMMU) outpatient department found a high frequency of insulin resistance (IR) 48.5 % in males and 56.5 % in females, based on modified metabolic syndrome (MetS) criteria. Internationally, frequencies varye.g in Iran 39 % of females and 28.3 % of males were IR bya similar approach.[14]

Obesity, particularly central adiposity, is a well-recognized driver of IR, via increased free-fatty acid flux from visceral fat and chronic low-grade inflammation impairing insulin signaling.

We used the HOMA2-IR model (via the Oxford calculator) because it better accounts for feedback between insulin and glucose than HOMA1. Prior studies support its improved accuracy for detecting IR and â-cell dysfunction.[15,16,17]

Using both percentile criteria (50th and 75th) and MetS criteria, we determined optimal cut-offs for HOMA2-IRaround 1.4 for the general adult population (P50) and 1.2-1.4 using MetS criteria, with the 75th percentile cut-offs higher (~2.0-2.4). Notably, a recent Japanese study of non-diabetic adults found an optimal HOMA-IR cut-off of 1.7 for the detection of MetS (sensitivity ~73 %, specificity ~70 %) among >6,800 participants.[18] Another large Spanish study found that using MetS criteria rather than simple percentiles lowered the cut-off from 3.46 to 2.05[19], which co relates with the findings of our study.

More recent work suggests that while HOMA-IR remains a useful surrogate, optimal thresholds differ by ethnicity, age and sex. For example, a 2022 Iranian sample identified an optimal cut-off of 1.95 (sensitivity ~68.4 %; specificity ~65.3 %) to detect MetS.[20]

Since the cut-off value of IR at the 50th percentile ranged between 1.4–1.7, and that determined by metabolic syndrome criteria ranged between 1.2–1.4, we suggest 1.4 as the optimal cut-off point for insulin resistance. This is supported by both percentile and metabolic syndrome criteria. This lower cut-offs (1.4) provided higher sensitivity and negative predictive value (NPV) compared to higher thresholds: thus they are more suitable for screening rather than confirming IR. Given the attendant cardiovascular and metabolic risks, adopting a lower cut – off may improve clinical utility in identifying individuals at risk.

We did not find significant variation of IR cut-off values by age or gender in our sample, which differs from a Spanish study which showed age- and sex-dependent thresholds.[19]

Conclusion:

The study identifies a HOMA-IR cut-off of 1.4 for detecting insulin resistance among Bangladeshi adults. These values offer a useful reference for clinicians and public health programs aiming to identify individuals at risk for metabolic disorders.

Limitations:

Single-center and the relatively short study duration might limit validity. Future multi-center studies with longer follow-up periods will provide more comprehensive insights.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there was no conflict of interest in this study.

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of Sir Salimullah Medical College

Mitford Hospital (SSMCMH) Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; had agreed on the journal to which the article had been submitted; and agreed to be account able for all aspects of the work.

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