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**Original Research Article**

# Identification of cut-off value for homeostatic model assessment for insulin resistance in children at a tertiary care hospital in Bangladesh

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## ABSTRACT

**Background:** Insulin resistance (IR) is associated with obesity, type 2 diabetes, dyslipidemia, hypertension, atherosclerosis, polycystic ovary syndrome, and non-alcoholic fatty liver disease. In recent years, IR has been increasingly reported in children. Among surrogate indices, the homeostatic model assessment of IR (HOMA-IR) is the most widely used.
**Methods:** A cross-sectional study was conducted at Bangladesh medical university, involving 613 children aged 6-18 years. Fasting insulin, glucose, and lipid profiles were measured, and HOMA-IR was calculated. Optimal cut-off values for IR were determined using percentile and modified ATP III metabolic syndrome criteria. Diagnostic accuracy was assessed using sensitivity, specificity, and the Youden index.
**Results:** HOMA-IR cut-off values at the 85$^{th}$ percentile ranged from 2.3 to 2.6, and by metabolic syndrome criteria from 2.0 to 2.4, with high sensitivity (93.2%) and specificity (60.1%). At the 95$^{th}$ percentile, cut-offs were higher (3.0-4.7) but less sensitive (78.6%) and specific (72.9%). A value of 2.4 was consistent across both approaches.
**Conclusions:** This study recommends 2.4 as optimal HOMA-IR cut-off for diagnosing IR in Bangladeshi children.

**Keywords**: HOMA-IR, Insulin resistance, Metabolic syndrome, Children, Bangladesh

## INTRODUCTION

Insulin resistance (IR), defined as the reduced physiological response of peripheral tissues to insulin, is a key factor in obesity, type 2 diabetes, metabolic syndrome, dyslipidemia, hypertension, atherosclerosis, polycystic ovary syndrome, and non-alcoholic fatty liver disease.[1,2] Previously considered exclusive to adults, IR is now recognized in children, with or without obesity.[3,4] It often precedes glucose intolerance by 1-2 decades, making early detection critical.[5,6]

Several methods detect IR, with the euglycemic-hyperinsulinemic glucose clamp as the gold standard.[7] However, its complexity and time requirements limit its use.[8] The HOMA-IR is a simple, cost-effective alternative.[9] HOMA-IR cut-off values vary by age, race, gender, and disease, with some studies using receiver operating characteristic (ROC) curves or percentile criteria for estimation.[10-16] In Bangladesh, no established HOMA-IR cut-off exists for children. This study aims to determine optimal HOMA-IR cut-off values for diagnosing IR in Bangladeshi children.

## METHODS

### *Study population*

This cross-sectional study, conducted from May 2019 to September 2020 at Bangladesh medical university's paediatric endocrinology clinic and outpatient/inpatient departments, enrolled 613 apparently healthy children aged 6-18 years. Children on systemic steroids, with chronic diseases (e.g., kidney, liver, pancreatic, endocrine, or autoimmune disorders), or using medications affecting glucose metabolism (e.g., sodium valproate, risperidone, cyclosporine, tacrolimus, glucocorticoids, growth hormone) were excluded.

### *Clinical and laboratory measurements*

Weight and height were measured using an electronic weighing machine and stadiometer to the nearest 0.2 kg and 0.1 cm, respectively. Waist circumference was measured midway between the lowest rib and iliac crest using a non-extensible tape during mid-respiration. Body mass index (BMI) was calculated as weight (kg) divided by height squared ($m^2$) and classified per CDC 2000 growth charts: normal weight ($\geq 5^{th}$ to $<85^{th}$ percentile), overweight ($\geq 85^{th}$ to $<95^{th}$ percentile), or obese ($\geq 9^{th}$ percentile).[17] Blood pressure was measured in a seated position after 5 minutes of rest using an appropriate cuff.

Pubertal status was assessed using Tanner stages: stage 1 (pre-pubertal) and stages 2-4 (pubertal).[18,19] Blood samples, collected after an 8-hour overnight fast, were analyzed for fasting insulin, glucose, 2-hour post-glucose load (1.75 g/kg), and lipid profiles using an Architect Plus ci4100 analyzer. Methods included glucose oxidase for serum glucose, microparticle enzyme immunoassay for insulin, glycerol phosphate oxidase for triglycerides, accelerator selective detergent for HDL cholesterol, cholesterol oxidase for total cholesterol, and Friedew Brittany's formula for LDL cholesterol.

### *Definition of metabolic syndrome and HOMA-IR calculation*

Metabolic syndrome was defined using modified adult treatment panel III (ATP III) criteria, requiring three or more of: WC $\geq 90^{th}$ percentile for age and sex, HDL cholesterol <40 mg/dL or treatment for this abnormality, triglycerides ≥150 mg/dL or treatment, blood pressure ≥130/85 mm Hg or previously diagnosed hypertension, fasting plasma glucose ≥5.6 mmol/L or previously diagnosed type 2 diabetes.[20]

HOMA-IR was calculated as fasting insulin (μU/mL)×fasting glucose (mmol/L)/22.5.[21]

### *Statistical analysis*

Analyses were performed with SPSS v25.0. Continuous variables are presented as mean±SD.

ROC curves were used to evaluate HOMA-IR cut-offs against MS. Diagnostic accuracy was assessed by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC). Youden's index (sensitivity + specificity-1) was used to determine the optimal cut-off. In children without MS, HOMA-IR cut-offs were additionally assessed using percentiles ($85^{th}$ and $9^{th}$).

### *Ethics statement*

The institutional review board of Bangladesh medical university approved the study. Written informed consent was obtained from participants parents.

## RESULTS

### *Baseline characteristics*

A total of 613 children aged 6-18 years were enrolled, comprising 47.3% boys and 52.7% girls. The mean±SD age of the study population was 11.28±2.47 years. Anthropometric and biochemical profiles are summarized in Table 1.

The mean body-mass index (BMI) was 23.19±5.78 $kg/m^2$. Among all participants, 45% were obese, 28% overweight, and 27% within the normal-weight range. Mean fasting plasma glucose and fasting insulin levels were 4.97±0.66 mmol/L and 16.02±10.88 μU/mL, respectively, corresponding to an average HOMA-IR value of 3.59±2.66.

The overall frequency of metabolic syndrome (MetS), defined according to the modified ATP III criteria, was 29.9%, slightly higher in girls (16.2%) than in boys (13.7%).

### *Determination of HOMA-IR cut-off values*

Percentile-based and ROC analyses were performed to determine the optimal HOMA-IR thresholds for identifying IR.

Table 2 demonstrates the diagnostic performance of the continuous metabolic score (MetS score) for identifying metabolic syndrome according to different percentile cut-offs and subgroup analyses. At the $85^{th}$ percentile (P=85) (cut-off 2.4), the MetS score showed the highest sensitivity (93.2%) but moderate specificity (60.1%), yielding a Youden Index of 0.53 and an AUC of 0.83. The $95^{th}$ percentile (P95) (cut-off 3.6) provided improved specificity (72.9%) but reduced sensitivity (78.6%), maintaining an overall balance (Youden index=0.52). The optimal cut-off value determined by the Youden index was 2.16, corresponding to a sensitivity of 91.8% and specificity of 60.5%.

When stratified by sex, the optimal cut-offs were 2.2 for boys and 2.13 for girls, both showing comparable

diagnostic accuracy (AUC=0.82; Youden index=0.52). The prepubertal group exhibited slightly better discriminative ability (AUC=0.83; Youden index=0.56) compared to the pubertal group (AUC=0.83; Youden index=0.53).

Overall, these results indicate that a HOMA-IR value around 2.4 provides a balanced and clinically relevant threshold for identifying IR among Bangladeshi children and adolescents.

***ROC curve analysis***

The ROC curves for the total population and for each subgroup (boys, girls, prepubertal, and pubertal) are presented in Figures 1-5.

All curves demonstrated strong discriminative performance of HOMA-IR in identifying children with metabolic syndrome, with areas under the curve (AUCs) ranging between 0.84 and 0.91. Taken together, the ROC curves visually confirm the numeric findings presented in Table 2, highlighting the robustness and consistency of HOMA-IR as a diagnostic tool across sex and developmental stages.

***Summary of key findings***

Mean HOMA-IR: 3.59±2.66. Optimal Youden-derived cut-off: 2.16 (overall); 2.2 (boys); 2.13 (girls). Physiological puberty-related increase: 2.0 (prepubertal)→2.4 (pubertal) and recommended unified screening cut-off: HOMA-IR=2.4.

**Table 1: Demographic, clinical and biochemical characteristics of study population, (n=613).**

| Characteristics | Mean±SD/ N (%) |
|---|---|
| **Age (in years)** | 11.28±2.47 |
| **Boys** | 290 (47.3) |
| **Girls** | 323 (52.7) |
| **BMI (kg/m²)** | 23.19±5.78 |
| Normal | 167 (27) |
| Overweight | 171 (28) |
| Obese | 275 (45) |
| **Systolic BP (mmHg)** | 100.27±11.51 |
| **Diastolic BP (mmHg)** | 67.30±9.75 |
| **Waist circumference (cm)** | 78.98±16.54 |
| **Fasting blood glucose (mmol/l)** | 4.97±0.66 |
| **2-hour plasma glucose (mmol/l)** | 6.14±2.52 |
| **Fasting insulin (µU/ml)** | 16.02±10.88 |
| **HOMA-IR** | 3.59±2.66 |
| **Triglycerides (mg/dl)** | 142.35±68.94 |
| HDL cholesterol (mg/dl) | 38.47±12.31 |
| Total cholesterol (mg/dl) | 168.92±39.45 |
| LDL cholesterol (mg/dl) | 102.56±35.89 |
| **Metabolic syndrome** | 29.9 |

**Table 2: HOMA-IR cut-off values summery.**

| Group/criterion | Cut-off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | AUC | Youden index |
|---|---|---|---|---|---|---|---|
| **Percentile P85 (total)** | 2.4 (range 2.3-2.6) | 93.2 | 60.1 | 52.0 | 95.0 | 0.83 | 0.53 |
| **Percentile P95 (total)** | 3.6 (range 3.0-4.7) | 78.6 | 72.9 | 52.3 | 89.9 | 0.80 | 0.52 |
| **MetS (total, Youden)** | 2.16 | 91.8 | 60.5 | 52.6 | 94.3 | 0.82 | 0.52 |
| **Boys (MetS)** | 2.2 | 91.7 | 60.0 | 51.9 | 94.3 | 0.82 | 0.52 |
| **Girls (MetS)** | 2.13 | 91.9 | 60.0 | 52.0 | 94.4 | 0.82 | 0.52 |
| **Prepubertal (MetS)** | 2.0 | 93.9 | 62.1 | 54.3 | 95.7 | 0.83 | 0.56 |
| **Pubertal (MetS)** | 2.4 | 93.2 | 60.1 | 52.0 | 95.0 | 0.83 | 0.53 |

*MetS-metabolic syndrome, PPV-positive predictive value, NPV-negative predictive value, AUC-area under the curve.

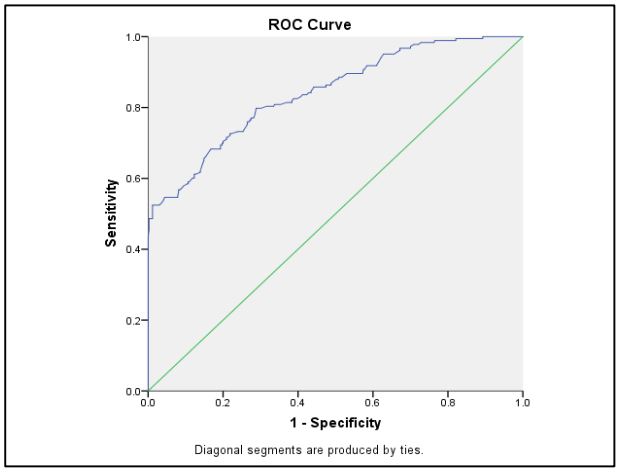


**Figure 1: ROC curve analysis of HOMA-IR determined by metabolic syndrome ATP III criteria in Bangladeshi children to be 2.16 with area under curve 0.842 and p<0.0001.**

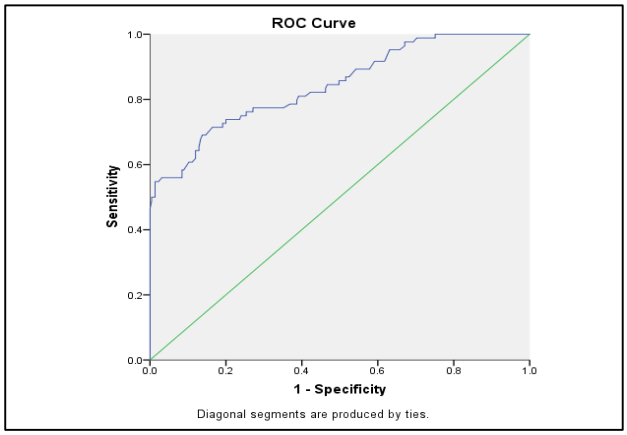


**Figure 2: ROC curve analysis of HOMA-IR determined by metabolic syndrome criteria in boys 2.2 with area under curve 0.843 and p<0.0001.**

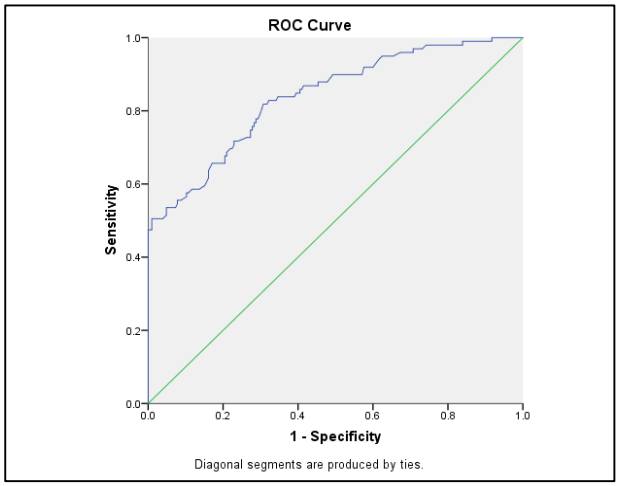


**Figure 3: ROC curve analysis of HOMA-IR determined by metabolic syndrome criteria in girls to be 2.13 with area under curve 0.838 and p<0.0001.**

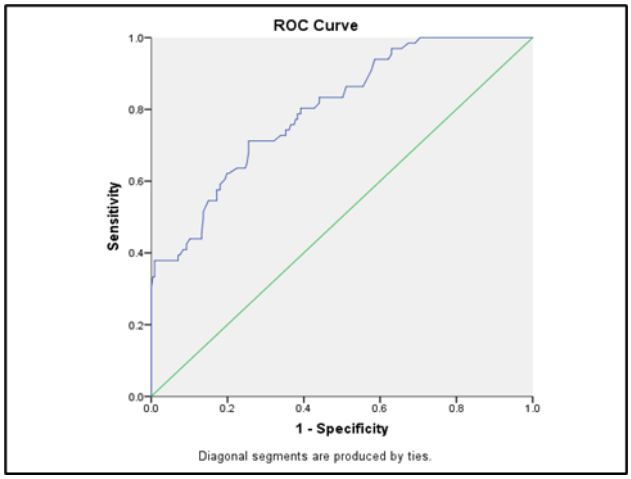


**Figure 4: ROC curve analysis of HOMA-IR determined by metabolic syndrome ATP III criteria in pre-pubertal children to be 2.0 with area under curve 0.799 and p<0.0001.**

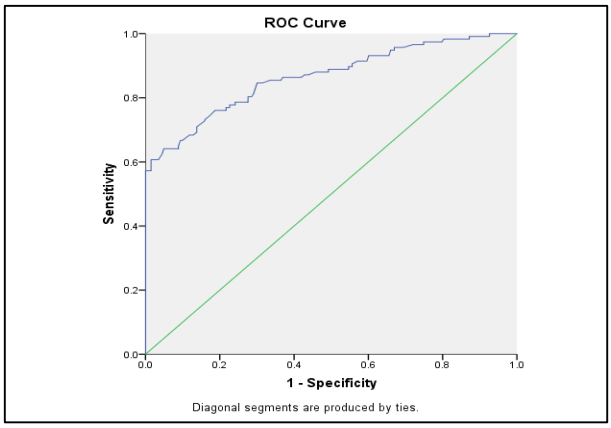


**Figure 5: ROC curve analysis of HOMA-IR determined by metabolic syndrome ATP III criteria in pubertal children to be 2.4 with area under curve 0.865 and p<0.0001.**

## DISCUSSION

IR is a crucial early abnormality in the pathway toward type 2 diabetes and other cardiometabolic diseases such as dyslipidemia, hypertension, non-alcoholic fatty liver disease, and polycystic ovary syndrome.[22] Its recognition during childhood is particularly important because intervention at an early stage can prevent or delay future complications.[24] In this study, the HOMA-IR was applied, which is widely accepted as a practical and low-cost alternative to the euglycemic clamp method.[7,8]

Our findings indicate that a HOMA-IR threshold of 2.4 is optimal for identifying insulin resistance in Bangladeshi children. This value was supported consistently by both the percentile approach (2.3-2.6 at the 85$^{th}$ percentile) and the metabolic syndrome criteria (2.0-2.4). The diagnostic accuracy was high, with sensitivity of 93.2% and a

negative predictive value of 97.5%, making it a strong tool for early screening (Table 4).

International comparisons show some variability, likely due to ethnic and environmental differences. Rocco et al reported 2.1 in Brazilian children, Yin et al found 2.3-3.0 in Chinese cohorts, and Shashaj et al observed 3.02 in Caucasian populations.[15,16] Despite these differences, our cut-off lies within the reported range, while providing population-specific evidence for Bangladeshi children. A key strength of our study is that it included normal-weight, overweight, and obese children, unlike many previous studies restricted to obese groups.[15,24-26] This broad representation improves the generalizability of our results.

The use of modified ATP III criteria, instead of the IDF definition, also allowed us to identify insulin resistance in non-obese children, an often-overlooked group.[23] Given that IR may occur independently of obesity, this approach adds clinical value. Although specificity was moderate, high sensitivity and negative predictive value are more important for a screening tool, since the priority is not to miss children at risk.[27]

Limitations of this study include its single-center design and cross-sectional nature. Longitudinal studies are required to confirm whether this cut-off predicts future development of metabolic syndrome or diabetes in Bangladeshi children. Despite these limitations, our study provides much-needed baseline data for clinical practice.

## CONCLUSION

A HOMA-IR cut-off of 2.4 is proposed as the most appropriate threshold for detecting IR in Bangladeshi children. This value is supported by both percentile and metabolic syndrome criteria, and shows high sensitivity for screening purposes. Applying this cut-off in practice could allow earlier recognition of children at risk, enabling preventive strategies against diabetes and other cardiometabolic disorders.

### *Recommendations*

Clinicians should adopt the HOMA-IR threshold of 2.4 in screening for IR in Bangladeshi children. Public health programs, particularly school-based initiatives, should integrate HOMA-IR screening to identify at-risk children. Multicenter and longitudinal studies are needed to validate these findings and assess long-term outcomes. Policymakers should incorporate this population-specific cut-off into national guidelines for pediatric screening and management of metabolic risk.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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