

Evaluation of routine laboratory markers for identifying insulin resistance in normal-weight adults

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ABSTRACT

Objective: To determine the frequency of insulin resistance in normal-weight adults and evaluate the ability of routine laboratory markers to identify insulin resistance.

Material and Methods: This Cross-sectional analytical study was conducted at the Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur, from June to December 2025. Adults aged 18–60 years with BMI 18.5–24.9 kg/m² were included. Fasting glucose, insulin, HbA1c, triglycerides, HDL-C, ALT, AST and uric acid were measured. HOMA-IR, triglyceride-glucose (TyG) index and TG/HDL-C ratio were calculated. Insulin resistance was defined as HOMA-IR ≥ 2.5 . Receiver operating characteristic analysis assessed discrimination.

Results: Among 246 adults, mean age was 36.2 (SD 8.6) years and 48 (19.5%) had insulin resistance. Compared with insulin-sensitive participants, those with insulin resistance had higher BMI, fasting glucose, HbA1c, triglycerides, ALT, AST, uric acid, TyG index and TG/HDL-C ratio, with lower HDL-C. TyG had the numerically highest AUC (0.815; 95% CI 0.752–0.878), with a cutoff of 8.481 providing 83.3% sensitivity and 65.7% specificity. TG/HDL-C had an AUC of 0.805. Each one-standard-deviation increase in TyG was associated with 4.26-fold higher adjusted odds of insulin resistance.

Conclusion: Insulin resistance was present in about one fifth of normal-weight adults. TyG and TG/HDL-C may offer simple, inexpensive screening tools for identifying individuals who require closer metabolic assessment, but population-specific validation is needed before routine clinical use.

Keywords: HDL cholesterol, HOMA-IR, Insulin resistance, Normal weight, Triglyceride-glucose index, Triglycerides

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INTRODUCTION

Body mass index (BMI) remains the most widely used indicator of overweight and obesity. It is simple and low cost, but provides limited information about metabolic health. Visceral adiposity, skeletal muscle mass, ectopic fat deposition and insulin sensitivity may vary significantly among individuals with the same BMI. A normal BMI can therefore provide false reassurance [1,2].

Metabolically unhealthy normal weight phenotype has received increased attention. These individuals have a normal BMI but have metabolic abnormalities typically associated with overweight and obesity. These may include dyslipidemia, impaired glucose regulation, hypertension and insulin resistance [1,3]. Recent work also shows that central adiposity and unfavorable body composition contribute to metabolic

risk among adults who would otherwise be classified as normal weight [4,5].

This issue is particularly relevant to South Asian population. Diabetes is found at a lower BMI in South Asians than many other western populations. Data from Pakistan and India has shown a greater incidence of diabetes among normal weight South Asian population as compared to normal weight White adults. Greater visceral or ectopic adiposity, relatively low lean mass and differences in insulin secretory capacity may contribute to this susceptibility [6, 7]. Reliance on BMI alone can lead to missing of a clinically important group that is at increased metabolic risk.

Insulin resistance often precedes overt hyperglycemia. Compensatory insulin secretion may maintain glucose concentration within normal range during the early stages despite reduced insulin secretion [8]. Direct measurement of insulin sensitivity using the hyperinsulinemic-euglycemic clamp is technically the best method, but is complex, time consuming and expensive and not used in routine practice [9]. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is a more practical measure but requires a fasting insulin measurement. There is still significant inter-assay variability among

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commercial insulin assays, making it difficult to compare insulin-based indices among different laboratories [10].

Several indices based on routinely measured biochemical parameters have been proposed. The triglyceride-glucose (TyG) index is a combination of fasting glucose and triglycerides. Both are closely related to insulin-resistant glucose and lipid metabolism. The index has shown reasonable performance as a screening marker for insulin resistance, although it should not be considered equivalent to a direct measurement of insulin sensitivity [11, 12]. The TG/HDL-C ratio is another simple marker that reflects the lipid disturbance related to insulin resistance [13]. Because fasting glucose contributes to both TyG and HOMA-IR, the observed relationship between these indices may be influenced by mathematical coupling.

These markers may be particularly useful in adults with normal BMI as metabolic testing is less likely to be performed when body weight appears reassuring. Recent studies have linked TyG with metabolically unhealthy normal weight, visceral adiposity and future metabolic disease [14,15]. Evidence from South Asian normal-weight cohorts also suggest that TyG may identify individuals at greater risk of dysglycemia [16].

This study was therefore conducted to determine the frequency of insulin resistance in normal-weight adults and to evaluate the utility of routinely available laboratory parameters to detect it. Particular emphasis was placed on markers that could be calculated or interpreted without additional specialized testing.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted in the Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur from June to December 2025 after approval from the Institutional Review Board / Ethics Committee (IRB) [ERC No. 1629/DME/QAMC/2025] dated . All participants gave written informed consent. Sample size was calculated using the OpenEpi version 3.01 sample-size calculator for a population proportion, using an expected prevalence of 20%, 95% confidence level and 5% absolute precision; the required sample was 246 participants.¹⁷

The inclusion criteria were adults between 18–60 years with a BMI range of 18.5–24.9 kg/m². The subjects were selected using the non-probability consecutive sampling method. Known diabetes mellitus, pregnancy, chronic kidney disease, chronic

liver disease, acute illness or a known endocrine disorder that may affect glucose metabolism were excluded. People on glucose-lowering drugs, lipid-lowering drugs, systemic corticosteroids or other drugs that significantly affect glucose or lipid levels were also excluded. Eligible adults were assessed against the predefined inclusion and exclusion criteria and enrolled consecutively until the required sample size was reached.

The height was measured without shoes, to the nearest 0.1 cm, and weight to the nearest 0.1 kg. BMI was calculated as weight in kilograms divided by height in meters squared.

The participants were asked to fast for 8–12 hours before blood sampling. Fasting plasma glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), low-density lipoprotein cholesterol (LDL-C), HbA1c and uric acid were measured using standard automated methods on Cobas c303 (Roche Diagnostics). The fasting insulin level was determined by electrochemiluminescence Cobas e411 (Roche Diagnostics). Internal quality control was performed daily using Roche PreciControl ClinChem Multi 1 and 2 for routine chemistry and PreciControl HbA1c for HbA1c. The laboratory also participated in the Bio-Rad EQAS programme, using Bio-Rad Lyphochek material for external quality assessment. Calibration was performed when a new reagent kit was installed, after major maintenance or repair or when quality-control results were out of control. HOMA-IR was calculated using fasting insulin (μU/mL) × fasting glucose (mg/dL)/405, following the method described by Matthews *et al.*¹⁸ HOMA-IR ≥2.5 was considered as insulin resistance. HOMA-IR ≥2.5 was used as the operational cutoff for insulin resistance, consistent with previous research in healthy Pakistani adults that included normal-weight participants. To assess the robustness of the findings to cutoff selection, sensitivity analyses were also performed using HOMA-IR thresholds of 2.0 and 3.0.¹⁹

The TyG index was calculated using established formula $\ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$.^{20,21} The TG/HDL-C ratio was determined by dividing fasting triglycerides by HDL-C, both of which were measured in mg/dL.

Data were analyzed using SPSS version 25. Paired bootstrap AUC comparisons and stratified 10-fold cross-validation were performed in Python. Normality was assessed using the Shapiro-Wilk test and

distribution plots. Normally distributed variables are reported as mean (SD) and non-normally distributed variables as median (IQR). Between-group comparisons used the independent-samples t test for age, BMI, fasting glucose, total cholesterol, LDL-C, HDL-C, AST, uric acid and TyG index, and the Mann-Whitney U test for HbA1c, triglycerides, TG/HDL-C ratio, ALT, fasting insulin and HOMA-IR. Sex is reported as n (%) and was compared using the chi-square test with continuity correction. Spearman rank correlation assessed associations of HOMA-IR with TyG index, TG/HDL-C ratio, fasting glucose, total cholesterol, triglycerides, LDL-C, HDL-C, ALT, AST, HbA1c, uric acid and BMI. Partial Spearman correlations of HOMA-IR with TyG index, TG/HDL-C ratio and triglycerides were calculated while controlling for fasting glucose. Receiver operating characteristic (ROC) analysis assessed the discrimination of TyG index, TG/HDL-C ratio, triglycerides, fasting glucose, HbA1c, ALT and uric acid for HOMA-IR-defined insulin resistance. AUCs with 95% confidence intervals were reported. Cutoffs were selected using the Youden index, and sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated. The AUC of TyG was compared with those of TG/HDL-C ratio, triglycerides and fasting glucose using paired nonparametric bootstrap resampling with 5,000 resamples. Sensitivity analyses repeated the ROC analysis using HOMA-IR cutoffs of 2.0 and 3.0. TyG and TG/HDL-C cutoffs were internally validated using stratified 10-fold cross-validation. In each fold, the Youden cutoff was derived from the training data and applied to the corresponding test data. Test-fold AUCs were summarized as mean (SD), and out-of-fold predictions were pooled to estimate sensitivity and specificity. Binary logistic regression was performed with HOMA-IR-defined insulin resistance (yes/no) as the dependent variable and standardized TyG index, age, sex and BMI as independent variables. Adjusted odds ratios with 95% confidence intervals were reported. Model fit was assessed using the likelihood-ratio test and McFadden pseudo- R^2 . Sex-specific ROC analyses were performed for TyG and TG/HDL-C, and a TyG-by-sex interaction term was tested in a separate adjusted model. All tests were two-sided, with $p < 0.05$ considered statistically significant.

Figure-1 shows routine biochemical signals that may accompany insulin resistance and the derived indices evaluated in this study.

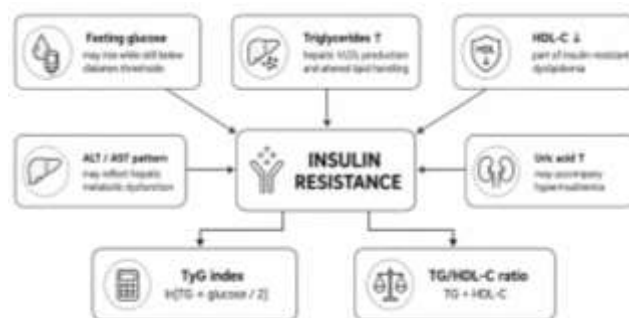


Figure 1: Routine laboratory signals of insulin resistance.

No single routine marker diagnoses insulin resistance; patterns and composite indices can strengthen screening.

RESULTS

A total of 246 normal-weight adults were included, comprising 152 (61.8%) women and 94 (38.2%) men. The mean age was 36.2 (SD 8.6) years and the mean BMI was 22.25 (SD 1.41) kg/m². Using HOMA-IR ≥ 2.5 , 48 (19.5%) participants were classified as insulin resistant.

Table 1 compares the insulin-sensitive and insulin-resistant groups. Age ($p=0.702$) and sex ($p=0.296$) did not differ significantly. BMI, fasting glucose, total cholesterol, triglycerides, LDL-C, TG/HDL-C ratio, ALT, AST, fasting insulin, HOMA-IR and TyG index were higher in the insulin-resistant group (all $p < 0.001$). HbA1c ($p=0.002$) and uric acid ($p=0.008$) were also higher, while HDL-C was lower ($p=0.031$). Table 2 shows positive correlations of HOMA-IR with all evaluated markers except HDL-C. The strongest correlations were with TyG index ($r=0.531$), TG/HDL-C ratio ($r=0.518$), fasting glucose ($r=0.500$) and triglycerides ($r=0.467$); the remaining positive correlations were weaker ($r=0.212$ – 0.383), while HDL-C was inversely correlated ($r=-0.271$). All correlations were statistically significant (all $p < 0.001$). After controlling for fasting glucose, the correlations remained significant for TyG index (partial $r=0.410$), TG/HDL-C ratio (partial $r=0.465$) and triglycerides (partial $r=0.404$), all $p < 0.001$.

Table 3 shows that TyG index had the highest observed AUC (0.815), closely followed by TG/HDL-C ratio (0.805) and triglycerides (0.791); fasting glucose, ALT, HbA1c and uric acid had lower AUCs of 0.762, 0.709, 0.645 and 0.639, respectively. At the selected cutoffs, TyG provided 83.3% sensitivity and 65.7% specificity, while TG/HDL-C provided 79.2% sensitivity and 71.2% specificity. Across markers, NPV ranged from 87.9% to 94.2%, PPV from 27.3% to 41.9%, LR+ from 1.55 to 2.98 and LR- from 0.25 to 0.57. Paired bootstrap comparisons showed no significant AUC difference between TyG and

TG/HDL-C ($p=0.500$) or between TyG and fasting glucose ($p=0.198$), whereas TyG had a higher AUC than triglycerides ($p=0.001$). ROC discrimination remained broadly similar using HOMA-IR cutoffs of 2.0 and 3.0. In stratified 10-fold cross-validation, mean AUCs were 0.810 (SD 0.085) for TyG and 0.790 (SD 0.083) for TG/HDL-C, with aggregated sensitivity/specificity of 81.2%/65.7% and 75.0%/69.2%, respectively.

Predictive values reflect the observed prevalence of 19.5%. Cutoffs are rounded for display; performance measures correspond to the selected ROC/Youden coordinate before rounding. Pairwise AUC p -values are from 5,000 paired bootstrap resamples; Panel B p -values are from multivariable logistic regression.

In Table 3, Panel B, standardized TyG was associated with higher odds of HOMA-IR-defined insulin resistance (adjusted OR 4.26, 95% CI 2.66–6.83; $p<0.001$), as was BMI (adjusted OR 1.54, 95% CI 1.17–2.04; $p=0.002$). Age (adjusted OR 1.01, 95% CI 0.97–1.06; $p=0.510$) and male sex (adjusted OR 1.38, 95% CI 0.64–2.98; $p=0.413$) were not significantly associated. The model likelihood-ratio test was significant ($p<0.001$; McFadden pseudo- $R^2=0.277$). Sex-specific ROC analysis showed TyG AUCs of 0.848 in men and 0.784 in women and TG/HDL-C AUCs of 0.809 and 0.795, respectively; the adjusted TyG-by-sex interaction was not significant (OR 1.14, 95% CI 0.44–2.93; $p=0.793$).

Table-I: Clinical and biochemical characteristics according to insulin resistance status

Variable	Insulin sensitive (n=198)	Insulin resistant (n=48)	p-value
Age, years	36.15 (8.73)	36.66 (8.20)	0.702
Male sex, n (%)	72 (36.4)	22 (45.8)	0.296
BMI, kg/m ²	22.10 (1.39)	22.89 (1.33)	<0.001
Fasting glucose, mg/dL	88.43 (6.77)	94.62 (5.64)	<0.001
HbA1c, %*	5.10 (4.95–5.26)	5.19 (5.10–5.36)	0.002
Total cholesterol, mg/dL	173.95 (23.37)	193.23 (23.21)	<0.001
Triglycerides, mg/dL*	94.15 (73.58–124.88)	141.40 (107.25–187.73)	<0.001
LDL-C, mg/dL	103.27 (19.30)	114.41 (18.06)	<0.001
HDL-C, mg/dL	50.44 (7.66)	47.86 (7.23)	0.031
TG/HDL-C ratio*	1.91 (1.45–2.53)	2.97 (2.49–3.74)	<0.001
ALT, U/L*	19.90 (16.12–24.53)	23.85 (21.20–29.12)	<0.001
AST, U/L	21.44 (3.59)	24.04 (3.00)	<0.001
Uric acid, mg/dL	4.84 (0.85)	5.23 (0.92)	0.008
Fasting insulin, μ U/mL*	5.23 (3.80–7.29)	14.14 (11.69–16.96)	<0.001
HOMA-IR*	1.16 (0.81–1.64)	3.30 (2.74–4.13)	<0.001
TyG index	8.34 (0.38)	8.83 (0.38)	<0.001

Data are presented as mean (SD), median (IQR) for variables marked with an asterisk, or n (%). P -values were calculated using the independent-samples t test for mean (SD) variables, the Mann-Whitney U test for asterisked variables and the chi-square test with continuity correction for sex.

Table-II: Correlation of routine markers with HOMA-IR.

Marker	Spearman correlation coefficient	p-value
TyG index	0.531	<0.001
TG/HDL-C ratio	0.518	<0.001
Fasting glucose	0.500	<0.001
Total cholesterol	0.264	<0.001
Triglycerides	0.467	<0.001
LDL-C	0.212	<0.001
HDL-C	-0.271	<0.001
ALT	0.383	<0.001
HbA1c	0.343	<0.001
Uric acid	0.277	<0.001
BMI	0.254	<0.001
AST	0.268	<0.001

Table-II p -values are from two-sided Spearman rank-correlation tests.

Table-III: ROC discrimination and multivariable logistic regression for HOMA-IR-defined insulin resistance.

Marker	AUC (95% CI)	Selected cutoff	Se/Sp (%)	PPV/NPV (%)	LR+/LR-
TyG index	0.815 (0.752–0.878)	8.481	83.3 / 65.7	37.1 / 94.2	2.43 / 0.25
TG/HDL-C ratio	0.805 (0.739–0.871)	2.461	79.2 / 71.2	40.0 / 93.4	2.75 / 0.29
Triglycerides	0.791 (0.724–0.859)	104.00 mg/dL	83.3 / 60.1	33.6 / 93.7	2.09 / 0.28
Fasting glucose	0.762 (0.692–0.832)	92.60 mg/dL	64.6 / 78.3	41.9 / 90.1	2.98 / 0.45
HbA1c	0.645 (0.565–0.724)	5.07%	87.5 / 43.4	27.3 / 93.5	1.55 / 0.29
ALT	0.709 (0.635–0.782)	21.00 U/L	79.2 / 59.1	31.9 / 92.1	1.94 / 0.35
Uric acid	0.639 (0.549–0.729)	5.07 mg/dL	64.6 / 62.6	29.5 / 87.9	1.73 / 0.57

Panel B. Multivariable logistic regression for HOMA-IR-defined insulin resistance

Predictor	Adjusted OR	95% CI	p-value	Unit / coding	Interpretation
TyG index	4.26	2.66–6.83	<0.001	per 1 SD	Higher odds
Age	1.01	0.97–1.06	0.510	per year	Not significant
Male sex	1.38	0.64–2.98	0.413	vs female	Not significant
BMI	1.54	1.17–2.04	0.002	per kg/m ²	Higher odds

Model LR $p < 0.001$; McFadden pseudo- $R^2 = 0.277$; outcome: HOMA-IR ≥ 2.5 (yes/no).

Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

DISCUSSION

The present study shows that insulin resistance is present in adults with normal BMI. The insulin-resistant group showed a consistently less favorable metabolic pattern, with higher glycemic and lipid markers, higher liver enzymes and uric acid and lower HDL-C. Among the routinely available indices, TyG had the highest observed AUC and remained associated with HOMA-IR-defined insulin resistance after adjustment for age, sex and BMI. The TG/HDL-C ratio performed nearly as well. In contrast, individual markers like fasting glucose, HbA1c, ALT and uric acid were less discriminative. These findings support the hypothesis that metabolic risk can be overlooked if normal BMI is considered a marker of metabolic health.

The frequency of insulin resistance in our cohort is comparable to other studies in normal weight individuals. Bo *et al* reported insulin resistance in about one fifth of normal weight adults using a HOMA-IR based definition which closely resembles the proportion observed in our study [17]. Simental-Mendía *et al* also found insulin resistance in 16% out of 1676 study participants with normal BMI [11]. López-Herrera *et al* showed that a metabolically unhealthy normal weight phenotype was present in 23.3% of adults from Colombia while the Tehran Lipid and Glucose Study reported metabolic unhealthiness in 19.4% of normal weight adults [5,22]. Different age groups, ethnicities and definitions were used by these studies. A few studies directly used HOMA-IR and others used clusters of metabolic abnormalities to measure insulin resistance. Sampling from the community, outpatient settings or selected healthy populations may also change the observed frequency.

The South Asian setting may further explain why insulin resistance was detectable despite normal BMI. Narayan *et al*. demonstrated that the metabolic susceptibility of South Asian adults in both India and Pakistan is lower than that of White adults, and that there is excess risk for diabetes at lower BMI than the threshold for overweight adults [6]. This indicates that BMI may not be an accurate measure of metabolic susceptibility in South Asians. Our results are also in

line with the hyperinsulinemic-euglycemic clamp study by Anoop *et al* which showed that in non-obese Asian Indian men insulin sensitivity was impaired at relatively low body weight [6,7]. Our findings are therefore consistent with a phenotype in which metabolic dysfunction appears before overt obesity becomes evident.

TyG was the strongest routine marker in our study. Similar findings have been observed in previous studies conducted on normal-weight Asian population. Kim *et al* found TyG cutoffs of 8.88 for men and 8.80 for women to define metabolically obese normal-weight older adults [14]. These values were slightly higher than ours most probably due to the difference in age and outcome definition. Jayashankar *et al* reported TyG cutoff above 8.61 for normal-BMI adults [16]. Although this value was close to ours, its discrimination for future diabetes was low. This may reflect the different outcomes studied. Our analysis assessed current HOMA-IR defined insulin resistance while their study evaluated incident diabetes over time.

The results also should be interpreted in the context of other large studies that have raised questions about the ability of TyG to substitute HOMA-IR. Only a moderate correlation was observed between TyG and HOMA-IR by Oliveira *et al*. who evaluated over 12,000 adults from ELSA-Brasil with an AUC of 0.742 [12]. This performance was lower than that observed in our study. This may be due to differences in population structure. While our analysis was of normal weight adults, ELSA-Brasil included adults with an older age and wider BMI range, whereas our analysis was restricted to normal weight adults. Lelis *et al* in a second ELSA-Brasil analysis reported only weak-to-moderate correlations and poor agreement between TyG and HOMA-IR indicating that the two indices might measure overlapping but different aspects of metabolic dysfunction [23]. This is a very important aspect to consider. Our results support TyG as a potential screening signal in normal-weight adults but not as a biochemical substitute for insulin-based assessment. These concerns have also been reported in large ELSA-Brasil analyses [12,23].

A key methodological consideration is mathematical coupling because fasting glucose is a component of both TyG and HOMA-IR. Sharing a component between calculated variables can inflate the observed association.²⁴ Importantly, the TyG-HOMA-IR association remained significant after controlling for fasting glucose, although the correlation decreased from $r=0.531$ to partial $r=0.410$. This attenuation suggests that part of the observed association may reflect the shared glucose component, although the relationship was not explained entirely by fasting glucose.

The TG/HDL-C ratio showed discrimination close to that of TyG. This is biologically plausible because insulin resistance is commonly accompanied by higher triglycerides and lower HDL-C. DeForest *et al* provided genomic evidence that the TG/HDL-C phenotype shares substantial genetic architecture with pathways related to insulin resistance [13]. A recent systematic review and meta-analysis by Zhong *et al* confirmed that increasing the TG/HDL-C ratio was linked to higher risk of type 2 diabetes in various populations [25]. However, that review showed considerable variation in how high and low ratios were defined. This supports our recommendation to use TG/HDL-C as a risk marker not suggest a cut-off level for diagnosis. Our data indicate that lipid patterning is an important metabolic marker even in the presence of normal BMI.

The individual laboratory markers were less informative when considered separately. Participants who were insulin-resistant had higher levels of both fasting glucose and HbA1c, but many were not at diabetic levels [8]. Triglycerides showed better performance, while ALT and uric acid had weaker associations [7]. This suggests that the overall biochemical pattern is more important than any single marker.

Although insulin-resistant participants had a higher BMI within the normal range, BMI alone did not clearly distinguish metabolic status. This is consistent with evidence that body composition and fat distribution provide metabolic information not captured by BMI, particularly in South Asian population [3-5].

The results are practically relevant in the laboratory as TyG and TG/HDL-C are calculated from the tests requested routinely in laboratory practice without further sampling and special assays. Unfavorable fasting glucose, triglyceride and HDL-C would warrant further metabolic evaluation in normal-weight adults, especially in high-risk South Asian populations. Automated calculation using laboratory

information systems might be considered following local validation. These indices should be used for risk recognition rather than diagnosis. A concerning pattern may prompt targeted assessment with waist measurement, fasting insulin with HOMA-IR, oral glucose tolerance testing or body-composition analysis. Fixed cutoffs should not be used in routine practice until validated for the population in which they are to be applied.

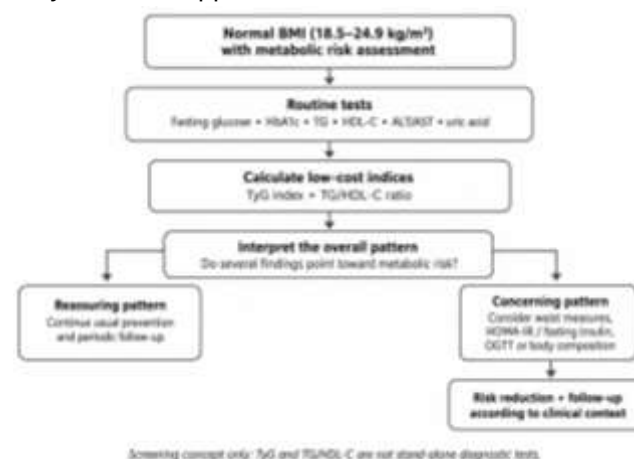


Figure-II: Proposed laboratory screening pathway for normal-weight adults. The pathway is intended for risk recognition and requires local clinical validation before implementation.

STRENGTHS AND LIMITATIONS

The main strength of this study is the focus on normal weight adults. This is a group in which metabolic risk may be overlooked. Multiple routine biochemical markers were compared with HOMA-IR using correlation, ROC analysis and adjusted regression. Relevance is added by the South Asian context as dysglycemia can be seen at lower BMI in this population.

Limitations include the cross-sectional, single-centre design and non-probability sampling, which limit generalizability and causal inference. HOMA-IR is a surrogate marker without a universally accepted cutoff, and waist circumference, body composition, visceral adiposity, lifestyle factors and family history were not assessed. Mathematical coupling remains a concern because fasting glucose is shared by TyG and HOMA-IR, although partial correlation attenuated but did not eliminate the association. Findings remained broadly consistent across alternative HOMA-IR cutoffs and 10-fold cross-validation. External validation in independent Pakistani or South Asian cohorts is required before the proposed cutoffs are adopted clinically. Sex-specific estimates should also be interpreted cautiously because of the smaller insulin-resistant subgroup.

CONCLUSION

Insulin resistance was identified in about one fifth of normal-weight adults. TyG and TG/HDL-C showed the highest discrimination among the routine markers evaluated such as fasting glucose, HbA1c, ALT and uric acid. It may serve as low-cost screening signals for HOMA-IR-defined insulin resistance. These indices should be used for risk recognition rather than diagnosis, and the proposed cutoffs require external population-specific validation before routine clinical application.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Imran Ali: Drafting the manuscript, acquisition, analysis, and interpretation of data. Critical review, literature search. Statistical review, critical review and discussion, final approval, responsible for every aspect of the research.

Saira Saleem: Data collection, data analysis and literature search. Critical review and discussion, final approval, responsible for every aspect of the research.

Hafiz Muhammad Salman Yousaf: Conception, data collection, formal Analysis, investigation, and resources, final approval, responsible for every aspect of the research

Sara Reza: Result analysis, review, final approval, responsible for every aspect of the research

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