Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 10s, https://carcinogenesis.com/

Association of Insulin Resistance Surrogates with NAFLD Progression and Disease Severity

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is increasingly recognized as the hepatic expression of metabolic dysfunction, closely linked to insulin resistance (IR). Surrogate markers such as the triglyceride-glucose (TyG) index, TyG-BMI, and TyG-WC have emerged as practical, low-cost tools for assessing IR and NAFLD risk. However, data from South Asian populations characterized by high metabolic risk is limited. ***Objective:*** To evaluate the association of TyG-index and TyG-based anthropometric indices with NAFLD presence and severity, and to determine their predictive accuracy for NAFLD among overweight and obese adults in Bangladesh. ***Methods:*** This cross-sectional study was conducted at the Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, from March 2023 to February 2024. A total of 253 adults (aged 18–75 years) with overweight or obesity were selected using purposive sampling. Clinical, anthropometric, and biochemical assessments were performed. Abdominal ultrasonography determined NAFLD diagnosis and grading. TyG-index, TyG-BMI, and TyG-WC were compared between groups and across NAFLD grades. ROC curves assessed predictive performance. ***Results:*** NAFLD prevalence was 51% (n=129). Among NAFLD subjects, Grade-I predominated (69%), followed by Grade-II (22%) and Grade-III (9%). NAFLD subjects had significantly higher TG, FPG, and ALT levels ($p<0.001$). TG, FPG, and ALT increased progressively with NAFLD grade. TyG-index, TyG-BMI, and TyG-WC were significantly higher in NAFLD subjects than controls ($p<0.001$). Across NAFLD grades, TyG-index and TyG-WC showed significant upward trends, highest in Grade-III. TyG-BMI did not differ significantly across grades. AUCs for prediction of NAFLD were: TyG (0.708), TyG-BMI (0.803), and TyG-WC (0.829). TyG-WC demonstrated the strongest predictive performance with optimal sensitivity and specificity. ***Conclusion:*** TyG-based indices, especially TyG-WC, are robust predictors of NAFLD among overweight and obese adults. TyG-index and TyG-WC also reflect disease severity. These low-cost markers offer practical advantages for early identification and risk stratification in resource-limited settings. Incorporating TyG-based indicators into routine metabolic evaluation may improve NAFLD detection and prevention strategies in South Asia.

Keywords: *NAFLD, Insulin resistance, TyG-index, TyG-BMI, TyG-WC, Hepatic steatosis, Overweight, Obesity.*

How to Cite: Sunjidul Haque, Tahmidul Islam, Broti Proma Biplab, Shaikhul Islam Shuja, Sumaiya Bashar, Ayesha Ferdous Jesun, Rehnuma Tarannum, Mozammel Hoque (2025). Association of Insulin Resistance Surrogates with NAFLD Progression and Disease Severity, *Journal of Carcinogenesis*, *Vol.24, No.10s*, 742-746

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most common chronic liver disorder worldwide, paralleling the global rise in obesity, insulin resistance, type 2 diabetes mellitus (T2DM), and other metabolic derangements [1–3]. The condition encompasses a spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), progressive fibrosis, cirrhosis, and hepatocellular carcinoma [4]. Its public health significance continues to expand as NAFLD now affects an estimated one-third of adults globally and is increasingly recognized in younger populations [5,6]. Early detection and risk stratification are essential to prevent disease progression, yet traditional diagnostic tools such as imaging and liver biopsy pose limitations imaging may be unavailable in resource-limited settings, while biopsy is invasive and unsuitable for population-level screening [7]. Growing evidence highlights the role of metabolic indices as practical tools for identifying individuals at higher risk of hepatic steatosis. Among these, the triglyceride-glucose (TyG) index has gained prominence as a reliable surrogate of insulin resistance, outperforming traditional measures in several cohorts [8,9]. Its extended variants TyG-BMI and TyG-WC integrate anthropometric parameters and may offer improved predictive accuracy for metabolic dysfunction and NAFLD severity [10–12]. However, the comparative performance of these indices across different NAFLD grades remains insufficiently understood, particularly in South Asian populations, where metabolic diseases behave differently due to unique genetic and anthropometric profiles [13]. This study evaluates the association of TyG-index, TyG-BMI, and TyG-WC with the presence and severity of NAFLD and assesses their diagnostic accuracy using ROC analysis. Understanding these relationships may support the development of simple, low-cost screening approaches particularly beneficial in clinical settings where advanced diagnostic facilities are limited.

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional study was conducted at the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, over a 12-month period (March 2023 – February 2024). Study subjects were recruited from the Hepatology Outpatient Department.

Sample Size and Sampling Method

A total of 253 adults aged 18–75 years with overweight or obesity were selected using purposive sampling.

Inclusion criteria

- Age 18–75 years
- BMI ≥23 kg/m² (Asian cutoff for overweight/obesity)
- Both genders
- Willingness to give written informed consent

Exclusion criteria

- Alcohol consumption >20 g/day
- Known chronic liver diseases (viral, autoimmune, or genetic)
- Pregnancy
- Use of hepatotoxic drugs or lipid-lowering agents
- Acute infection or critical illness

Ethical Considerations

The study received approval from the Institutional Review Board of BSMMU. Written informed consent was obtained from all participants after explaining the study purpose.

Data Collection Procedures

Clinical and Anthropometric Assessment

A structured questionnaire captured demographic and clinical information. Anthropometric measurements included:

- Height
- Weight
- BMI (categorized as overweight 23–24.9 kg/m²; obese ≥25 kg/m²)
- Waist circumference (WC)

Ultrasonographic Assessment

Upper abdominal ultrasonography (USG) was performed at the Department of Radiology, BSMMU by an experienced radiologist blinded to biochemical results. NAFLD was diagnosed and graded as:

- **Grade I:** Mild steatosis
- **Grade II:** Moderate steatosis

- **Grade III:** Severe steatosis

Subjects were categorized into:
- **Non-NAFLD (reference group)**
- **NAFLD group** (Grades I–III)

Biochemical Analysis
Fasting (8–12 hours) venous samples were assessed for:
- Fasting plasma glucose (FPG)
- Lipid profile: TG, LDL-C, HDL-C
- Alanine aminotransferase (ALT)

Calculation of TyG and Composite Indices
The following formulas were used:
TyG-index = ln [TG (mg/dL) × FPG (mg/dL) / 2]
TyG-BMI = TyG × BMI
TyG-WC = TyG × WC

Statistical Analysis
Data analysis was performed using SPSS version 27.0. Continuous variables were assessed for normality, and appropriate statistical tests were applied accordingly. Mann–Whitney U tests were used for non-parametric comparisons between the NAFLD and non-NAFLD groups, while independent t-tests were applied to parametric variables. Categorical data were compared using the Chi-square test. For evaluating differences across NAFLD severity grades, both Kruskal–Wallis tests and one-way ANOVA were employed, depending on data distribution. The predictive performance of TyG-index, TyG-BMI and TyG-WC was assessed using receiver operating characteristic (ROC) curve analysis. A p-value <0.05 was considered statistically significant for all analyses.

RESULTS

Table 1. Prevalence and Distribution of NAFLD Grades

Variable	Value
Total NAFLD prevalence	**51% (n = 129)**
Grade-I NAFLD	**69%**
Grade-II NAFLD	**22%**
Grade-III NAFLD	**9%**

In the study population, the overall prevalence of NAFLD was 51% (129 subjects). Among individuals diagnosed with NAFLD, Grade-I steatosis constituted the majority (69%), followed by Grade-II (22%), while Grade-III represented the smallest proportion at 9%. This distribution indicates that early-stage fatty liver disease predominated in the cohort.

Table 2. Comparison of Metabolic and Liver Biomarkers Between NAFLD and Non-NAFLD Subjects

Biomarker	Comparison Result
Triglycerides (TG)	**Higher in NAFLD**, $p < 0.001$
Fasting Plasma Glucose (FPG)	**Higher in NAFLD**, $p < 0.001$
Alanine Aminotransferase (ALT)	**Higher in NAFLD**, $p < 0.001$

When comparing metabolic and hepatic biochemical parameters, subjects with NAFLD exhibited significantly elevated levels of TG, FPG, and ALT relative to non-NAFLD participants ($p < 0.001$ for all). These findings highlight the strong metabolic burden associated with NAFLD. Moreover, each of these biomarkers showed a progressive increase with advancing NAFLD grade, indicating a severity-dependent relationship.

Table 3. TyG-Based Indices in NAFLD vs Controls

Index	Comparison Result
TyG-index	**Higher in NAFLD**, $p < 0.001$
TyG-BMI	**Higher in NAFLD**, $p < 0.001$
TyG-WC	**Higher in NAFLD**, $p < 0.001$

All three TyG-related indices TyG-index, TyG-BMI, and TyG-WC were significantly higher among NAFLD subjects compared with controls ($p < 0.001$). When stratified across grades, TyG-index and TyG-WC increased progressively, reaching their highest values in Grade-III NAFLD. In contrast, TyG-BMI did not show significant variation across grades, despite being elevated in NAFLD overall.

Table 4. ROC Performance of TyG-Related Indices for Predicting NAFLD

Index	AUC Value
TyG-index	**0.708**
TyG-BMI	**0.803**
TyG-WC	**0.829**

Receiver operating characteristic analysis demonstrated varying predictive strengths of the TyG-derived indices. The TyG-index showed moderate discriminatory ability (AUC 0.708), whereas TyG-BMI performed better (AUC 0.803). The strongest predictive capacity was observed for TyG-WC, which yielded the highest AUC (0.829) and provided the most favorable balance between sensitivity and specificity for identifying NAFLD.

DISCUSSION

In this study, the prevalence of NAFLD was 51%, aligning with recent regional and global reports demonstrating an increasing burden of fatty liver disease in populations with rising metabolic risk profiles [1,4,13]. The predominance of Grade-I steatosis in this cohort is consistent with epidemiological evidence showing that the majority of individuals with NAFLD present in early-stage disease, although a substantial proportion may still harbor significant metabolic dysfunction [2,5]. The progressively higher levels of TG, FPG, and ALT observed across NAFLD grades further support the established relationship between metabolic abnormalities and hepatic fat accumulation, reflecting underlying insulin resistance and hepatic inflammation [6–9]. A notable finding of the present study is the strong association of TyG-index, TyG-BMI, and TyG-WC with NAFLD. All three indices were significantly higher among individuals with NAFLD compared to controls, corroborating previous work that positions TyG-derived parameters as accessible markers of insulin resistance and hepatic steatosis [8–11]. The progressive rise in TyG-index and TyG-WC across NAFLD grades suggests these markers may reflect not only the presence but also the severity of steatosis. TyG-BMI, although elevated in NAFLD overall, did not differ significantly between grades, possibly indicating that BMI alone does not capture fat distribution patterns or visceral adiposity as effectively as waist circumference a limitation reported in other studies as well [12,14]. The ROC analysis revealed that TyG-WC demonstrated the highest predictive performance for NAFLD (AUC 0.829), surpassing both TyG-index and TyG-BMI. This finding aligns with previous research indicating that indices incorporating central obesity parameters such as waist circumference provide superior discriminatory ability for metabolic syndrome and related conditions [10,11,14]. Given that visceral adiposity plays a pivotal role in hepatic fat deposition and insulin resistance, the enhanced performance of TyG-WC is biologically plausible and clinically meaningful. These observations underscore the potential utility of TyG-based indices as low-cost, non-invasive screening tools for NAFLD, particularly in resource-limited settings where access to ultrasonography or advanced imaging may be constrained. Among the indices assessed, TyG-WC emerges as the most robust predictor and may be valuable in early triaging of high-risk individuals for further evaluation. However, while the results are encouraging, they should be interpreted with attention to the study's limitations, including potential variability in ultrasound-based grading and the cross-sectional nature of the dataset, which restricts causal inference. Prospective studies incorporating diverse populations and longitudinal follow-up would help further elucidate the predictive value of TyG-related markers for NAFLD onset and progression [7,15]. Overall, the study reinforces the growing recognition of TyG-derived indices particularly TyG-WC as practical tools to identify individuals at increased risk of NAFLD. Integrating these indices into routine metabolic screening may enhance early detection efforts and improve risk stratification, ultimately contributing to more efficient NAFLD management strategies.

CONCLUSION

This study demonstrates that TyG-index, TyG-BMI, and especially TyG-WC are significantly associated with NAFLD and can reliably predict its presence among overweight and obese adults. TyG-index and TyG-WC also correlate with disease severity. These simple, cost-effective markers can serve as valuable tools for early detection and risk stratification in clinical settings, aiding timely intervention to prevent disease progression.

Recommendations

- Integrate TyG-based markers into routine metabolic screening for overweight/obese adults.
- Use TyG-WC preferentially when predicting NAFLD risk.
- Target preventive interventions (lifestyle modification, weight reduction) in individuals with elevated TyG markers.
- Future longitudinal studies should explore predictive value for fibrosis and NASH.

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