

## Correlation of Triglyceride-Glucose Index and HOMA-IR (Insulin Resistance) in Patients with Prediabetes and Type 2 Diabetes Mellitus

Subrata K. Barua<sup>1</sup> Shantanu Dutta<sup>2</sup> Chandan Saha<sup>3</sup>

### Abstract

**Background:** Diabetes is a prevalent metabolic disorder linked to increased cardiovascular morbidity and mortality, which cannot be solely attributed to hyperglycemia or conventional cardiovascular risk factors like smoking or hypercholesterolemia. Intensive glycemic control using insulin to achieve near-normal glycemia does not significantly reduce macrovascular complications when compared to conventional glycemic control. The triglyceride glucose index is a significant indicator of the progression from prediabetes to type 2 diabetes mellitus. This study explored the correlation between triglyceride glucose index and HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) in prediabetes group and type 2 diabetes mellitus group.

**Materials and methods:** This Cross-sectional analytical study was carried out in the Department of Biochemistry at Institute of Applied Health Sciences. After conducting non-probability purposive sampling methods 25 prediabetes and 25 type diabetes patients were selected. Fasting blood glucose, fasting lipid profile and fasting insulin was measured. The triglyceride Glucose Index (TyG) and HOMA-IR (Homeostatic model assessment)-IR were calculated by following formula :-

Triglyceride Glucose Index (TyG) =  $\ln [Fasting Triglycerides (mg/dL) \times Fasting Glucose (mg/dL)]/2$ .

HOMA-IR =  $Fasting Insulin (\mu\text{IU}/\text{ml}) \times Fasting Glucose (\text{mmol}/\text{l})/22.51$ .

**Results:** There is a significant mean difference in BMI, Fasting insulin, fasting blood glucose, triglyceride, HDL-C, triglyceride index and HOMA-IR between prediabetes and type 2 diabetes group. There is a significant positive correlation of TyG with HOMA-IR in prediabetes group and type 2 diabetes mellitus group. ROC curve Test the TyG value to predict type 2 diabetes mellitus. TyG index exhibits higher AUC 0.94 with CI (0.88-1.00).

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1.□Associate Professor of Biochemistry  
□ Institute of Applied Health Sciences (IAHS) Chattogram.  
2.□Assistant Professor of Biochemistry  
□ Institute of Applied Health Sciences (IAHS) Chattogram.  
3.□Assistant Professor of Biochemistry  
□ Chandpur Medical College, Chandpur.

**\*Correspondence:** Dr. Subrata K. Barua  
□ Cell : 01711 93 46 46  
□ E-mail: [drsubratakbarua@gmail.com](mailto:drsubratakbarua@gmail.com)

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**Conclusion:** The study shows significant differences in key metabolic markers between prediabetes and type 2 diabetes mellitus, with a strong positive correlation between TyG index and insulin resistance in both groups.

**Key words:** HOMA-IR; Insulin resistance; TyG; Type 2 diabetes mellitus.

### Introduction

A metabolic imbalance that promotes the onset of type 2 diabetes mellitus is a hallmark of Insulin Resistance (IR) which is a metabolic disorder defined by a diminished cellular response to insulin.<sup>1</sup> This phenomenon arises when insulin levels are elevated as a result of insulin resistance, along with a rise in triglyceride levels. Hypertriglyceridemia leads to increased transport of free fatty acids to the liver, thereby enhancing hepatic glucose synthesis.<sup>2</sup> The primary mechanisms involved in the pathogenesis of type 2 diabetes mellitus are insulin resistance and inadequate insulin secretion.<sup>3</sup> Previous researches indicate early functional defects in  $\beta$  cells already exist in pre-diabetes.<sup>4,5</sup> Considering the critical importance of  $\beta$  cell dysfunction in the progression and prognosis of type 2 diabetes mellitus, identifying a marker that can detect and assess  $\beta$  cell function at the earliest stage is crucial.<sup>6</sup> In response to glucose stimulation,  $\beta$  cells demonstrated dynamic and biphasic insulin production, marked by first-phase and second-phase responses.<sup>7</sup> First-Phase Insulin Secretion (FPIS) refers to the rapid release of insulin by  $\beta$  cells in response to intravenous glucose within 10 minutes or oral glucose within 30 minutes. Second-Phase Insulin Secretion (SPIS) is defined by a gradual and moderate rise in insulin levels following prolonged stimulation.<sup>8</sup> To assess the functionality of  $\beta$ -cells, it is essential to track insulin secretion. At present, the methods that have been proven to evaluate  $\beta$ -cell activity encompass two main tests: the intravenous glucose tolerance test (IVGT) and the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).<sup>9,10</sup>

Additionally, significant clinical usage of the homeostasis model assessment of the insulin resistance index is not financially practical, despite it being the most accessible marker for evaluating insulin resistance in clinical situations.<sup>1</sup> A thorough statistical metric that integrates fasting glucose and triglyceride levels is the Triglyceride-Glucose index (TyG index).<sup>2</sup> Because of its simplicity and lack of time and expense constraints, the TyG index is well-suited for usage with large populations and has several advantages in clinical settings.<sup>2</sup> Blood Triglycerides (TG) and Fasting Plasma Glucose (FPG) levels were used to construct the Triglyceride-Glucose index (TyG) which has been associated with a number of chronic diseases, such as metabolic syndrome, metabolic fatty liver disease, cardiovascular disease and metabolic fatty liver.<sup>11-14</sup> Recent studies uncovered a correlation between the TyG index and insulin resistance.<sup>15,16</sup> However, whether TyG is associated with the insulin secretion activity of  $\beta$ -cells is still unclear. The main causes of  $\beta$ -cell differentiation and death, which ultimately result in  $\beta$ -cell malfunction, are lipotoxicity and glucotoxicity.<sup>17</sup> Recent investigations indicate that obese individuals with elevated fasting insulin levels, although normal fasting glycemia, exhibit increased free fatty acids compared to lean control patients.<sup>18,19</sup> There is strong evidence that higher HOMA-IR (Insulin resistance) correlates positively with a higher TyG index and both tend to rise with increasing measures of adiposity or obesity linking insulin resistance, glucose-lipid dysmetabolism and excess fat mass in type 2 diabetes. The observations support the notion that increased free fatty acids may directly induce fasting hyperinsulinemia, resulting in insulin resistance.<sup>20</sup> This study analyzed the relationship of Triglyceride Glucose index (TyG) with HOMA-IR in both prediabetes and type 2 diabetes group.

#### Materials and methods

This cross-sectional analytical study was carried out on 50 patients in the Department of Biochemistry at Institute of Applied Health Sciences. The study was conducted from December 2024 to February 2025. The study was undertaken after approval by the Ethical Review Committee of Institute of Applied Health Sciences. Informed consent was obtained from each patient.

After conducting non-probability purposive sampling methods 25 prediabetes and 25 type diabetes patients was selected. Fasting blood glucose, fasting lipid profile and fasting insulin was measured. The Triglyceride Glucose index (TyG) and HOMA-IR (Homeostatic Model Assessment)-IR were calculated by following formula:-

$$\text{Triglyceride Glucose index (TyG)} = \ln [\text{Fasting triglycerides (mg/dL)} \times \text{Fasting glucose (mg/dL)}]/2.$$

$$\text{HOMA-IR} = \text{Fasting insulin } (\mu\text{IU/ml}) \times \text{Fasting glucose (mmol/l)}/22.51$$

Fasting blood glucose is measured using the hexokinase enzymatic method, where glucose is phosphorylated by hexokinase in the presence of ATP to form glucose-6-phosphate, which is then converted by Glucose-6-Phosphate Dehydrogenase (G6PD) with simultaneous reduction of NADP to NADPH.

Fasting insulin is measured using a Chemiluminescent Immunoassay (CLIA) a highly sensitive technique based on antigen-antibody binding. In this method, insulin in the sample binds to specific antibodies labeled with a chemiluminescent marker.

#### *Inclusion and exclusion criteria*

- Patients who were not merely diabetic and whose fasting blood glucose levels were between 6.1 to 6.9 mmol/l were considered prediabetes.
- Patients who were diagnosed with diabetes and whose fasting blood glucose levels were between  $\geq 7$  mmol/l on OGTT were considered diabetes mellitus.

IBM-SPSS V26.0 for Windows analysed and evaluated all the data. A p-value  $< 0.05$  indicates statistical significance. 'Variables were presented as mean  $\pm$  SEM, SD. The Kolmogorov-Smirnov Test checked for data normality and a p-value larger than 0.05 showed non-significant result. At  $p < 5\%$ , 95% confidence was considered statistically significant. For continuous data, patient characteristics were given as mean  $\pm$  standard deviation. For categorical variables, percentage and frequency distribution were employed.

## Results

**Table I** Demographic characteristics among the study population (n=50)

Variable	Prediabetes group (n=25)	Type 2 diabetes group (n=25)	p-value
Age	40.96 ± 10.2	49.83 ± 11.1	0.009*
Gender	Male 12 (52.2%)	11 (47.8%)	0.7
	Female 13 (48.1%)	14 (51.9%)	

\*p-value significant at < 0.05

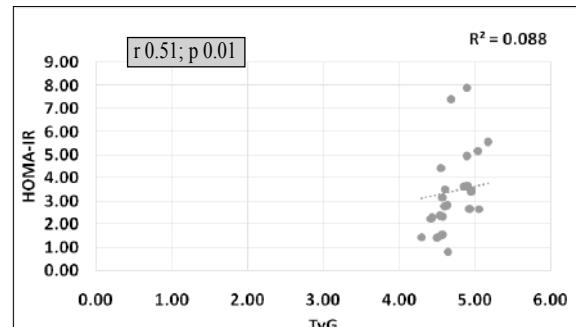
Table 1 shows a significant difference in mean age between the prediabetic group and the type 2 diabetic group.

**Table II** Biochemical and anthropometric analysis among the study population (n=50)

Variable	Prediabetes group (n=25)	Type 2 diabetes group (n=25)	p-value
BMI (kg/m <sup>2</sup> )	22.32±3.50	30.55 ± 4.7	0.001*
Fasting insulin µIU/ml	11.61±5.81	33.42±17.49	0.001*
Fasting blood glucose (mmol/l)	6.56±0.23	17.14±7.81	0.0001*
Total cholesterol (mg/dl)	182.08±52.03	186.16±49.20	0.7
Triglyceride (mg/dl)	119.0±55.02	192.87±83.47	0.001*
LDL-C (mg/dl)	120.32±45.66	120.83±38.51	0.5
HDL-C (mg/dl)	44.84±9.67	36.83±8.14	0.0001*
TyG	4.72±0.23	5.4±0.33	0.03*
HOMA-IR	3.4±1.7	27.2±5.4	0.001*

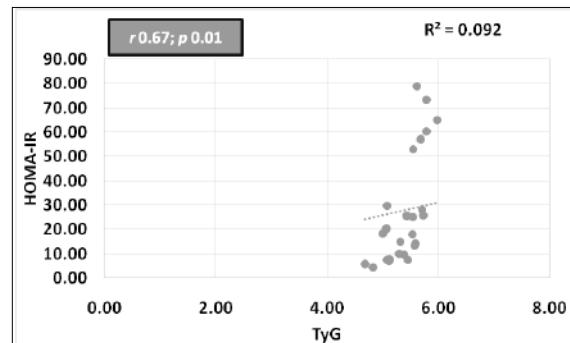
\* Independent sample t-test.

Table II shows that there is a significant mean difference in BMI, Fasting insulin, fasting blood glucose, triglyceride, HDL-C, triglyceride index and HOMA-IR between prediabetes and type 2 diabetes group.



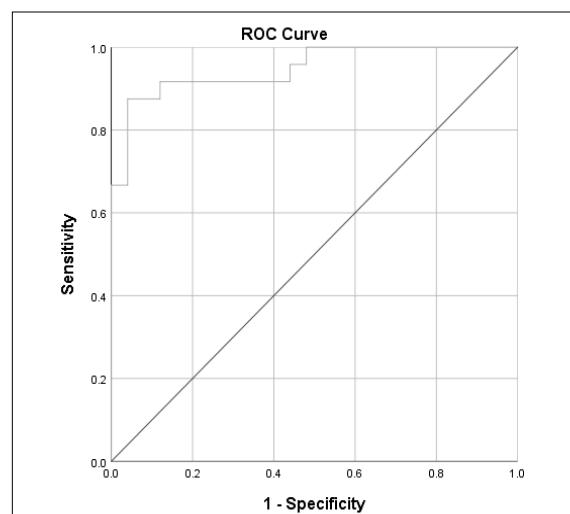
There is a significant positive correlation of TyG with HOMA-IR in prediabetes group

**Figure 1** Correlation of Triglyceride glucose index and HOMA-IR in prediabetes group (n=25)



There is a significant positive correlation of TyG with HOMA-IR in diabetes mellitus group

**Figure 2** Correlation of Triglyceride glucose index and HOMA-IR in diabetes mellitus group (n=25)



ROC curve Test the TyG value to predict type 2 diabetes mellitus. TyG index exhibits higher AUC 0.94 with CI (0.88-1.00).

**Figure 3** ROC Curve

## Discussion

According to the study of Wang Z et al. & Sun Y et al. Type 2 diabetes mellitus constitutes a substantial proportion of the total incidence of diabetes mellitus.<sup>21,2</sup> Each incremental unit in the TyG index correlates with a nearly tenfold increase in the risk of Type 2 diabetes mellitus, indicating a direct relationship between the TyG index and Type 2 diabetes mellitus risk. This study reveals a significant mean difference in the triglyceride index between the prediabetes and type 2 diabetes mellitus groups (Table II). The ROC curve test indicates that the TyG value is effective in predicting type 2 diabetes mellitus.

TyG index exhibits higher AUC 0.94 with CI (0.88-1.00) (Figure 3).

The TyG index demonstrates superior predictive capability for the onset of type 2 diabetes compared to its individual components, as evidenced by a larger area under the curve (AUC = 0.75, 95% CI 0.70–0.81) relative to fasting plasma glucose (AUC = 0.66, 95% CI 0.60–0.72) and triglyceride levels (AUC = 0.71, 95% CI 0.65–0.77).<sup>22</sup>

An increasing number of adults are being recognised as meeting the diagnostic criteria for Metabolic Syndrome (MetS). Recent studies indicate a concerning increase in the prevalence of MetS among younger populations, suggesting that these conditions are increasingly impacting individuals beyond just adults and the elderly.<sup>23</sup> The TyG index demonstrates a direct correlation with multiple metabolic risk factors, establishing it as a valuable instrument for identifying populations at heightened risk for metabolic disorders.<sup>23</sup>

Primo D et al. & Nabipoorashrafi S A et al. indicates that the TyG index serves as a more reliable predictor of MetS than HOMA-IR and other metabolic indicators.<sup>24,25</sup> The strong association between the TyG index and MetS may aid in reducing both the incidence and progression of this syndrome.<sup>23</sup>

There is a significant positive correlation of TyG with HOMA-IR in prediabetes group and diabetes mellitus group. (Figure 1,2)

### Limitation

This was a single-centre study.

Long-term follow-up was beyond the scope of the study.

### Conclusion

The Triglyceride-Glucose (TyG) index is a reliable and cost-effective marker for assessing insulin resistance.<sup>23</sup> It is derived from fasting triglyceride and glucose levels, making it an accessible alternative to the HOMA-IR. Studies have shown a strong correlation between a higher TyG index and increased insulin resistance, which is a key factor in metabolic disorders like type 2 diabetes and cardiovascular disease.<sup>23</sup> The 'TyG index is particularly useful for early detection and risk stratification in clinical and epidemiological settings. Its simplicity and predictive value make it a valuable tool for managing metabolic health.'

### Recommendation

Depending upon the study findings, the following recommendations are suggested:

- A prospective multicentered study is recommended
- Association of complications of diabetes with TyG should be tested
- Correlation between inflammatory biomarker and TyG need to be observed.

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### Contribution of authors

SKB-Conception, design, acquisition of data, data analysis, interpretation of data, drafting, critical revision & final approval.

SD-Design, acquisition of data, data analysis, drafting & final approval.

CS-Data analysis, interpretation of data, critical revision & final approval.

### Disclosure

All the authors declared no conflicts of interest.

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