ORIGINAL ARTICLE

Assessment of Triglyceride/Glucose Index as a Predictor of Insulin Resistance in Comparison with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR): in a Referral Laboratory

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ABSTRACT

Objective: To investigate triglyceride glucose index (TyG index) as a predictor of insulin resistance (IR) in comparison with homeostasis model assessment for insulin resistance (HOMA-IR) for the screening of DM in healthy adult population

Study Design: Cross-sectional comparative study.

Place and Duration of Study: The study was done at Chemical Pathology & Endocrinology Department, Armed Forces Institute of Pathology, Rawalpindi from 01st June 2022 to 31st May 2023 over a period of one year.

Materials and Methods: The study comprised 307 healthy individuals coming for laboratory investigations to our laboratory after routine annual checkup at Combine Military Hospital, Rawalpindi. Individuals of both genders aged between 18 and 35 years were included and initial history of any previous medical condition was taken. All the participants with previous history of any chronic disease were excluded. Healthy individuals who were disease free were included. Blood sample was taken in clot activator and sodium fluoride tube for lipid profile, serum insulin fasting and blood glucose fasting, respectively. Formula used for estimation of HOMA-IR was:

$HOMA\text{-}IR = \frac{\text{FPG} \times \text{Insulin}}{22.5}$. The equation used for TyG index was natural log of fasting plasma glucose and triglycerides divided by 2 i.e. $\ln\left(\frac{\text{FPG} \times \text{TG}}{2}\right)$.

Results: A comparative analysis was done using SPSS version 29.0 and revealing a significant positive correlation between the TyG index and HOMA-IR with an r value of 0.79 and *p* value = 0.001 where *p* value <0.01 is considered as significant.

Conclusion: TyG index can be used as a surrogate marker of HOMA-IR to predict insulin resistance in healthy adults population.

Key Words: *Diabetes Mellitus, HOMA-IR, Insulin Resistance, Metabolic Syndrome, TyG Index.*

Introduction

In this era of technology where information and services are readily accessible the lack of active lifestyle and increasing trend toward unbalanced diet, our world is developing many diseases which were uncommon before. The most catastrophically spreading non-communicable diseases affecting every single household in this time and age are diabetes mellitus, metabolic syndrome, obesity occurring at a very early age. Many of the ways to fight these wildly spreading diseases are addressing the root cause which is now identified as insulin resistance.[1]

Insulin resistance(IR) with a pivotal role in the development of metabolic disorders, like type 2 diabetes and cardiovascular diseases has become a significant factor to be detected at an early stage.[2] IR can be defined as a condition of decreased sensitivity of target tissues to regularly available insulin in circulation. IR is also an attribute to dyslipidemia, obesity, glucose intolerance and hypertension.[3] Dyslipidemia due to insulin resistance occurs by increased triglycerides levels, decreasing HDL levels and changing the composition of LDL molecules which ultimately leads to obesity and intima changes

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at vascular levels leading to hypertension.[4]

Worldwide the prevalence of IR varies over a range of 15.5 to 46.5%.[5] While in Pakistan, it is reported to be at 26.7% by Azeem *et al.,*[6] accurate assessment of IR is essential for early detection and customized intervention strategies. Hyperinsulinemic-Euglycemic clamp (HIEC) is considered as gold standard for estimation of IR but due to its complexity and extreme cost it is difficult to use in daily life and in smaller setups.[7] Keeping in view of this, the HOMA-IR has been widely used as a substitute indicator for IR. However, recent studies have proposed an alternative and potentially more practical tool for IR assessment which is TyG index.[8]

Among routine risk factors, the fasting blood glucose (FBG) and triglycerides (TG) are well known for their part to foresee the progress of DM. Raised FBG levels in impaired fasting glucose range have been observed to be an autonomous risk factor for type 2 diabetes.[9]

HOMA-IR is determined by fasting glucose and fasting insulin levels, and it provides an estimation of IR by evaluating the ability of insulin to reduce glucose production by the liver.[13] Pakistan is a developing country, as a nation we do not have access to many efficient and gold standard procedures due to lack of resources and high raising inflation.

Moreover, many studies have been done in our region for determination and utilization of TyG index as surrogate marker for IR for developing diabetes mellitus for high risk groups.[15] But a little work has been done on evaluation of this marker in Pakistan for this purpose in adult healthy individuals.[16]

Although HOMA-IR has demonstrated its usefulness in the screening of IR, it requires measurements of insulin, which are not always available in routine clinical practice.[14] Contrary to this, the TyG index requires only the measurement of fasting glucose and triglycerides, which are routinely measured in clinical laboratories, making it a more feasible tool for extensive assessments.

The TyG index is a new index recommended as a replacement of HOMA-IR. The TyG index is an effortless and simply calculated value. The formula to obtain the TyG index is: $\text{TyG index} = \ln\left(\frac{FPG \times TG}{2}\right)$.[10]

Thus, a strong surrogate marker for insulin resistance due to its close association with the gold standard HIEC technique is TyG index.[11] TyG index can be used as marker of IR, not only for DM but also for other diseases like metabolic syndrome.[12] Extensive literature review shows that scanty work has been done to assess the association of HOMA-IR and TyG index in patients with T2DM in Pakistan.

In our study, we not only focused on TyG index but also compared it with HOMA-IR which is a well recognized marker for determination of IR. So, our study aimed to provide some strong evidence for utilization of TyG index as a predictor of IR in comparison with HOMA-IR for the screening of DM in healthy adult population.

Materials and Methods

This cross-sectional study was conducted in the Department of Chemical Pathology & Endocrinology, Armed Forced Institute of Pathology, Rawalpindi from 1st June 2022 to 31st May 2023 after getting ethical approval from the Institutional Review Board of Armed Forced Institute of Pathology, Rawalpindi with letter reference number: FC-CHP-26/READ-IRB/21/659.

Sample size calculation was performed using World Health Organization sample size calculator which came out to be 307. Participants from 18 – 35 years who came for their annual checkup at Combined Military Hospital, Rawalpindi were selected for the study. Individuals of both genders were selected and initial history of any chronic medical condition was taken. All the participants with previous history of any chronic disease like diabetes mellitus, chronic kidney disease, ischemic heart disease and hypertension etc. were excluded. Only healthy individuals who were disease free were included which was confirmed by their history and most recent available laboratory investigations. Any individual with previously diagnosed pre-diabetes, on any special diet, pregnant females and lactating mothers were also excluded. 5ml of venous blood by aseptic technique were collected in yellow top gel tubes and sodium fluoride grey top tube. Serum/plasma centrifuged at 3500 revolutions per minute (RPM) for 5 minutes and analysed for serum lipid profile, serum insulin fasting and plasma glucose fasting.

Spectrophotometric technique was used to measure serum lipid profile and plasma glucose fasting on Siemens ADVIA 1800 Chemistry Analyzer and

chemiluminescence technique was used to measure serum insulin fasting on Advia Centaur XP. Statistical Package for Social Sciences (SPSS) version 29.0 was used for data analysis. Results were mentioned as mean ± standard deviation (SD). Pearson correlation analysis was used to examine the relationship between the TyG index and HOMA-IR. Independent t-test was applied to compare TyG index with the cutoff of HOMA-IR.

Results

A total of 307 healthy individuals with age group 18-35 years irrespective of gender were enrolled in our study. The split between the male and female was 215 (70%) and 92 (30%) shown in Fig. I. The mean age of study participants was 33 ± 6 years.

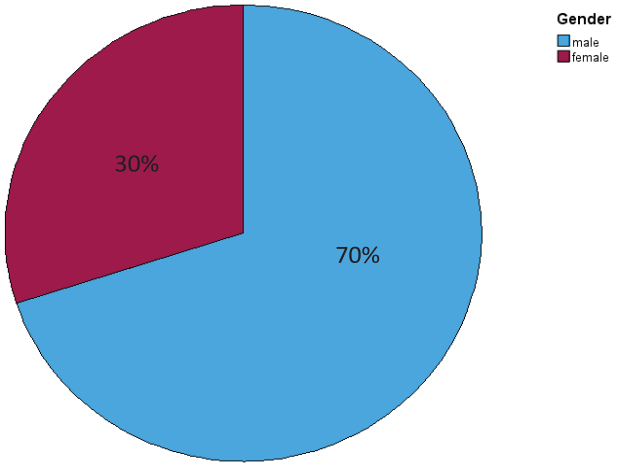

Figure 1: Distribution of Gender between the Participants

Mean and SD for serum lipid profile, serum insulin fasting and plasma glucose fasting were calculated. Mean ± SD for total cholesterol, triglyceride, LDL-C, HDL-C, glucose and insulin were 4.28±0.9 mmol/L, 1.70±0.5 mmol/L, 2.46±0.74 mmol/L, 1.01±0.29 mmol/L, 5.55±0.76 mmol/L, 11.2±4.8 µIU/ml respectively shown in Table I

Table I: Mean Value for Initial Investigations

Parameter	Mean Value
Total Cholesterol (<5.2 mmol/L)	4.28±0.9
Triglyceride (0.4-1.6 mmol/L)	1.70±0.5
LDL-C (<3.2mmol/L)	2.46±0.74
HDL-C (>1.04 mmol/L)	1.01±0.29
Glucose (< 5.6 mmol/L)	5.55±0.76
Insulin (5-25 µIU/ml)	11.2±4.8

HOMA-IR was calculated using formula: $HOMA\text{-}IR = \frac{\text{FPG} \times \text{Insulin}}{22.5}$, and already established cutoff of 2.22 was considered for insulin resistance. While for TyG index, equation used was $\text{TyG} = \ln\left(\frac{\text{FPG} \times \text{TG}}{2}\right)$.[10] The values calculated for each patient for both indices. Shapiro-Wilk test was applied to check the data distribution, which came out to be parametric. For correlation between the two indices, Pearson correlation was applied and r value= 0.79, *p* value= 0.001 (*p* value ≤ 0.01 considered significant) were observed as shown in Table II.

Table II: Pearson Correlation between HOMA-IR and TyG Index

	HOMA-IR		TyG Index	
Parameters	R value	*p* value	R value	*p* value
HOMA-IR	.	.	0.798**	0.001**
TyG Index	0.798**	0.001**	.	.

**Correlation is significant at the ≤0.01 level. HOMA-IR: Homeostasis Model Assessment for Insulin Resistance, TyG Index: Triglyceride glucose index

Individuals were separated in two groups on the basis of HOMA-IR cutoff i.e. >2.22. Both groups were compared with TyG index by applying independent t-test which came out to be significant i.e. *p* value less than 0.05 shown in Table III. TyG index score for Group 1 was 1.17 ± 0.21 and TyG index score for Group 2 was 1.70 ± 0.26.

Table III Comparison of TyG Index with Group 1 and Group 2 of HOMA-IR

HOMA-IR	Group 1* (N=120)	Group 2** (N=187)	*p* value
TyG Index	1.17 ± 0.21	1.70 ± 0.26	0.001***

* Group 1 with HOMA-IR cutoff value of <2.22
**Group 2 with HOMA-IR cutoff value >2.22
****p* value is significant at less than <0.05.HOMA-IR: Homeostasis Model Assessment for Insulin Resistance, TyG Index: Triglyceride glucose index

Discussion

In this study, 307 healthy individuals were included. Mean and SD for total cholesterol, triglyceride, LDL-c, HDL-c, glucose and insulin were 4.28±0.9 mmol/L, 1.70±0.5 mmol/L, 2.46±0.74 mmol/L, 1.01±0.29 mmol/L, 5.55±0.76 mmol/L, 11.2±4.8 µIU/ml respectively. TyG index with HOMA-IR was compared using Pearson Correlation which showed correlation with r value=0.798. This showed that TyG index can be used for determination of IR even if the HOMA-IR calculation is not possible.

A study done at Dow University by Kanpurwala *et al.*,[17] for TyG index evaluation showed its significance in different groups and showed high significance in

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group with higher risk of developing IR i.e. offspring of parents who has DM. In their study, they only used TyG index with lipid profile and no marker for IR was used. While in our study we took only the healthy individual without any family history of DM and we used HOMA-IR for comparison of TyG index.

Many studies have compared the TyG index and HOMA-IR in various populations and have found TyG index to be comparable or even superior in identifying insulin resistance. Kang *et al*.,[18] compared TyG index and HOMA-IR in adolescents and found the correlation to be significant at r value= 0.41, while in our study we compared both indices in adults with a significant correlation at r value=0.79. So, they concluded that TyG index can be used at an early age for the detection of insulin resistance. This goes in accordance with our study which also suggests TyG index usage for screening of IR.[2]

Lee *et al*.,[19] carried out a cohort study in Korea over a period of 4.5 years and suggested the superiority of TyG index in comparison to other indices. In their study, they enrolled 5,354 non-diabetic subjects of middle-age and followed the cases for 4.5 years closely assessing the subjects for developing diabetes. They concluded that TyG index is more efficient in detecting in IR than the other indices available including HOMA-IR with r value= 0.27 and *p* value <0.0001 when compared with non-diabetics and diabetics individuals. While, we only focused our study to comparison of TyG index with HOMA-IR which showed TyG index to be comparable to HOMA-IR.

Locateli *et al.,*[20] used the same indices to compare in South American obese adolescent and adult population and suggested it to be a reliable marker for assessment of IR. He also added another index to improve the efficacy of TyG index i.e. TG/HDL-C index, which also uses the day-to-day profiles to assess the IR risk. In our study, we took all the individuals from general population with different BMIs and did not considered BMI as the major confounding factor in the determination of both indices. Nonetheless, our study showed higher indices as the BMI increases.

Selvi *et al.,*[21] in their study took one step further and estimated utilization of TyG index for assessment of glycemic control in diabetics. In their study, they enrolled 140 patients of T2DM and divided them into 2 groups with good glycemic control of HbA1c value <7.0% and poor glycemic control of HbA1c value >7.0%. They concluded that TyG index can be efficiently used in assessment of TyG index as compared with HbA1c and HOMA-IR with r value= 0.46 and *p* value =0.001. While our study also showed a strong comparison between these 2 markers with r value=0.79 and *p* value <0.001. Thus, TyG index is proved to be a reliable marker, not only for risk estimation, but also management of DM.

Lv *et al*.,[22] performed a cross-sectional study on patients of T2DM and checked utilization of TyG index for estimation of diabetic kidney disease (DKD). For this purpose, they took 1432 patients, and compared their TyG index alongwith microalbuminuria and eGFR. In their study, they showed significant correlation between the TyG index and development of DKD, claiming it to be a potential marker for DKD risk evaluation. Our study lacked the determination of role of TyG index in diabetic population, which can be also be helpful in our region as most diabetic patients donot have access to state of the art labs performing robust techniques.

Many studies were carried out to assess the significance of TyG index in diseases other than DM. One of the studies was carried out by Song *et al*.,[23] for evaluation of non-alcoholic fatty liver disease (NAFLD) utilizing TyG index. In their study, they included 225 patients in their study diagnosed with different grades of NAFLD and TyG and its modified indices were compared in these different grades. TyG index along with its modified indices came out to be useful for evaluation of NAFLD. As we focused on TyG index role in IR we were not able to compare its role in other disease. Thus, TyG index is not only efficient for screening and monitoring of DM but can also be utilized for diagnosis and monitoring of other diseases, proving its utilization for broader spectrum.

Conclusion

The TyG index shows promise as a practical and accessible surrogate marker for insulin resistance in adults, potentially surpassing the limitations associated with the HOMA-IR method. Its strong correlation with insulin resistance and association with metabolic disorders suggests that the TyG index can be a valuable addition to routine clinical practice

and epidemiological studies.

Limitations of study

Multiple other factors like BMI, family history, lifestyle evaluation and activity levels which are considered important for the identification of insulin resistance are important for more focused approach to tackle this havoc. This was single centered study, in which we have used cross-sectional data.

Recommendations

Standardized cut-offs for our population should be established to ensure consistent interpretation and clinical application of the TyG index. So further investigation, validation, and consensus among the medical community are necessary before widespread adoption in clinical practice. For evaluation of cutoff in our region, study should be done with the gold standard test which is HIEC and it is currently not available in Pakistan. Moreover, in future a multi-centric long-term study can be done to confirm the importance of this index in various other ethnic populations. Further studies could investigate the longitudinal predictive value of TyG for various health outcomes or evaluate its utility in guiding interventions for IR and related conditions.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.