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Study To Establish Triglyceride Glucose Index's Correlation With Various Markers Related To Insulin Resistance

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Abstract

Background: Diabetes Mellitus is a complex metabolic disorder, which results from absolute or relative deficiency in insulin secretion and or its action. Triglyceride Glucose Index (TyG index) calculated as the product of Triglyceride (TG) and Fasting Plasma Glucose (FPG) levels presents moderate power as a surrogate marker for estimating IR. Present study was aimed to establish triglyceride glucose index's correlation with various markers related insulin resistance. **Material and Methods:** Present study was cross sectional study, conducted in patients > 18 years age, newly detected type 2 diabetes mellitus, patients with impaired fasting glucose. Individuals were grouped in to Insulin resistant group (Group IR +) and Insulin resistance absent group (Group IR-) according to ATPIII criteria. **Results:** In present study, out of 120 subjects, 70 were males and 50 were females. 73 had signs of Insulin resistance, while 47 did not have. There was a positive correlation between TyG levels and SBP, between TYG levels and DBP, a positive correlation between TyG levels and FBS, a positive correlation between TyG levels and PPBS, a positive correlation between TYG levels and TC, a positive correlation between TyG levels and TG, a negative correlation between TYG levels and HDL & a positive correlation between TyG levels and LDL. Majority of the study subjects in IR -ve group are distributed < 3 HOMA Score group (97.87%) and 3-5 HOMA Score group in IR +ve group (57.53%), thereby giving a statistical significance. There is a positive correlation between TyG levels and HOMA score. Sensitivity of TyG was 84%, specificity of TyG was 83%, positive predictive value of TyG was 64% & negative predictive value of TyG was 93%. **Conclusion:** Age, BMI, waist circumference, WHR, fasting and postprandial blood sugars and all the lipid parameters. TyG index cutoff was calculated. Those with 8.65 were definitely diabetics.

Keywords: triglyceride glucose index, insulin resistance, HOMA IR, diabetes mellitus

Introduction

Diabetes Mellitus is a complex metabolic disorder, which results from absolute or relative deficiency in insulin secretion and or its action".[1] There has been a continuous increase in the global prevalence of diabetes and its devastating effects on life expectancy and quality of life of individuals.

It has been suggested that a derangement of lipid metabolism is an early event contributing to the development of both hyperinsulinemia and insulin resistance.[2] Insulin resistance (IR) involves reduced muscle and adipose tissue sensitivities to insulin and reduced ability of the liver to suppress hepatic glucose production and output. IR is considered a major ri.sk factor for type 2 diabetes and cardiovascular diseases (CVD).[3,4] Because of the clinical importance of IR, the ability to identify individuals with IR before the development of cardiometabolic diseases is of paramount importance. Although the hyperinsulinemic euglycemia clamp remains the gold standard for measuring IR, its practical clinical application is limited by the labor intensiveness and cost and by ethical concerns.[5]

Therefore, a simple, reliable, and reproducible index for measuring IR is urgently required. It has been

demonstrated that the product of Triglyceride (TG) and Fasting Plasma Glucose (FPG) levels Triglyceride Glucose Index (TyG index) presents moderate power as a surrogate marker for estimating IR. The superiority of the TyG index in identifying IR was also reported in many other studies.[6] With these findings, a highly efficient substitute measure to establish IR can be easily applied in our clinical settings to measure the same in large scale of population where impending diabetes is at a escalating trend. Present study was aimed to establish triglyceride glucose index's correlation with various markers related insulin resistance

Material And Methods

Present study was single-center, cross sectional study, conducted in department of General Medicine, at Bharati vidyapeeth medical college & hospital, sangli, India. Study duration was of 6 months (March 2022 to September 2022). Study approval was obtained from institutional ethical committee.

Inclusion Criteria

Patients > 18 years age, either gender, Newly detected type 2 diabetes mellitus, patients with impaired fasting glucose, willing to participate in present study

Exclusion Criteria

1. Type 1 diabetes
2. Patient already on insulin or insulin sensitisers, lipid lowering drugs, steroids, antipsychotics etc.
3. Gestational diabetes
4. Secondary diabetes
5. Patient in ketoacidosis or extremely sick.

Study was explained to patients in local language & written consent was taken for participation & study. All persons were analysed with proforma with detailed history taking and anthropometry, vitals, system examination and require investigations were carried out. Data regarding clinical history and relevant information about cardiovascular disease (coronary heart disease, cerebrovascular disease, peripheral arterial disease), cancer and psychiatric diseases, lifestyle behaviour including cigarette smoking (none, former smoker or current smoker), daily alcohol intake (yes/no) and lifestyle pattern (physically active/sedentary behaviour) was noted.

Anthropometric measurements (weight, height and BMI) and BP, were taken as per standardized methods. BMI was calculated as the body mass divided by the square of the body height and expressed in units of kg/m2. Waist circumference, hip circumference, neck circumference and waist hip ratio were also measured .

Routine biochemical data including FPG, fasting insulin (done using CLIA method , for calculating HOMAIR), Total cholesterol (TC), TG, HDL cholesterol (HDL-C), and LDL cholesterol (LDL-C) were also retrieved. Blood samples were drawn after an 8-h of fasting and analyzed in a central laboratory with Chemistry Analyzer under strict quality control. FPG was measured through the hexokinase method. TC, HDL-C and TG were determined using enzymatic colorimetric tests and LDL-C was calculated using 134 the Friedewald formula.

The TyG index was calculated as

ln[fasting Triglycerides (mg/dl) x Fasting glucose (mg(dl)/2].

Individuals were grouped in to Insulin resistant group (Group IR +) and Insulin resistance absent group (Group IR-) according to ATPIII criteria (Individuals with 3 or more of following 5 abnormalities were considered to have insulin resistance syndrome [IRS] :

1. abdominal obesity WC > 102 cm in men and > 88 cm in women
2. elevated BP systolic BP >= 130 mm hg or diastolic BP >= 85 mm hg
3. hypertriglyceridemia >= 1.7mmol/l
4. HDL <= 1.04mmol/l in men and <1.29 mmol/l in women
5. High fasting blood glucose >= 6.1mmol/l).

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

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In present study, out of 120 subjects, 70 were males and 50 were females. 73 had signs of Insulin resistance, while 47 did not have. Majority of the study subjects in IR -ve group are distributed in 41-50 years age group (40.43%) and same age group in IR +ve group (41.10%) (p=0.4844, unpaired t test), thereby showing no statistical significance . Majority of the study subjects in IR -ve group are males (59.57%) and same too in IR +ve group (57.53%) (p=0.8249, chi square test), showing no significant statistical association.

Table 1- General characteristics

	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
Age groups (in years)			
≤ 40	12 (25.53 %)	17 (23.29 %)	
40-49	19 (40.43 %)	30 (41.1 %)	
50-59	15 (31.91 %)	25 (34.23 %)	
60-69	1 (2.13 %)	1 (1.37 %)	
70-79			
Mean age	46.26 ± 7.42	47.26 ± 7.81	0.4844
Gender			
Male	28 (59.57 %)	42 (57.53 %)	0.8249
Female	19 (40.43 %)	31 (42.47 %)	

There was a positive correlation between TyG levels and age, indicated by the Pearson's R Correlation value of 0.21 with a poor statistical significance with a p-value of 0.0232.

Regression Statistics - TyG Vs Age	
Pearson's R	0.21
R Square	0.04
P value - ANOVA	0.0232

Majority of the study subjects in IR -ve group had normal BMI (89.35%) and were overweight in IR +ve group (56.16%) (p= <0.0001), showing a statistical significance.

Table 2 - BMI distribution

BMI groups	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
Normal	42 (89.36 %)	5 (6.85 %)	
Overweight	3 (6.38 %)	41 (56.16 %)	
Obese	2 (4.26 %)	27 (36.99 %)	
Mean BMI	23.21 ± 2.38	29.03 ± 2.22	< 0.0001

There was a positive correlation between TYG levels and BMI. This is indicated by the Pearson's R Correlation value of 0.65 and a statistically significant p-value of <0.0001.

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Regression Statistics - TyG Vs BMI	
Pearson's R	0.65
R Square	0.42
P value ANOVA	<0.0001

Majority of the study subjects in IR -ve group had 90-100 cms waist circumference group (91.49%) and 101-110 cms waist circumference group in IR +ve group (80.82%) (p= <0.0001, unpaired t test) , thereby showing a statistical significance.

Table 3 - Waist circumference versus Insulin resistance

Waist circumference	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
≤ 90	2 (4.26 %)	1 (1.37 %)	
91-100	43 (91.49 %)	13 (17.81 %)	
101-110	2 (4.26 %)	59 (80.82 %)	
Mean waist circumference	95.31 ± 3.29	102.87 ± 3.6	< 0.0001

There is a positive correlation between TYG levels and waist circumference. This is indicated by the Pearson's R Correlation value of 0.21 statistically insignificant with a p value of 0.0208.

Regression Statistics - TyG Vs WC	
Pearson's R	0.21
R Square	0.04
P value ANOVA	0.0208

Majority of the study subjects in IR -ve group had ≤ 0.80 waist hip ratio (36.17%) and > 1.00 waist circumference group in IR +ve group (67.12%) (p= <0.0001, unpaired t test), thereby showing a statistical significance.

Table 4- Waist hip ratio VS Insulin resistance

Waist circumference	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
≤ 0.8	17 (36.17 %)	4 (5.48 %)	
0.81-0.9	12 (25.53 %)	2 (2.74 %)	
0.91-1	10 (21.28 %)	18 (25.53 %)	
>1	8 (17.02 %)	49 (80.82 %)	
Mean waist hip ratio	0.89 ± 0.18	1.02 ± 0.14	< 0.0001

There was a positive correlation between TyG levels and waist hip ratio, indicated by the Pearson's R Correlation value of 0.30 and a statistically significant p value of 0.0007.

Regression Statistics - TyG Vs WHR	
Pearson's R	0.30
R Square	0.09
P value ANOVA	0.0007

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No statistical significance was noted with regards to blood pressure (SBP & DBP) among group IR (-) & IR (+). The mean FBS values are 104.91 mg/dl in IR -ve group and 173.66 mg/dl in IR +ve group (p <0.0001, unpaired t test). The mean PPBS values are 120.98 mg/dl in IR -ve group and 202.32 mg/dl in IR +ve group (p <0.0001, unpaired t test). Hence there is significant statistical association.

The mean cholesterol values are 150.47 mg/dl in IR -ve group and 219.22 mg/dl in IR +ve group (p <0.0001, unpaired t test). The mean TGL values are 113.64 mg/dl in IR -ve group and 198.76 mg/dl in IR +ve group (p <0.0001, unpaired t test). The mean HDL values are 37.91 mg/dl in IR -ve group and 22.88 mg/dl in IR +ve group (p <0.0001, unpaired t test). The mean LDL values are 102.85 mg/dl in IR -ve group and 146.78 mg/dl in IR +ve group (p <0.0001, unpaired t test). Lipid parameters on analyzing gave a statistical significance.

There was a positive correlation between TyG levels and SBP, between TYG levels and DBP, a positive correlation between TyG levels and FBS, a positive correlation between TyG levels and PPBS, a positive correlation between TYG levels and TC, a positive correlation between TyG levels and TG, a negative correlation between TYG levels and HDL & a positive correlation between TyG levels and LDL.

Table 5- Blood parameters

Parameters	Group IR (-) (n=47)	Group IR (+) (n=73)	P value	Pearson's R	R Square	P value ANOVA
SBP	129.79 ± 10.13	131.26 ± 11.18	0.4665	0.17	0.03	0,0625
DBP	84.02 ± 5.66	84.22 ± 6.03	0.8577	0.17	0.03	0,0576
FBS	104.91 ± 32.41	173.66 ± 55.06	< 0.0001	0.85	0.73	<0.0001
PPBS	120.98 ± 33.34	202.32 ± 66.69	< 0.0001	0.82	0.68	<0.0001
Lipid profile						
Total Cholesterol	150.47 ± 14.48	219.22 ± 28.69	< 0.0001	0.7	0.49	<0.0001
Triglycerides	113.64 ± 43.93	198.78 ± 76.74	< 0.0001	0.85	0.73	<0.0001
HDL	37.91 ± 7.73	22.88 ± 6.7	< 0.0001	-0.59	0.34	<0.0001
LDL	102.85 ± 14.95	146.78 ± 16.93	< 0.0001	0.68	0.46	<0.0001

Majority of the study subjects in IR -ve group are distributed in 5.01-10 µIU/mL fasting insulin group (78.72%) and 10.01-15.00 µIU/mL fasting insulin group in IR +ve group (54.79%) (p= <0.0001, unpaired t test), thereby showing statistical significance . There is a positive correlation between TyG levels and fasting insulin.

Table -6 FASTING INSULIN VS INSULIN RESISTANCE

Fasting insulin (µIU/mL)	Group IR (-) (n=47)	Group IR (+) (n=73)	P value	Pearson's R	R Square	P value ANOVA
≤ 5	5 (10.64 %)	0				
5.01-10	37 (78.72 %)	27 (36.99 %)				
10.01-15	5 (10.64 %)	40 (40.79 %)				

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>15	0	6 (8.22 %)				
Mean age (mean ± SD)	7.64 ± 1.91	11.17 ± 2.75	< 0.0001	0.16	0.03	0.0822

Majority of the study subjects in IR -ve group are distributed < 3 HOMA Score group (n=46, 97.87%) and 3-5 HOMA Score group in IR +ve group (n=42, 57.53%) (p= <0.0001, unpaired t test), thereby giving a statistical significance. There is a positive correlation between TyG levels and HOMA score. This is indicated by the Pearson's R Correlation value of 0.79 and a statistically significant correlation with a p value of less than 0.0001.

Table 7- HOMA IR vs insulin resistance

HOMA IR Score	Group IR (-) (n=47)	Group IR (+) (n=73)	P value	Pearson's R	R Square	P value ANOVA
<3	46 (97.87 %)	6 (8.22 %)				
3-5	1 (2.13 %)	42 (57.53 %)				
>5	0	25 (34.25 %)				
Mean HOMA IR Score (mean ± SD)	1.83 ± 0.42	4.55 ± 1.05	< 0.0001	0.79	0.79	<0.0001

Majority of the study subjects in IR -ve group are distributed > 8.5 triglyceride and glucose index group (n=26, 55.32%) and same group in IR +ve group (n=67, 91.78%) (p <0.0001, unpaired t test), having good statistical significance.

Table 8 - Triglyceride glucose index vs insulin resistance

triglyceride and glucose index group	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
≤8.5	21 (44.68 %)	6 (8.22 %)	
>8.5	26 (55.32 %)	67 (91.78 %)	
Mean triglyceride and glucose index group	8.66 ± 0.54	9.64 ± 0.62	< 0.0001

Majority of the study subjects in IR -ve group are diagnosed as no metabolic syndrome (n=37, 78.72%) and same too in IR +ve group (n=57, 78.08%) (p=0.9337, chi squared test). No statistical significance is achieved with regards to metabolic syndrome.

Table 9- Metabolic syndrome vs insulin resistance

Metabolic syndrome	Group IR (-) (n=47)	Group IR (+) (n=73)	P value
Present	10 (21.28 %)	16 (21.92 %)	0.9337
Absent	37 (78.72 %)	57 (78.08 %)	

Sensitivity of TyG is high, meaning that 84% of those with DM will have a positive test result with TyG, Specificity of TyG is high, meaning that 83% of those without DM will have a negative test result with TyG. Positive predictive value of TyG is high, meaning 64% of individuals with positive TyG test will actually have DM. Negative predictive value of TyG is high, meaning 93% of individuals with negative TyG test will actually not have DM. HOMA IR

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Sensitivity of HOMA IR is high, meaning that 79% of those with DM will have a positive test result with HOMA IR. Specificity of HOMA IR is high, meaning that 69% of those without DM will have a negative test result with HOMA IR. Positive predictive value of HOMA IR is high, meaning 48% of individuals with positive HOMA IR test will actually have DM. Negative predictive value of HOMA IR is high, meaning 90% of of individuals with negative HOMA IR test will actually not have DM

Table 10 – Accuracy analysis

Accuracy Analysis	Cut Off	Sensitivity	Specificity	PPV	NPV	LR +	LR -	AUC	P value
TyG	8.65	0.84	0.83	0.64	0.93	4.87	0.19	0.900	<0.0001
HOMA IR	3.54	0.79	0.69	0.48	0.90	2.57	0.30	0.855	<0.0001

Discussion

Diabetes is a major health issue in most of the South East Asian countries, especially in India where carbohydrates form the bulk of staple food Sedentary life style and decrease in day to day physical activities along with high calorie junk foods which is popular among the youth is another important factor in the increase in trend of diabetes worldwide.

Every second individual in the world will be affected by diabetes soon. India has the largest diabetic population in the world and is infamously dubbed as "The Diabetic capital" of the world. According to Indian council of Medical Research (ICMR), India is faced with galloping diabetes epidemic, approximately more than 70 million patients are affected with diabetes in India and this number is projected to cross beyond hundred million by the year 2030.[2,3]

Type 2 diabetes mellitus has foremost clinical and social, impact, but its causal pathophysiology is below par to be understood. Since the disease is diagnosed as a disorder of carbohydrate metabolism, i.e., hyperglycemia, the possible contribution of abnormal lipid metabolism to its etiology has been largely overlooked.[4] The predominant, obesity related form of diabetes is characterized by hyperinsulinemia, resistance to insulin-mediated glucose disposal in skeletal muscle, and elevated plasma free fatty acid and triglyceride levels.[7,8]

The prime intention of this study is to test whether the novel and simple marker of insulin resistance (i.e) TyG-Index, associates with the presence of carotid atherosclerosis, and other metabolic and anthropometric parameters and above all its efficiency when compared with the classic HOMA IR which is being used for insulin resistance estimation in a wide basis.[7] Kajaija et al.,[9] which stated that there is no statistical significance to TyG index with regards to age and gender. This study also brought a interesting finding that TyG index gradually increased with age in those with normal glycemia and with fasting glucose in the range 101–125 mg/dl, while there was a slow but progressive decrease in individuals with glycaemia of >125 mg/dl.

The decreased difference in mean waist hip ratio in IR -ve group compared to IR +ve group was 0.13 points, showing a 13% reduction, establishing a independent positive association with insulin resistance. These findings were consistent with yet another study done by Tingting du et al.,[10] in a set of Chinese population which brought out similar results (significant statistical association of lipid parameters and TyG index). However, it also brought out an interesting fact that models with lipid ratios were consistently superior to lipid variables used alone for prediction.

The difference in the percentages of metabolic syndrome patients in IR -ve group and IR +ve group (0.64) was found to be statistically insignificant (p >0.05), the difference in the percentages of carotid intimal thickness in IR -ve group and IR +ve group was found to be statistically insignificant (p = 0.1083). HOMA score increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 1.63 unit increase in HOMA

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score there is a 1 unit increase in TyG among the study subjects.

The diagnostic effectiveness or diagnostic accuracy in relation to TyG test is an excellent case finding or diagnostic test with high specificity and PPV suggesting that false positives are very rare. It is also a good screening test with high sensitivity and NPV suggesting that high false negative tests will occur rarely compared to HOMA IR. TyG index also gave a positive correlation with HOMA IR; Indeed, the ROC curve analysis showed that TyG index had the largest AUC, thus demonstrating its superior performance in recognizing IR than HOMAIR

Our study is consistent with the findings of another study done by Irace et al [119] conducted in an Italian cohort which proved that TyG index is better compared to HOMA IR in assessing insulin resistance. Our study also have got a consistency with a similar study done in a argentinal cohort by Giselaunger et al [120] which first came up with the proof that TyG index is a good discriminant of metabolic syndrome .

All patients who are insulin resistant should advised to undergo strength training, endurance exercise (walking 5 days a week for about 30 minutes a day) and other anaerobic activities; avoidance of smoking and tobacco ; low carb , high protein diet is advised ; foods rich in omega 3 fatty acids are also encouraged; vitamin D and magnesium supplements are added along with follow up medical checkup .

Our study had few limitations. First, because of the cross sectional design, the associations were not prospective and causality cannot be inferred. Further longitudinal study is necessary to confirm if TyG index may predict future occurrence of IR. Secondly, because the study includes south Indian individuals, the results cannot be generalized to other ethnicity; As triglyceride levels varies according to ethnicity, further research is required to evaluate TyG index in different populations

Conclusion

TyG index established a positive correlation with Age, BMI, waist circumference, WHR, fasting and postprandial blood sugars and all the lipid parameters. TyG index cutoff was calculated. Those with 8.65 were definitely diabetics. If these data are established in future observations, and in other populations, the TyG-Index could be converted in to a simple but effective tool for risk assessment in daily clinical practice.

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