

Association of Triglyceride/High-Density Lipoprotein Cholesterol (Tg/Hdl-C) Ratio and Triglyceride-Glucose (Tyg) Index with Hba1c in Patients with Type 2 Diabetes Mellitus - A Retrospective Study

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ABSTRACT

Background: One of the most prevalent non-communicable diseases worldwide, including in India, is diabetes mellitus (DM), which is also a major public health concern. Hyperglycemia, or elevated blood glucose levels, is a hallmark of this chronic metabolic disorder that results from either insufficient insulin action or synthesis, or both. Microvascular and macrovascular problems include diabetic nephropathy, retinopathy and neuropathy, coronary artery disease, peripheral arterial disease, and stroke can develop early if type 2 diabetes is left untreated and uncontrolled. Triglyceride-glucose index (TyG index) calculated according to fasting blood glucose (FBG) and triglyceride (TG) measurements can also be used as an indicator of insulin resistance. The aim of this study was to evaluate the association of TG/HDL-C ratio and TyG index with glycated hemoglobin levels in Type 2 diabetic patients.

Materials and Methods: The current research investigated Serum lipid profile, TyG index, TG/HDL-C and glycemic status to examine different metabolic alterations in Type 2 DM patients with good glycemic control compared to poor glycemic control. Standard methods were followed.

Results: TyG index was higher in patients with poor glycemic control (HbA1c \geq 7%) compared to patients with good glycemic control (HbA1c<7%). TyG index are positively associated with HbA1c levels in Type 2 DM patients.

Key words: Diabetes mellitus, Triglyceride-glucose index, serum lipid profile.

INTRODUCTION:

Diabetes mellitus (DM) is a major public health concern as well as one of the most common non-communicable diseases in the world, including India. This chronic metabolic disease is characterized by hyperglycemia (increased blood glucose levels) caused due to deficiency in insulin production, action or both [1]. The majority of people with diabetes (90–95%) have Type 2 Diabetes Mellitus (T2DM) [2]. Type 2 diabetes mellitus (Type 2 DM) is a metabolic disorder characterized by hyperglycemia due to combination of insulin resistance and/or inadequate insulin secretion [3]. Insulin resistance (IR) leads to impaired glucose tolerance, and plays an important pathophysiological role in the development of diabetes and is a hallmark of obesity, dyslipidemias, hypertension, and other components of the metabolic syndrome [4,5,6].

The higher prevalence of lipid abnormalities in diabetes mellitus has been attributed to insulin resistance and its associated complications. Effective glycemic control and enhancing insulin sensitivity are essential in order to reduce the risk of developing diabetes complications [7].

The golden method of evaluating insulin resistance is hyperinsulinemic euglycemic glucose clamp (HEGC) [8]. It is more complex, too costly, time-consuming and invasive method that is not feasible for routine clinical application. Alternatively, the homeostasis model assessment for insulin resistance (HOMA-IR) index is widely used in clinical practice to evaluate insulin resistance using fasting state measurements [9]. However, the plasma insulin or C-peptide assay is expensive, or it is not easily available in all laboratories and has poor reproducibility. Thus, there is a need for new biomarkers that are easier to detect and more affordable.

Recently, some novel and simple indicators have been reported to be reliable surrogate indexes of IR, such as the triglyceride-glucose (TyG) index and the triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio.

Triglyceride-glucose index (TyG index) calculated according to fasting blood glucose (FBG) and triglyceride (TG) measurements can also be used as an indicator of insulin resistance. The TyG index is calculated as $\ln [\text{fasting TG (mg/dL)} \times \text{FBG (mg/dL)} / 2]$ [10].

Majority of studies conducted to date have explored association between TG/HDL-C ratio and insulin resistance in diabetic patients (11, 12). However, studies that aimed to assess association between TG/HDL-C ratio and glycemic control, and association between TyG index and glycemic control are limited. Therefore, the aim of this retrospective study was to evaluate the association of TG/HDL-C ratio and TyG index with glycosylated hemoglobin levels in Type 2 diabetic patients.

AIM:

To find out the association of Triglyceride/HDL-cholesterol (TG/HDL-C) ratio and Triglyceride-Glucose index (TyG index) with glycemic control (HbA1c) in patients with Type 2 DM.

OBJECTIVES:

1. To calculate TG/HDL-C ratio and Triglyceride-Glucose index in type 2 DM patient with good and poor glycemic control
2. To find out the association of Triglyceride/HDL cholesterol (TG/HDL-C) ratio and Triglyceride-Glucose index (TyG index) with HbA1c in patients with type 2 DM.

MATERIALS AND METHODS:

The results of 490 Type 2 diabetes mellitus patients, aged 30 to 60, receiving treatment with hyperglycemic medications, were gathered from the ASOTA at a tertiary care center in Puducherry between September 1, 2020, and August 31, 2021. This study was a retrospective investigation. The individuals were split into two groups based on their HbA1c levels: the excellent glycemic control group (if their HbA1c was less than 7.0%) and the poor glycemic control group (if their HbA1c was greater than 7.0%). Participants in this study were not allowed to have type 1 diabetes mellitus, be pregnant, or have a history of hyperthyroidism, hypothyroidism, autoimmune disorders, cardiovascular illness, liver disease, renal disease, or muscular diseases.

METHODOLOGY:

The glucose oxidase technique was used to measure the fasting plasma glucose (FG) level. A high-performance liquid chromatography was used to measure HbA1c. High-density lipoprotein cholesterol (HDL-C) levels were assessed using a direct homogeneous enzymatic approach, serum total cholesterol (TC) was estimated using the cholesterol oxidase method, and serum triglyceride (TG) levels were estimated using the glycerol oxidase method. Using Friedewald's equation, the low-density lipoprotein cholesterol (LDL-C) was determined.

The TG/HDL-C ratio was calculated by dividing the serum concentration of TG by HDL-C measured in mg/dL [13]. TyG index was calculated based on formula: $\ln [\text{TG (mg/dL)} \times \text{FG (mg/dL)} / 2]$, according to the previous studies [14, 15].

Bergmeyer HU and Bernt E (1974) methodology was followed for estimation of fasting and postprandial plasma glucose by Hexokinase Method HU [16].

Determination of Glycosylated Hemoglobin (HbA1c) by Cation-Exchange HPLC Method was followed by Hoshino et al., 1988 [17].

Allain et al. (1974) standard method was followed for the estimation of Total Cholesterol by CHOD-PAP Enzymatic Method [18].

Estimation of Triglyceride by Glycerol 3 P-Oxidase-Peroxidase Method (GPO-POD) by Bucolo and David (1973) and estimation of HDL-Cholesterol by immuno FS-Homogeneous Direct Method by Warnick et al. (1982) [19,20].

Low-density Lipoprotein-Cholesterol (LDL-C) and Very Low-Density Lipoprotein (VLDL-C) by Calculation Method Friedewald et al., (1972) [21].

STATISTICAL ANALYSIS:

JASP 0.14 software was used to analyze the data and the results are presented as Mean±SD. The independent t test was used to assess the group mean differences. The association between the

TyG index, HbA1c, and TGL/HDL was evaluated using Pearson's correlation analysis. Statistical significance was defined as a two-sided p-value of less than 0.05.

RESULTS:

Baseline characteristics:

Table 1 shows the baseline characteristics and anthropometric measurement of Type 2 diabetic subjects with good and poor glycemic control.

The mean age of the type 2 diabetes with good glycemic control and poor glycemic control subjects were 48 ± 12 and 49 ± 11 years respectively. There was no significant difference observed in age group between two groups, $p=0.434$.

Anthropometric measurement:

BMI: The mean BMI level was significantly increased (26.82 ± 3.36 , $p=0.000$) in diabetic subjects with poor glycemic control than diabetic subjects with good glycemic control as shown in the table 1.

Table 1: Baseline characteristics and anthropometric measurement among Type 2 diabetic patients with good glycemic control and poor glycemic control subjects

Parameters	Group I (Type 2 DM with good glycemic control) N=345	Group II (Type 2 DM with poor glycemic control) N=145	p value
Age (Years)	48 ± 12	49 ± 11	0.434
Gender (%)	M - 193 (55.94%) F - 152 (44.06%)	M - 74 (51.03%) F - 71 (48.97%)	
Body Mass Index (BMI)	24.67 ± 2.90	26.82 ± 3.36	<.001*

* $p<0.05$ significant; Data are expressed in Mean \pm standard deviation; p values are estimated between two groups by using Student 't' test.

Glycemic status: The mean fasting plasma glucose (FBS), Post Prandial plasma glucose and glycated hemoglobin (HbA1c) levels were significantly increased (172 ± 74 ; 260 ± 82 ; 9.2 ± 1.82 , $p<.001$) in Type 2 Diabetic patients with poor glycemic control when compared to Type 2 Diabetic patients with good glycemic control (91 ± 14 ; 128 ± 37 ; 5.9 ± 0.47) as shown in table 2. The mean duration of diabetes was more than 5 years in both groups. A significant difference was observed for duration of diabetes among two groups by using Student 't' test, $p<0.001$.

Table 2: Comparison of glycemic status among study groups

Parameters	Group I (Type 2 DM with good glycemic control) N=345	Group II (Type 2 DM with poor glycemic control) N=145	p value
Fasting plasma glucose (mg/dL)	91 ± 14	172 ± 74	<.001*
Post Prandial plasma glucose (mg/dL)	128 ± 37	260 ± 82	<.001*
HbA1c (%)	5.9 ± 0.47	9.2 ± 1.82	<.001*
Duration of diabetes	7.29 ± 2.44	8.77 ± 3.58	<.001*

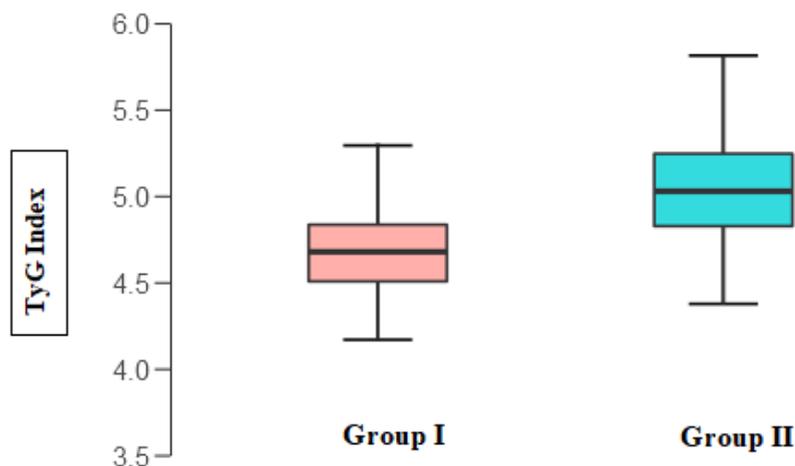
* $p<0.05$ significant; Data are expressed in Mean \pm standard deviation; p values are estimated among two groups by using student "t" test; HbA1c=Glycosylated haemoglobin.

Serum lipid profile: Table 3 represents the comparison of serum lipid profile between the study groups. The mean serum total cholesterol (221 ± 63), triglycerides (167 ± 76) and VLDL-C (34 ± 16) levels were

significantly increased ($p < .001$) in Type 2 diabetes with poor glycemic controls compared to Type 2 diabetes with good glycemic control. However, there is no significant difference observed in mean serum HDL-C and LDL-C between two groups.

Serum TyG index and TG/HDL-C ratio: The mean serum TyG index and TG/HDL-C ratio levels were significantly increased ($p < .001$) in Type 2 diabetes with poor glycemic control when compared to Type 2 diabetes with good glycemic control using student t test as shown in table 3 and figure 1.

Table 3: Comparison of serum lipid profile, TyG index and TG/HDL-C ratio among study groups

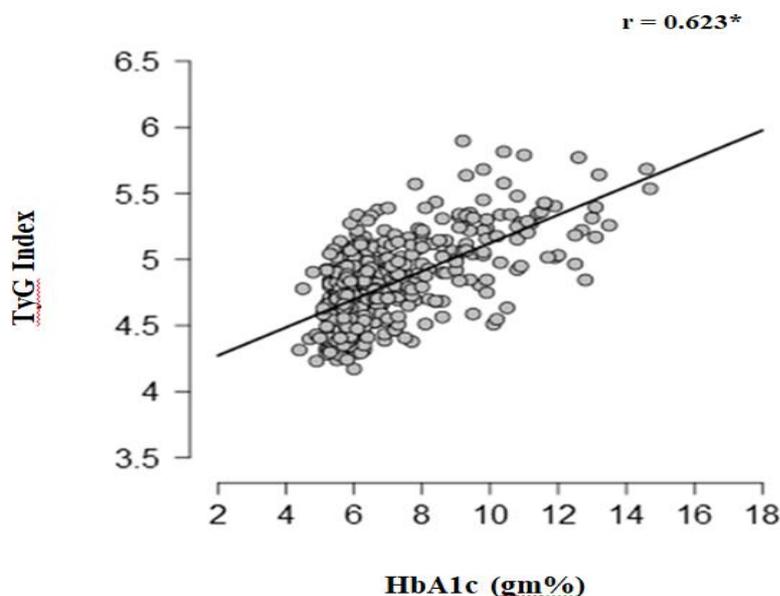


Parameters	Group I (Type 2 DM with good glycemic control) N=345	Group II (Type 2 DM with poor glycemic control) N=145	p value
Serum Total Cholesterol (mg/dL)	216 ± 48	221 ± 63	0.426
Serum Triglycerides (mg/dL)	145 ± 67	180 ± 69	<.001*
Serum HDL-Cholesterol (mg/dL)	51 ± 11	44 ± 09	<.001*
Serum LDL-Cholesterol (mg/dL)	136 ± 43	141 ± 58	0.371
Serum VLDL-Cholesterol (mg/dL)	29 ± 13	35 ± 14	<.001*
TyG index	4.69 ± 0.24	5.04 ± 0.33	<.001*
TG/HDL-C Ratio	3.02 ± 1.73	4.28 ± 1.82	<.001*

* $p < 0.05$ significant; Data are expressed in Mean ± standard deviation; p values are estimated among two groups by using student “t” test; HDL=High density lipoprotein, LDL=Low density lipoprotein, VLDL= Very low density lipoprotein; TyG index = Triglyceride-Glucose index; TG = Triglyceride; HDL-C = High density lipoprotein cholesterol.

Figure 1: Comparison of TyG index between the study groups

Correlation between Glycemic control VS TyG Index & TG/HDL-C Ratio in Type 2 diabetic



subjects:

Pearson’s correlation analysis showed a significant positive correlation between TyG index and glycemic control [(r = 0.623, p<0.001) (Fig. 2), as shown in table 4.

Table 4: Association of glycemic control with TyG index and TG/HDL-C Ratio

Parameters		Pearson’s Correlation (r)	p Value
HbA1c Vs	TyG Index	0.623*	< .001*
	TG/HDL Ratio	0.297	<.001*

* p<0.05 significant,

Figure 2: Correlation between TyG index Vs HbA`c

DISCUSSION:

The results of the present study have shown that TyG index are positively associated with HbA1c levels in DM2 patients and was higher in patients with poor glycemic control (HbA1c>7%) compared to patients with good glycemic control (HbA1c<7%). However, these associations were weak, between TG/HDL-C and glycemic control was found in Type 2 DM subjects but the mean levels was significantly increased in patients with poor glycemic control (HbA1c>7%) compared to patients with good glycemic control (HbA1c<7%).

The results of the present study was in concordance with the earlier work that that included 143 patients with DM2 not taking lipid-lowering medications, which found that patients with HbA1c more than 6.5% had higher triglyceride and lower HDL-C that served as markers of poor glycemic control in mentioned study [22].

Earlier studies have shown that TG/HDL-C ratio is independently related to insulin resistance, obesity and metabolic syndrome [23, 24]. McLaughlin et al. investigated the use of TG/HDL-C ratio in detecting insulin resistance in overweight individuals and found that a TG/HDL-C value above 3.0 mg/dL was a better marker of insulin resistance than triglycerides or insulin levels [25]. In the present study, average value of TG/HDL-C ratio was 3.02 mg/dL in HbA1c <7% group and 4.2mg/dl in in HbA1c >7% suggesting that patients in both Type 2 DM group were also insulin resistant.

TyG index is a marker of insulin resistance and has been correlated with the hyperinsulinaemic-euglycaemic clamp test and with the homeostatic model assessment of insulin resistance (HOMA-IR) [26, 27,28]. Our results are in agreement with the results from the earlier study that evaluated whether TyG

index and TyG derived indices (TyG-WC and TyG-BMI) were associated with long the term glycemic control. The study found that TyG indices were significantly correlated with HbA1c and were significantly increased in the diabetics with poor glycemic control [29].

Although earlier studies have shown that the TG/ HDL-C and TyG index could be useful markers of insulin resistance and glycemic control, the study by Er et al. showed that TyG was more efficient than TG/ HDL-C for identifying insulin resistance [30].

CONCLUSION:

The current research investigated Serum lipid profile, TyG index, TG/HDL-C and glycemic status to examine different metabolic alterations in Type 2 DM patients with good glycemic control compared to poor glycemic control. In the current study TyG index was higher in patients with poor glycemic control (HbA1c \geq 7%) compared to patients with good glycemic control (HbA1c $<$ 7%). TyG index are positively associated with HbA1c levels in Type 2 DM patients. However, these associations were weak, between TG/HDL-C and glycemic control found in Type 2 DM subjects.

HbA1c is relatively expensive and not available in most primary health care centers in undeveloped countries. Hence, the present study concludes that, TyG index could be used as an alternative test that is inexpensive and routinely available could have potential use for primary care physician in follow up of patients with confirmed Type 2 DM patients with poor glycemic control.

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