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ASSOCIATION OF GLYCATED HEMOGLOBIN WITH TRIGLYCERIDE TO HDL-CHOLESTEROL RATIO IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Diabetic patients have 2-4 folds higher Cardiovascular disease (CVD) risk when compared to non-diabetics. High HbA1c could be a sign of high triglycerides levels which may predict CVD risk factors in patients with type 2 Diabetes mellitus. Elevated TG: HDL-C ratio may be closely associated with poor glycemic control. The purpose of the study was to investigate the relationship between hemoglobin A1c and TG: HDL-C ratio in type 2 diabetic patients. The study included a total of 100 subjects in which 50 subjects with a history of T2DM for at least 5 years and 50 controls. Patients were assigned to two groups based on HbA1c, those with good glycemic control who had HbA1c ≤7.0 % and poor glycemic control who had HbA1c >7.0 %. For all subjects, HbA1c, FBS and lipid profile and TG/HDL-C ratios were assessed. Data analyzed using descriptive statistics and correlated by Pearson correlation coefficient. Results showed that higher Mean ±SD for lipid parameters, fasting blood sugar and HbA1c in T2DM cases than controls. There is highly significant correlation of TG: HDL-C ratio and HbA1C (r=0.347, p=0.0004) in subjects with poor glycemic control.HbA1c positively correlated with TC (r=0.0154, p=0.87), TG (r=0.295, p=0.002), whereas negatively correlated with HDL-C in subjects with poor glycemic control. These findings suggested that TG/HDL-C ratio should be focused in management of T2DM. A strong correlation between HbA1c and various lipid parameters especially TG/HDL-C ratio may suggest the importance of glycaemic control and dyslipidemia.

KEYWORDSType 2 Diabetes Mellitus, Cardiovascular disease; TG: HDL-Cholesterol; HbA1C.

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Introduction

Diabetes mellitus (DM)is a chronic disease characterized by hyperglycemia either due to low insulin secretion, or insulin resistance in peripheral tissues[1].Chronic hyperglycemia leads to the development of microvascular and macrovascular complications and can damage bodily systems if left untreated. The prevalence of DM is more than 500 million globally and recent reports showed that in India 77 million people were diagnosed with this disease in 2021 which is expected to increase more than 134 million by 2045 [2].Individuals with type 2 Diabetes mellitus (T2DM) have double risk of all-cause mortality with CVD being the major cause [3]. When compared to non-diabetics, diabetic patients have 2-4 folds higher CVD risk [4].

Glycated hemoglobin (HbA1c) is routinely used to measure glycemic control in patients with diabetes, and it is formed by non-enzymatic glycosylation of hemoglobin. HbA1c is used as a marker to predict the occurrence of microvascular and macrovascular complications in diabetic patients [5]. A recent study reported that high HbA1c could be a sign of high triglyceride (TG) levels which may predict CVD risk factors in patients with T2DM[6]. Elevated triglycerides have been associated with increased risk of cardiovascular disease in diabetics [7,8]. The pro-atherogenic properties of small low density lipoprotein (LDL) particles might be related to their ability to penetrate the arterial wall and thereby making them more susceptible to oxidation, indirectly linked with coronary artery disease [9]. HbA1c values not only reflect glycemic control but are also the main factor in determining the risk of diabetes-related complications [10] and mortality [11]. It has been projected that a decrease in the HbA1c value by 0.2% could lower mortality by 10% [12]. A high triglyceride /high density lipoprotein (TG/HDL) ratio leads to endothelial dysfunction. T2DM patients with good glycemic control had nearly 3-4 times decreased TG/HDL-C ratio. Hence high TG/HDL-C ratio may be closely associated with poor glycemic control [13].

Diabetes mellitus can lead to complications including cardiovascular disease (CVD). Glycated hemoglobin and its association with CVD can be mediated through modulation of risk factors such as dyslipidemia. Glycemic control has an impact on serum lipid levels. Increased fat levels often occur in patients with poor glycemic control [14].Decreased insulin action resulting in activation of hormone sensitive lipase that cause lipolysis, releases more free fatty acids that

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enter into liver leads to increased synthesis of TG and total cholesterol (TC) [15].It is suggested that correlation of HbA1c with blood lipids may enable its use as a dual marker for glycaemic status and dyslipidemia. There are many studies available on association between glycated hemoglobin and lipid parameters in diabetic patients and shows conflicting results, some studies show the positive associations between HbA1c and lipid parameters and some others shows it as negative correlation. Studies on association between HbA1c and TG/HDL-C ratio in T2DM individuals are scanty, hence this study was undertaken to determine the relationship between HbA1c and blood lipid concentrations especially TG/HDL-C ratio in T2DM patients.

Materials and Methods

This cross sectional study was conducted at NRI Medical College Hospital, Chinakakani, Guntur district of Andhra Pradesh State (India). The study included a total of 100 subjects in which 50 subjects with a history of type 2 diabetes mellitus for at least five years and 50 controls. Patients were assigned to two groups depending on their HbA1c, patients with good glycemic control who had HbA1c ≤7.0% (Controlled DM) and those with poor glycemic control who had HbA1c >7.0% (uncontrolled DM). Necessary approval for the study has been obtained from the Institutional Ethics Committee and an informed consent in writing was taken from every participant.

From the overnight fasted (10-12 h) subjects, 5 mL of venous blood was collected and analyzed on Vitros 5600 Fully Automated Analyzer for fasting blood sugar (FBS),post prandial blood sugar (PPBS)and Lipid profile parameters. Total cholesterol and triglycerides were determined enzymatically with the cholesterol oxidase peroxidase, 4-aminophenazone (CHOD-PAP) [16]. and glycerophosphate oxidase-peroxidase-4aminophenazone (GPO-PAP) [17]. techniques respectively. Estimation of HDL-Cholesterol and Direct LDL-Cholesterol were carried out by Non-HDL precipitation [18] and cholesterol esterase and oxidase methods. The TG/HDL-C ratio was calculated by dividing the serum TG level by HDL-C value. HbA1c was estimated by high performance liquid chromatography using D-10 Bio-Rad automated analyzer.

Results

A total of 100 participants were recruited in study in which 50 are known cases of T2DM and 50 are age matched non diabetic's acts as controls. Table-1 shows the Mean ±SD of TC, TG, LDL-

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C, HDL-C, TG/HDL-C ratio in cases and controls. Elevated levels of TC, TG, LDL-C TG/HDL-C ratio and depleted HDL-C were observed in T2DM cases than in controls and these differences were highly significant ($p<0.01$). Table 2 shows Mean ±SD of some biochemical Parameters in controlled and uncontrolled Type 2 Diabetic patients in which FBS ($t=6.91$, $p=0.0001$), PPBS ($t=7.104$, $p=0.0001$), TG ($t=2.49$, 0.01), LDL-C ($t=2.54$, $p=0.01$) and TG/HDL-C ($t=3.27$, $p=0.001$)

are elevated and HDL-C levels are depleted in those with poor glycemic control than with good glycemic control and the difference is statistically highly significant for TG and HDL-C.

Figure-1 shows the correlation between HbA1c and TG/HDL-C ratio in T2DM patients. It was observed that a positive correlation of HbA1c with TG/HDL-C ($r=0.347$ and $p=0.0004$). Figure-2 shows the positive correlation of HbA1c with TC in diabetic cases ($r=0.0154$, $p=0.87$) which is statistically insignificant. Figure-3 shows the positive correlation of HbA1c with TG in diabetic cases ($r=0.295$, $p=0.002$) which is highly significant. Figure-4 shows the negative correlation of HbA1c with HDL-C in diabetic cases ($r=-0.348$, $p=0.0003$) which is highly significant. A significant negative association indicating the elevation of the later and decrease in the former. Figure-5 shows the correlation of HbA1c with LDL-C in diabetic cases ($r=-0.135$, $p=0.18$) in which there is no association.

Table 1: Distribution of biochemical parameters in Type 2 diabetic cases and controls

Variables	CASES (n=50)		CONTROLS (n=50)		t-value	p-value
	Mean	SD	Mean	SD		
FBS (mg/dl)	156.02	50.03	92.34	6.53	-8.92	0.0001*
PPBS(mg/dl)	211.34	62.44	113.26	25.41	-10.28	0.0001*
HbA1C (%)	8.14	1.55	5.82	0.26	-10.43	0.0001*
Total cholesterol (mg/dl)	185.10	39.06	179.72	40.56	-0.676	0.5
TG(mg/dl)	170.78	89.68	126.14	54.63	-3.006	0.003*
HDL-C(mg/dl)	37.60	7.59	44.92	9.77	4.18	0.0001*
LDL - C(mg/dl)	112.47	37.07	109.92	37.99	-0.342	0.73
TG/HDL(mg/dl)	4.85	3.12	3.03	1.55	-3.69	0.0004*

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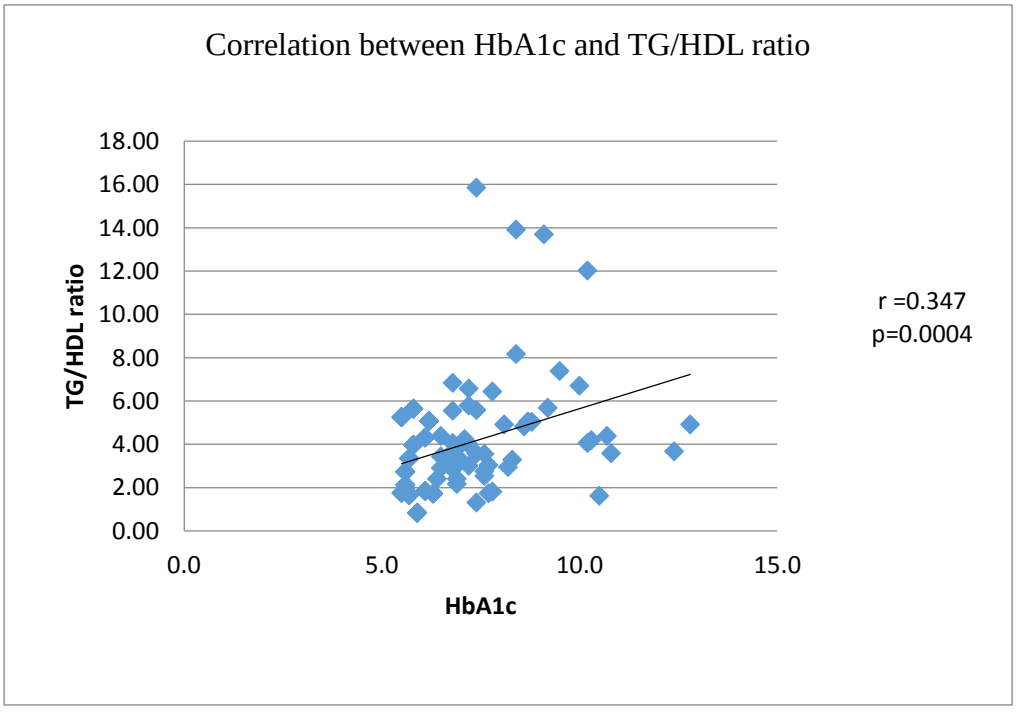
*p<0.05 was considered as significant.

Table 2: Lipid Parameters in controlled and uncontrolled Type 2 Diabetic patients

Variables	HbA1c ≤ 7.0 % (n=24)		HbA1c > 7.0 % (n=26)		t-value	p-value
	Mean	SD	Mean	SD		
FBS (mg/dl)	116.57	28.42	171.36	48.37	6.91	0.0001*
PPBS(mg/dl)	160.00	40.74	231.31	58.12	7.104	0.0001*
HbA1C (%)	6.74	0.19	8.68	1.50	9.07	0.0001*
Total cholesterol (mg/dl)	195.07	44.92	181.22	36.49	-1.69	0.09
TG(mg/dl)	142.36	47.37	181.83	99.89	2.49	0.01*
HDL-C(mg/dl)	40.07	6.40	36.64	7.87	-2.39	0.01*
LDL - C(mg/dl)	126.50	39.93	107.50	34.60	-2.54	0.01*
TG/HDL(mg/dl)	3.61	1.29	5.33	3.49	3.27	0.001*

* p<0.05 was considered as significant.

Figure 1: Correlation of HbA1c with TG: HDL-C in Type 2 Diabetic patients



r: correlation coefficient; p<0.05 was considered as significant.

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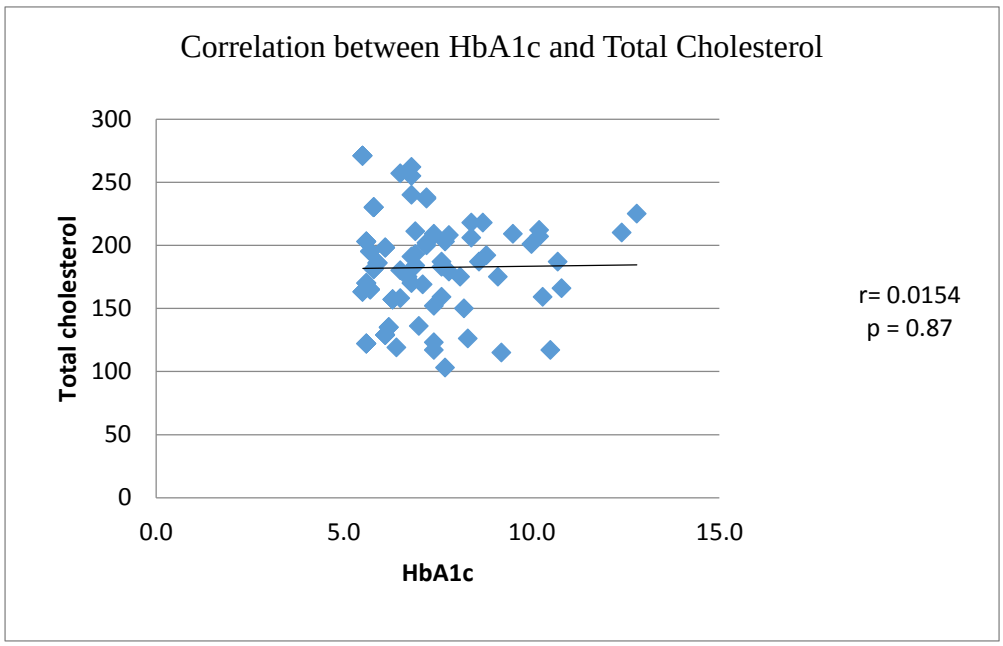
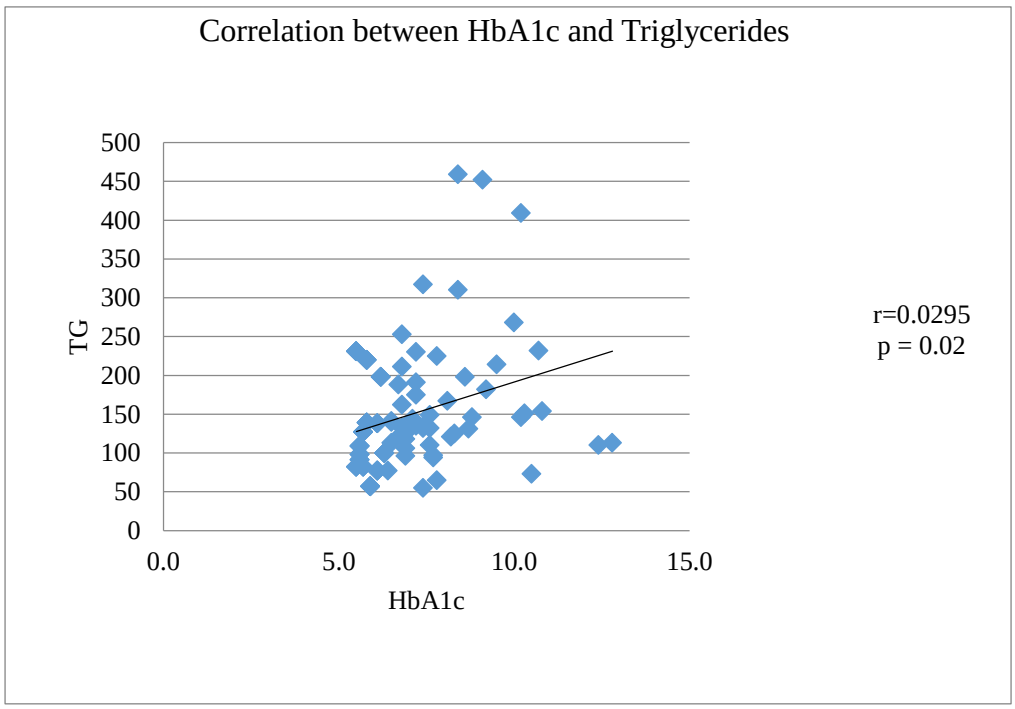
Figure 2: Correlations between HbA1c and Total cholesterol in Type 2 Diabetic subjects.



r: correlation coefficient; p<0.05 was considered as significant.

Figure 3: Correlation of HbA1c with TG in diabetic cases.



r: correlation coefficient; p<0.05 was considered as significant.

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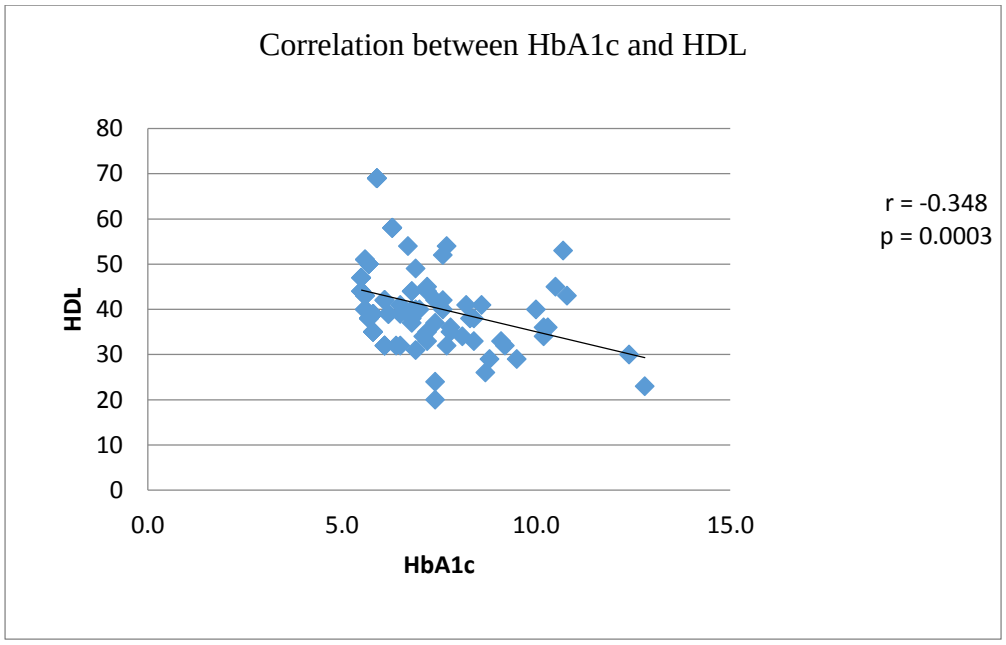
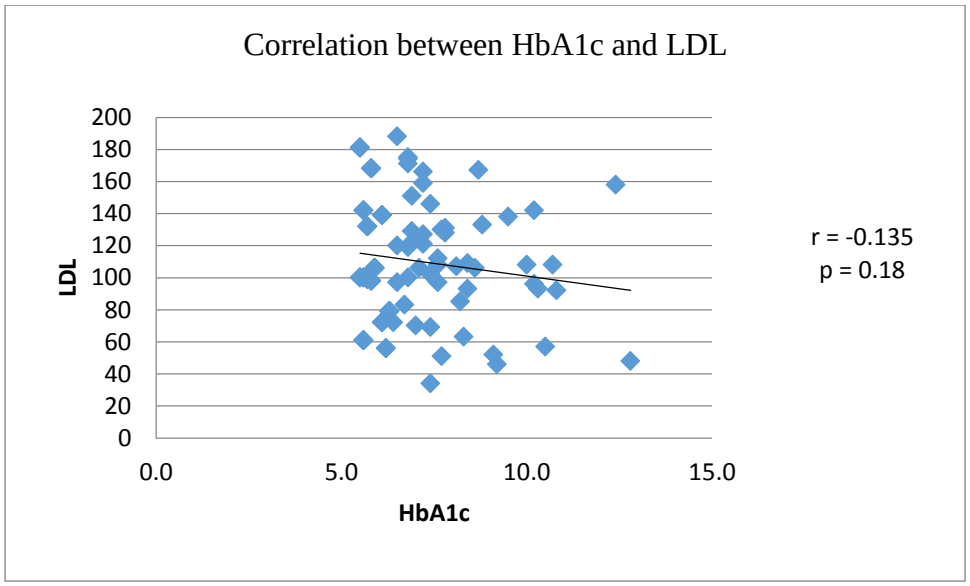
Figure: 4 Correlation of HbA1c with HDL-C in diabetic cases.



r: correlation coefficient; p<0.05 was considered as significant.

Figure 5: Correlation of HbA1c with LDL-C in diabetic cases



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Discussion

T2DM with poor glycemic control is one of the common cause of hyperlipidemia, and an important risk factor for CAD [19].In diabetics the risk of vascular disease is mainly due to lipid abnormalities. In the present study TC, TG, LDL, FBS, PPBS and HbA1c are higher and HDL-C levels are lower in T2DM cases when compared to control group who are non-diabetics. Similar results obtained in a study of Traoreet al [20]. Our results are in accordance with another study which included 186 non-diabetics, 238 pre diabetics and 576 diabetics. [21]. The mean value of FBS, TC, LDL and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. But, mean value of HDL was found to be higher in patients with good glycemic control than those with poor glycemic control. Consistent with our study found by Ghariarab et al study in which significantly higher FBS, PPBS and TG are found in individuals with poor glycemic control [22].

In the present study, HbA1c had strong positive association with some lipid parameters like TC and TG and negative association with HDL in diabetic individuals. Similar results were obtained by the study of Erciyas et al., in diabetic patients [23].Notably, there is weak correlation was observed between glycated hemoglobin with LDL-C in DM patients. This result was in accordance with findings of Hussain et al. who found that patients with HbA1c value greater than 7.0% had significantly higher value of TC, LDL-C compared with patients with an HbA1c value up to 7.0% [12]. The result was inconsistent with findings of Samdani et al. [24]who reported that there was a significant positive correlation between HbA1c especially with LDL-C. Another study reported that HbA1c had no significant correlation with lipid parameters except TG [25]. A study by Bhattacharjee et al. reported that patients with HbA1c $\geq$ 7% had a significant increase in TC, LDL-C, TG, TC/HDL-C and LDL-C/HDL-C ratio and a decrease in their HDL-C levels as compared to patients with HbA1c < 7.0% which is in concordance with the present study[26]. Dyslipidemia in T2DM might be caused by reduced insulin production that affects the synthesis of apolipoprotein in liver which regulates activity of lipoprotein lipase and cholesterol ester transport protein [27].

Raised TG/HDL ratios in patients with T2DM acts as predictor of cardiovascular disease [28]. The major finding of the study was significant elevation of TG/HDL-C in subjects with poor glycemic control which is in concordance with the earlier finding [13] and reliable

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biomarker in CAD risk prediction. These findings are in accordance with a study by Laverdyet al, that included 143 T2DM patients with poor glycemic control had high TG and low HDL-C levels. positive and independent association between TG/HDL ratio HbA1c has been reported. Our results are in concordance with the results of the study 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 [29].

A lower TG/HDL-C in subjects with good glycemic control than those with poor control indicated a greater proportion of HDL-C's role in reducing the risk of CHD and vice versa. It has also been indicated that the elevation in TG/HDL-C is the single most powerful predictor of extensive CHD [30,31] and the atherogenic link between high TG/HDL-C is due to higher concentration of TG-rich VLDL-C in plasma. The latter generates small and dense LDL-C during lipid exchange and lipolysis that accumulate in the circulation forming HDL-C particles of similar characteristics which undergo accelerated catabolism leading to atherogenesis [32].

Conclusion

The findings of the present study suggested that a significant correlation between HbA1c and various lipid profile parameters especially TG/HDL-C ratios, and may suggest the importance of glycaemic control as well as in managing dyslipidemia. T2DM patients should be educated to monitor their blood glucose levels and lipid levels regularly and also about lifestyle modifications and dietary changes to target good glycemic status so as to reduce the risk of CVD in later life. Further studies are warranted in reducing the risk of CVD in Type 2 diabetic patients.

Limitations of the study

It lacks follow-up or interventions besides being a single-centered study with a small sample size. However, multi-centered studies with large sample sizes are needed to understand the severity of the problem and validate/generalize the findings.

Conflict of interest

The authors declare that there is no conflict of interest.

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