ABSTRACT
Our study aimed to find utility of HbA1c as indicator of dyslipidemia in patients with type 2 diabetes mellitus. This study is an attempt to determine the correlation between hemoglobin A1c (HbA1c) and serum lipid profile and to evaluate the importance of HbA1c as an indicator of dyslipidemia in South Indian Patient with T2DM. Total cholesterol (TC), high density lipoprotein cholesterol (HDLC), low density lipoprotein cholesterol (LDLC), triglyceride (TG) and HbA1c levels were evaluated. Test of significance was calculated by unpaired Student's 't' test. Correlation studies (Pearson's correlation) were performed between HbA1c and serum lipid profile. Significance was set at p<0.01. Significantly higher mean serum levels of TC, TG and LDL-C and significantly lower mean serum levels of HDL-C were noted in patients with diabetes. Significant correlations were observed between HbA1c value and serum levels of TC, TG and LDL-C (p<0.01) but no significant correlation of HbA1c value with LDL-C in diabetes patient. Apart from a reliable glycemic index, HbA1c can also be used as a predictor of dyslipidemia and thus early diagnosis of dyslipidemia can be used as a preventive measure for the development of CVD in patients with T2DM.

KEYWORDS: HbA1c, dyslipidemia, Correlation, Retrospective Study.

1. INTRODUCTION
The estimated prevalence of diabetes (type 1 and type 2 combined, both diagnosed and undiagnosed) in people aged 20–79 years has risen from 151 million (4.6% of the global population at the time) to 463 million (9.3%) today. Without sufficient action to address the pandemic, we predict 578 million people (10.2% of the population) will have diabetes by 2030. That number will jump to a staggering 700 million (10.9%) by 2045. Diabetes is a serious threat to global health that respects neither socioeconomic status nor national boundaries. People living with diabetes are at risk of developing a number of serious and life-threatening complications, leading to an increased need for medical care, a reduced quality of life, and undue stress on families. Diabetes and its complications, if not well managed, can lead to frequent hospital admissions and premature death. Globally, diabetes is among the top 10 causes of death. Despite the stark truth the data represent, there is a positive message: with early diagnosis and access to appropriate care, diabetes can be managed and its complications prevented. Furthermore, type 2 diabetes can often be prevented and there is compelling evidence to suggest it can be reversed in some cases. In recent years, the World Health Organization (WHO) and the United Nations (UN) have set global targets to encourage action to improve care and strengthen healthcare systems. These actions include reducing premature death from non-communicable diseases (NCDs), including diabetes, by 30% by 2030, establishing national diabetes plans and achieving universal health coverage (UHC) by 2030. These are important steps towards guaranteeing access to affordable high quality care and alleviating financial catastrophe for the close to 580 million who will then be living with diabetes. However, many countries still lack a national diabetes plan, and at least half the world’s population does not have full coverage for essential health services. Most countries are also falling short of the WHO 2025 target of halting the rise of type 2 diabetes. Urgent national actions are required to improve type 2 diabetes prevention and the management of all types of diabetes. Governments will need to adopt a health-in-all-policies approach to secure the best possible care and quality of life for people living with diabetes.1-3

No wonder diabetes is called “Silent Killer”. There is a higher risk of cardiovascular disease in people with type 2 diabetes; these patients have more than two-fold increased risk for cardiovascular death compared with persons without diabetes.4-6 Dyslipidemia, which is one of the most important risk factors for coronary artery
disease, is more prevalent among adults with type 2 diabetes mellitus than in the general population with a four to six fold greater cardiovascular mortality.[5-8] Typical pattern of diabetic dyslipidemia include an abnormally high level of triglycerides (TG), a high proportion of small dense low density lipoprotein cholesterol (LDL), low high density lipoprotein cholesterol (HDL), and postprandial lipemia.[9-11] The higher prevalence of lipid abnormalities in diabetes mellitus has been attributed to insulin resistance or deficiency that affects key enzymes and pathways in lipid metabolism.[12-15] So, hyperglycemia, dyslipidemia and coronary artery disease relate well with each other in type 2 diabetes and it has been proposed that higher prevalence of cardiovascular disease in type 2 diabetes is due to chronic uncontrolled hyperglycemia[16,17] and hence strict control of hyperglycemia and dyslipidemia can be preventive. Studies have suggested HbA1c to be an independent risk factor for coronary heart disease[18-21] and stroke and it has also been seen that risk of cardiovascular disease increases by 18% with every 1% increase in value of HbA1c in diabetic.[22-25] Also, it has been calculated that a reduction of 0.2% in the value of HbA1c reduces mortality due to cardiovascular events by 10%.[13] In a country like India where a significant number of people belong to below poverty line group and are unable to take the blood tests as frequently as advised, using HbA1c as a dual marker i.e. marker for hyperglycemia and dyslipidemia would be of much help while treating patients.[26-29] It should be understood that HbA1c cannot replace the utility of lipid profile, but if presence of certain correlation is discovered between the two, HbA1c could be considered for early determination of dyslipidemia and hence could help in assessing CV risk.[30-33] Hence this study was undertaken to observe correlation of HbA1c with lipid profile in south Indian population. HbA1c provides a reliable measure of chronic glycemia and correlates well with the risk of long-term diabetes complications, so that it is currently considered the test of choice for monitoring and chronic management of diabetes.[34-39] However, the cut-point of HbA1c from the diagnostic point of view is still controversial. Among diabetics, the blood glucose levels increase in the blood and the glucose attaches to the hemoglobin molecule in a concentration-dependent manner.[40-43]

2. METHODOLOGY
The present retrospective cross-sectional study was accomplished at the Medicare Group of Hospitals, Hyderabad, India between September 2020 and January 2021, either diagnosed as type 2 diabetic as per American Diabetes Association guidelines 2020 or already taking treatment for type 2 diabetes were considered in the study. There were 196 T2DM patients selected for the study (141 females and 55 males), and the data were collected through a review of the electronic profiles of patients by using the medical electronic file system used at the Medicare Group of Hospital. Biochemical data such as fasting plasma glucose (FPG), HbA1c and lipid profile, along with the patient’s age, gender, were also taken from the electronic file system. The inclusion criteria allowed for only patients who were regularly seeing their physician and whose electronic file was up to date.

All records were categorized into two groups according to their HbA1c levels. The data were evaluated via the SPSS statistical package version 16.0. Pearson’s correlation test was performed to examine various correlations. Independent sample Student’s t test (two tailed) was used to compare means of different parameters. All p values less than 0.01 were considered statistically significant. The value of HbA1c was given as a percentage of the total hemoglobin and values of all other parameters were given in mg/dl. All values are expressed as mean ± standard deviation (SD) or standard error of the mean.

Study design and location
A cross-sectional study was conducted from September 2020 to January 2021 and patients suffering from COVID19 were excluded from the study. Records of south Indian patients with T2DM visiting an outpatient department in the Medicare Group of Hospitals, a Tertiary care Hospital, located Hyderabad, India were included in the study.

3. RESULTS AND DISCUSSION
The participants’ data were analyzed gender-wise. The females had significantly higher values for HbA1c (p<0.01), triglycerides (TGs) (p<0.01), high-density lipoprotein cholesterol (HDL-C) (p<0.01) and low-density lipoprotein cholesterol (LDL-C) (p<0.01) compared to the males. The study subjects were grouped according to their level of HbA1c (good glycemic index <7%, and poor glycemic index >7%). In both groups, no significant differences were found in any of the parameters other than TGs (p=0.268) and HbA1c (p<0.01). An analysis of the correlation between HbA1c and other parameters exhibited a significant correlation with TG (r=0.16, p=0.020), while no significant relationship was observed with the other variables. The linear regression results indicated that HbA1c values were associated with TGs (p=0.020) and were independent of age, BMI, TC, LDL-C, HDL-C and FPG levels.

This study is a cross-sectional study involving 196 type 2 diabetic patients. The correlation of long term glycemic control represented by HbA1c has been found out with parameters of lipid profile.

The mean value of HbA1c, TC, LDL-C and LDL-C were slightly higher in female compared with male patients, but the differences were not statistically significant. Although the mean levels of TC and the TC/HDL-C ratio were slightly lower in women than in men, these differences were statistically non-significant, as shown in Table.1.
We have classified dyslipidemia according to NCEP ATP III guidelines and found out that hypercholesterolemia, hypertriglyceridemia and increased LDL-C was seen in 39%, 49% and 32% of subjects respectively. Level of HDL-C was low in 39% of females and 12% of males. Also, 59% of patients had good glycemic control as suggested by HbA1c level <7%. HbA1c was found to have significant positive correlation with TC (r=0.207, <0.01), LDL (r=0.808, <0.01), and TG (r=0.268, <0.01) and significant negative correlation with HDL (r= -0.897, <0.01) and HDL/LDL ratio (r= -0.995, <0.01).

Significant correlation of level of HbA1c with S. lipid profile.

Table 2: Correlation of HbA1c with S. lipid profile.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TC(^a)</th>
<th>HDL(^b)</th>
<th>LDL(^a)</th>
<th>HDL/LDL(^b)</th>
<th>Triglycerides(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c(^a)</td>
<td>0.207*</td>
<td>-0.897*</td>
<td>0.808*</td>
<td>-0.995*</td>
<td>0.268*</td>
</tr>
<tr>
<td>*p &lt;0.01</td>
<td>p &lt;0.01</td>
<td>p &lt;0.01</td>
<td>p &lt;0.01</td>
<td>p &lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Pearson’s correlation, \(^b\)Spearman rho correlation.

* Correlation is significant at 0.01 level.

To see the utility of HbA1c as a marker of dyslipidemia, we divided subjects into two groups, good and poor glycemic control groups depending upon the levels of HbA1c as <7% and >7% respectively. The mean value of 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 and HDL/LDL ratios was found to be higher in patients with good glycemic control than those with poor glycemic control. These differences were significant at the level of p <0.01 (Table 3).

Table 3: Comparison of lipid profile between subjects with good and poor glycemic control.

<table>
<thead>
<tr>
<th>HbA1c (^a) (mg/dl)</th>
<th>(&lt;7)</th>
<th>(\geq7)</th>
<th>*p’ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (^a) (mg/dl)</td>
<td>5.23±39.2</td>
<td>189.24±39.5</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>HDL (^b) (mg/dl)</td>
<td>47.1±5.1</td>
<td>51.9±5.1</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>LDL (^a) (mg/dl)</td>
<td>87.6±7.9</td>
<td>108.2±19.1</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>HDL/LDL (^b)</td>
<td>0.5±0.12</td>
<td>0.29±0.18</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Triglycerides (^b) (mg/dl)</td>
<td>151 (107,183)</td>
<td>174 (120,234)</td>
<td>0.03**</td>
</tr>
</tbody>
</table>

\(^a\) Independent t-test , \(^b\) Mann Whitney U test.

Significant correlation of level of HbA1c with parameters of lipid profile suggests utility of HbA1c as a marker of dyslipidemia in addition to chronic hyperglycaemia and hence should be analysed accordingly. Our study adds to the existing literature suggesting HbA1c as an indicator for dyslipidemia. We noted a significant difference in lipid parameters in two groups (\(<7.0%\) and \(>7.0%\)) of HbA1c. This may indicate that HbA1c can be used as a potential biomarker for predicting dyslipidemia in patients with T2DM in addition to glycemic control. Hence, early diagnosis can be accomplished through relatively inexpensive blood testing and may be utilized for screening high-risk patients with DM for timely intervention with lipid-lowering drugs.

4. CONCLUSION

Significant correlation of level of HbA1c with parameters of lipid profile suggests utility of HbA1c as a marker of dyslipidemia in addition to chronic hyperglycaemia and hence should be analysed accordingly. Our study adds to the existing literature suggesting HbA1c as an indicator for dyslipidemia. We noted a significant difference in lipid parameters in two groups (\(<7.0%\) and \(>7.0%\)) of HbA1c. This may indicate that HbA1c can be used as a potential biomarker for predicting dyslipidemia in patients with T2DM in addition to glycemic control. Hence, early diagnosis can be accomplished through relatively inexpensive blood testing and may be utilized for screening high-risk patients with DM for timely intervention with lipid-lowering drugs.

5. Conflict of interest

Authors declare no conflict of interest in this critical review.

6. ACKNOWLEDGMENT

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7. REFERENCES


