"ASSOCIATION BETWEEN GLYCAEMIC CONTROL AND LIPID PROFILE IN TYPE 2 DIABETES MELLITUS"

Dr. Desai Jabbar V 1 Dr. U.T. Mane 2
Assistant Professor, Department of Medicine, Krishna Institute of Medical Sciences, Krishna Institute of Medical Sciences Deemed to be University ,Karad
Email :- dr.jabbardesai@gmail.com

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Introduction

Diabetes mellitus refers to a group of metabolic disorders that share a common phenotype of hyperglycaemia. There are several distinct types of DM which are caused by a complex interaction between genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1] DM is the chronic illness that requires constant medical care and patient's self-management to prevent its acute and chronic complications and also to reduce risk of long- term effects. Care of Diabetes is complex and it also requires many issues, beyond the glycaemic control, which needs to be addressed. A large evidence exists which supports a range of interventions to improve the diabetes outcomes.[2]

Dyslipidaemia is commonly seen in diabetes. Type 2 DM is one of the most common secondary causes of hyperlipidaemia. The relationship between hyperlipidaemia and vascular complication of diabetes has long been of interest because both tend to occur with greater frequency in Type 2 DM. Insulin resistance and obesity combines to cause dyslipidemia and hyperglycemia and hyperlipidemia have additive cardiovascular risk. It is recommended that patients with DM should be treated as if they already have coronary artery disease.

Hence identification, critical evaluation, and follow-up of serum lipid profile in Type 2 DM continue to be important.[3]

Incidence of diabetes in rural and urban part of India has been gradually and constantly increasing. It will be the major cause of death in 21st century in India. In condition of sustained hyperglycemia like in diabetes mellitus, the glycated haemoglobin increases substantially. Also, in diabetes mellitus, increased percentage of glycated haemoglobin is associated with dyslipidemia. Patient with type 1 diabetes with good glycemic control are generally not dyslipidemic. But, type 2 diabetes patients are usually dyslipidemic even after relative good glycemic control.[5] The estimated number of people with diabetes worldwide is expected to increase from 366 million in 2011 to 522 million in 2030, at an average annual growth of 2.7% which is 1.7 times the annual growth of total world adult population. Type 2 diabetes mellitus (T2DM) accounts for more than 90% of all patients with diabetes worldwide. The prevalence of diabetes in adult is showing an upward trend from 6.4% in 2010 to an estimated 7.8% in 2030. The majority of

this increase will, however, occur in the developing world. The lipid abnormalities associated with diabetes are better termed as " Dyslipoproteinemia" or "Dyslipidemia", rather than "Hyperlipoproteinemia‖ or —Hyperlipidemia" because there may be changes in both, the quantity and quality of lipoproteins. Dyslipidemia is more common in type 2 diabetes and is major contributor to the high risk of CHD seen in this condition. The most frequent form of quantitative dyslipidemia is increased Triglyceride. The other quantitative dyslipidemia associated with type 2 diabetes is low HDL cholesterol and the low HDL cholesterol usually persists despite achievement of glycemic control.[6] Glycated haemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients. Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for cardiovascular disease in patients with or without diabetes.[7]

AIM OF STUDY

To assess the relationship between glycaemic control and serum lipid profile in type-2 diabetes mellitus.

OBJECTIVES

1. To measure HbA1c level in type 2 diabetes mellitus patients.
2. To measure lipid profile in type 2 diabetes mellitus patients.
3. To assess the association between Glycated Haemoglobin and Lipid profile parameters.

Review of Literature

- **EARLY 19th CENTURY**

By the early 19th Century, chemical tests have been devised which can detect excess sugar in the urine. It was not until the Franco-Prussian War, when the French Physician Bouchardat noticed that restricted diets helped his patients, that calorie intake is recognised as important.

- **1869**

Medical student Paul Langerhans reveals that the pancreas contains two types of cells, of which one secretes tiny cells islets. The function of these cells is currently unknown; they go on to be referred to as the —Islets of Langerhans‖.

- **1889**

Joseph von Mering and Oskar Minkowski remove pancreases from dogs and discover that they develop the symptoms of DM.

- **EARLY 1900S**

Jean de Meyer and Sir Edward Albert Sharpey-Schafer both independently propose the name —insulin‖, it is believed, in reference to the tiny cell islands in the pancreas – the islets of Langerhans. Insulin is Latin for —insula‖, meaningisland.

- **1936**

Sir Harold Percival publishes research which divides diabetes into type 1 and type 2 based on the degree of insulin sensitivity in patients.

- **1940S**

Insulin treatments continue to develop and by 1945 the life expectancy of someone with diabetes is increasing. By 1945, a newly-diagnosed 10-year-old has a life expectancy of 45 years; a 50-year-old might live for another 16 years.

Dr Elliot Proctor Joslin and his staff develop the first hospital blood glucose monitoring system. Joslin also sets up The Victory Medal award in 1947 to celebrate patients who live with diabetes for 25 years and have no health complications regarding their kidneys, eyes and blood vessels.

Helen Free develops the Clinistix –dip-and-read‖ urine test which allows instant monitoring of blood glucose levels.

- **1980S**

Humulin, the first biosynthetic human insulin, is approved for distribution in several countries. It is identical to the structure of human insulin and has the advantage of being less likely to lead to allergic reactions than animal insulin. The first insulin pen delivery system, called the NovoPen, is introduced by Novo Nordisk in 1985.

- **1991**

The World Health Organisation launches World Diabetes Day in response to the rapid rise of diabetes around the world. It is held on November 14, the birthday of Frederick Banting.

- **1992**

Medtronic releases the MiniMed 506 insulin pump, which delivers meal bolus memory and daily insulin totals.

- **1993**

The landmark Diabetes Control and Complications Trial (DCCT) report is published, demonstrating that regular activity and good nutrition help to improve diabetes control and stave off the risk of long-term health complications.

- **2013**

The University of Cambridge trials an artificial pancreas which combines thetechnology of an insulin pump with a continuous glucose monitor.

Pathophysiology of Dyslipidemia in Type 2 Diabetes Mellitus

The underlying pathophysiology of diabetic dyslipidemia is complex and still not well understood. Hypertriglyceridemia, low HDL-cholesterol and a predominance of small dense LDL can be detected years before the clinical diagnosis of type-2 diabetes in insulin-resistant, pre-diabetic individuals with normal glucose concentrations.[9] Thus, hyperglycemia alone cannot fully explain the lipid changes. Insulin resistance is believed to be the main trigger for diabetic dyslipidemia. Hypertriglyceridemia is considered the dominant lipid abnormality in insulin resistance and plays a pivotal role in determining the characteristic lipid profile of diabetic dyslipidemia. Elevated triglyceride levels are the result of increased production and decreased clearance of triglyceride-rich lipoproteins in both fasting and non-fasting states. Increased production of very low density lipoprotein (VLDL), the main transporter of fasting triglycerides, is a prominent feature of insulin resistance.[9] Patients with Type 2 diabetes present with a wide variety of lipid patterns. This reflects the fact that many factors influence the plasma lipid profile. Genetic factors, concomitant diseases, lifestyle, medications and other factors all affect lipid values and may thus alter the lipid patterns observed in diabetic patients. Many Type 2 diabetic patients are characterized by a typical mixed dyslipidemia, thus by hypertriglyceridemia, low HDL-C and the predominance of small dense LDL, while total cholesterol may be normal or elevated. LDL-C concentration is often only mildly elevated and is usually not the predominant abnormality.[10]

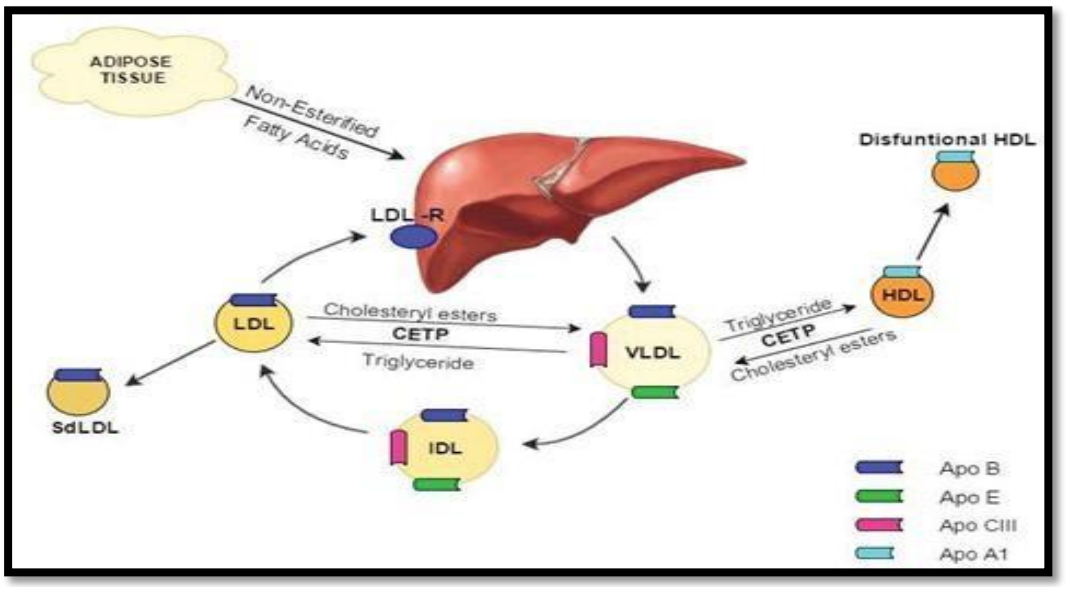
Following are the dyslipidemia components associated with type 2 diabetes

- Increased TG and TG-rich lipoproteins
- Increased postprandial TG
- Low HDL-C
- Low apo A-I
- Decreased small HDL, prebeta-1 HDL, alpha-3 HDL

- Increased apo B
- Increased LDL particle number
- Increased small, dense LDL
- Increased apo C-III
- Increased non-HDL-C
- Increased oxidized and glycated lipids.[11]

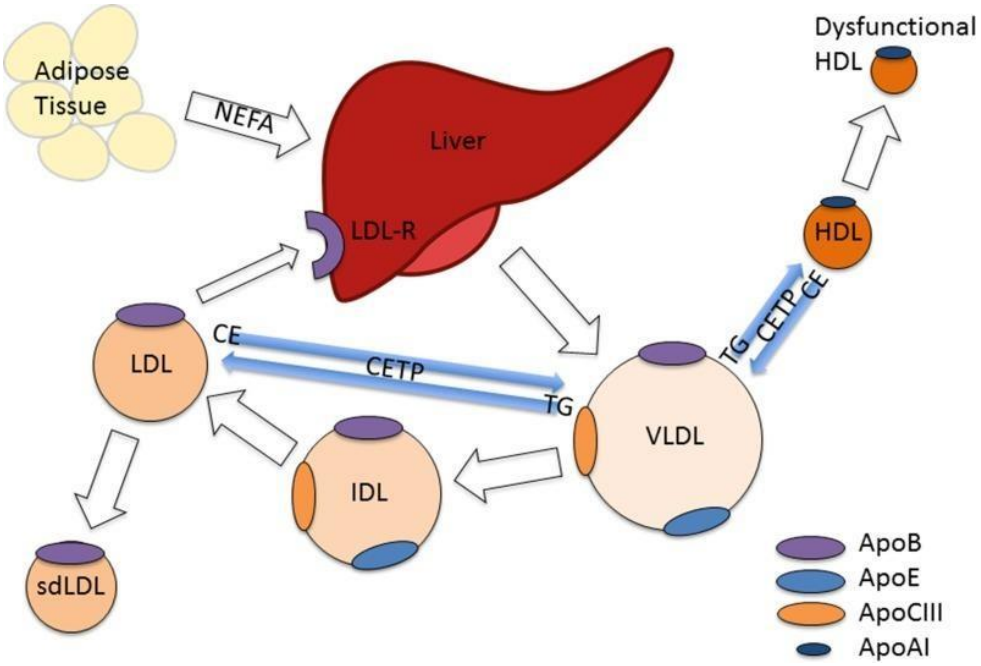
Insulin resistance/deficiency in type 2 diabetics in association with other factors like adipocytokines, hyperglycemia lead to qualitative, quantitative and kinetic changes in normal lipid metabolism including :

(1) Increased VLDL.
(2) Increased LDL.
(3) Decreased HDL. [12]



The above figure showed the normal Lipid metabolism.[12]

A number of factors may contribute to the alterations in lipid metabolism observed in patients with diabetes, including insulin deficiency or resistance, adipocytokines, and hyperglycemia. Insulin deficiency or resistance activates intracellular hormone-sensitive lipase which increases the release of non- esterified fatty acids (NEFA) from triglycerides stored in the more metabolically active centrally distributed adipose tissue. High circulating levels of NEFA increase hepatic triglyceride production. Increased hepatic triglyceride synthesis is associated with increased secretion of apolipoprotein B (apoB). Furthermore, the normal inhibitory effect of insulin on hepatic apoB production and triglyceride secretion in VLDL is lost, and the VLDL secreted islarger and more triglyceride-rich. The tendency to hypertriglyceridemia is further augmented by reduced VLDL catabolism. Lipoprotein lipase located on vascular endothelium largely determines the rate of removal of triglycerides from the circulation. In contrast to intracellular hormone-sensitive lipase this lipoprotein lipase may be down regulated in states of insulin resistance or deficiency. This reduction in lipoprotein lipase activity also contributes to postprandial lipemia. The following figure showed the qualitative changes in lipoprotein in diabetes.[14]



There are many tests to diagnose the diabetic complications, for Diabetic retinopathy, we do many tests some of which are Ophthalmoscopy which is done in clinical examination and Fundus fluorescein angiography (FFA). This study has been conducted to evaluate the use of Fundus fluorescein angiography (FFA) in DM patients and its comparison with clinical evaluation for early detection and diagnosing stages of diabetic retinopathy. [6-8]

Various Studies

Study conducted by Abhishek Gupta, Vinod Kumar Tyagi, Sunil Kumar Virmani showed that out of all 150 type 2 diabetic study participants, 100 were male and 50 were female by gender. Overall prevalence of dyslipidemia in the study participants was found to be 94.7% (47 females, 95 males). Among these 94 patients (62.7%) had hypercholesterolemia, 87 (58%) had hypertriglyceridemia, 93 (62%) low HDL levels, 119 (79.3%) had high LDL levels, 87 (58%) had high TC HC ratio, 125 (83.3%) had Non HDL cholesterol. About 65 patients out of 150 were found to be obese (BMI>25) i.e. 43.3% cases were obese. Mean lipoprotein levels showed higher levels in females than males, but the difference was statistically not significant. Comparison of mean lipoprotein level in patients with normal and high BMI did not show statistical significance. There was no significant difference in the number of patients with dyslipidemia among normal and high BMI category.[15]

Aleksandra Klisic and etal conducted cross sectional study to find out association between unfavourable lipid profile and glycemic control in type 2 diabetes patients. As expected, significantly higher TC, LDL-c, TG (5.75 [4.94–6.38]; 3.48 ± 1.09; 2.02 [1.54–3.17]; p = 0.029, p = 0.018, and p = 0.001, respectively) were found in the highest HbA1c tertile group, as compared with the lowest (5.16 [4.40–5.70]; 3.06 ± 0.92; 1.59 [1.14–2.04],
respectively) and intermediate HbA1c (5.32 [4.84–6.29]; 3.30 ± 0.97; 1.87 [1.74–2.11], respectively) tertile group. In addition, significantly higher calculated indexes (VAI, LAP) were found in the highest HbA1c tertile group (3.23 [1.82–5.62] and 87.78 [76.10–98.91]; p < 0.001, respectively), as
compared with the lowest (2.30 [2.00–2.65] and 67.06 [59.72–75.32],
respectively) and intermediate HbA1c (2.95 [2.60–3.35] and 87.89 [77.98– 99.07], respectively) tertile group. On the other hand, significantly lower HDL-c (1.07 [1.00–1.14]) was found in the highest HbA1c tertile group (p =

0.015), as compared with the lowest (1.20 [1.14–1.27]) and intermediate (1.18 [1.12–1.25]) HbA1c tertile group.[18]

Anju Sharma et al. conducted a case-control Study to see dyslipidemia in patients of type 2 diabetes mellitus. The study results showed that the mean fasting blood sugar in cases were found to be 140.98 ± 42.0 and in control it was 75.14 ± 8.43. Also, the mean HbA1c in cases and control was 7.78 ± 1.87 and 4.77 ± 0.56 respectively. The total cholesterol in control group was 148 ± 32 and in cases was 208 ± 78. It was also observed that the difference between total serum cholesterol levels of normal individuals and patients of type 2 diabetes was statistically highly significant (p <0.001), with the patient group having significantly higher levels than the normal group.[19]

Funmilayo Esther Omotoye and Grace Tanimoowo Fadupin evaluated lipid profile in type 2 diabetes mellitus patients at urban tertiary health facility in Nigeria and found that the mean age of respondents was 57.82 ± 3.3 years, about 70.0% of diabetic patients presented at least one lipid abnormality. Elevated LDL-C, Total Cholesterol, Triglyceride, and reduced HDL-C levels were noted in 34%, 36%, 12%, and 72% of the patients, respectively. Combination of elevated LDL and reduced HDL-C was the most prevalent of combined lipid abnormalities. There was significant difference between Triglyceride and blood glucose (p-value < 0.05).[23]

From study conducted by H.A. Khan et al.: Glycaemic control and lipid profile, we came to know that there was a highly significant correlation between HbA1c and FBG (R2=0.685, P=0.000). Both HbA1c and FBG exhibited direct correlations with cholesterol, TG and LDL and an inverse correlation with HDL(p-value < 0.05); all these correlations were significant except FBG vs. HDL where p-value was 0.08.[24]. Also, study conducted by Hanish R Jain et al, showed that the average duration of diabetes ranged from 4 to 12. While, mean value all range of lipid fractions except HDL-C are higher in diabetes when compared to controls. However, statistical significance is high for TG, HDL-C, VLDL-C, and low power TC, LDL -C.[3]

From the study conducted by Khansaa A. I. Albaroodi et al, we came to know that 1014 outpatients with type 2 diabetes were enrolled in the study, All the enrolled patients had FPG measurements through the evaluation period, while only 81.9% (n = 830) had HbA1c measurements. Female patients constituted 54% and more than half of the study population were Chinese (54.1%) andthe rest were Malay and Indian ethnic. Two thirds of participants had diabetes mellitus during the last 10 years, and 43% of them had two comorbidities (hypertension and dyslipidemia). Out of all 830, about 92.9% (771 Patients) were having HbA1c value more than 6 while of all 1014 study participants 73.2% (742 Patients) were having Fasting plasma glucose more than 6.7 mmol/l indicating poor glycemic control in maximum participants. It also showed that patients with hypertension and dyslipidaemia concurrently had the highest HbA1c (p = 0.015). There were significant differences between groups based on number of the complications in terms of the HbA1c level; patients with two complications had the highest HbA1c level (8.5 ± 2%).[27] The study by Kusum Bali and Amarjit Singh Vij showed that there were 55.1% male and 44.9% female with mean age 52.7 ± 11.43; 42.8% patients were urban and 57.2% rural. The mean body mass index (BMI) was 26.8 ± 5.48 (male: 25.4 ± 4.62 and female: 28 ± 5.31). Dyslipidemia was found in 81.8% patients. The most commonly elevated lipid was LDL-C (59.3%) followed by TG (57.2%) and TC (36.5%). The HDL-C was decreased in 34.4% patients. The distribution of dyslipidemia among the different age groups was almost similar: 82.6% in < 45 years, 82.9% in 45-60 years and 83.7% in > 60 years, the difference was not statistically significant (p = 0.998).[28]

P.Muraliswaran et al. conducted the study in the rural hospital in Pondicherry showed significant correlation between HbA1c and lipid profile parameters between the two groups (less than 7% and more than 7% of HbA1c). The results suggested the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular disorder in type 2 diabetes.[30] Neha Yadav et al. in their study divided study participants into 3 groups based

on HbA1c. Out of total patients enrolled 48% were male and 52% were female. There was no significant difference in male: female ratio between different groups. The data showed that TG level was maximum in group III and was minimum in group I. Comparison between the group shows a significant difference between all the groups (p <0.001). A significant positive correlation (Correlation coefficient 0.67, p <0.001) was also observed between level of TG and HbA1c. Similarly, LDL level was also highest in group III with a significant difference with other two groups (p <0.05). Also, a positive correlation (Correlation coefficient 0.64, p <0.05) was observed between LDL and HbA1c. On the other hand, HDL was lowest in group III as compared to groups I and II (p <0.001) and a negative correlation (Correlation coefficient - 0.716, p <0.001) was seen between HDL and HbA1c.[31]

Study conducted by Ram Vinod Mahato and et al. showed that among total 294 type 2 diabetic individuals included in this study, 180 were male and 114 were female. The mean age ± SEM of male and female patients were 62.72 ± 10.24 and 55.86 ± 12.08 years respectively. Hypercholesterolemia was found in 82(27.89%) individuals. Similarly, hypertriglyceridemia was found in 186(63.26%) individuals, decreased HDL-C was found in 46(15.6%) individuals and increased LDL-C was found in 140(47.6%) individuals. Among the diabetic individuals, 106(36.05%) individuals had only one abnormal lipid profile parameter, 88(29.93) had two abnormal lipid parameter and 68(23.12%) individuals had more than 2 abnormal lipid profile parameters. According to NCEP-ATP III guideline, 92(80.70%) females out of 114 and 150 (83.33 %) males out of 180 were dyslipidemic. Highly significant correlation was observed between FBG and HbA1c (p=0.000). HbA1c also demonstrated direct and significant correlations with TC (p=0.017), LDL-C (p=0.015), LDL- C/HDL-C ratio (p=0.011), Non-HDL-C (p=0.011) and Risk ratio (p=0.005). The correlation of HbA1c with TAG was positive (p=0.169) and with that of HDL-C was negative (p=0.596) but it was statistically non-significant.[32]

Saurabh Sultania et al. conducted Study of Lipid Profile in Type 2 Diabetes Mellitus Patients and its correlation with HbA1c at Rohilkhand medical college and hospital. The study results showed that there was highly significant difference in mean HDL in diabetic patients (39.66 ± 10.17) and controls (52.02 ± 11.15) (p<0.0001). Also, a highly significant difference was found in mean triglyceride in diabetic patients (185.70 ± 76.87) and controls (125.22 ± 17.14) (p<0.0001). There was no significant correlation found between HbA1c and TC, LDL, HDL, TG.[35] The study by Ishaq et al showed that of 239 cases, 96 (40%) were male and 143 (60%) were female. The mean age of males was 53.32 ± 12.4 years and that of females was 50.3 ± 14.0 years (p = 0.08). Of 239 patients, 53 (22%) patients with T2DM had controlled glycaemia (HbA1c <6.5) and 186 (78%) patients had uncontrolled glycaemia (HbA1c ≥6.5). Pearson's correlation of HbA1c with all lipid parameters except VLDL was statistically significant. HbA1c, however, had an inverse correlation with HDL and had a significant direct correlation with FBG (Pearson correlation 0.247; p ≤ 0.001).[36]

Siva Prabodh et.al in their study concluded that among 100 Type - 2 DM patients, only 21% were under good glycaemic control, 61% cases had dyslipidemia with higher Total Cholesterol (204± 40.24), higher Triglycerides (166.26 ± 58.68) and lower HDL-C (39.56±9.09) mg/dl, where p- value 0.001 which is highly significant. HbA1c is having a strong positive correlation with Total Cholesterol and Triglycerides whereas a strong negative correlation with HDL which is highly significant. 53% cases had hypertension with SBP (126.2±13.28) and DBP (82.87±7.66) mmHg and the p- value is < 0.0001 which is highly significant. HbA1c is having weak positive correlation with SBP and DBP which is not significant.[37]

Study by Alireza Arab et al. found that overall, 484 patients (328 females and 156 males) were studied. Mean age of patients was 56.61 ± 12.65 years. Mean duration of the disease was 13.52 ± 7.55 years. Mean level of HbA1c, triglycerides, cholesterol, LDL and HDL was 8.93 ± 1.76, 159.88 ± 93.91,
172.54 ± 44.53, 97.25 ± 43.99, and 45.81 ± 12.18 mg/dl, respectively. There was a

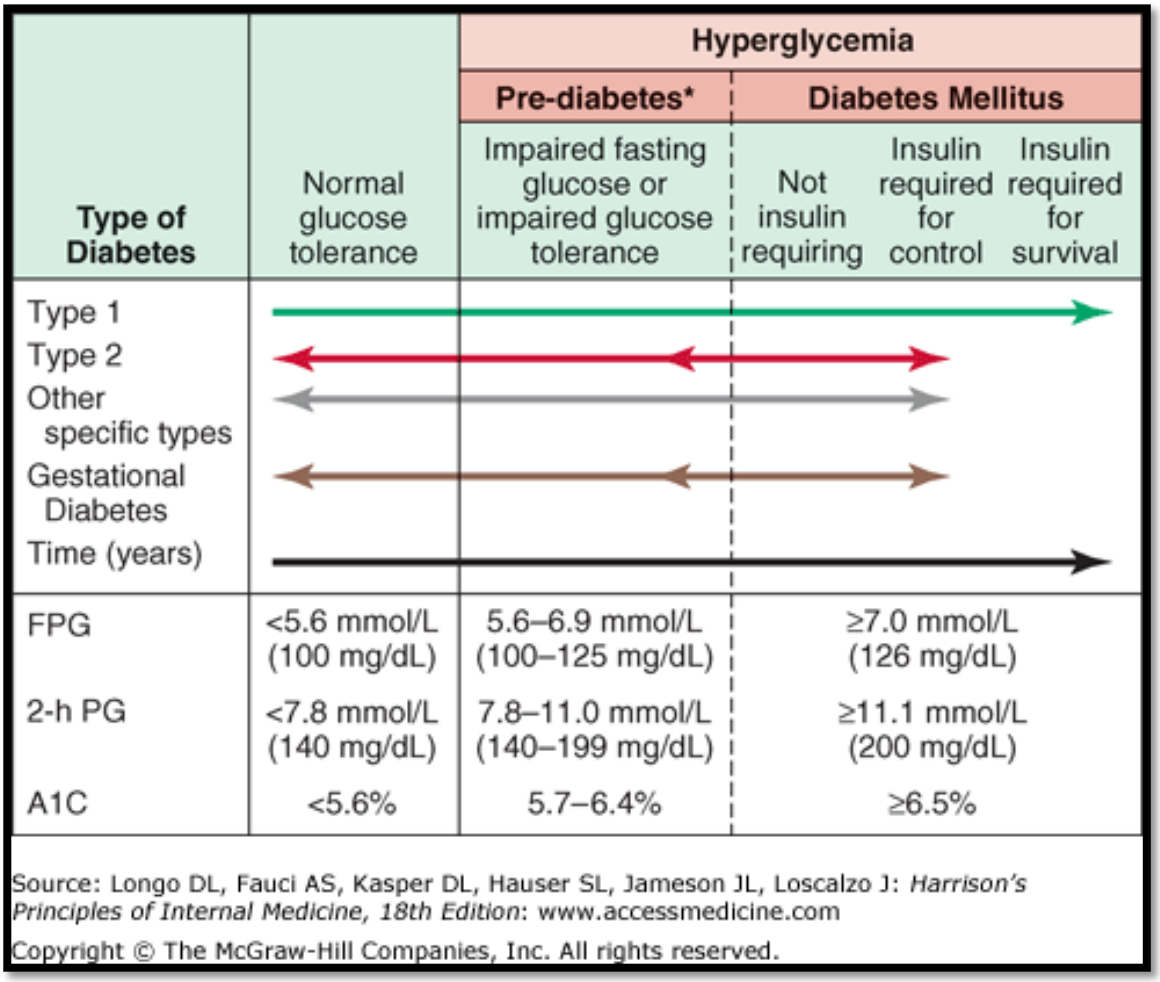
statistically significant correlation between HbA1c level and serum cholesterol (p=0.001), triglyceride (p=0.009), low-density lipoprotein (p=0.003) and FBS (p=0.0001). However, there was no statistically significant relationship between HbA1c and high-density lipoprotein levels (p= 0.8). High level of HbA1c is associated with dyslipidemia and can be used as predictors of cardiovascular disease in type 2 diabetes patients.[42]

The study conducted by DC Pant, AB Mowar, N Chandra showed that significant co-relation between HbA1c and ACS severity depicted in form of single/multi-vessel disease. Mean HbA1c of patients with single vessel disease was 7.67±0.71 and of patients with multi-vessel disease was 10.78±1.44. Significant inverse co-relation was also found between HDL and ACS severity with mean HDL in SVD patients 41.62±11.12 and in patients with MVD it was 25.92±8.67. Significant co-relation was also found between LDL and ACS severity with mean LDL in SVD patients 96.15±31.79 and in patients with MVD it was 162.83±36.74. Significant co-relation was also found between total cholesterol and ACS severity. With mean total cholesterol 164.13±33.44 in patients with SVD and mean 216.33±41.22 in patients with MVD. Significant direct co-relation was also found between HbA1c and total cholesterol, LDL and inverse significant co-relation with HDL.[43] Also, the study conducted by Dr. Anand showed significant correlation between HbA1c and lipid profile parameters between the two groups (less than 7% and more than 7% of HbA1c). The results suggested the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular disorder in type 2 diabetes.[44] The study conducted by Dr. Premkumar K.S. et.al. showed that the mean HbA1c 8.03%, Total Cholesterol 194.5 mg/dl, TGL 118, HDL 41.3 mg/dl, VLDL 35 mg/dl, LDL 115 mg/dl was seen in patients having Diabetes for less than 5 years and the mean HbA1c 8.45%, Total Cholesterol 199.4 mg/dl, TGL177 mg/dl, HDL39.5 mg/dl, VLDL37.9 mg/dl, LDL 122mg/dl was seen in patients having Diabetes for more than 5 years. By comparing both the groups it is found that there was no significant difference in lipid levels with effect to duration though HbA1c, was found to be elevated.[45 -48]

Criteria for the diagnosis of DM:

ADA guidelines for type 2 DM (2018): [53]

1. Fasting Blood sugar levels ≥126 mg/dL (7.0 mmol/L).
2. Two hour Postprandial sugar levels ≥200 mg/dL (11.1 mmol/L)
3. HbA1C ≥6.5% (48 mmol/mol).
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl (11.1 mmol/L).



The classic symptoms of hyperglycaemia include polyuria, polydipsia, and unexplained weight loss. [54-56]

Classification of DM:

1) Primary-

a) Type 1 (autoimmune)
   i. Immune mediated
   ii. Idiopathic

b) Type 2 (Non- autoimmune)

c) Other types

-Genetic defects of beta cell dysfunction:

E.g. Maturity onset DM in young MODY 1 (HNF-4 alfa mutation) MODY 2 (glucokinase mutation) MODY 3 (HNF-1 alfa mutation)
MODY 4 (insulin promoter factor mutation) MODY 5 (HNF-1 beta mutation)

-Genetic defects of insulin secretion

- Type A insulin resistance
- Lipoatropic DM
- Leprechaunism
- Rabson-Mendenhall syndrome

2) Secondary

- To disease associated with pancreas e.g. pancreatitis.
- Pheochromocytoma, hyperthyroidism and acromegaly
- To hormonal abnormalities like Cushing's syndrome.
- To insulin receptor antibodies
- To drugs and chemical induced
  e.g. thyroid hormones, glucocorticoids
- Associated with genetic syndromes

e.g. Down's syndrome, Klinefelter's syndrome, Turners syndrome

Several studies have found a strong association

between prevalence of DM and overweight and obesity.[62] There is also a substantial role of geneticfactors in determining the risk of type 2 DM.[63]

A study in India indicates that more than 50% of people with DM have got poor glycemic control, uncontrolled hypertension, and dyslipidaemia and a large percentage have diabetic vascular complications.[64] Another study on Indian data shows that the common risk factors such as greater duration of DM, hypertension, poor metabolic control are more prone to develop diabetic complications.[65]

Materials and Methods

Study area and setting:

The study was conducted at Krishna Hospital and Medical Research Centre, a tertiary care hospital and teaching institute in Maharashtra.

Source of Data: The study was carried on patients with diagnosis of type 2 Diabetes mellitus who were admitted in wards and attending Out Patient Department over the period of October 2017 to March 2019 in Krishna Institute of Medical Sciences, Karad.

Study design:

A cross sectional study of type 2 diabetic patients.

Study period:

The present study was conducted for 18 months, from October 2017 to March 2019.

Sample size:

According to a study conducted by Nyasatu G. Chamba et al. the prevalenceof dyslipidemia in type 2 diabetes patients was 83 %. So

P = 83 %

Q = 1-p = 1-0.83 = 0.17

D = absolute error = 10% = 0.1

$$N = \frac{4 \times 0.83 \times 0.17}{0.1 \times 0.1}$$

= 56 64. N ~ 60

For statistical reasons and better yield, sample size taken as 100. N =100

SELECTION OF PARTICIPANTS

Type 2 diabetic patients attending the Out Patient Department, Indoor patients, patients admitted in Intensive Care Unit at KIMSDU, Karad were selected for the study.

Inclusion Criteria:

All the patients who were willing to participate in the study, provided they were

- Patients above 18 years of age
- Patients diagnosed as Type 2 Diabetes Mellitus

Exclusion Criteria:

- Newly diagnosed diabetic patients who are not on treatment.
- Non diabetics.
- Patients diagnosed as Type 1 diabetes mellitus.
- Patients with hepatic, renal, endocrine disorders.
- Patients who are on lipid lowering agents.
- Patients who are not willing to participate in the study.

Informed consent:

Patients presenting with type 2 diabetes mellitus were screened for the eligibility. The patients fulfilling the selection criteria were explained about the nature as well as purpose of the study in English and / or local language they understand. A written informed consent was obtained from those who were willing to participate in the study.

Ethical clearance:

The study also obtained the permission of the institutional ethics committee (IEC). Permission was also taken from head of departments.

Laboratory Investigations:

1. Blood sugar levels
   - Fasting blood sugar levels

- Postprandial blood sugar levels
- Random blood sugar levels

2. Glycosylated haemoglobin (HbA1c)
3. Other routine investigations

Procedure:

- Under all aseptic precautions, 7ml of blood was collected from the cubital vein after 6-8 hours of fasting
- Blood was collected in

a. EDTA sodium fluoride vacutainer (1ml) for fasting blood sugar levels and post prandial blood sugar levels.
b. EDTA vacutainer (2ml) for glycosylated haemoglobin (HbA1c).

- After 2 hours of meals, 1ml of blood was collected in EDTA sodium fluoride vacutainer.
- Blood sugar levels (Fasting, Postprandial and Random) were calculated by Trinder's method (Glucose Oxidase-Peroxidase Method) automatically on EM360 Transasia machine.

- Glycosylated haemoglobin (HbA1c) as calculated by particle enhanced immuneturbidimetric test (automatically) on EM360 Transasiamachine.

Normal Values:

1. Fasting BSL: 70-110 (mg/dl)
2. Postprandial BSL: 150-180 (mg/dl)3. HbA1c: 5.6-6.5 (%)

Diagnosis of type 2 Diabetes mellitus

ADA guidelines for type 2 Diabetes mellitus (2018):

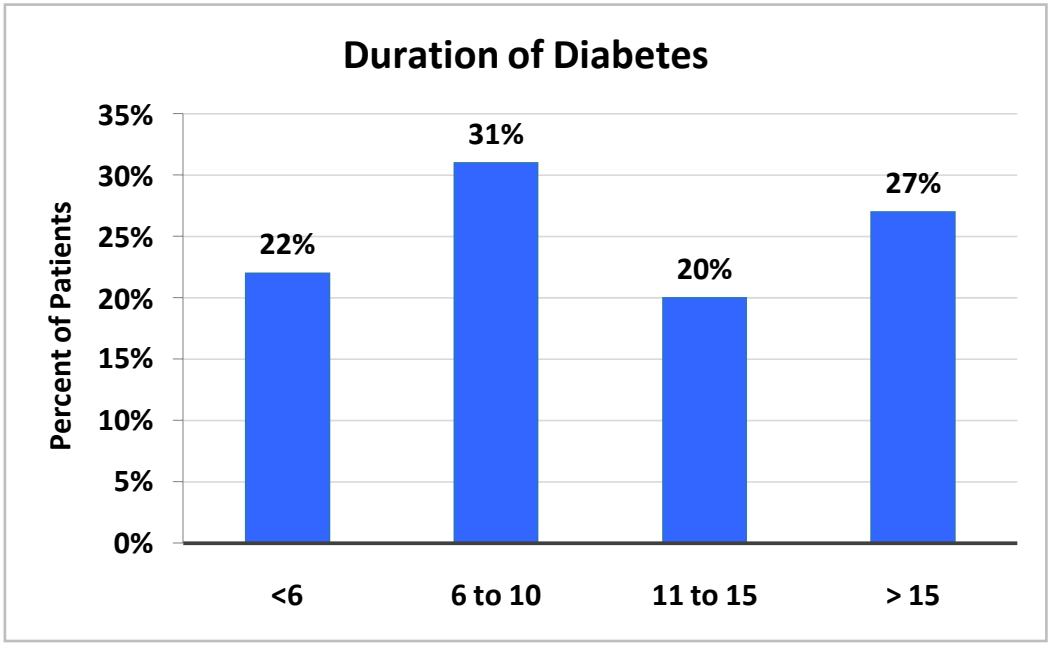
1. Fasting Blood sugar levels ≥126 mg/dl (7.0 mmol/L)
2. Two-hour postprandial sugar levels ≥200 mg/dl (11.1 mmol/L)
3. HbA1c≥6.5 % (48 mmol/mol)
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/L).

- **Weight Measurements**
- Weights of the participants will be measured to the nearest 0.1kg. The scale will be placed on a hard surface. The participants will then be asked to stand in the centre of the platform bare footed with their weight distributed evenly to both feet.
- **Height Measurement**
- Heights of participants will be measured to the nearest 0.5cm using wall mounted stadiometer. Participants will be asked to remove their sandals and made to stand upright with their back to the height rule.
- **Waist Circumference**
- Waist circumference of the participants measured at a level midway between the lower rib margin and iliac crest with the tape all around thebody in supine position.
- Participants will be made to stand with their feet close together and their weight equally distributed to each leg.
- **Hip Circumference**
- Hip circumference measured as the maximal circumference over the buttocks.
- **Body Mass Index (BMI)**
- BMI will be calculated as weight kg/height squared (kg/m²) and patients will be considered as normal weight if their BMI comes < 25 kg/m² , overweight if their BMI is from 25 to 29 kg/m² and obese if their BMI is≥ 30 kg/m².

Table 1: Distribution of patients based on duration of diabetes

Duration of Diabetes in years	Frequency (n)	Percent (%)
<6	22	22
6 to 10	31	31
11 to 15	20	20
> 15	27	27
Total	100	100
Mean: 10.36 ± 6.10		

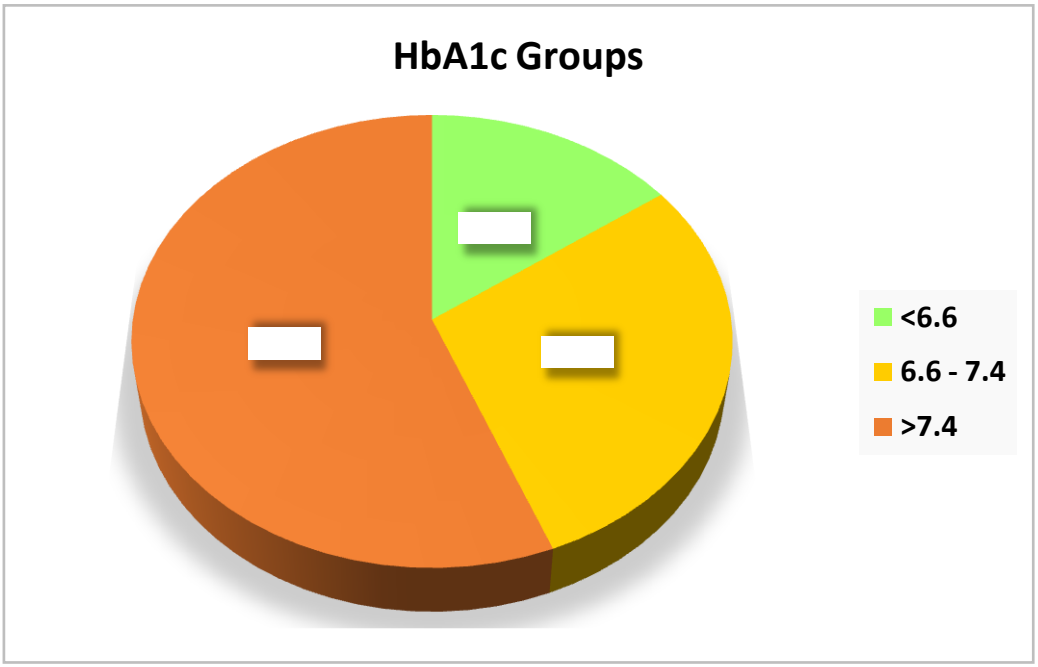
Figure 1: Distribution of patients based on duration of diabetes



Most common HbA1c group seen in our study was >7.4, in 56 patients (56%) followed by 6.6-7.4 in 26 patients (29%). Only 15 patients (15%) had good sugar control with HbA1c values less than 6.6. The mean level of HbA1c was
7.85 ± 1.34 %. (**Table 4, Figure 4)**

Table 2: Distribution of patients based on HbA1c levels		
HbA1c levels	**Frequency (n)**	**Percent (%)**
<6.6	**15**	**15**
6.6 - 7.4	**29**	**29**
>7.4	**56**	**56**
Total	**100**	**100**
Mean: 7.85 ± 1.34 %		

Figure 2: Distribution of patients based on HbA1c levels



Only 15 patients (15%) had good sugar control with HbA1c values less than 6.5, rest 85 patients (85%) had poor control with HbA1c more than 6.5. (**Table5, Figure 5)**

Table 5: Group statistics

Group Statistics					
	Sugar Control	**n**	**Mean**	**S.D.**	**'p' Value**

Age	**Poor (HbA1c ≥ 6.5)**	**85**	**56.07**	**12.029**	**0.43**
	Good (HbA1c < 6.5)	**15**	**53.33**	**13.367**	
FBS	**Poor (HbA1c ≥ 6.5)**	**85**	**162.46**	**62.659**	**0.30**
	Good (HbA1c < 6.5)	**15**	**144.67**	**45.780**	
PPBS	**Poor (HbA1c ≥ 6.5)**	**85**	**263.93**	**82.295**	**0.23**
	Good (HbA1c < 6.5)	**15**	**237.00**	**54.487**	
TC	**Poor (HbA1c ≥ 6.5)**	**85**	**180.28**	**48.464**	**0.035**
	Good (HbA1c < 6.5)	**15**	**151.67**	**43.897**	
TRIG	**Poor (HbA1c ≥ 6.5)**	**85**	**195.22**	**76.625**	**0.016**
	Good (HbA1c < 6.5)	**15**	**143.93**	**63.697**	
HDL	**Poor (HbA1c ≥ 6.5)**	**85**	**43.28**	**9.862**	**0.09**
	Good (HbA1c < 6.5)	**15**	**48.53**	**16.366**	
VLDL	**Poor (HbA1c ≥ 6.5)**	**85**	**45.53**	**16.314**	**0.09**
	Good (HbA1c < 6.5)	**15**	**37.87**	**13.158**	
LDL	**Poor (HbA1c ≥ 6.5)**	**85**	**103.25**	**45.380**	**0.14**
	Good (HbA1c < 6.5)	**15**	**84.87**	**38.197**	
Duration of Diabetes	**Poor (HbA1c ≥ 6.5)**	**85**	**10.33**	**6.009**	**0.91**
	Good (HbA1c < 6.5)	**15**	**10.23**	**6.833**	

The mean levels of total cholesterol was 180.28 ± 48.46 in poor sugar control patients and 151.67 ± 43.90 in good sugar control patients, were showing significant correlation (p= 0.035). Levels of total cholesterol were lower in patients with good sugar control, showing positive correlation.

Mean levels of triglycerides, 195.22 ± 76.63 in poor sugar control patients and 14.93 ± 63.70 in good sugar control patients were showing significant correlation (p = 0.016). Levels of triglycerides were lower in patients with good sugar control, showing positive correlation.

There was no any significant correlation found

between the sugar control and age, FBS, PPBS, LDL, VLDL but they all were showing positive correlation, that's with increase in these values, there was increased chances of poor sugar control with higher levels of HbA1c.

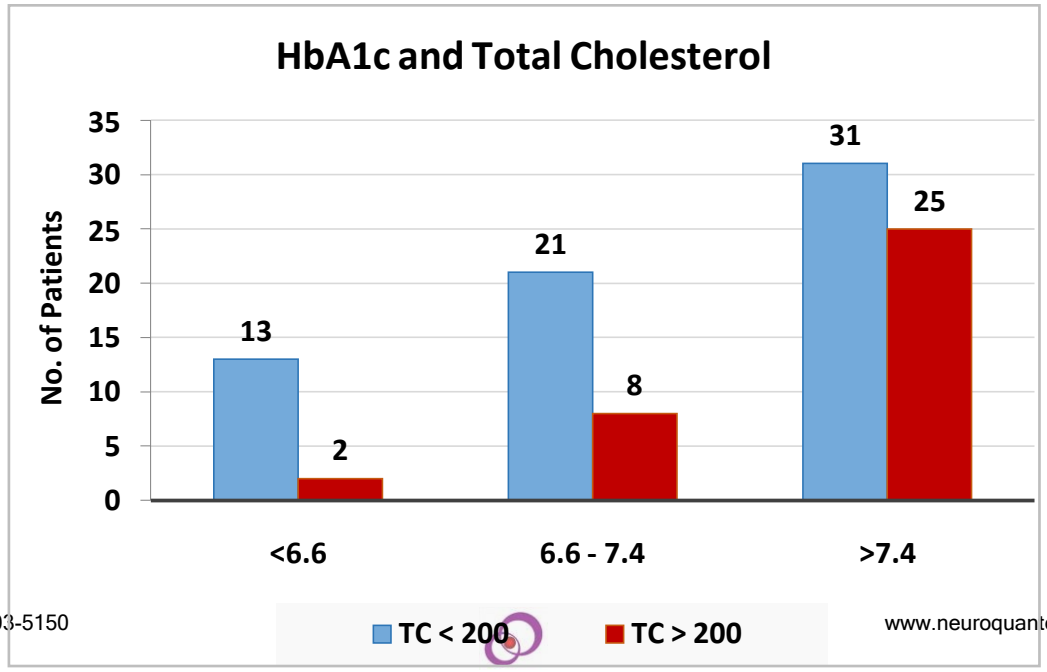
Only HDL showed Negative correlation with sugar control, as lower mean HDL values of 43.28 ± 9.26 were associated with higher HbA1c values suggesting poor sugar control as compared to higher mean HDL values of 48.53 ± 16.37 seen in lower HbA1c levels suggesting good sugar control.

Table 6: HbA1c levels and Total Cholesterol > 200

HbA1c levels	TC > 200		Total
	No	Yes	
<6.6	13	2	15
6.6 - 7.4	21	8	29
>7.4	31	25	56
Total	65	35	100

X^2= 6.09 p = 0.048 (statistically significant)

Figure 3: HbA1c levels and Total Cholesterol



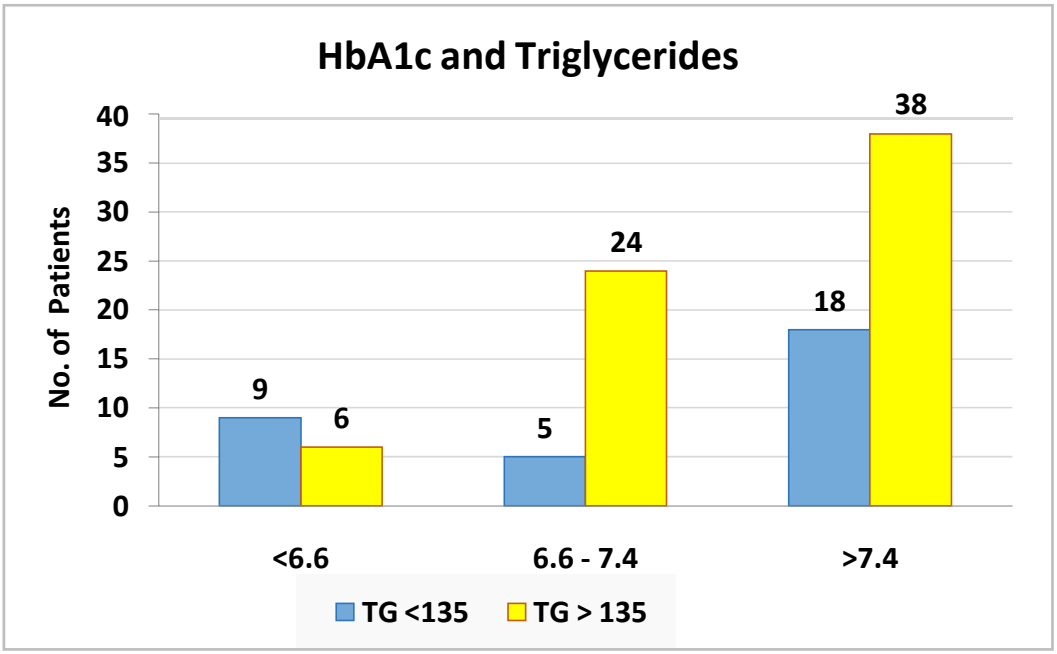
Significant association was seen between the HbA1c Groups and triglyceride levels. TG levels > 135 were seen more in patients with poor sugar control (38%) as compared with the patients with good sugar control (6%). (p = 0.016)

Table 7: HbA1c levels and TG > 135

HbA1c levels	TG > 135		Total
	No	Yes	
<6.6	9	6	15
6.6 - 7.4	5	24	29
>7.4	18	38	56
Total	32	68	100

X^2= 8.31 p = 0.016 (statistically significant)

Figure 4: HbA1c levels and TG



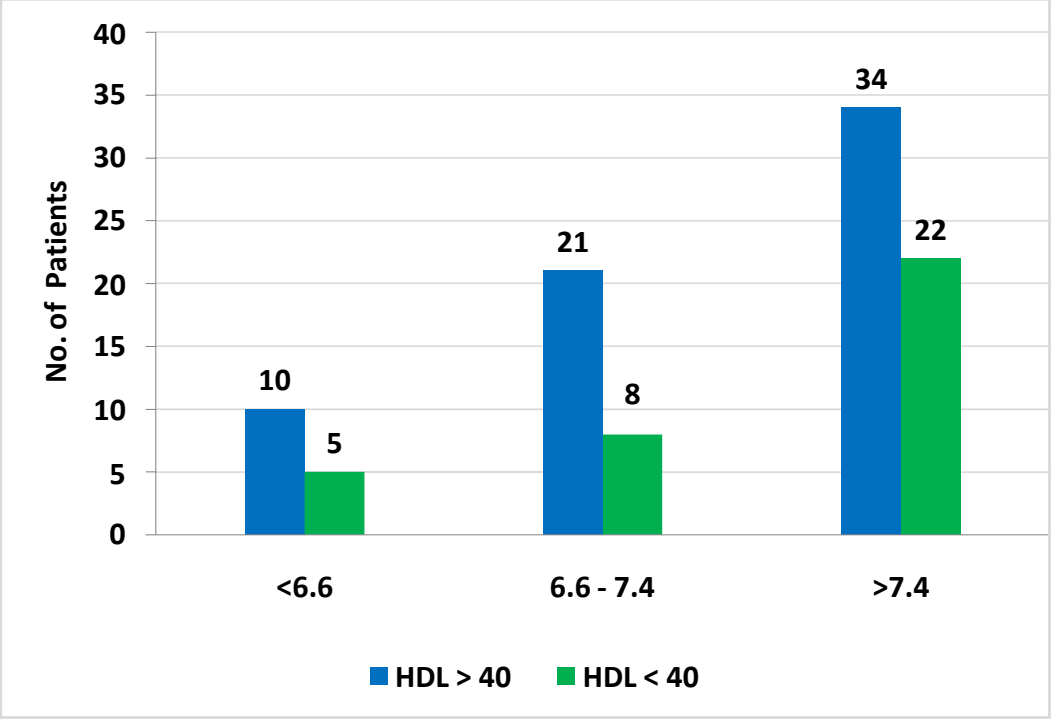
No significant association was seen between the HbA1c levels and HDLlevels < 40. (p=0.56)

Table 8: HbA1c levels and HDL < 40

HbA1c levels	HDL < 40		Total
	No	Yes	
<6.6	10	5	15
6.6 - 7.4	21	8	29
>7.4	34	22	56
Total	65	35	100

X^2= 1.71 p = 0.56 (statistically insignificant)

Figure 5: HbA1c levels and HDL



No significant association was seen between the HbA1c Groups andVLDL > 30 (p = 0.62).

Discussion

- The study by **Sanjay Thorat** had 17% patients with good control, in our study it was less and was 15%. [70]
  Mean levels of total cholesterol, 180.28 ± 48.46 in poor sugar control patients and 151.67 ± 43.90 in good sugar control patients were showing significant correlation (p= 0.035). Levels of total cholesterol were lower in patients with good sugar control, showing positive correlation.
- The study by **Vithpala Praveena et al** had mean values of total cholesterol in poorly control group 175 ± 52.26 and in well control group 150.4 ± 38.26, these are comparable with the current study and there is correlation seen similar to the current study. [71]
- In the study by **Samatha P et al**, there was no correlation seen between HbA1c and total cholesterol level while in our study there was correlation seen. [66]
- The study by **Sanjay Thorat** had no correlation with total cholesterol while in the current study it was found. [70]
  Mean levels of triglycerides, 195.22 ± 76.63 in poor sugar control patients and 143.93 ± 63.70 in good sugar control patients were showing significant correlation (p = 0.016). Levels of triglycerides were lower in patients with good sugar control, showing positive correlation.
- The study by **Vithpala Praveena et al**, had mean values of total triglyceride in poorly control group 170 ± 99.35 and in well control group 118 ± 43.92. These are lower than the current study and thereis correlation seen similar to the current study. [71]
- In the study by **Samatha P et al**, there was no correlation seen between HbA1c and triglyceride level while in our study there was correlation seen. [66]
- The study by **Sanjay Thorat** had no correlation between Triglycerides and HbA1c, while in our study there was correlation seen. [70]
  There was no any significant correlation found between the sugar control and age, FBS, PPBS, LDL, VLDL but they all were showing positive correlation, that's with increase in these values, there was increased chances of poor sugar control with higher levels of HbA1c.
- The study by **Satarupa Dash** had no correlation of VLDL similar tothe current study.[69]
- The study by **Vithpala Praveena et al**, found correlation between LDL,VLDL,FBS, while in our study no such correlation was seen. [71]
- In the study by **Samatha P et al,** they found correlation between HbA1c and fasting glucose levels while in our study it was not there.[66]
- The study by **Sanjay Thorat** had association between age and HbA1c, while in the current study it was not seen and had correlation with FBS LDL, VLDL while in the current study it was not found. [70]
- The study by **Baljinder Singh et al**, had correlation with LDL which was not seen in the current study.[73]

Only HDL showed Negative correlation with sugar control, as lower mean HDL values of 43.28 ± 9.26 were associated with higher HbA1c values suggesting poorsugar control as compared to higher mean HDL values of 48.53 ± 16.37 seen in lower HbA1c levels suggesting good sugar control.

- The study by **Vithpala Praveena et al**, had mean values of HDL in poorly control group 40.71 ± 8.91 and in well control group 42.3 ± 9.38. These are lower than the current study and there is no correlation seen while in the current study we found negative correlation.[71]
- In the study by **Samatha P et al**, there was no correlation seen between HbA1c and HDL level while in our study there was negative correlation seen.[66]

No Significant association was seen between the HbA1c levels andage

groups. (p = 0.38)

- The study by **Baljinder Singh et al**, had no association of age and HbA1c similar to the current study.[72]

No any significant association was seen between the HbA1c levels and gender. (p = 0.07)

No any significant association was seen between the HbA1c levels and duration of diabetes. (p = 0.82)

Significant association was seen between the HbA1c Groups and Total Cholesterol levels. TC levels > 200 were seen more in patients with poor sugar control (25%) as compared with the patients with good sugar control (2%). (p = 0.048)

- The study by **Baljinder Singh et al**, had association of total cholesterol and HbA1c similar to the current study.[72]

Significant association was seen between the HbA1c Groups and triglyceride levels. TG levels > 135 were seen more in patients with poor sugar control (38%) as compared with the patients with good sugar control (6%). (p = 0.016)

No significant association was seen between the HbA1c levels and HDLlevels < 40. (p=0.56)

No significant association was seen between the HbA1c Groups and VLDL >30 (p = 0.62).

No any significant association was seen between the HbA1c Groups and LDL > 130 (p = 0.26).

- The study by **Devkar et al.** found association between poor glycemic control and deranged lipid profile, similar association was seen in our study, seen between total cholesterol and triglyceride levels with HbA1c levels.[67]
- The study by **Samdani TS et al**, had no association of HbA1c and high LDL and low HDL this is similar to the current study. There was association of triglyceride and cholesterol seen in our study but was absent in the study by Samdani TS et al.[73]
- The study by **Abdulazeez Sulaiman Safo** had no association of TC, LDL, HDL, TC. But in the current study we had correlation of TG and TC.[68]

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