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Glycated hemoglobin disorders in patients with diabetes and hyperlipidemia

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ABSTRACT

This study is an attempt to evaluate the diagnostic value of Glycated haemoglobin (HbA1c) in predicting diabetic dyslipidemia. Venous blood samples were collected from 154 type 2 diabetic patients. The whole blood and sera were analyzed for HbA1c, fasting blood glucose (FBG) and lipid profile panel test. Dyslipidemia was defined as per the National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP) III guidelines. Diabetes was defined as per American diabetes association criteria.. HbA1c demonstrated positive and significant correlations with total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and LDL-C ratio, non-HDL-C and TC/HDL-C ratio. Patients with HbA1c value>7.0% had significantly higher value of TC, Triacylglycerol (TAG), LDL-C, LDL-C/HDL-C ratio,non-HDL-C and TC/HDL-C ratio as compared to the patients with HbA1c ≤ 7.0%. However,. HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control.

Keywords: Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, Lipid Profile panel, Biomarker.

اضطرابات الهيموجلوبين السكري لدى مرضى السكري والدهون

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الملخص

هذه الدراسة هي محاولة لتقييم هيموجلوبين السكري (HbA1c) في التنبؤ بخلل شحوم الدم الناتج عن مرض السكري. تم جمع عينات الدم الوريدي من 154 مريضاً مصاباً بداء السكري من النوع الثاني. تم تحليل الدم الكامل والأمصال لنسبة HbA1c ومستوى السكر في الدم الصائم (FBG) واختبارات الدهون. تم تعريف اضطراب شحوم الدم وفقًا للمبادئ التوجيهية للبرنامج الوطني لتعليم الكوليسترول (NCEP) ولجنة علاج البالغين III. (ATP) تم تعريف مرض السكري وفقًا لمعايير الجمعية الأمريكية لمرض السكري. أظهر HbA1cارتباطات إيجابية ومهمة مع الكوليسترول الكلي(TC) ، وكوليسترول البروتين الدهني منخفض الكثافة(LDL-C) ، وكوليسترول البروتين الدهني عالي الكثافة (HDL-C) ونسبةLDL-C ، غير -نسبة HDL-Cو .TC/HDL-C كان لدى المرضى الذين لديهم قيمةHbA1c> 7.0 ٪ قيمة أعلى بكثير من TC، ونسبة(TAG) Triacylglycerol ، وLDL-C، ونسبةLDL-C/HDL-C ، ونسبة غير HDL-C ونسبة TC/HDL-C مقارنة بالمرضى الذين يعانون من نسبةHbA1c> 7.0 ٪ .نسبة .HbA1c ≥ 7.0% لكن. يمكن استخدام HbA1c كمؤشر حيوي محتمل للتنبؤ بخلل شحوم الدم لدى مرضى السكري من النوع 2 بالإضافة إلى التحكم في نسبة السكر في الدم.

INTRODUCTION

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke). Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular deaths. The lipid abnormality (dyslipidemia) associated with type 2 diabetes typically consists of elevated triglycerides and decreased HDL cholesterol level **(Howard, 1995)**. In such individuals, LDL cholesterol levels are generally not significantly abnormal, although they may be somewhat elevated in whites **(Harris ,1991)** and lower in other racial/ethnic groups. The frequently mild abnormality in LDL cholesterol concentration associated with diabetes belies a qualitative abnormality in the LDL structure, i.e. decreased size and increased density of the LDL particle**(Siegel ,1996).** Even when LDL cholesterol is normal or within a range that might be

considered low in diabetic individuals, LDL appears to be very potent contributor to the development of coronary heart disease CHD **(Howard *et al* ,2000)**

In addition to VLDL, LDL levels are also somewhat increased in diabetic individuals under poor control probably accounting in part for their increased risk for cardiovascular disease (CHD). the study revealed that HbA1c, and serum lipid para Type 2 diabetes is associated with significant cardiovascular morbidity and mortality. Although low-density lipoprotein cholesterol levels may be normal in patients with type 2 diabetes, insulin resistance drives a number of changes in lipid metabolism and lipoprotein composition that render low-density lipoprotein cholesterol and other lipoproteins more pathogenic than species found in patients without type 2 diabetes. A number of lipid-lowering agents, including statins, fibrates, niacin, and bile acid sequestrants, are available to target normalization of the entire lipid profile. Despite use of combination and high-dose lipid-lowering agents, many patients with diabetes do not achieve lipid targets. Meters total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, lipoprotein **Murat *et al*.(2010).**

MATERIALS AND METHODS

The study comprised of a total of 154 Type 2 diabetic patients who visited the Medicine OPD of, king George medical college Luknow , India. Ethical clearance obtained for the study from the hospital. Venous blood samples collected from all the patients after at least 12 hours fasting into centrifuge tubes. The blood allowed to clot and then centrifuged at 3000 rpm for 15 min at room temperature. The glycohaemoglobin (HbA1c) estimated by Ion exchange resin method and the serum analyzed for total cholesterol by Enzymatic method and triglycerides by Enzymatic colorimetric method and HDL-Cholesterol estimated by Cholestrol

Phosphotungstate method and LDL-Cholesterol by Friedewald formula as shown below.

LDL-C = TC - HDL-C – (TG/5).

The serum glucose determined by using the glucose oxidase enzymatic method. All the parameters under investigation were determined in the serum of the subjects using commercially available reagent kits. estimated. For serum lipid reference level National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP ATP III guideline hypercholesterolemia defined as TC > 200 mg/dL, high LDL-C when value > 100 mg/dL, hypertriglyceridemia > 150 mg/dL and low HDL-C when value < 40 mg/dL. Dyslipidemia defined by presence of one or more than one abnormal serum lipid concentration. Values of HbA1c were given as % of total hemoglobin and values of all other parameters were given in mg/dL. All values were expressed as mean ± SD.

Results

Diabetic patients were classified into 2 groups as per their glycemic index; first group consists of patients with HbA1c value ≤7.0 % and second group consists of patients with HbA1c value >7.0%. The mean of the parameter when the HbA1c >7%. HbA1c ;fasting blood sugar ;postprandial blood sugar total -cholesterol, triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein were 8.48±1.07%; 159.92 ±52.6 mg/dL; 241.62 ±64. 2 mg/dL; 241.67 ±29.06 mg/dL; 225.43±67 mg/dL; 45.5±13.28 mg/dL; 151.09 ±33.34mg/dL; The data were evaluated by Microsoft Excel statistical package. Pearson’s correlation test was performed to examine, according to NCEP-ATPIII guideline, Value of HbA1c was given as percentage of total haemoglobin and

values of all other parameters were given in mg/dl. All Values are expressed as mean ± standard deviation.

Table : Mean ± SD of HbA1c & lipid profile of type 2 diabetics when the HbA1c > 7

Parameter	SD ±Mean
FBG (mg/dL)	159.92 ±52.6
P.P BG (mg/dL)	241.62 ±64.2
TC (mg/dL)	241.67 ±29.06
TAG (mg/dL)	225.43±67
HDL (mg/dL)	45.5±13.28
LDL (mg/dL)	151.09 ±33.34
VLDL (mg/dL)	45.09±13.4

TC- total cholesterol, HDL- high density lipoproteins, LDL-low density lipoproteins, VLDL- very low density lipoproteins, TG- triglycerides

Further, it was found that glycated haemoglobin (HbA1c) was positively and significantly related with fasting blood sugar(R=0.08) ,postprandial blood sugar (R= 0.104), total cholesterol (R=0.21), high density lipoproteins (R=0.2), triglycerides (R= 0.189) and very low density lipoproteins (R=0.189). However, low density lipoproteins (R=0.194).

Association between glycaemic control and serum lipid profile in type 2 diabetic patients when the HbA1c >

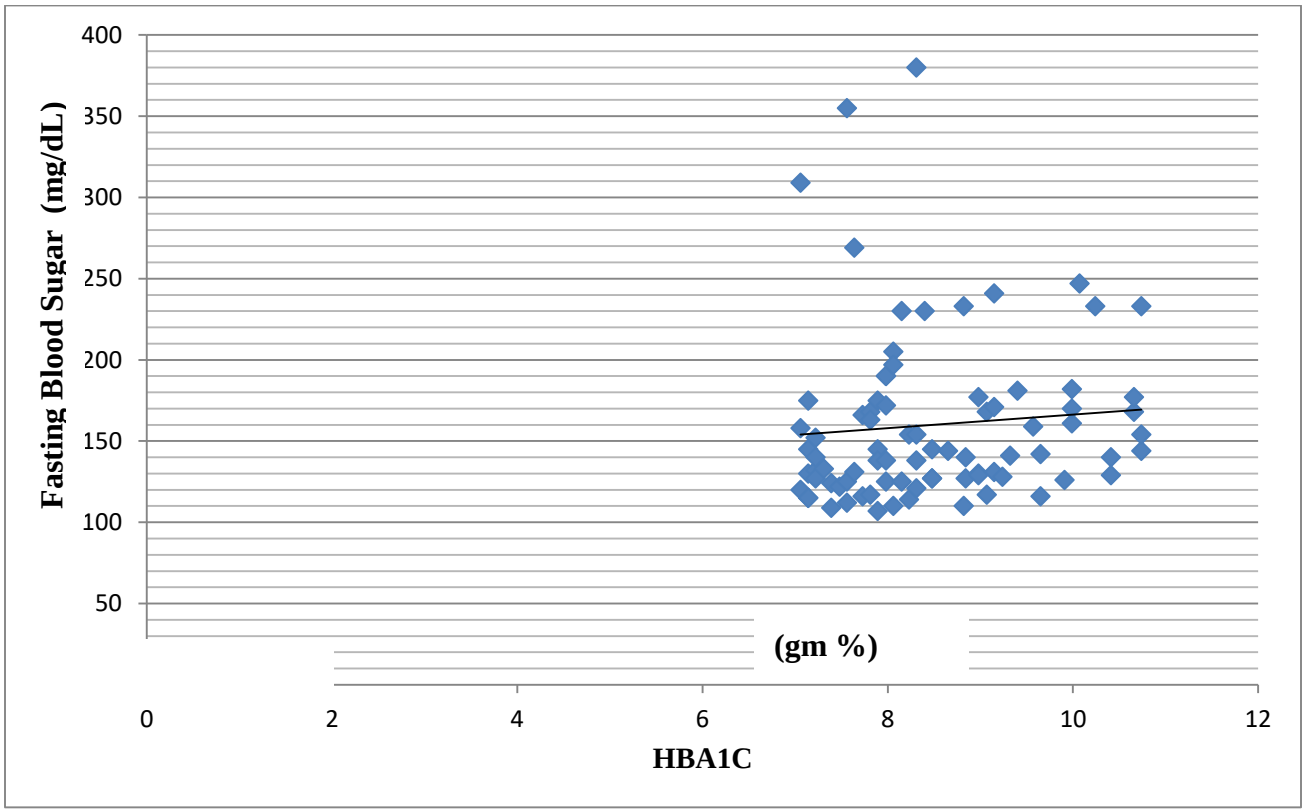

Figure 4.2.1: Correlation between HbA1c and FBG (R=0.08) in patients.

Figure 4.2.1 is a plot between the fasting blood sugar and HbA1c level, the graph shows that the HbA1c level is increasing with the increasing level of fasting blood sugar, so it shows positive correlation. The formation rate of HbA1c (that is product of glucose +Hb) is totally dependent on the sugar level in the body. So in diabetes the formation rate of HbA1c become more rapid due to the presence of high blood sugar (glucose).

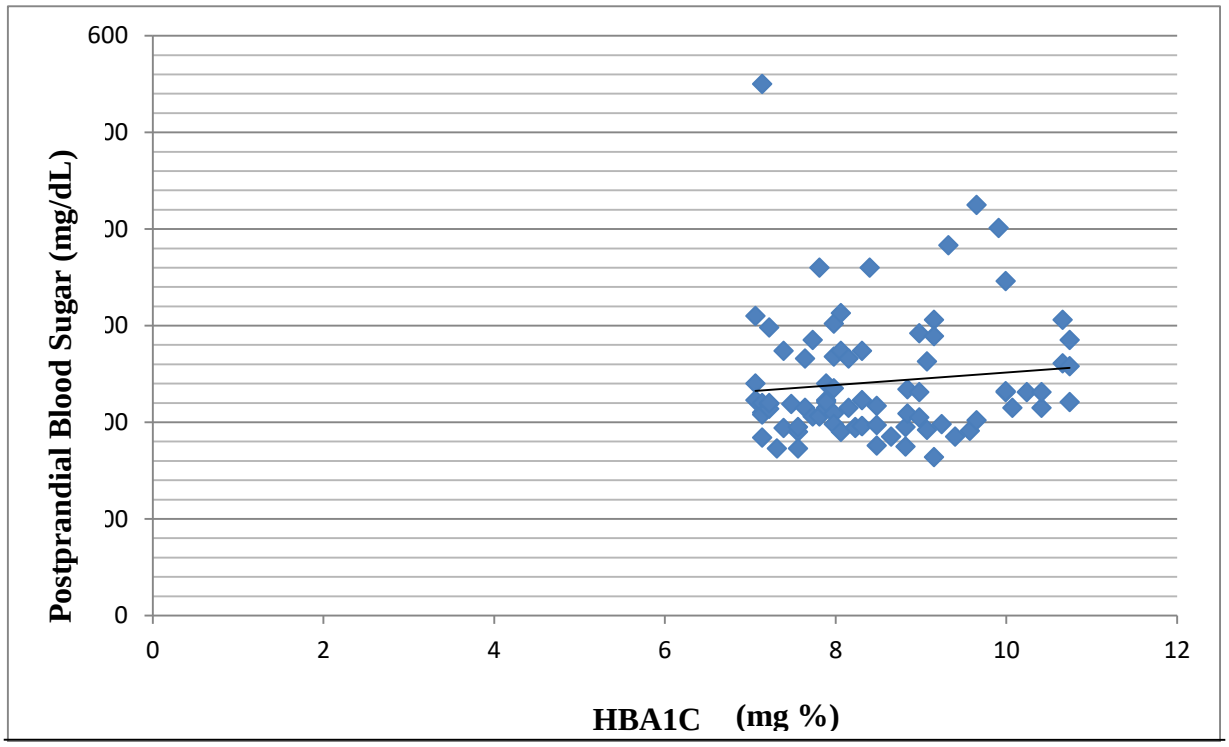

Figure 4.2.2: Correlation between HbA1c and PPBS (R=0.104) in patients.

Figure 4.2.2 is a plot between the postprandial blood sugar and HbA1c level. The graph shows that the HbA1c level is increasing with the increasing level of postprandial blood sugar so it shows positive correlation. The formation rate of HbA1c (that is product of glucose +Hb) is totally depending up on sugar level in the body. So in diabetes the formation rate of HbA1c become more rapid due to the presence of high blood sugar (glucose).

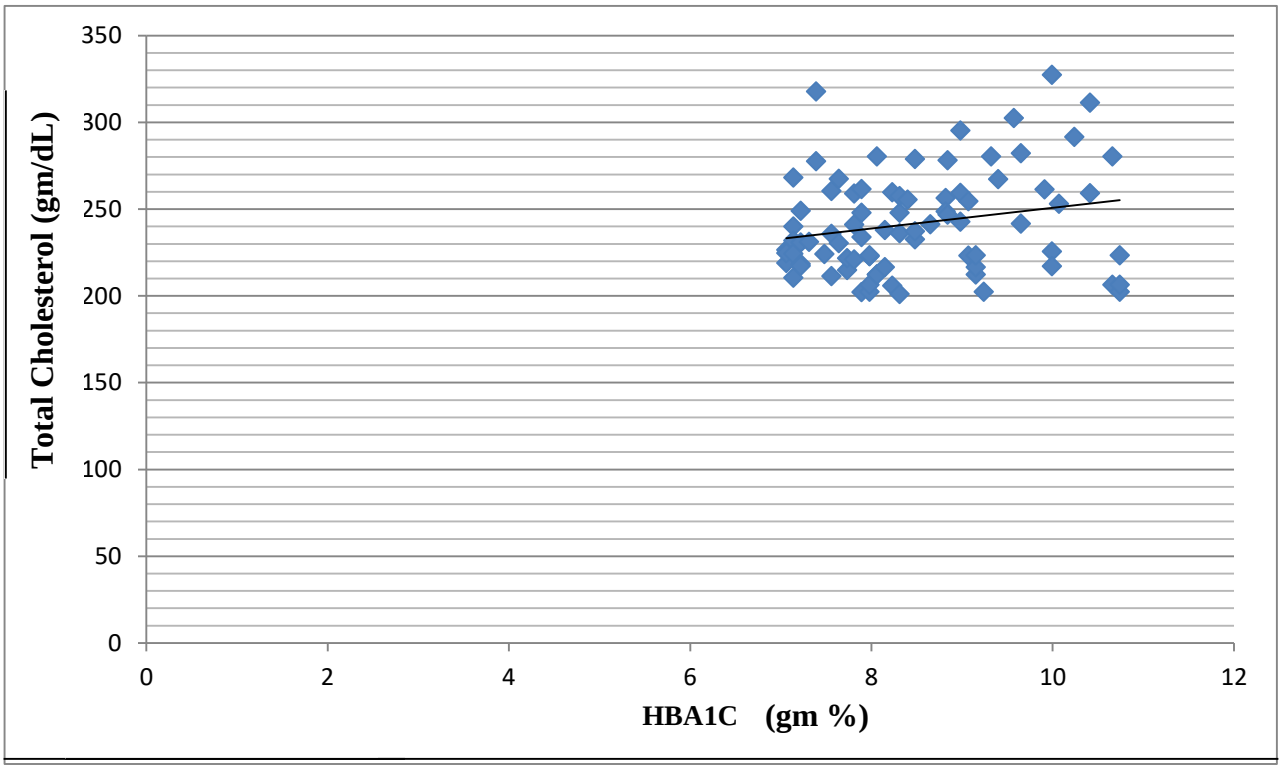

Figure 4.2.3: Correlation between HbA1c and TC (R=0.22) in patients.

Figure 4.2.3 is a plot between the total cholesterol and HbA1c level, the graph show that the HbA1c level is increasing with the increasing level of total cholesterol so it show positive correlation. In the diabetes condition when change in sugar level occurs it leads to disturbance in formation rate of acetyl co-A ultimately it will change the balance formation rate of acetyl co-A and effects on Krebs cycle. At this clinical condition most of the acetyl co-A molecules will go for cholesterol synthesis and associated factors. So formation rate of cholesterol become high in diabetes.

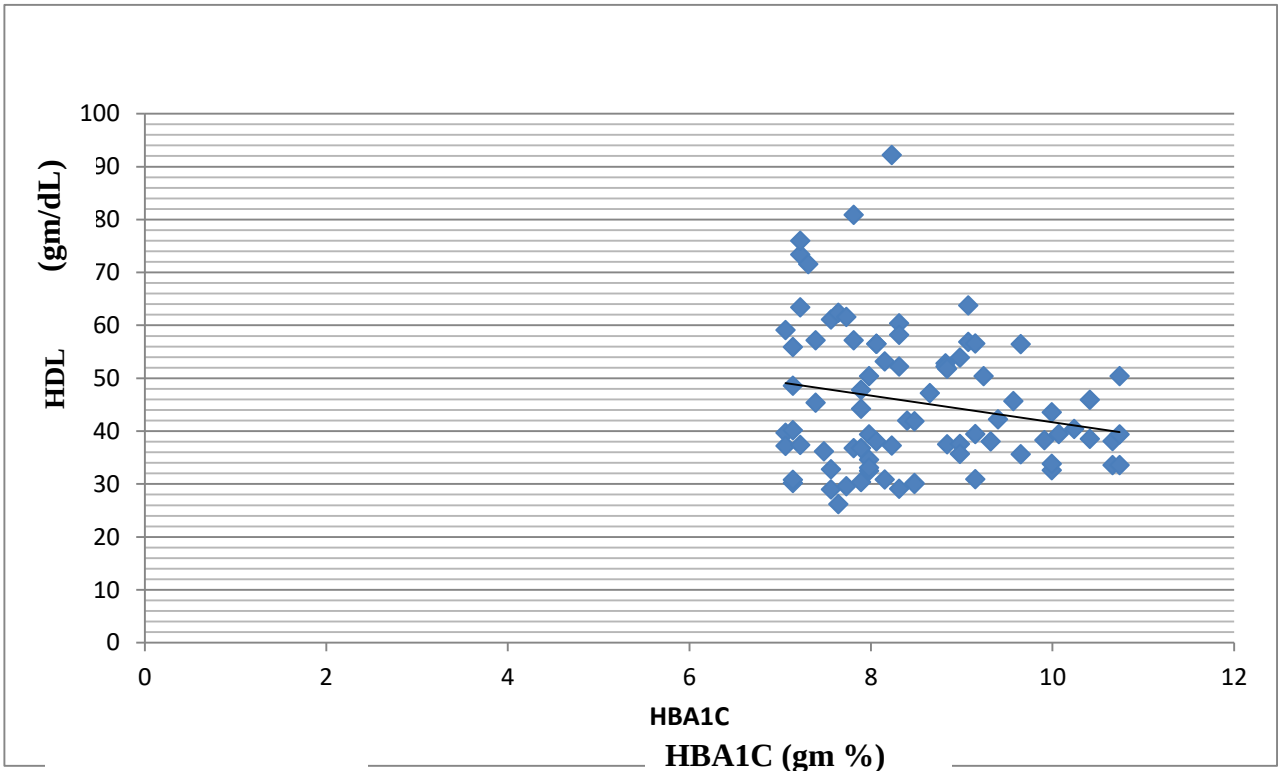

Figure 4.2.4: Correlation between HbA1c and HDL (R= -0.2) in patients.

Figure 4.2.4 is a plot between the high density lipoprotein and HbA1c level, the graph shows that the HbA1c level increase as the level of high density lipoprotein decrease so it show negative correlation. HDL is a transport for cholesterol. The relation between HDL and cholesterol is inversely proportional when cholesterol level become high the HDL level becomes low automatically in the body. In the diabetes there is high HbA1c and side by side high cholesterol so there is a decrease in HDL level.

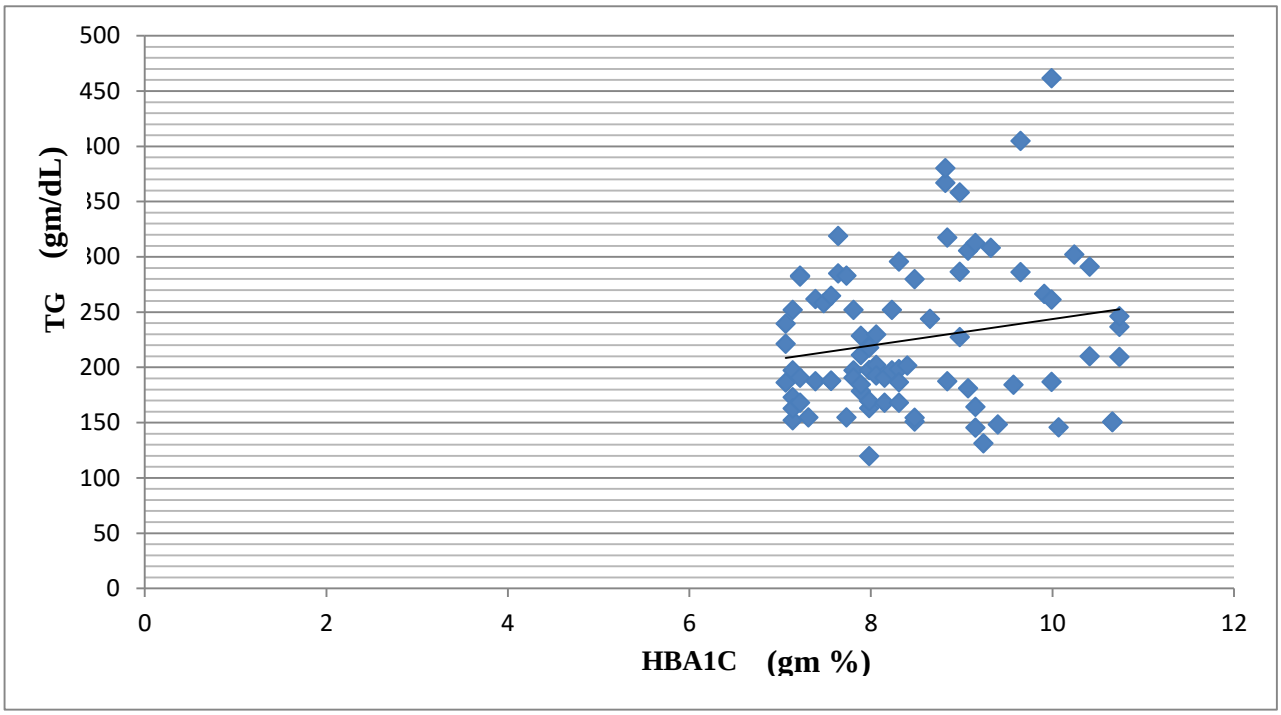

Figure 4.2.5: Correlation between HbA1c and TG (R=0.189) in patients.

Figure 4.2.5 is a plot between the triglycerides and HbA1c level, the graph show that the HbA1c level increases with the increasing level of triglycerides it show a positive correlation. Triglycerides are simple lipids and in diabetes when the intermediate metabolism between carbohydrate, protein and lipids get disturbed due to high sugar level which further disturbs the lipid metabolism and thereby resulting in formation of more triglycerides.

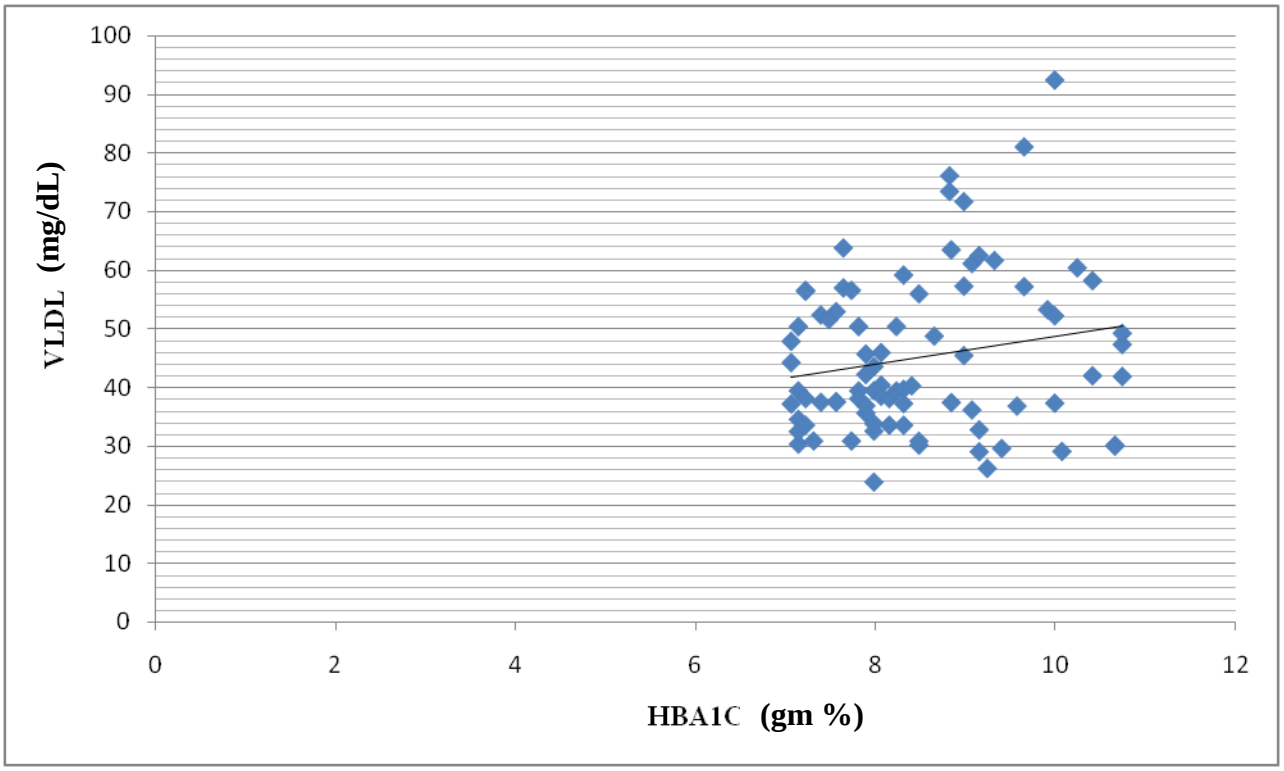

Figure 4.2.6: Correlation between HbA1c and VLDL (R=0.189) in patients.

Figure 4.2.6 is a plot between the very low density lipoprotein and HbA1c level, The graph shows that the HbA1c level increases with the increasing level of very low density lipoprotein so it show positive correlation. The VLDL is lipoprotein responsible for transportation of cholesterol from liver to peripheral tissues. Liver is the site where formation of VLDL is going on. Due to high cholesterol in diabetes with high HbA1c which results formation the of the high VLDL level.

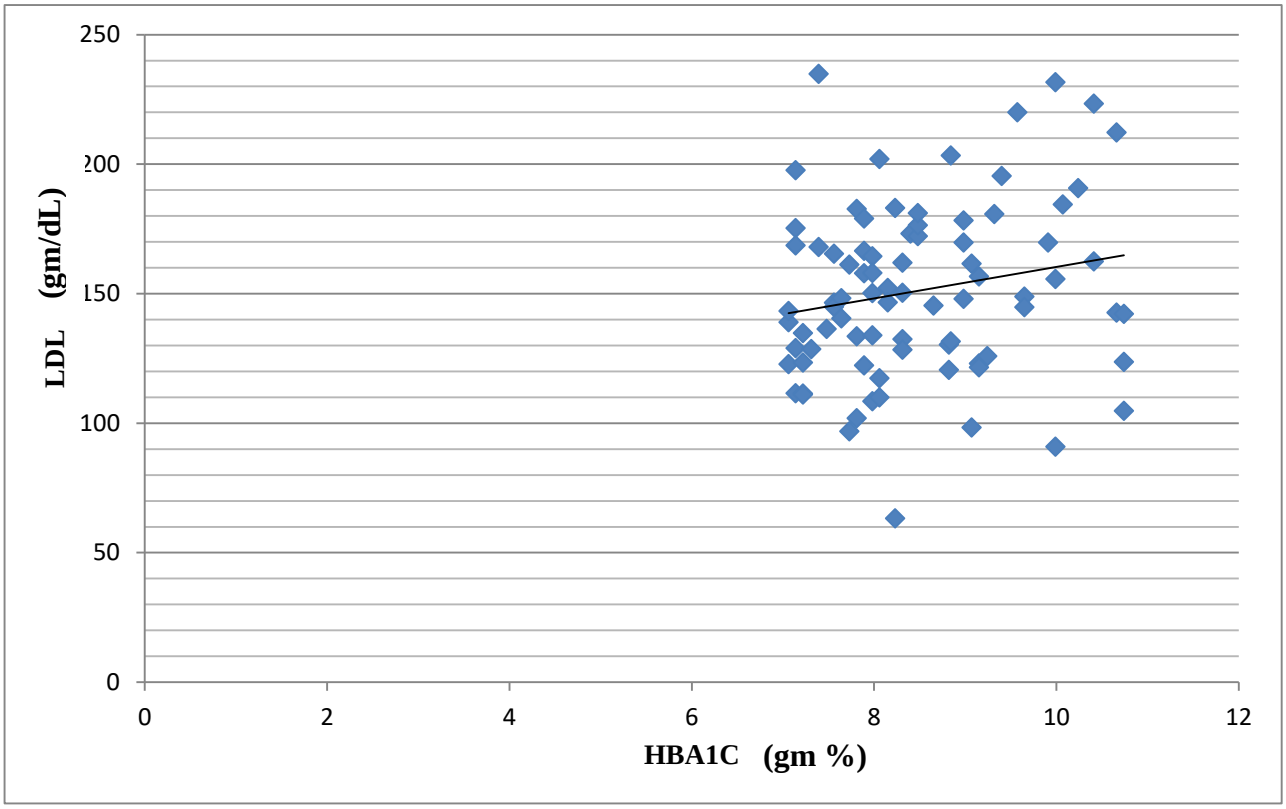

Figure 4.2.7: Correlation between HbA1c and LDL (R=0.19) in patients.

Figure 4.2.7 is a plot between the low density lipoprotein and HbA1c level, the graph shows that HbA1c level increases with increasing level of low density lipoprotein, so it show positive correlation. The LDL is lipoprotein responsible for transportation of cholesterol from liver to peripheral tissues. Liver is the site where formation of LDL is going on. Due to high cholesterol in diabetes with high HbA1c leads to high formation of more LDL.

Discussion:-

the results of the present study suggest the importance of glycemic control in order to manage dyslipidaemia and risk for cardiovascular diseases in type 2 diabetics. This study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C levels which are well known risk factors for cardiovascular diseases. Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in Diabetes mellitus **Goldberg ,I.J.,(1996).** Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LpL may be altered in DM **Tavangar *et al*.,(1992)**The main disorder in lipid metabolism was hypertriglyceridemia in our study The correlation of HbA1c with non-HDL-C was found to be more significant than correlation of HbA1c with other lipid parameters except for LDL-C/ HDL-C and Risk ratio in our study. The measurement of Non-HDL-C is simple which can be conducted even in non-fasting state of patients and can be determined regardless of TAG concentration. Hence, Non-HDL cholesterol can be of great value in determining dyslipidemia in diabetic subjects.

Conclusion:

Significant correlation between HbA1c and various circulating lipid parameters and significant difference of lipid parameters in two groups (≤7.0% and >7.0%) of glycated hemoglobin indicates that HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control hence early diagnosis can be accomplished through relatively inexpensive blood testing**.** Early diagnosis of dyslipidaemia can be used as a preventive measure for the development of cardiovascular disease (CVD) in type 2 diabetics. Hence it is

evident from the study that in diabetic condition one should routinely evaluate his\her blood sugar values along with glycemic index as well as lipid and lipoprotein parameters as preventive measures and to reduce the burden of secondary complications.

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