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RESEARCH ARTICLE

CORRELATION BETWEEN HEMOGLOBIN A1C AND SERUM LIPID PROFILE WITH TYPE 2 DIABETES: A CROSS-SECTIONAL STUDY

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Abstract

Background: Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Patients with type 2 diabetes (T2DM) have an increased prevalence ofdyslipidemia, which contributes to their high risk of cardiovascular diseases (CVDs). 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 with Type II diabetes mellitus.

Methods: The study had 240 participants between the age groups of 20-70 years included 80 males and 40 females in diabetic group whereas the control group included 78 males and 42 females. T.cholesterol, Triglycerides, HDL were calculated by semi automated analyzer and LDL and VLDL were calculated by Friedewald's Formula. HbA1c was measured by turbidMetric Method.

Results: Data was represented as mean ± standard deviation or median with statistically significant values of T. Cholesterol, LDL, HDL, TGs and HbA1c ($P < 0.001$). There was a significant positive correlation between HbA1c, TC, TG, and LDL-C. Patients with HbA1c value greater than 7.0% had significantly higher value of cholesterol, LDL-C, and compared with patients with an HbA1c value up to 7.0%.

Conclusion: Significant positive correlation of HbA1c with Lipid profiles in our study suggests that HbA1c can also be used as a predictor of dyslipidemia in addition to a glycemic control parameter for prevention of complication.

Introduction:-

Diabetes has become one of the most common chronic diseases all over the world. Diabetes can cause directly or indirectly damage to people and cause metabolic abnormalities and different complications, which is harm to health and survival, resulting in lower quality of life and increased risk of death[1].

Diabetes mellitus (DM) is a chronic metabolic disorder that occurs as a result of a complex interaction of genetic, environmental factors, and lifestyle choices[2].Diabetes mellitus (DM) describes a constellation of metabolic disorders characterised by hyperglycemia and disturbances to carbohydrate, fat, and protein metabolism resulting from insulin

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deficiency, insulin resistance, or both and Type 2 diabetes mellitus (T2DM), a heterogeneous, complex, multifactorial metabolic disorder characterized by severe hyperglycemia, is the most dominant form[3].

It is a silent epidemic that is growing at a steady rate and the International Diabetes Federation has estimated a burden of 642 million diabetics on health services of all the parts of the world by 2040[4].

Diabetes mellitus is associated with a considerably increased risk of premature atherosclerosis, particularly coronary heart disease (CHD) and peripheral arterial disease. Although more recent analyses have suggested a less marked effect, most authorities consider diabetes to confer at least a two fold excess risk, independently from other conventional risk factors. Even in people without diabetes, fasting blood glucose concentration and glycated hemoglobin (HbA1c) are associated with the risk of vascular disease[5].

In type 2 diabetes an increased cardiovascular risk often exists for many years before the onset of biochemical hyperglycemia. During this period obesity and insulin resistance are often present, associated with hypertension and dyslipidemia, usually referred to as metabolic syndrome.[6] These risk factors may lead to the early development of CHD and may account for the increased incidence of diabetes in the period following a diagnosis of cardiovascular disease[7].

Glycated hemoglobin analysis in blood provides evidence about in individual's average blood glucose levels during the previous two to three months, which is the predicted half-life of red blood cells (RBCs)[8].

Proteins are often glycated during several enzymatic reactions when the conditions are physiologically favorable. However, in the case of hemoglobin, the glycation occurs by the nonenzymatic reaction between the glucose and the N-terminal end of the β-chain, which forms a Schiff base.During the readjustment, the Schiff base is converted into Amadori products, of which the best known is HbA1c (Fig. 1).In the Initial step of glycated hemoglobin formation, hemoglobin and the blood glucose interact to form aldimine in a reversible reaction. In the secondary step, which is irreversible, aldimine is gradually converted into the stable ketoamine form[9].

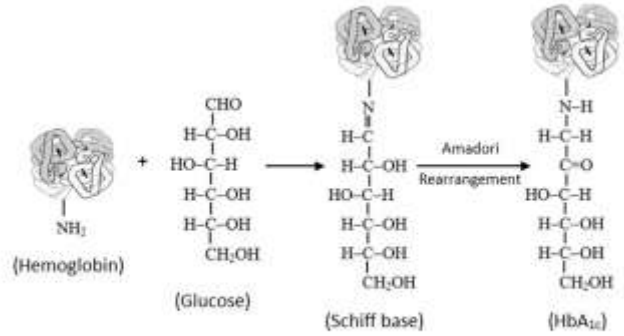


Figure 1. Formation of glycated hemoglobin (HbA1c) from the binding of glucose to hemoglobin.

This study was an attempt to determine lipid abnormalities associated with Type-2 Diabetes Mellitus and association between glycated hemoglobin (HbA1c) levels and serum lipid profile to assess the importance of HbA1c as an indicator of dyslipidemia and future risk of cardiovascular disease.

Materials and Methods:-

The present study is prospective study, will be carried out in the Department of Biochemistry and Department of General Medicine**,** Index Medical College, Hospital & Research Center (IMCHRC)**,** Indore. The cases were selected from those who attended the medicine outpatient department (OPD) during the period of 1 year (January 2019 to December 2019) at IMCHRC, Indore.

Inclusion criteria & Exclusion criteria:

All cases and control were included with age group of 18-65 years in both male and female. Cases and healthy control suffering from immune deficiency disease were included as patients with known case of hypothyroidism, Cushion's syndrome were excluded from the study. Patients diagnosed with the Type 2 diabetes were included

whereas Type I diabetes patients were excluded from the study. In the selection of patients, patients below age of 18 years or known or suspected with pregnancy were excluded.

Sample Collection
After 12 hours overnight fast, 6.0 ml of blood was collected from each subject by venipuncture with standard blood collection technique in a plane vial for serum separation, sodium fluoride vial for plasma and EDTA vial for HbA1c estimation. Plasma was collected again after two hours of post meal for the postprandial glucose estimation.

Parameters Measured
The following parameters were measured in this study:
1. Serum fasting blood sugar (FBS)
2. Lipid Profile
3. HbA1c.

Serum FBS was measured by GOD-POD method with the help of Randox RX, a fully automatic analyzer. Estimation of serum Cholesterol, serum Triglyceride & serum HDL was done by CHOD – POD method, GPO-POD Method & CHO-POD Method respectively. VLDL and LDL were calculated by Friedewald's Formula. HbA1c was measured by turbidimetric immunoassay with the help of HPLC Method. The assays were performed according to the manufacturers' instructions.

Statistical analysis
Data were analyzed using Statistical Package for Social Science version 20 (IBM, SPSS Statistics 20), and graphs were generated with the help of GraphPad Prism 5 and Microsoft Excel. The results were considered significant if $p < 0.05$.

Ethical clearance was obtained from Institutional Ethics Review Committee (IERC). All healthy volunteers were enrolled and a written informed consent was taken. The proforma included, name, age, sex, dietary habit, personal history of disease (if any), smoking habit, drinking habit, socioeconomic status and occupation.

Results:-

The study had 240 participants between the age groups of 20-70 years. The diabetic group included 80 males and 40 females whereas the control group included 78 males and 42 females (Table 1). In the controls, the mean serum TC, HDL and LDL levels were 180.34 mg/dl, 49.75 mg/dl and 112.56 mg/dl respectively and In the diabetic Patients, mean Serum TC, HDL and LDL levels in this group were 214.74 mg/dl, 40.28 mg/dl and 126.75 mg/dl respectively which was shown in Table 2. The age wise distribution in both the study groups is shown in (Graph 1).

Table No. 1:- Gender wise distribution of subjects in control group (normal Healthy individuals) and Study group (Type -2 Diabetes Patients).

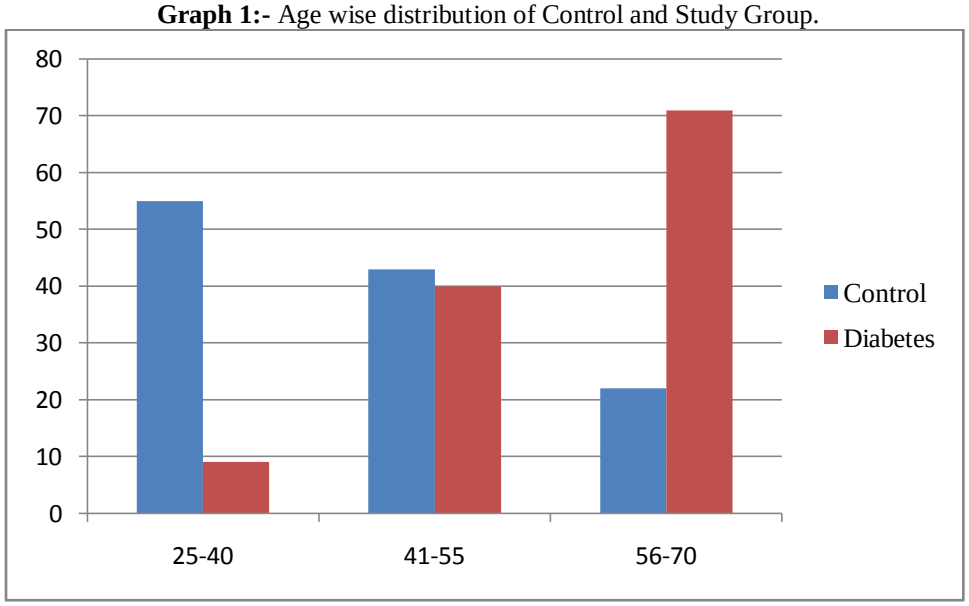
Groups	Male	Female	Total
Healthy Control	78 (65%)	42 (35%)	120 (100%)
Type 2 Diabetes	80 (66.66%)	40 (33.33%)	120 (100%)
Total	158 (65.83%)	82 (34.15%)	240 (100%)

Table No. 2:- Showing means serum levels of lipid parameters in diabetic patients and healthy individuals.

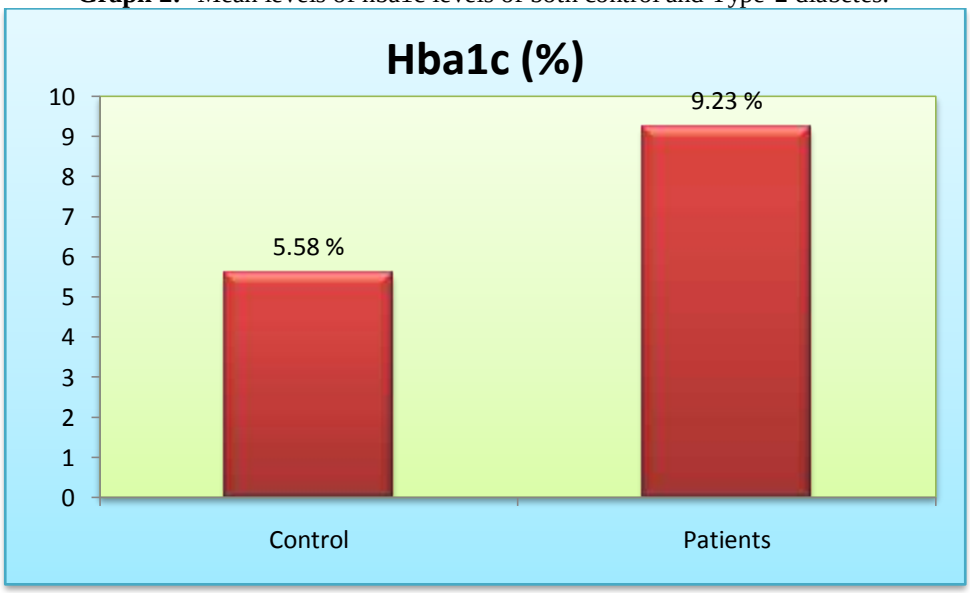
Variables	Healthy individual (Controls)	Diabetic patients (Cases)	p-Value
T. Cholesterol (mg/dl)	180.34± 29.47	214.74± 50.88	<.001**
Triglyceride (mg/dl)	135.37 ±24.82	195.20±123.24	<.001**
HDL(mg/dl)	45.79±24.45	40.28±7.46	0.009**
LDL(mg/dl)	112.56±27.43	126.75±26.77	0.009**

**: Significant at 1% level of significance
*P -Value <.001 considered as statistically significant

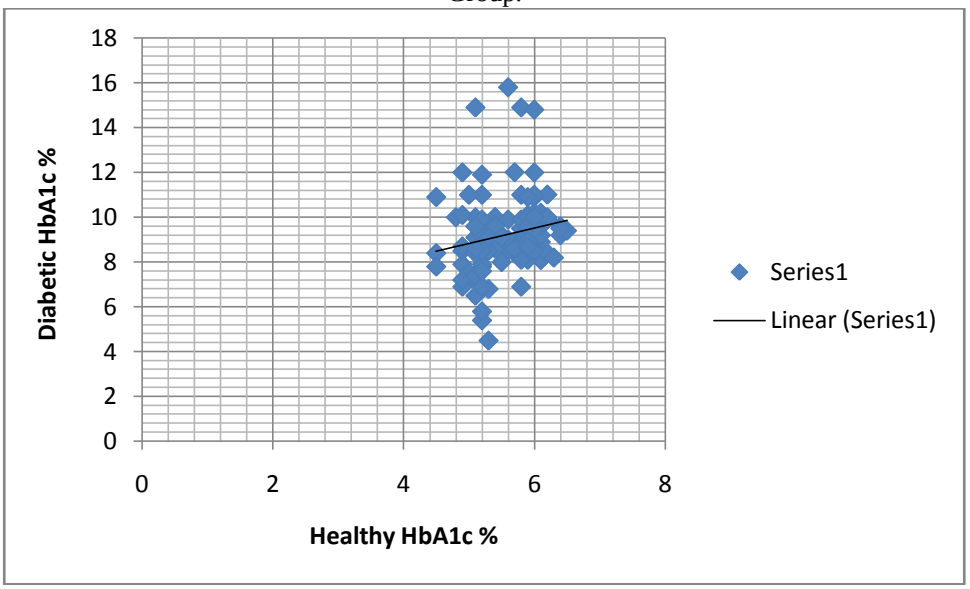
Graph 1:- Age wise distribution of Control and Study Group.



Graph 2:- Mean levels of hba1c levels of both control and Type-2 diabetes.



Graph 3:- Scatter plot showing Correlation values between healthy HbA1c Group & Diabetic Type II HbA1c Group.



Discussion:-

Diabetes is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from insufficient action of insulin. Diabetes mellitus is the common causes of macrovascular and microvascular complications[10]. Patients with diabetes mellitus have higher susceptibility to develop a variety of severe complications of these the common is Nephropathy, Cardio vascular Disease[11].

The aim of our study was to find an association between lipid profile and HbA1c in healthy control and type 2 diabetic subjects. Ethical clearance was granted by the scientific and ethical committee of the institution. The study was conducted in Index Medical College, Hospital & Research Center (IMCHRC)**,** Indore; patients were selected from medicine OPD. Consent was taken before sample collection from the patients. The present study included total 240 subjects, a control group of 120 subjects and study group of 120 subjects diagnosed with Type 2 Diabetes mellitus.

In our study out of 120 patients in each group, there were 42 females and 78 males in healthy group and 40 female with 80 male in diabetic group. In present study, we estimated BMI of both control and type 2 diabetes mellitus patients. We found significantly increased BMI level in diabetes group as compare to control healthy group ($p \leq 0.001$). In Present study, Mean values of HbA1c were 5.58 % and 9.23 % in healthy individual and type-2 diabetic respectively. They were found to be significantly increased in study group as compared to control subjects (Graph 2) ($p \leq 0.001$). This is in accordance with Kurai Z. Chako[12] who also found elevated level of HbA1c in type 2 diabetic patients compared to Healthy subjects. Shanmuga Priya[13], Yurong Zhang[14]**,** Shahram Haddadinezhed[15] also support our results.

Atherosclerosis is a disease of different sized arteries characterized by any of fatty streak, fibrous plaque or complication lesions. A number of epidemiological studies has revealed that highly elevated lipid and cholesterol levels are linked with an increased incidence of atherosclerosis. The presence of a sub molecules of LDL has emerged as a powerful genetic risk factor for coronary artery disease (CAD) raising the question of Dyslipidema and its relation to CAD.[16]

Dyslipidemia in diabetes is common and is characterized by hypertriglyceridemia (HTG) with decreased levels of high-density lipoprotein (HDL)-cholesterol. Whilst low-density lipoprotein (LDL) - cholesterol levels are usually not elevated there is a preponderance of small dense LDL particles which appear to be more atherogenic[17].

In present study, we found highly significant increase in Total cholesterol, Triglyceride level and LDL level in type 2 diabetic group as compare to healthy control. There is significant decrease level of HDL in type 2 diabetic group as compare to healthy group. (Table 2) ($p \leq 0.001$)

The mean HDL in control group was 45.79 mg/dl and in Patients group it was 40.28 mg/dl. The mean HDL in two groups was compared using independent sample t-test. The result of t-test indicates that the mean HDL in patients groups was significantly lower than the mean HDL in controls (t= 2.359, p=0.019).The mean TG in control group was 135.37 mg/dl and in Patients group it was 195.20 mg/dl. The mean TG in two groups was compared using independent sample t-test. The result of t-test indicates that the mean TG in patients groups was significantly lower than the mean TG in controls. ($p<0.001$).The mean LDL in control group was 112.56 mg/dl and in Patients group it was 126.75 mg/dl. The mean LDL in two groups was compared using independent sample t-test. The result of t-test indicates that the mean LDL in patients groups was significantly lower than the mean LDL in controls (t= -2.633, p=0.009)

Our study is concurrent with study of Bishwajit Bhowmik[18], Muhammad Khurram[19] Stamauli M[20]. Bishwajit Bhowmik et al 2018 found the lipid parameters (especially TG and HDL-C) among patients with T2DM and prediabetes, is warranted in this population considered to be the epi-center for T2DM or CAD. Muhammad Khurram et al 2013 concluded in their study that uncontrolled glycemia and dyslipidemia are common in type 2 DM patients and also found Dyslipidemia in terms of hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL is significantly more frequent among uncontrolled diabetics. Stamouli M et al 2014 found 70.0% of diabetic patients presented at least one lipid abnormality. Elevated LDL-C, elevated Total Cholesterol, elevated TG, and reduced HDL-C levels were noted in 28.37%, 36.37%, 39.01%, and 30.12% of the patients, respectively. The combination of elevated TG and reduced HDL-C was the most prevalent of the combined lipid abnormalities.

In Present study, Elevated levels of TG, cholesterol, LDL & reduced levels of HDL were observed. This indicates the influence of Type 2 DM patients with lipid abnormalities might cause CVD risk in future.

The Scatter plot showing correlation between Healthy HbA1c group and Diabetic HbA1c group were shown in Graph 3. In our present study, there is positive correlation between HbA1c with serum triglyceride and LDL in diabetic patients. Our results are consistent with another study, as it also reporting significant relationship between these parameters. However, these results are inconsistent with the results of numerous other studies that have stated no significant relationship between HbA1c and TC and LDL-C[21].Further, our results show a statistically non-significant negative link between HbA1c and HDL-C. Shanmuga Priya et al 2020 in their studies found

Significant positive correlation of HbA1c with lipid profiles and also suggests that HbA1c can also be used as a predictor of dyslipidemia in addition to a glycemic control parameter for prevention of complication[13].
Further a study conducted by Anand et al. established that serum HbA1c levels, adequate glycemic control, and lipid profile screening help to identify high-risk patients for timely diagnosis of hyperlipidemia, hence decreases the incidence of cardiovascular diseases and peripheral vascular complications through appropriate interventions[22].

Conclusion:-

The findings of the present study showed a significant positive correlation between HbA1c with Total Cholesterol, Triglycerides, LDL and negative correlation with HDL and VLDL. We conclude that a high proportion of diabetes patients have poor glycemic control and dyslipidemia. The findings of our study show that HbA1c which is gold standard in the analysis of glycemic control together with its strong correlation with the lipid profile which makes an ideal marker for predicting dyslipidemia in type 2 DM. Thus, dual biomarker capacity of HbA1c (glycemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients for timely intervention with lipid lowering drugs and thus preventing adverse cardiovascular events.

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Competing Interests

The authors declare that we have no conflict of interests to declare.

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