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A CLINICAL STUDY OF HBA1C AS THE MARKER OF CIRCULATING LIPIDS IN TYPE 2 DIABETES PATIENTS.

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ABSTRACT

Aims: The objective of this study was to determine the correlation of HbA1c with circulating lipids in patients with Type 2-diabetes and to find out whether HbA1c can be used as a predictor of circulating Lipids in T2DM. Materials and Methods: The research used a sample of 100 patients who had fulfilled the inclusion criteria and got admitted in a tertiary medical college hospital in south India. HbA1c and FLP tests were done and their relation was analysed. **Statistical analysis used:** Data analysis was done using a method that is standardized and certified by the NGSP, to determine the correlation between HbA1c and each variable in the FLP. The respective scatter plot was designed with a regression analysis. A follow up study was done after a period of six months to analyze how each variable in FLP was changing with variation in HbA1c. This was done by Spearman's Rho and Pearson's correlation test. **Results:** The results indicated a positive correlation between HbA1c and S. Cholesterol, LDL and TG. There was a negative correlation between HbA1c & HDL. That is, higher the HbA1c value, lower was the value of HDL. In the follow up study, it was found that increase or decrease of HbA1c was associated with a corresponding increase or decrease in S. Cholesterol, LDL and TG. A Negative correlation of HbA1c with HDL was shown only in the female population in the follow up study. Conclusions: The study concluded that HbA1c could be used as a predictor of Dyslipidemia among the type 2-diabetes patients.

KEYWORDS : T2DM, HbA1c, S. Cholesterol, TG, LDL, HDL, VLDL.

Introduction

Diabetes mellitus is a disease whereby the body of an individual indicates the presence of high level of blood sugar. High blood sugar is caused by the deficiency of insulin secretion. Type 2-diabetes results from the ineffectiveness of the body to use insulin. Several factors cause diabetes. These factors are categorized as either genetic or lifestyle induced. [1] The pancreas do not produce enough insulin to maintain the sugar level in blood. The result of the insulin imbalance results in high blood sugar level in the body. [2] Type 2- diabetes increases the risk of developing cardiovascular disease. Diabetes is also associated with a development of coronary artery disease and hypertension.

The first identified trait of haemoglobin was the predominant type, glycated hemoglobin that is also known as HbA1c.[3,4] Four decades ago, through a process known as ion exchange chromatography, it was found to be a minor part of the normal adult hemoglobin. Preliminary studies showed that in this predominant type, glycation was prevalent at the N-terminal valine of the hemoglobin ß-chain.[5]Health organizations such as International Federation of Clinical Chemistry (IFCC) have proposed that the predominant glycated hemoglobin can be defined in one or more sites of the haemoglobin molecule as part of glucose glycation[6]. In the past, HbA1c was thought to represent an average glycemia over a period of between 6 and 8 weeks. However, it has been demonstrated that glycation of hemoglobin proceeds for 120 days, the entire life cycle of the human red cell. Nevertheless, within these 120 days, the recent glycemia exhibits total control on the HbA1c value. [7]

HbA1c levels are used to demonstrate the measure of the average glycemic control. Therefore, it is considered the best indicator of scrutiny of glycemia. [8] Research also shows a positive linear correlation between HbA1c & dyslipidemia. [9] The aim of this paper is to analyze and demonstrate the relationship between HbA1c and lipids in patients with type 2 diabetes.

II. Subjects and Methods

Totally 100 Type 2-DM patients with diabetes were involved in the research. All the participants were explained the details regarding the study, and a written consent was issued to them to make them aware of the research and the objectives. Each patient was given a form to fill; they were required to indicate their health history; personal history, and history of diabetes in the family, diet habits, and the history of any complications of Diabetes that they are having. Anthropometric values and blood tests were done. HbA1c and FLP were obtained from lab testing.

The information was analysed to find the relationship between HbA1c and variables from lipids, in a Scatter plot and a line of regression was drawn.[12] After the initial tests, a follow-up study was conducted six months later to evaluate the changes in FLP according to change in HbA1c. This study was done with Pearson's correlation test.

Those included in the research were patients either continuing with medication or the newly detected patients with type 2-diabetes mellitus. The patients were asked to make follow ups with repeat sugars every month, so that the dose of insulin or OHA can be

adjusted.

The researchers noted that it was necessary not to add these patients on drugs, such as OCPS, HRT, diuretics or steroids as they are known to change the FLP.[13] Any patients put on those drugs were excluded from the study.

All the 100 participants were contacted by telephone for the follow up in the next six months. Out of the 100 patients, 50 patients came for the follow-up. Out of the 50 patients who did not come for follow up, 15 patients developed at least one complication of Type 2-Diabetes Mellitus. Further, 5 from them had expired during the period of study due to some complication. 35 of the patients enrolled in the study could not turn up for a follow-up.

III. Statistical Analysis

Data analysis, done using a method that is standardized and certified by the NGSP, was done to determine the correlation or the relationship between HbA1c and each variable in the FLP. The respective scatter plot was designed with a regression analysis. A follow up study was done after a period of six months to analyse how each variable in FLP was changing with variation in HbA1c. This was done by Spearman's Rho and Pearson's correlation test. Patient information collected included their present conditions, personal health history, in-patient outpatient records, dietary habits, treatment, and their blood groups.

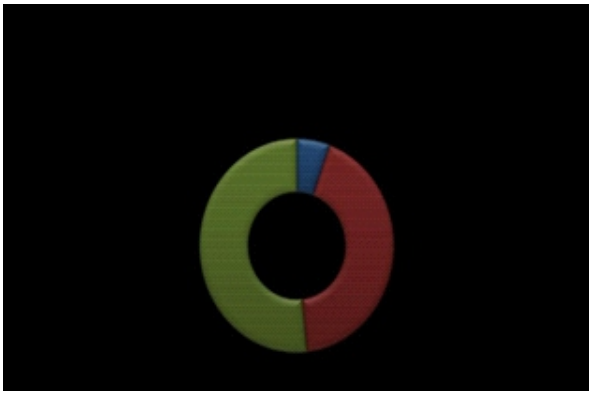
IV. Ethical Concern

Ethical clearance was obtained from the Ethical committee meeting conducted by the Institutional Ethics Committee.

V. Results

HbA_1C VALUES

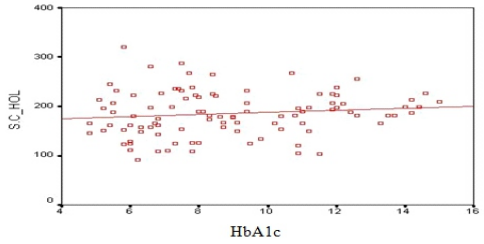
Table.1. shows that HbA1C values in control was present only in 5% of the study group and poor glycemic control (7-9%) was present in 43%. However only 52% (>9%) of high HbA1C groups are present.



HBA_1C	% of patients
<7	5
7-9	43
>9	52

Fig 1. Correlation between HbA1C and Cholesterol Values

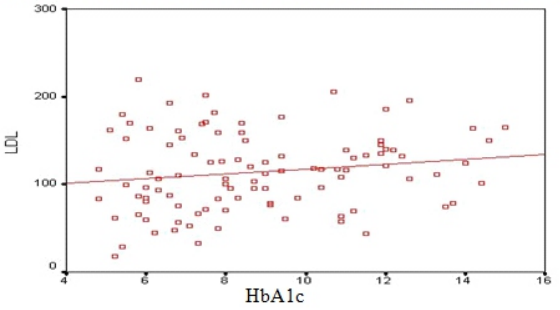
Figure 1: scatter plot with line of regression HbA1c & Cholesterol.



There exists a positive correlation between HbA1c & S. Cholesterol values overall among the 100 patients included in the present study. That is, in patients with higher HbA1c values, S. Cholesterol values were also found to be high.

Fig.2. HbA1C and LDL Values

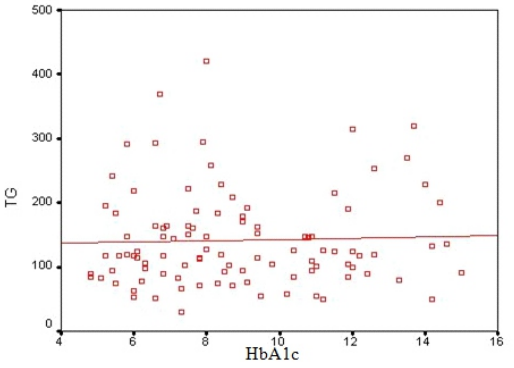
Figure 2: scatter plot with line of regression HbA1c & LDL



There was a positive correlation between HbA1c & LDL values overall among the 100 patients included in the study. That is, in patients with higher HbA1c values, LDL values were also found to be high.

Fig.3. HbA1C and TG Values

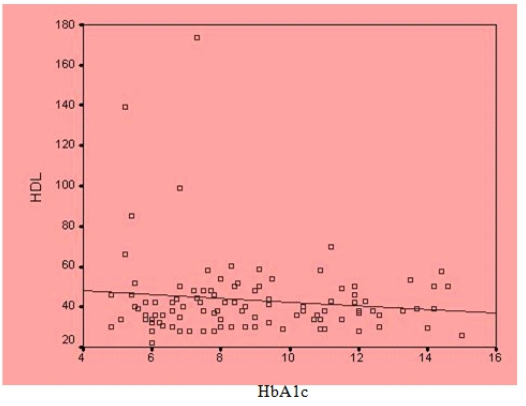
Figure 3: scatter plot with line of regression HbA1c & TG



There was a Positive correlation between HbA1c & TG values overall among the 100 patients included in the study. That is, in patients with higher HbA1c values, TG values were also found to be high.

Fig.4. HbA1C and HDL Values

Figure 4: scatter plot with line of regression HbA1c & HDL.



There was a Negative correlation between HbA1c& HDL values overall among the 100 patients included in the study. That is, in patients with higher HBA1C values, HDL values were found to be low.

Table.2. The characteristics of the correlation between the HbA1c and the lipids for 50 patients who showed up for the follow-up are summarized in the table.

		DHBA1C	DCHOL	DTG	DHDL	DVLDL	DLDL
DHBA1C	Pearson Correlation	1	.255	.072	.208	-.031	.299*
	Sig. (2-tailed)	.	.074	.619	.148	.830	.035
	N	50	50	50	50	50	50
DCHOL	Pearson Correlation	.255	1	.346*	-.032	.092	.700**
	Sig. (2-tailed)	.074	.	.014	.828	.524	.000
	N	50	50	50	50	50	50
DTG	Pearson Correlation	.072	.346*	1	-.246	.504**	.137
	Sig. (2-tailed)	.619	.014	.	.085	.000	.345
	N	50	50	50	50	50	50
DHDL	Pearson Correlation	.208	-.032	-.246	1	-.075	-.280*
	Sig. (2-tailed)	.148	.828	.085	.	.606	.049
	N	50	50	50	50	50	50
DVLDL	Pearson Correlation	-.031	.092	.504**	-.075	1	-.017
	Sig. (2-tailed)	.830	.524	.000	.606	.	.908
	N	50	50	50	50	50	50
DLDL	Pearson Correlation	.299*	.700**	.137	-.280*	-.017	1
	Sig. (2-tailed)	.035	.000	.345	.049	.908	.
	N	50	50	50	50	50	50

Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Relationship Characteristics: Correlation coefficient shows the strength of the relationship between two related variables. It ranges from - 1 to +1. Positive correlation co-efficient indicates that the variables are related to each other. P values less than 0.05 are significant and P values less than 0.005 are highly significant.

VI. Discussion:

DM refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[14] Several distinct type of DM are caused by a complex interaction of genetic and environmental factors. It is a leading cause of End-Stage Renal Disease, Non-traumatic lower extremity amputations, Adult blindness and Cardiovascular diseases. DM will be the leading cause of morbidity and mortality for the forseable future. The aim of the present study was to determine the correlation of HbA1c with circulating lipids in patients with T2DM.

In this study it was found that HbA1c has a positive and significant correlation with LDL (P-value is < 0.05). That is, in patients with higher HbA1c values, LDL values were also found to be high and this correlation was found to be significant, or most of the patients in our study, with poorly controlled T2DM were found to have high levels of LDL cholesterol.

HbA1c has a positive correlation with S. Cholesterol and TG, that is in patients with higher HbA1c values, S. Cholesterol and TG were also found to be high, or patients with poorly controlled T2DM have high levels of TG and total Cholesterol.

A negative correlation was found between HbA1c and the values of HDL; that is patients with high HbA1c values had correspondingly low values of HDL or patients with poorly controlled T2DM had low HDL Cholesterol values.

The level of HbA1c has no major significant variations in both male and female counterparts. A negative correlation was established in the relationship between BMI and HbA1c. However, this relationship did not have a significant influence on the study findings.

Finally, in the follow-up studies after six months, the changes in HbA1c showed a Positive and Significant correlation with LDL (P-value is 0.035). That is an increase or decrease of HbA1c over a period of six months was showing an increase or decrease of LDL respectively, in majority of the patients. The changes in HbA1c showed a Positive correlation with S. Cholesterol (P-value is 0.074) and TG (P-value is 0.619). That is an increase or decrease of HbA1c over a period of six months was showing an increase or decrease of S. Cholesterol. & TG respectively, but this correlation was not statistically significant. The changes in HbA1c showed a Positive but Insignificant correlation with HDL (P-value is 0.148). The changes in HbA1c showed a Negative but Insignificant correlation with VLDL (P-value is 0.830). This means that as the patient was improving in diabetic control with medications within the six months study period, there was a corresponding lowering of S. cholesterol, LDL, and TG in the same client.

VII. Conclusion:

This study ascertains through its findings that HbA1c endures the ability of predicting serum lipid profile in both male and female diabetic patients.[15,16] Thus, a 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.

References:

1. Balasubramanian, S. "Characteristics of Predictors of Progression and Strategies in Type 2 Diabetes Mellitus in a Multiethnic Population."InS. Balasubramanian, Predicting Type 2 Diabetes Mellitus (pp. 223-240), University of Leicester. 2012.
2. William C. Knowler, Sharon L., and Ronald D. Goldberg. HbA1C as Predictor off Diabetes and as an Outcome in the Diabetes Prevention Program. Journal of Medicine, 2014.
3. Sell,David R. and Genuth Saul. Glycation Products as Markers of and Predictors of the Progression of Diabetic Complications. Annals of the New York Academy of Science, 2005.
4. Mekelin, K. "Insulin Glargine or NPH Combined With Metformin in Type 2 Diabetes."Journal of Diabetes Studies, 2006. 400-442.
5. Yuri, P. Therapy Strategy in Newly Diagnosed Type 2 Diabetes According to HbA1c. Relevant Endocrinology, 2015.
6. Lerner, N., Shani, M., and S.Vinker."Marking Type 2 Diabetes Mellitus Using HemoglobinA1c: A Community-based Historic Cohort Study."Eur J Gen Pract., vol. 20, no. 2, 2014, pp.6-20.
7. Edelman,David, and Maren K. Olsen. "The utility of Hemoglobin A1c in Predicting Diabetes Risk."Journal of General Internal Medicine, vol. 19, no. 12, 2004, 1175-1180.
8. Calcaterra,F. and Simonetta Lombardi. "Plasma Glucose Levels throughout the Day and HbA1c correlations in Type 2 Diabetes."DiabetesCare,no. 24,2001, pp.2023–2029.
9. Cederholm, O. "New Aspect of HbA1c as Risk Factor for Cardiovascular Diseases in Type 2 Diabetes."InternationalMedication,vol. 268, no.5, 2010, pp. 471-82.
10. John, D."Predicting the Glycemic Response to Gastric Bypass Surgery in Patients with Type 2 Diabetes."Journal of Diabetes Care, vol. 36, no. 1, 2013, pp. 20-6.
11. Giugliano, G. "Relationship of Baseline HbA1c and Reduction Following Insulin Therapy in Type 2 Diabetes."DiabeticMedicine,vol. 28, no. 2, 2011, pp.247-248.
12. Aicha, L. "HbA1c as the Predictor of Dyslipidemia in Algerian Type 2 Diabetes Patients."Roman Journal of Diabetes Nutrition and Metabolic Diseases, 2012. 23- 25.
13. Oscar, M. V. In Metformin- Treated Type 2 Diabetes Mellitus, Weekly Dulaglutide was not inferior to HbA1c Levels. Annas of Internal Medicine, 2014.
14. Nathan, D. M. International Experts Report on the Role of HbA1C in Diagnosing Diabetes. International Journal of Diabetes, 2017.
15. Khan, H. andS.A. Sobki."Association Between Glycemic Control and Serum Lipids Profile in Type 2 Diabetic Patients HbA1c Predicts Dyslipidemia."Journal of Clinical and Experimental Medicine,vol. 7, no. 1, 2007, pp.24-30.
16. Lingling, H. "HbA1c- Based Score Model for Predicting Death Risk in Patients with Type 2 Diabetes Mellitus."Journal of Diabetes Research,vol. 2017, 2017, pp.2-8.