GLYCATED HEMOGLOBIN AS A BIOMARKER TO PREDICT DYSLIPIDEMIA IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To establish the correlation between glycated hemoglobin (HbA1c) and lipid profile in patients with type 2 diabetes mellitus (T2DM).

Study Design: Correlation study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi (PEMH), Medical Outpatient department (OPD), from Nov 2017 to May 2018.

Methodology: A total of 160 patients with type 2 diabetes mellitus of both genders, 30-70 years of age presenting in OPD were included in study, while those with T1DM, CKD stage 3 and above, infection or diabetic foot, any endocrine disease and female patients with pregnancy were excluded from the study. The blood samples were taken for blood sugar random (BSR), blood sugar fasting (BSF), haemoglobin A1c (HbA1c), lipid profile and results were collected next day. The Pearson correlation test was used to analyze correlations.

Results: Among 160 patients the mean age was 57.28 ± 10.13 years, 81 (50.6%) were males while 79 (49.4%) were females. The 34 (21.20%) patients had good, while 125 (78.80%) had poor glycaemic control using haemoglobin A1c of 7% as a cut off. A positive and statistically significant correlation was observed between haemoglobin A1c and total cholesterol (r=0.233, p<0.01), triglycerides (r=0.172, p<0.05), and a correlation which was positive but statistically not significant was observed between haemoglobin A1c and LDL-C (r=0.105, p=0.260) while a statistically insignificant negative correlation was observed between haemoglobin A1c and HDL-C (r=-0.041, p=0.652).

Conclusion: A significant positive correlation was found between haemoglobin A1c and total cholesterol and triglycerides. Haemoglobin A1c can also be used as a biomarker to predict dyslipidemias in patients with type 2 diabetes mellitus.

Keywords: Dyslipidemia, Glycated Hemoglobin, Type 2 DM.

INTRODUCTION

Diabetes mellitus is a complex disease which is characterized by an increased levels of glucose in the blood (hyperglycemia). The hyperglycemia is due to either insulin deficiency or resistance or due to combination of both[1]. In most of the cases the diabetes is either type 1 or type 2. The T1DM results when destruction of pancreatic islet B cell leads to absolute deficiency of insulin. So, insulin therapy in the form of exogenous insulin is required to avoid ketosis and for reduction of blood glucose levels.

The T2DM predominantly occurs in adults. In T2DM, circulating insulin is sufficient to prevent ketosis but insufficient to prevent hyperglycemia. Initially, there is hyper- insulinemia to overcome the resistance of the tissues to the insulin. Both genetic and environmental factors combine to cause increased insulin resistance. But later on, in addition to insulin resistance there is progressive loss of Beta cells. The elevated blood sugar levels result into micro-vascular and macro vascular changes affecting many organs causing diabetic nephropathy, peripheral neuropathy, stroke and retinopathy.

The number of diabetic patients is increasing worldwide. Globally it is estimated that >451 million patients who had diabetes in 2017 and this figure is estimated to reach 693 million by 2045[2]. The prevalence of diabetes in Pakistan is also on the rise. Currently about 11.77% of total population is having diabetes in Pakistan[3]. Most of these patients are suffering from T2DM[4]. This

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can be considered as pandemic which mostly involves T2DM and there are almost 5 million deaths each year due to Diabetes and its related complications. There is an increased risk of mortality especially cardiovascular mortality[5]. Diabetic patients who also have abnormal lipids that is dyslipidemia are more prone to cardiovascular disease and deaths[6]. Researchers have shown that approximately 77.5% patient with T2DM have dyslipidemias[7]. HbA1c, is used as a biomarker to monitor long term glycemic control and thus it predicts the risk for development of long term diabetic complications[4,8]. In T2DM patients, HbA1c levels <7% were associated with 35-76% reduction in micro vascular complications[9]. In addition to long term glycemic control the HbA1c also predicts abnormal lipid profile in patients with T2DM[4,8,10]. The aim of this study was to identify to dyslipidemias in our population and the correlation of lipid profile with HbA1c. The elevated HbA1c can give the treating physicians an insight about the abnormal lipid profile without doing lipid profile studies and thus patients with an increased cardiovascular risk can be identified. If dyslipidemias are identified earlier in course of disease and they are treated with lipid lowering drugs such as statins than cardiovascular morbidity and mortality can be significantly reduced[11,12].

METHODOLOGY

The diagnosed cases of T2DM of both genders between 30-70 years were included in the study while patients with type 1 diabetes, chronic kidney disease stage 3 and above, infection or diabetic foot patients, who had recent major surgery, nephropathy, Ischemic Heart disease, thyroid disease and any other endocrine disease, female patients with pregnancy or lactating mothers, and patients who refused to cooperate were excluded from the study.

The permission was sought from institutional ethics review committee. The sample size was calculated with the help of correlation sample size calculator using level of significance 5%, power of the test 90%, correlation coefficient (r) of 0.430, observed in previous studies[8]. The cases satisfying the selection criteria were selected from medical OPD by non-probability consecutive sampling. An informed verbal consent was obtained from every patient. The venous blood samples were taken under strict aseptic measures for HbA1c, fasting plasma glucose, 2-hour plasma glucose, serum lipid profile (LDL-C, HDL-C, Triglycerides, Total cholesterol). The samples were sent to Pathology Laboratory PEMH and AFIP Rawalpindi. The results were collected next day.

The data were analyzed using SPSS-17. Mean and standard deviations for LDL-C, HDL-C, Triglycerides, total cholesterol, HbA1c, age and duration of diabetes were measured. Frequency and percentages were calculated for good and poor glycemic control. Pearson Correlation coefficient (r) was calculated to measure correlation between HbA1c and cholesterol, HbA1c and Triglycerides, HbA1c and LDL-C, HbA1c and HDL-C using Pearson correlation test. The independent sample t-test was used to compare means between patients with good and poor glycemic control. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 160 patients with T2DM were included in the study. The mean age in the study was 57.23 ± 10.14 years with range from 34 to 75 years. The distribution of gender of patients in terms of frequency and percentage was also calculated for both male and female patients.

Table-I: Mean values of lipid and glucose parameters.

Parameter	Mean ± SD
HbA1c (%)	9.28 ± 2.16
Total Cholesterol (mmol/L)	4.98 ± 1.20
LDL-C (mmol/L)	2.84 ± 0.91
TGs (mmol/L)	2.85 ± 1.72
HDL-C (mmol/L)	1.05 ± 0.34
BSF (mmol/L)	11.00 ± 4.57
BSR (mmol/L)	13.81 ± 6.13
Duration of diabetes (years)	6.22 ± 4.03
Age (years)	57.23 ± 10.14

There were 81 (50.6%) males and 79 (49.4%)

females. The descriptive statistics like mean for HbA1c, total Cholesterol, LDL-C, TGs, HDL-C, BSF, BSR and duration of diabetes was calculated as shown in table-I.

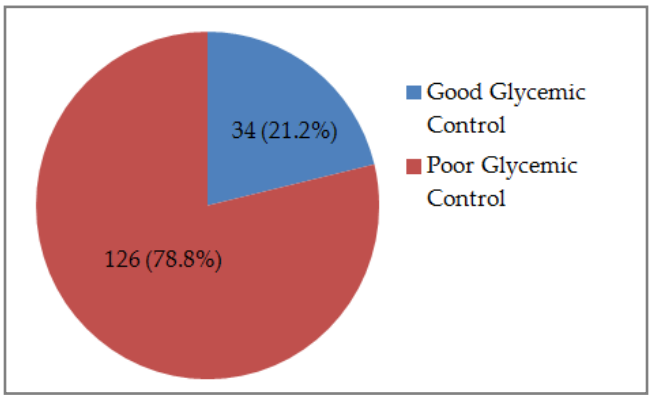

Figure: Patients with good & poor glycemic control.

The frequency of patients having good glycaemic control was 34 (21.2%), while 126 (78.8%) had poor glycaemic control (figure).

Out of 81 male patients 22 (27.2%) had good while 59 (72.8%) had poor glycaemic control while out of 79 female patients 12 (15.2%) had good while 57 (84.8%) had poor glycaemic control. Among patient with age between 30-45 years, 7 (25.9%) had good while 20 (74.1%) patients had poor glycaemic control, while patients between 46-60 years of age 14 (19.2%) had good 59 (80.8.1%) had poor glycaemic control, and those patient with age range between 61-75 years 13 (21.7%) had good, while 47 (78.3%) had poor glycaemic control.

The correlation between HbA1c and BSF, BSR using pearson correlation test was checked which found to be significantly positive for BSF, BSR, with Pearson coefficient value, as shown in table-II. The correlation between HbA1c and

Table-II: Correlation between HbA1c, lipid and blood glucose parameters.

Parameter	Pearson Coefficient Value	Correlation	*p*-value	Significance
HbA1c/Total cholesterol	0.233	Positive	0.003	<0.05
HbA1c/Triglycerides	0.172	Positive	0.031	<0.05
HbA1c/LDL-C	0.105	Positive	0.260	>0.10
HbA1c/HDL-C	-0.041	Negative	0.652	>0.10
HbA1c/ BSF	0.443	Positive	0.000	<0.01
HbA1c/BSR	0.516	Positive	0.000	<0.01
BSF/BSR	0.700	Positive	0.000	<0.01

Table-III: Descriptive statistics of lipid parameters.

Lipid Parameter	Lipid Control	Descriptive Stats
Total cholesterol	Optimal Abnormal	85 (53.1%) 74 (46.3%)
Triglycerides	Optimal Abnormal	50 (31.2%) 110 (68.8%)
LDL-C	Optimal Abnormal	48 (30%) 112(70%)
HDL-C	Optimal Suboptimal	72 (45.6%) 106 (66.2%)

Table-IV: Comparison of means in patients with good and poor glycemic control.

Parameter	Good Glycaemic Control	Poor Glycaemic Control	*p*-value
BSF (mmol/L)	7.87 ± 3.23	11.82 ± 4.52	0.010*
BSR (mmol/L)	9.48 ± 4.43	15.01 ± 6.01	0.013*
HbA1c (%)	6.43 ± 0.47	10.03 ±1.78	0.000*
Total Cholesterol (mmol/L)	4.42 ± 0.922	5.13 ± 1.22	0.028*
TGs (mmol/L)	2.09 ± 3.057	1.34 ± 1.75	0.002*
LDL-C (mmol/L)	2.58 ± 0.87	2.9 ± 0.92	0.246
HDL-C (mmol/L)	1.05 ± 0.166	1.06 ± 0.38	0.361

**Statistically Significant*

Total Cholesterol, Triglycerides (TGs), Low density lipoproteins (LDL-C), High density lipoproteins (HDL-C) using Pearson correlation test was checked which found to be significantly positive for Total cholesterol, TGs while there was statistically insignificant positive and statistically insignificant negative correlation between HbA1c and LDL-C with Pearson coefficient values as shown in table-II.

Most patients had more than one type of dyslipidaemias.The frequencies of different types of dyslipidaemias were assessed andareshown in table-III.

The comparison of means in patients with good and poor glycaemic control is shown in table-IV.

DISCUSSION

The diabetes mellitus (DM) is complex metabolic disorder which results in increased blood sugar levels and it has wide range of effects in different body organs. The DM is cause of significant morbidity and mortality. It has many micro and macro-vascular complications[13]. The most important of all is cardiovascular and cerebrovascular complications leading to CAD and strokes in diabetics. The diabetics are at increased risk of these complications as compared to general population[14]. So, optimal glycemic control is advocated to reduce these complications[15]. The diabetics having dyslipidemias with poor glycemic control are at further increased risk of microvascular complications[16]. In our study, 78.80% people had poor glycemic control defined as HbA1c levels of >7% which was more than a study conducted by Pushpita *et al*. in India (63%) and by Atif *et al* in Pakistan (73.5%)[17]. The mean HbA1c was 6.4% ± 0.46 in those with good glycaemic control which was less in comparison with study by Rajagopal *et al* (7.33 ± 0.14) while it was 10.06% ± 1.85 in those with poor glycaemic control which was more than Rajagopal *et al*. (9.72 ± 0.17)[18]. Various studies done in past at national and international level showed that prevalence of dyslipidemias is very high in diabetics, ranging from 35% to 97.8%[19]. Any kind or combination of dyslipidemias can occur in diabetics[20]. Those patients having good glycaemic control had generally decreased total cholesterol, TGs, LDL-C and increased HDL-C levels as compared to those with poor glycaemic control[21]. So, it means that good glycaemic control has a positive effect on lipid profile consistent with previous studies[21,25].

The HbA1c is used to predict glycaemic control over the period of last 3 months[4,22]. The HbA1c has a direct positive correlation with BSR and BSF. In a systemic review and meta-analysis, the Pearson correlation coefficient (r) between BSR and HbA1c was found to be 0.68, with a slightly lower Pearson correlation coefficient of 0.61 between BSF and HbA1c, consistent with our study results[23]. The study also showed a positive correlation between HbA1c, total cholesterol and TGs, similar to various studies done in the region in the past but with different Pearson coefficients values, while there was statistically insignificant positive and negative correlation was found between HbA1c and LDL-C[5,9,11,24]. So, HbA1c in addition to its role in long term monitoring of glycaemic control, can serve as biomarker to predict dyslipidaemias in patients with T2DM as there is positive correlation between HbA1c and blood sugar levels as well as lipid parameters in patients with T2DM. So, HbA1c can help the physicians to be more vigilant for increased risk of various atherosclerotic cardiovascular complications associated with these dyslipidaemias in patients with T2DM. The treatment of dyslipidaemias with lipid lowering drugs such as statins can help in preventing microvascular complications associated with diabetes[4,8,10]. The lipid research clinics coronary primary prevention trial showed that with reduction in Triglycerides by 1%, there is a reduction of CAD risk by 2%[16,25]. Similarly Helsinki heart study showed that a mean increase in HDL-C by 12% and decrease in LDL-C by 11% resulted in 34% decrease in CAD risk.

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CONCLUSION

Glycated haemoglobin (HbA1c) levels correlates with the serum lipid profile. So, in addition to predicting glycaemic control it provides additional information about the circulating lipids and thus dyslipidaemia in T2DM patients. Glycated haemoglobin can serve as a screening test for dyslipidaemias to help the physician in clinics to identify patients with T2DM, who are at increased cardiovascular risks.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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