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Original Research Article

Significance of HbA1c test is a stable indicator of triglycerides in diagnosis and prognosis of diabetic patients

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ABSTRACT

Background: The main purpose of the study was to highlight the relationship between glycosylated hemoglobin (HbA1c) and triglyceride levels in type 2 diabetes mellitus (DM). Insulin resistance is associated with the elevated triglycerides (TG), and persons with type-2 diabetes are insulin resistant However, it is unknown what level of glycemia that causes an increase in TGL. Hence Therefore I am interested to determine the quantitative relationship between the hemoglobin A1C (HbA1c) and TGL.
Methods: This descriptive study was conducted at GVPIHC&MT Marikavalasa, Visakhapatnam-4. The study population included 100 patients (not discriminate male/ female) of type 2 DM not on lipid lowering medication and 100 subjects without DM as controls from the department of General Medicine. For statistical analysis, Chi-square and Pearson's correlation coefficient was used to find the association between triglyceride and HbA1c.
Results: The association of high triglyceride was evaluated in type 2 DM group of HbA1c, with a cut-off value 7% patients had high triglycerides and showed a significant association with high HbA1c levels at $p<0.0001$.
Conclusions: It has been shown from this study Triacylglycerol level are high with HbA1c (with a cut-off value 7%) level was found higher in diabetic patients when compared with the controls. Therefore, proper glycemic control should be maintained by maintaining HbA1c level less than 6.0% to prevent multifactorial disorder of diabetic complications.

Keywords: Diabetes mellitus, Glycated hemoglobin, Triglycerides

INTRODUCTION

Type 2 diabetes mellitus is one of the prevalent diseases increasing health burden in both developed and underdeveloped countries Diabetes mellitus is actually a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. In 1979, the National Diabetes Data Group developed a classification and diagnosis scheme for diabetes mellitus.[1] The common threat of this disease is poor glycemic control predisposing to micro- and macro-vascular complications. Microvascular complications include neuropathy, retinopathy, and nephropathy. Macrovascular complications are coronary artery and peripheral artery disease.[2,3]

Dyslipidemia is one of the common conditions associated with a poor glycemic control in type 2 DM. The pathogenesis of dyslipidemia in type 2 DM is a decrease in activity of lipoprotein lipase due to insulin deficiency or resistance. Under the action of insulin, enzyme lipoprotein lipase metabolizes lipids in a healthy

individual. In type 2 DM, the relative insulin deficiency and decreased adiponectin causes decrease lipoprotein lipase activity resulting in high levels of low-density lipoprotein (LDL), triglyceride and low levels of high-density lipoprotein (HDL). Qualitative defects in LDL are also seen in type 2 diabetes including atherogenic, glycated or oxidized LDL further amplifying the risk of atherogenesis.[4,5]

Dyslipidemias is one of the modifiable risk factors for coronary artery disease in type 2 diabetes. Atherogenic or diabetic dyslipidemia is defined by a profile of low- and high-density lipoprotein and high triglycerides. It is an independent predictor of coronary artery disease or silent myocardial ischemia.[6,7] High triglycerides can be dictated by many factors including genetic or acquired.[8] To rule out other causes, include the patients without any familial dyslipidemia or history of alcohol intake. As these two factors also play a role in increasing triglycerides as compared to polygenic etiologies like obesity, insulin resistance or diabetes mellitus.[9,10]

The literature review was evident that hypertriglyceridemia is linked to high glucose levels and increased risk of type 2 diabetes.[11,12] In my study, correlation of HbA1c with high triglycerides signifies. HbA1c as a direct marker of hypertriglyceridemia and an indirect marker of risk assessment of coronary artery disease. It is important to understand the concept of insulin resistance and dyslipidemia predisposing to atherosclerosis.[13,14] Cholesterol lowering through secondary prevention by lifestyle changes or statin therapy has tremendously improved cardiac outcome in diabetes.[3]

Glycated hemoglobin A1c (HbA1c) has been accepted as an accurate and reliable test both to establish diagnosis and to evaluate glycemic control in patients with diabetes.[15,16] Currently, the worldwide epidemic of type II diabetes encompasses 90% of people with diabetes around the world, and most of them are obese. DM is a chronic metabolic disorder in which blood glucose level increases. This increase in blood sugar level increases the risk of both micro and macrovascular diabetic complications.

Hypertriglyceridemia is common in patients with diabetes (>30-60%) and it is known to be transiently elevated by uncontrolled hyperglycemia usually in the setting of recent diabetes diagnosis or poor glycemic control (due to inadequate insulin activity and lipolysis).[17-19]

Therefore, not well controlled diabetes, and consequently high HbA1c, is associated with high triglyceride levels. Glycoproteins of special interest are glycated hemoglobin (GHB) and similar proteins, which are used to monitor longterm glucose control in people with diabetes mellitus. In addition, GHb is a measure of the risk for the development of complications of diabetes. Chemically, glycation is the nonenzymatic addition of a sugar residue to amino groups of proteins. Human adult hemoglobin (Hb) usually consists of Hb A (97% of the total), HbA2 (2.5%), and HbF (0.5%). HbA is made up of four polypeptide chains, two α and two β-chains.

Formation of glycated hemoglobin

Formation of GHb is essentially irreversible, and the concentration in the blood depends on the lifespan of the red blood cells (average 120 days) and the blood glucose concentration. Because the rate of formation of GHb is directly propotional to the concentration of glucose in the blood the GHb concentration represents the integrated values for glucose over the preceding 6-8 weeks.[20] This provides an additional criterion for assessing glucose control because GHb values are free of day-to-day glucose fluctuations and are unaffected by recent exercise or food ingestion. The contribution of the plasma glucose concentration at a given time point to the ultimately measured GHb depends on the time interval before blood is sampled; the concentrations of glucose at recent time points provide a larger contribution to GHb than do earlier values, at least partly because more of the red cells survive from the recent time point than from the more remote time point. The plasma glucose in the preceding 1 month determines 50% of the HbA1c whereas days 60-120 determine only 25%. After a sudden alteration in blood glucose concentrations, the rate of change of HbA1c is rapid during the initial 2 months, followed by a more gradual change approaching steady state 3 months later. The half- time is 35 days.[21]

There are several causes for high triglyceride levels, but probably, the most important one is obesity. Triglycerides are stored in our fat cells and are used as an energy source through hormonal management between meals. If regularly eat more than and are able to burn, metabolic mechanisms will promote fat cells to storage the excess of calorie intake and carbohydrates, in particular.

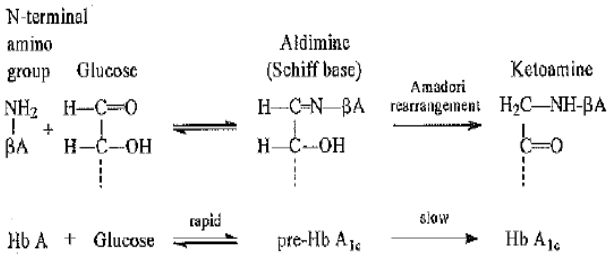

Figure 1: Formation of HbA1c.
(Source: Tietz Clinical Chemistry, 4th Edition)

METHODS

This descriptive study was conducted from October 2019 to February 2020 at GVPIHC & MT Marikavalasa, Visakhapatnam-41 A total of consenting 100 patients of type 2 diabetes mellitus were enrolled over a period of 5.0 months. The consent taken from the study subjects.

The study population included 100 patients (not discriminate Male/ Female) of type 2 our age limit was 18 and above, DM not on lipid lowering medication and 100 subjects without DM as controls from the department of General Medicine. Detailed history, anthropometry and clinical examination were recorded from the all patients.

Inclusion criteria

100 Patients with type 2 diabetic, DM not on lipid lowering medication.

Exclusion criteria

Patients with thyroid disorder, Pregnancy, Diabetic nephropathy, Patients with chronic illness, Patients with Type-1 diabetes mellitus, Patients with suffering from renal, hepatic diseases.

Sample collection

5 ml of Venous blood samples were collected after 12-hour fasting and dispensed into lithium heparin bottles. Plasma was obtained by centrifugation for 5 min at 3,000 rpm and separated into plain bottles for analysis concentrations were assayed at the institution, based on the IFCC (International Federation of Clinical Chemistry) methods for measurement of triglyceride levels and glycated hemoglobin (HbA1c) for a period of 05 months.

Serum TGL levels, were estimated by glycerol Oxidase-Peroxidase method with Semi Auto analyser (Lab life CHEM MASTER, RFCL) using commercial reagents (ERBA for TGL); the normal ranges are TGL: 35-160mg/dl). were compared between the two groups. HbA1c (cut off value 7%) analysis was performed with Fluorescence Immunoassay: (FIA)

Statistical analysis

Chi-square and Pearson's correlation coefficient was used for statistical analysis and data were expressed as the mean and standard deviation.

RESULTS

During the period from October 2019 to February 2020 in the Department of Medicine, Gayatri Vidya Parishad Health Care and Medical College, Marikavalasa, Visakhapatnam. A total No of 200 cases were studied (HbA1c and TGL) by dividing them into two groups Controls 100 and Cases 100 and observation made were tabulated.

Table 1 shows that mean serum TGL of cases (168.819±134.764) is having higher level as compared to the mean value of controls (82.324±10.536). This increase is statistically highly significant (<0.0001).

Table 1: TGL (mg/dl) levels in both cases and controls.

Group	TGL	Mean±SD	Z value	P value
Cases	100	168.819±134.764	6.5568	<0.0001
Controls	100	82.324±10.536		

Table 2: HbA1c (%) levels in both cases and controls.

Group	HbA1c	Mean±SD	Z value	P value
Cases	100	6.464±1.559	8.6210	<0.0001
Controls	100	5.050±0.629		

The above Table 2 shows that mean HbA1c of cases (6.464±1.559) is having higher level as compared to the mean value of controls (5.050±0.629). This increase is statistically highly significant (<0.0001).

DISCUSSION

Diabetes is a multifactorial disorder having a wide range of lipid abnormalities. In type 2 diabetes mellitus, there is an increased incidence of hyper-triglyceridemia.[22,23] This study evaluated the correlation between glycated haemoglobin (HbA1c) and triglycerides level and the results showed that there is a significant correlation between high HbA1c and high triglyceride. This may in turn help in predicting the triglyceride status of type 2 diabetics from the degree of glycemic control and therefore identifying patients at increased risk from cardiovascular events.[24,25]

There are several causes for high triglyceride levels, but probably, the most important one is obesity. Currently, the worldwide epidemic of type II diabetes encompasses 90% of people with diabetes around the world, and most of them are obese. Therefore, not well controlled diabetes, and consequently high HbA1c, is associated with high triglyceride levels.

In most of the studies, there is a correlation found between glycemic control and dyslipidemia.[26] In a recent study, it was evident that there was a positive correlation between HbA1c and high triglycerides and HbA1c can be used as a potent marker for dyslipidemia and mitigate the macro- and micro-vascular complications of disease.[27]

Diabetes is an independent risk factor for developing cardiovascular risk. Cardiovascular events are also the most common cause of death in diabetes.[28,29] Gluco-centric medications might help in improving glycemic control but their role in preventing cardiovascular disease is limited. The existence of plasma hyperglicemia causes alterations in the proteins, so that the same as there is an increase. In the HbA1c, altered lipoproteins responsible of the metabolism of triglycerides, such as VLDL. Another cause is the added resistance in adipose tissue,

often associated with obesity, which increases the levels of triglycerides.

High HbA1c means that the blood glucose concentration has remained high for a long period of time. This level of glucose represents failure of insulin or elevated resistance to it.

Considering that endothelial LpL and lipase in adipose tissue are sensitive to insulin, but to the contrary, the absolute or relative deficiency may cause an increased release of free fatty acids by adipose tissue that conveys the liver as VLDL (high plasma triglyceride concentration) and if in addition the endothelial LpL activity is decreased by the same relative deficiency of insulin, VLDL are metabolized much more slowly the consequence is hypertriglyceridemia.

Increasing evidence points towards insulin resistance lead to hyper-triglyceridemia, an important risk factor for developing atherosclerotic cardiovascular event and peripheral artery disease. According to my study, high HbA1c (cut-off of 7%) increased the risk of hypertriglyceridemia ($p<0.0001$).

Interpretation

The interpretation of GHb depends on the red blood cells having a normal lifespan. Patients with hemolytic disease or other conditions with shortened red blood cell survival exhibit a substantial reduction in GHb.[30]

GHb concentrations can still be used to monitor these patients when their red cell survival is not changing, but values must be compared with previous values from the same patient. Individuals with recent significant blood loss have falsely low values.

CONCLUSION

In this study, there is a significant correlation between glycemic control (HbA1C) and triglyceride levels in patients with type 2 diabetes in this population. Admitting this has important clinical implications in day-to-day clinical practice as many patients with high HbA1c will have associated hyper-triglyceridemia Therefore proper glycemic control should be maintained by maintaining HbA1c level less than 6.0% to prevent multifactorial disorder of diabetic complications.

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