

ORIGINAL ARTICLE

Glycosylated Hemoglobin (HbA1c) as a Marker for Dyslipidemia in Type 2 Diabetes MellitusHENNA KHALID¹, MARIAM RIAZ², MOMINA KHADIJA ABBASI³, ABDUL HASEEB⁴¹Associate Professor, Histopathology Department, WM & DC, Abbottabad²Associate Professor, Pathology Department, WM & DC, Abbottabad³Associate Professor, Histopathology Department, Watim Medical & DC, Rawat⁴Senior Lecturer, Pathology Department, WM & DC, AbbottabadCorresponding author: Dr. Henna Khalid, Email: hennakhalid@rocketmail.com, Cell: +923350523150**ABSTRACT****Objective:** The purpose of this research was to examine the effectiveness of HbA1c as a predictor of dyslipidemia in patients with Type-2 Diabetes Mellitus.**Study Design:** Cross-sectional**Place and Duration:** Department of Pathology; Women Medical & Dental College Abbottabad in collaboration with Jinnah International Hospital, Abbottabad; April 2022 – September 2022**Methods:** After obtaining their agreement, a total of 110 people with Type-2 diabetes mellitus were included in the research. Statistics and background information were recorded. Fasting lipid profile (cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, and cholesterol/HDL), HbA1c, creatinine, and electrocardiogram were conducted as part of the comprehensive systemic examination to detect the presence of complications or co-morbidities. Mean, frequency, and correlation analyses are performed in SPSS 22.0. When doing a correlation analysis, the Pearson Chi-square test was typically utilized.**Results:** Twenty-two patients (20%) had an HbA1c below 7%, whereas eighty-eight patients (80%) had a HbA1c beyond 7%. Dyslipidemia was seen in 62 individuals (56.4%). Direct connections were found between HbA1c and BMI, cholesterol, triglycerides, and low-density lipoprotein (LDL), while an inverse correlation was found between HbA1c and high-density lipoprotein (HDL). When comparing female and male patients, females were shown to have considerably greater TG levels. HbA1c levels were also significantly correlated with the presence of metabolic syndrome, particularly among women (P<0.003).**Conclusion:** According to the findings of our research, HbA1c is not only useful as a biomarker of long-term glycaemic control, but it is also an excellent predictor of lipid profile.**Keywords:** Lipid Profile, Dyslipidemia, Type 2 Diabetes mellitus, HbA1c**INTRODUCTION**

One of the pandemics that have emerged in recent times is diabetes mellitus type 2 (Type 2 Diabetes). It is anticipated that 220 million individuals would be affected by the time the year 2020 rolls around. Today, diabetes is regarded as one of the most significant diseases in the field of medicine and is a primary focus of research in the area of chronic medicine. It is one of those illnesses that cannot be treated but can only be managed in order to avoid the long-term microvascular and macrovascular consequences that are associated with it¹.

Patients who have type 2 diabetes are more likely to experience certain complications, and new evidence has surfaced to support the benefits of glycemic control in addition to the control of blood pressure and lipid levels in the prevention or delay of the onset and severity of complications caused by diabetes. The degree to which one is able to keep their blood glucose level under control might predict the likelihood of developing a variety of issues¹⁻³.

The glycosylated haemoglobin, often known as the HbA1c test, is used to evaluate how well glucose levels have been managed over the course of the past three months. Therefore, in comparison to fasting blood glucose and postprandial blood glucose, which both only represent the immediate control, it is a more accurate indication of blood glucose. Dyslipidemia is present in around half of all type 2 diabetes individuals. If you have type 2 diabetes, you are more likely to have lipid problems than if you have type 1 diabetes. Dyslipidemia is a frequent secondary cause of type 2 diabetes, especially if glycemic control is inadequate, which is itself a significant risk factor for atherosclerosis and coronary heart disease¹⁻³.

Type 2 diabetes is a growing public health problem in countries across the world, with serious consequences for individuals' health as well as their societies' healthcare infrastructures and citizens' standard of living. There are 415 million persons with diabetes mellitus, according to the latest data from the International Diabetes Federation (IDF) (DM). In most countries, the percentage of persons with type 2 diabetes mellitus

is rising, and by 2040 the number of people with the disease is projected to reach 642 million, or one in eleven people³. About 80% of the world's population with the illness lives in nations with median or lower incomes⁴.

The Israeli Security Forces now include Pakistan and Afghanistan in its definition of "Middle East and North Africa." Type 2 diabetes affects about 9.7% of the Middle Eastern and North African population, or about 37 million people⁵. Due to the country's political unrest, however, data on the disease's prevalence, complications, and mortality rates in Afghanistan is scarce. Following a worldwide demographic adjustment, experts predict that 9.9% of the world's adults will have diabetes mellitus by 2030, up from an estimated 8.6% in 2010.^{1,6}

In 2015, diabetes mellitus was the cause of death for 342,000 people among this part of the world.^{4,5} Approximately 51.3% of all deaths in people under the age of 60 were attributable to diabetes mellitus. Multiple factors may contribute to these avoidable deaths, including the rapid transformation of the local environment and way of life, the difficulty of making an accurate diagnosis, and the inadequacy of the local healthcare system to effectively treat the growing number of people who suffer from diabetes.⁸

To put it simply, diabetes mellitus is a metabolic disorder that has far-reaching effects on many bodily processes. As a result, this factor adds to the already substantial morbidity associated with the illness. Atherosclerosis is a direct result of diabetes mellitus and greatly increases the risk of cardiovascular disease (CVD) in comparison to those who do not have DM. Illnesses come in a wide variety of forms, and cardiovascular disease (CVD) is only one of them. In addition to being the top cause of mortality among people with type 2 diabetes, cardiovascular disease is also more likely to affect those who already have the condition.⁴

Diabetes mellitus increases the chances of hypertension, and dyslipidemia, all of which are already significant contributors to cardiovascular disease.¹⁰

Glycemic control is often evaluated using haemoglobin A1c, which was deemed the gold standard after being used in the Diabetes Control and Complications Trial (DCCT).^{11,12} It is

regarded to be the gold standard marker and has showed substantial connection with lipid profile of Type 2 diabetes patients in various research investigations. There is a lack of local published data on HbA1c and diabetic dyslipidemia to rule out the possibility of a linear or inverse linear link between the two. This research is warranted by the fact that the phenotypic and genotypic variations in this area differ from those in other Asian, European, and Western locations. The purpose of this research was to ascertain whether a causal connection of this kind exists. If this association holds, it could aid in the early and aggressive treatment modalities of the specific patient, decreasing the morbidity and mortality and the heavy cost that must be allowed to exist afterward to satisfy the demands of managing cardiorespiratory fitness, ischaemic stroke, and other micro or microvascular complications or problems.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Pathology Women Medical & Dental College Abbottabad in collaboration with Jinnah International Hospital, Abbottabad and comprised of 110 patients with type-2 diabetes mellitus. After obtaining informed written consent detailed demographics of enrolled cases including age, sex and BMI were recorded. Patients who were pregnant, as well as those who had serious health conditions like heart failure, kidney failure, unmanaged or refractory hypertension, or severe concomitant disease, were not allowed to participate in the trial.

The ages of the patients in the research varied from 30 to 60. Serum samples were tested using commercially available kits for glucose (both fasting and non-fasting), total cholesterol, triglycerides, LDL and HDL cholesterol, urea, and creatinine. A transabdominal ultrasonography examination at 24-hour intervals to measure kidney size; Urine protein and creatinine clearance were taken into account with the ECG to identify the presence of chronic renal illness and ischemic heart disease. To determine HbA1c levels, a Boronate affinity test was performed.

Diabetic patients were divided into two groups according to their glycemic indices: those with haemoglobin (HbA1c) of less than 7.0% (indicating good control) and those with an A1c of greater than 7.0%. (representing poor control). The Asian modified National Cholesterol Education Program Patients Over the age Panel (NCEP ATP III) defines hypercholesterolemia as the following: total cholesterol >200 mg/dl, high low density lipoproteins cholesterol (LDL-C) once value >100 mg/dl, hypertriglyceridemia as triglyceride >150 mg/dl, and low High-density lipoproteins cholesterol (HDL-C) when value 40 mg/dl. Dyslipidemia is clinically diagnosed when more than one of the aforementioned abnormalities in blood lipid content is present. Similarly, the diagnosis of Metabolic Syndrome requires the presence of three or more of the following symptoms.

1.A Waist Circumference that is greater than 90 centimeters for men and 80 centimeters for women. 2. Triglyceride (TG) concentration in the blood at than 150 mg/dL (1.69 mmol/L). 3. HDL-C levels below 40 mg/dL (1.04 mmol/L) in men and 50 mg/dL (1.29 mmol/L) in women. 4. Fasting serum glucose level of at least 110 mg/dL (6.05 mmol/L); Blood pressure of at least 130/85 mm Hg.

The data is presented as a mean + standard deviation of the mean. t-tests for independent samples were used for statistical analysis. If the probability level was less than 0.05, the findings were considered to be significant. In order to determine if there is a relationship between the independent variables (age, gender, duration of diabetes, body mass index, and haemoglobin A1c and the dependent variable (serum lipid profile), the Pearson chi square test was performed. In order to conduct statistical tests, SPSS version 22 is utilized.

RESULTS

Among all patients, females were higher in numbers 72 (65.5%) as compared to males 38 (34.5%). Mean age of the patients was

51.4±8.43 years and had mean BMI 27.16±13.37 kg/m². Mean duration of diabetes was 6.3±4.21 years. There were 63 (57.3%) cases had rural residency and 47 (42.7%) patients had urban residency.(table-1)

Table-1: Demographically details of enrolled case

Variables	Frequency	Percentage
Gender		
Male	38	34.5
Female	72	65.5
Mean age (years)	51.4±8.43	
Mean BMI (kg/m ²)	27.16±13.37	
Mean Duration of DM (years)	6.3±4.21	
Residency		
Rural	63	57.3
Urban	47	42.7

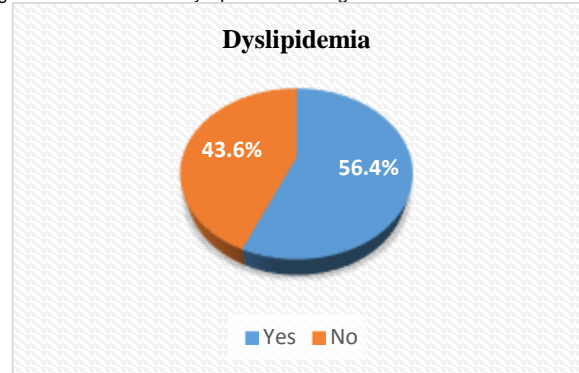
Twenty-two patients (20%) had a HbA1c below 7%, whereas eighty-eight patients (80%) had a HbA1c beyond 7%.(table 2)

Table-2: Level of HbA1c among all cases

Variables	Frequency	Percentage
HbA1c		
<7%	22	20
>7%	88	80

Dyslipidemia was seen in 62 individuals (56.4%) while 48 (43.6%) cases had no dyslipidemia. (figure 1)

Figure-1: Association of dyslipidemia among all cases



Direct connections were found between HbA1c and BMI, cholesterol, triglycerides, and low-density lipoprotein (LDL), while an inverse correlation was found between HbA1c and high-density lipoprotein (HDL).(table 2)

Table-2: The relationship between HbA1c, BMI and lipids, as measured by Pearson's correlation

Variables	Pearson Correlation, 1 Sig. (2-tailed)
HbA1c (1)	
BMI	0.234(**),0.003
cholesterol	0.187(*),0.030
low-density lipoprotein (LDL)	0.158(*),0.039
Triglycerides	0.269(**),0.003
Cholesterol/ HDL	-0.050, 0.639
high-density lipoprotein (HDL)	-0.220(**)0.008

When comparing female and male patients, females were shown to have considerably greater TG levels. HbA1c levels were also significantly correlated with the presence of metabolic syndrome.(table 3)

Table-3: Body Mass Index, Hemoglobin A1c, and Lipid Profile Data for Males and Females

Variables	Male	Female
BMI	26.11±3.98	26.63±3.26
CHO	171.12±21.97	179.0±37.9
TGs	160.12±19.80	166.14±41.18
LDL	100.6±21.53	107.7±40.17
HDL	43.19±21.17	37.8±10.19
CHO/HDL	4.7±8.63	5.8±4.67
HbA1c	8.99±6.18	8.45±7.37

DISCUSSION

If a subject has dyslipidemia and an increased HbA1c, they are now regarded to have an independent risk factor for cardiovascular disease. This is the case even if the subject does not have diabetes. The estimated risk of cardiovascular disease rises by 18% among diabetics for every 1% increase in absolute HbA1c levels in the diabetic population. In non-diabetic individuals, a favorable link between HbA1c and CVD has been established even when the HbA1c levels are within the normal range. [13]

There is accumulating evidence that fat cells that are resistant to insulin create more free fatty acids, which suggests that insulin resistance plays a substantial role in the pathogenesis of diabetic dyslipidemia. The buildup of free fatty acids in the liver is the root cause of fatty liver disease. This accumulation encourages the production of triglycerides as well as the release of apolipoprotein B and very low density lipoprotein cholesterol. The fact that high levels of circulating insulin are also linked to low HDL levels [14] suggests that this may be a shared factor in the present study; although we did not measure insulin to confirm this hypothesis, the presence of metabolic syndrome and a higher body mass index both lend credence to the idea that insulin resistance is a contributing factor to rising HbA1c levels.

In current 110 patients of type-2 diabetes were presented. Among all patients, females were higher in numbers 72 (65.5%) as compared to males 38 (34.5%). Mean age of the patients was 51.4 ± 8.43 years and had mean BMI 27.16 ± 13.37 kg/m². Mean duration of diabetes was 6.3 ± 4.21 years. There were 63 (57.3%) cases had rural residency and 47 (42.7%) patients had urban residency. These findings were comparable to the previous studies.[15,16] In our study, twenty-two patients (20%) had a HbA1c below 7%, whereas eighty-eight patients (80%) had a HbA1c beyond 7%. Dyslipidemia was seen in 62 individuals (56.4%). Results were comparable to the previous study.[17] Direct connections were found between HbA1c and BMI, cholesterol, triglycerides, and low-density lipoprotein (LDL), while an inverse correlation was found between HbA1c and high-density lipoprotein (HDL). These findings were in line with the previous study.[18] When comparing female and male patients, females were shown to have considerably greater TG levels. HbA1c levels were also significantly correlated with the presence of metabolic syndrome.[19]

Our findings show that hypertension is the single most important risk factor for developing Type 2 DM. A total of 46% of our male patients and 58% of our female participants were found to have hypertension in addition to Type 2 diabetes. Our results are consistent with those of a previous research by Lastra, which found that 50% of their type 2 diabetic participants also suffered from hypertension. Hyperinsulinemia, a characteristic of insulin resistance in type 2 diabetes, causes vascular smooth muscle cell proliferation, which in turn raises vascular stiffness [20]. Vasodilation is also impaired, oxidative stress is raised, and the inflammatory process in the vascular wall is initiated. The cumulative impact is a loss of the body's natural ability to maintain a healthy vascular tone, which shows itself as an increase in vascular resistance and a subsequent rise in blood pressure (BP). The antinatriuretic effects of insulin contribute to the renal retention of salt and, hence, to the development of hypertension.[21]

CONCLUSION

According to the findings of our research, HbA1c is not only useful as a biomarker of long-term glycemic control, but it is also an excellent predictor of lipid profile.

REFERENCE

1. Ramachandran A. In: Das S, Moses CR, editors. Epidemiology of Type 2 Diabetes and Its Complications in India, Moses Manual on Diabetes Mellitus. New Delhi: IJCP Group of Publications; 2007. p. 36-45
2. Powers AC. Diabetes Mellitus Harrison's Principles of Internal Medicine. 18th ed., Vol. 2. Ch. 344. 2012. p. 2968-3003.
3. McFarlane SM, Castro J, Kirpichnikov D, Sowers JR. Hypertension in diabetes mellitus. Joslin's Diabetes Mellitus. 14th ed., Vol. 57. Philadelphia, PA: Lea & Febiger; 2005. p. 969-73.
4. Tabish SA. Is diabetes becoming the biggest epidemic of the twenty-first century? *Int J Health Sci* 2007; 1: V-VIII.
5. International Diabetes Federation. Middle East and North Africa at a glance. *IDF Diabetes Atlas*. 6th ed., <http://www.idf.org/sites/default/files/attachments/MENA%20factsheet.pdf> (2014, accessed 25 August 2016).
6. Saeed KMI. Prevalence and predictors of diabetes mellitus in Jalalabad City, Afghanistan-2013. *Iran J Diabetes Obes* 2014; 1: 1-8
7. VinodMahato R, Gyawali P, Raut PP, et al. Association between glycaemic control and serum lipid profile in type 2 diabetic patients: glycated haemoglobin as a dual biomarker. *Biomed Res* 2011; 22: 375-380.
8. International Diabetes Federation. Middle East and North Africa. *IDF Diabetes Atlas*. 7th ed., <http://www.worlddiabetesfoundation.org/sites/default/files/Middle-east.pdf> (2015, 25 August 2016).
9. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, et al. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength? *World J Diabetes* 2014; 5: 444-470.
10. Zahidullah M, Aasim M, Khan I, et al. Evaluation of patients with coronary artery disease for major modifiable risk factors for ischemic heart disease. *J Ayub Med Coll Abbottabad* 2012; 24: 102-105.
11. AHA- Guideline on the Management of Blood Cholesterol: Executive Summary. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *National Guidelines: 10 Nov*. 2018. Available at: <https://healthmetrics.heart.org/wp-content/uploads/2018/11/2018-Guideline-on-the-Management-of-Blood-Cholesterol-Executive-Summary.pdf>.
12. Hussain A, Ali I, Ijaz M, Rahim A. Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: hemoglobin A1c prognosticates dyslipidemia. *Ther Adv Endocrinol Metab*. 2017;8(4):51-57. doi:10.1177/2042018817692296
13. Naqvi S, Naveed S, Ali Z, Ahmad MS, Khan AR, et al. Correlation between Glycated Hemoglobin and Triglyceride Level in Type 2 Diabetes Mellitus. *Cureus*. 2017;9(6):e1347. doi: 10.7759/cureus.1347
14. Tanweer S, Illahi Y, Amatya B, Naeem A, Tareen ZF. Frequency of the metabolic syndrome in type 2 diabetic subjects attending the diabetes clinic of Nishtar Medical College and Hospital, Multan. *Ann Punjab Med Coll*. 2011;5(1):53-58.
15. Kidwai SS, Nageen A, Bashir F, Ara J. HbA1c - A predictor of dyslipidemia in type 2 Diabetes Mellitus. *Pak J Med Sci*. 2020 Sep-Oct;36(6):1339-1343.
16. Alzahrani SH, Baig M, Aashi MM, Al-Shaibi FK, Alqarni DA, Bakhamees WH. Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study. *Diabetes Metab Syndr Obes*. 2019 Aug 29;12:1639-1644.
17. Sama Al-Shaheeb, Husham Kamil Hashim, Athir Kadhim Mohammed, Haider Abdulkareem Almashhadani, Ali Al Fandi Volume 7 / Issue 3 / 29
18. Naqvi S, Naveed S, Ali Z, Ahmad MS, Khan AR, et al. Correlation between Glycated Hemoglobin and Triglyceride Level in Type 2 Diabetes Mellitus. *Cureus*. 2017;9(6):e1347. doi: 10.7759/cureus.1347
19. Beigh HS, Jain S. Prevalence of metabolic syndrome and gender differences. *Bioinformation*. 2012;8(13):613-
20. Lastra G, Syed S, Kurukulasuriya LR, Manrique C, Sowers JR. Type 2 diabetes mellitus and hypertension: an update. *Endocrinol Metab Clin North Am*. 2014;43(1):103-122.
21. Villalpando GC, Meigs BJ, Ferrannini E. Hypertension and Diabetes Mellitus. Coprediction and Time Trajectories. *Hypertension*. 2018;71:422-428