Association between lipid indices and glycated haemoglobin to detect cardiovascular diseases in diabetic patients: A retrospective cross-sectional study

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Abstract- Diabetes mellitus is a major risk factor for cardiovascular disease (CVD), significantly increasing both morbidity and mortality. Glycated hemoglobin (HbA1c) is widely used as a marker of glycemic control to assess CVD risk in diabetic patients. This study aimed to explore the association between lipid profiles, HbA1c levels, and CVD in diabetic patients from Punjab, Pakistan. A retrospective cross-sectional analysis was conducted on 211 diabetic patients with a confirmed diagnosis of CVD. Demographic, anthropometric, and biochemical data were collected for a comprehensive analysis of correlations and regression. The study found that diabetic patients with poor glycemic control (HbA1c >7%) had significantly higher body mass index (BMI), fasting blood glucose (FBG), systolic blood pressure (SBP), cholesterol, and triglyceride levels compared to those with better glycemic control (HbA1c <7%). Poor glycemic control was strongly associated with an increased incidence of ischemic heart disease (33.33%), coronary artery disease (13.82%), and stroke (11.38%). Correlation and regression analysis showed that HbA1c levels were significantly influenced by SBP ($p < 0.035$), triglycerides ($p < 0.025$), FBG ($p < 0.041$), and microvascular complications ($p < 0.037$). This study emphasizes the importance of regular monitoring of HbA1c and lipid profiles to predict and manage CVD risk in diabetic patients. It also lays the groundwork for designing interventions targeting lipid management to reduce CVD risk, with a recommendation for future longitudinal studies to establish a clearer relationship between glycemic control and CVD outcomes in diabetic patients.

Keywords- Type 2 Diabetes Mellitus, HbA1c, Lipid profile, Cardiovascular diseases, Glycemic control, Risk factors, Cross-sectional study

I. INTRODUCTION

Hyperglycemia, commonly associated with diabetes mellitus (DM), is a metabolic syndrome that arises due to defective secretion or impaired action of insulin [1]. The onset of type 2 diabetes mellitus is a complex process and account to 85% to 90% of all diabetes cases around the globe [2]. It significantly contributes to the development of cardiovascular diseases (CVD) as individuals with diabetes are at 2 to 4 times higher risk of morbidity and mortality compared to non-diabetic individual with any cardiovascular disease. Effective care management of diabetes is critical in reducing the risk of CVD, beginning with a reliable method to monitor blood glycaemic control such as glycated haemoglobin (HbA1c). HbA1c is a most reliable measure and recognized indictor to assess the blood sugar level for period of 2 to 3 months. Current guidelines often recommend a specific and patient-centred measure over a generic threshold for assessing glycemic control [3].

HbA1c had proven as a reliable indicator of plasma glucose due to its reflection of the non-enzymatic bonding of glucose to haemoglobin. Achieving a level of HbA1c below than 7% is considered as a good glycemic control. The levels of HbA1c can be altered due to impact of multiple factors including adherence to medications, sugar intake, physical activities and non-communicable disease such as CVD [3], [4]. Previous investigations have suggested that HbA1c could serve as a biomarker for predicting CVD. The significant association between HbA1c levels and CVD has long been a concern for healthcare professionals [5], [6]. Diabetic patient, particularly those with dyslipidemia are more susceptible to CVD, resulting in an increased cardiovascular mortality rate. Individuals at the early stage of diabetes or reaching positive diagnostic threshold are considered at high risk of for CVD-related death. Notably, diabetic patients and those patients who have diabetes and CVD systematically underrated for explore risk factors for CVD [7].

The association of DM and CVD is already known with diabetes is being listed among the risk factors for the development of CVD including coronary artery disease [8]. Diabetic patients are more prone to have relative risk of incidence, morbidity and mortality of CVD with adverse outcomes as compared to non-diabetic patients. Over the past three decades, the early mortality rate in result of myocardial infarction in the public community has declined drastically however; it remains significantly higher in diabetic patients [9]. Whenever a heart attack occurs outside or in other place away from the healthcare setting, diabetic patients have higher chance of death compared to non-diabetic counterparts. Despite this, there is controversy by continuously debating related to strong positive association between DM and development of CVD. Numerous observational studies have demonstrated that higher levels of HbA1c are horizontally linked with an increased risk of CVD as well as mortality rate [7]. In contrast, a meta-analysis study has shown that minor risk in CVD is decreased with a 1% reduction in HbA1c level but the risk of stroke-related mortality was unchanged with glycemic control [10].

The American college of cardiology foundation, the American heart association task force on practical guidelines, the

Canadian cardiovascular society recommended that HbA1c measurement should be used to identify CVD risk in asymptomatic patients. It is also highlighted that the patients with any CVD often require long-term medications, which has been linked to the development of diabetes [11]. Various studies also suggested that HbA1c level can be a risk factor that independently predicts CVD regardless of diagnosis of T2DM. HbA1c levels are lined to a composite index of cardiac, cerebral and peripheral vascular syndromes in diabetic patients. Although the association between HbA1c and CVD has been documented in many countries, similar information regarding the general population of Pakistan remains scarce. Therefore, the presented study was designed to investigate the association between lipid profiles and HbA1c levels from diabetic patients with cardiovascular disease.

II. MATERIAL AND METHODS

Study Area

Study setting and sample size

A retrospective cross-sectional study was conducted from July 2023 to May 2024. The study population were selected from secondary and tertiary hospitals in Punjab Pakistan. A total of 211 participants were selected by calculating through following formula integrated in Open Epi version 3.

$n = [DEFF*Np(1-p)]/[d^2/Z_2\ 1\text{-}\alpha/2*(N-1)+p*(1-p)]$

Here "n" represents the sample size, DEFF= design effect, N= total population size, p= estimated proportion, 1-p= proportion of population, d= margin of error and $Z_2\ 1\text{-}\alpha/2$ = confidence level at 95%. The calculated sample size was 197.

Data collection

A written informed consent was obtained from all participants and they were informed about confidentiality of the study. Data were collected from participants who fulfilled eligible criteria. The inclusion criteria for participants were those having diagnosed type 2 diabetes mellitus, visiting hospital for treatment, more than 35 years of age and complain of CVD. The exclusion criteria included the type 1 DM patients and diabetic patients lower than 35 years of age, only diabetic without CVD and only CVD without diabetes. All patients' anthropometric measurements including age, weight, height, BMI and duration of DM, blood pressure and laboratory parameters including cholesterol, triglyceride, HbAIc, HDL-C, LDL-C and fasting blood sugar were noted.

Statistical analysis

For statistical analysis, SPSS version 21 was employed to compute mean and standard error mean of variables. Utilizing mean of each parameter, the comparison and correlation was determined using independent sample t-test. A linear regression analysis was computed to explore association between HbA1c and other variables including lipid profile, anthropometric measurements and CVD at significant level of >0.05.

Ethical Consideration

The study was conducted after obtaining ethical approval from the Institutional Review Board following a thorough review of the study's objectives, methods and informed consent (IRB no. MN/199/2023).

III. RESULTS

Of 211 respondents comprising 72 males and 139 females, male respondents (54.24±9.02) were slightly older than females (51.81±7.44) with non-significant association (p=0.082). The duration of diabetes was also similar with average duration of 11.42±4.99 years in males compared to 13.90±3.08 years in females (Table 1). Females had a significantly (p=0.001) higher BMI (32.22±5.09 kg/m²) compared to males (29.12±3.44 kg/m²). Females exhibited higher systolic (144.8±5.74 vs 125.2±3.93 mmHg) and diastolic blood pressure (88.11±3.45 vs 79.8±2.04 mmHg) than males. Compared to males, females had worse cholesterol level (169.09±36.83 vs 143.04±38.4 mg/dl) with higher HDL-C (48.63±16.45 vs 40.95±12.56 mg/dl) and LDL-C (108.83±34.93 vs 88.71±30.64 mg/dl). However triglyceride levels were lower in females (129.69±76.90 mg/dl) compared to males (147.04±96.51 mg/dl). Females had higher levels of HbA1c (7.79±2.22% vs 7.14±2.04%) and fasting blood sugar (FBS) (239.49±24.8 vs 221.38±17.3 mg/dl). Both parameters including HbA1c and FBS were statistically significant (p=0.024 and p=0.009, respectively) (Table 1).

Variables	Males (n = 72) Mean±SEM	Females (n=139) Mean±SEM	Total (n=211) Mean±SEM	*p*-value
Age (yrs)	54.24±9.02	51.81±7.44	53.03±12.74	0.082
Duration of DM (yrs)	11.42±4.99	13.90±3.08	12.86±3.79	0.856
BMI (kg/m^2)	29.12±3.44	32.22±5.09	30.6±5.82	0.001*
SBP (mmHg)	125.2±3.93	144.8±5.74	133.89±4.81	0.047*
DBP (mmHg)	79.8±2.04	88.11±3.45	84.59±3.10	0.059
Cholesterol (mg/dl)	143.04±38.4	169.09±36.83	170.35±39.80	0.019*
Triglyceride (mg/dl)	147.04±96.51	129.69±76.90	142.54±85.46	0.039*
HbAIC (%)	7.14±2.04	7.79±2.22	7.66±1.98	0.024*
HDL-C (mg/dl)	40.95±12.56	48.63±16.45	46.89±15.4	0.037*
LDL-C (mg/dl)	88.71±30.64	108.83±34.93	89.74±32.38	0.007*
FBG (mg/dl)	221.38±17.3	239.49±24.8	235.44±17.4	0.009*

Note: *: Significant (p<0.05)

Table 1: Gender-wise comparison of basic characteristics and lipid profile of participants

While categorizing patients as per their glycemic control, 88 respondents had HbA1c lower than 7% and 123 respondents had HbA1c greater than 7%. Patients with poor glycemic control had a significantly higher BMI (32.46±5.71 vs 30.74±5.09 kg/m²), triglyceride level (148.55±97.01 vs 126.21±69.24 mg/dl), FBG (161.44±56.21 vs 124.16±46.92 mg/dl), systolic (136.74±4.81 vs 129.25±2.06) and diastolic blood pressure (82.04±3.46 vs 81.10±3.91) and cholesterol level (163.29±36.41 vs 169.35±37.49) compared to those with better glycemic control (Table 2).

Table 2: Comparison of basic characteristics and lipid profile of type 2 diabetes mellitus patients according to their glycemic control

Variables	HbAIC level <7 (n=88) Mean±SEM	HbAIC level ≥7 (n=123) Mean±SEM	*p*-value
Age (yrs)	60.5±11.43	58.98±12.59	0.342
Duration of DM (yrs)	14.21±2.11	10.29±1.43	0.290
BMI (kg/m^2)	30.74±5.09	32.46±5.71	0.043*
SBP (mmHg)	136.74±4.81	129.25±2.06	0.349
DBP (mmHg)	82.04±3.46	81.10±3.91	0.909
Cholesterol (mg/dl)	163.29±36.41	169.35±37.49	0.181
Triglyceride (mg/dl)	126.21±69.24	148.55±97.01	0.022*
HDL-C (mg/dl)	49.41±16.81	47.68±16.01	0.248
LDL-C (mg/dl)	98.83±36.11	103.51±33.89	0.360
FBG (mg/dl)	124.16±46.92	161.44±56.21	0.039*

Note: *: Significant (p<0.05)

Patients with poor glycemic control had a higher prevalence of coronary artery disease (13.82% vs 4.54%), ischemic heart disease (33.33% vs 5.68%) and stroke (11.38% vs 3.41%) compared to patients with better glycemic control. On the other hand angina was more frequent among patients with better glycemic control (35.23%) compared to patients with poor glycemic control (15.45%). Microvascular complications were more prevalent among patients with better glycemic control (51.14%) as compared to patients with poor glycemic control (26.02%) (Table 3).

Table 3: Incidence of cardiovascular diseases on the basis of glycemic control

Variable	HbAIC level <7 (n =88) %(n)	HbAIC level ≥7 (n = 123) %(n)
Coronary artery disease	4.54% (n =4)	13.82% (n = 17)
Angina	35.23% (n =31)	15.45% (n = 19)
Ischemic Heart	5.68% (n =5)	33.33% (n = 41)
Stroke	3.41% (n =3)	11.38% (n = 14)
Microvascular complications	51.14% (n =45)	26.02% (n =32)

Correlation analysis indicated a strong association between HbA1c and SBP (r= -0.036, p=0.029), cholesterol (r=0.234, p=0.031), triglyceride (r=0.153, p=0.022), FBG (r=-0.083, p=0.038) and microvascular complications (r=0.141, p=0.013). Regression analysis showed that HbA1c was significantly influenced by factors such as systolic blood pressure (b=-0.101, p=0.034), cholesterol (b=0.103, p=0.051), triglycerides (b=0.349, p=0.024), FBG (b=-0.040, p=0.040) and microvascular complications (b=0.293, p=0.036) (Table 4).

Table 4: Correlation analysis and linear regression analysis of T2DM patients showing dependency of HbA1C on other variables

Variable	Correlation		Regression analysis	
	Coefficient	p-value	Unstandardized coefficient b	p-value
Age (yrs)	-0.063	0.374	-0.051	0.611
Duration of DM (yrs)	-0.126	0.092	-0.304	0.171
BMI (kg/m^2)	0.042	0.636	0.293	0.728
SBP (mmHg)	-0.036	0.029*	-0.101	0.034*
DBP (mmHg)	0.031	0.255	0.394	0.417
Cholesterol (mg/dl)	0.234	0.031*	0.103	0.051
Triglyceride (mg/dl)	0.153	0.022*	0.349	0.024*
HDL-C (mg/dl)	-0.079	0.281	-0.126	0.238
LDL-C (mg/dl)	-0.088	0.159	-0.541	0.589
FBG (mg/dl)	-0.083	0.038*	-0.040	0.040*
Coronary artery disease	0.040	0.806	0.138	0.912
Angina	-0.953	0.644	-0.981	0.860
Ischemic Heart	-0.793	0.408	-0.718	0.567
Stroke	-0.762	0.805	-0.944	0.968
Microvascular complications	0.141	0.013*	0.293	0.036*

Note: *: Significant (p<0.05)

IV. DISCUSSION

Several studies have shown a high prevalence of cardiovascular diseases (CVD) in patients with type 2 diabetes mellitus (T2DM) around the globe [12], [13], [14]. It is difficult to diagnose silent CVD at an early stage, but it can become complicated in diabetic patients. Therefore, disturbances in lipid parameters may serve as early diagnostic markers for CVD [15]. The current study provides insight into the relationship between T2DM and CVD by evaluating lipid profiles and HbA1c levels. Numerous studies have indicated that diabetic patients exhibit an increased prevalence of lipid abnormalities. The findings of the current study align with existing observations regarding HbA1c as a marker for both glycemic control and CVD risk prediction in diabetic populations [16], [17]. Overall, the findings of the current study reveal that diabetic patients with poor glycemic control experience severe dyslipidemia and have significantly higher levels of cholesterol, triglycerides, systolic blood pressure

(SBP), and fasting blood glucose (FBG). The elevation of these parameters suggests a higher risk of CVD complications in diabetic patients. These findings are consistent with observations made in previous studies conducted in India, Pakistan, and China [18], [19], [20]. Current findings indicate a strong positive relationship between HbA1c and triglyceride levels as per reported by previous studies. The increased level of triglyceride in T2DM patients may partially arise due to insufficient production of insulin, which cause the liver to secret more low-density lipoprotein and delayed removal of triglyceride-rich lipoproteins mainly due to increased substrate for triglyceride synthesis [21].

The findings of the current study highlighted an absence of the correlations between the levels of HbA1c and total cholesterol, which is in accordance of the observations of previous study [22]. This study also proved that the female patients had higher HbA1c levels, worse cholesterol profile and hypertension compared to male diabetic patients. There is conclusive evidence that diabetic women are at higher risk of developing CVD than diabetic men due to the severe lipid abnormalities and perhaps, effects of sex hormones on distribution of adipose tissues in the body. The positive relationship between HbA1c levels and poor glycemic control shows that poor glycemic control increases the CVD risk factors. This finding supports the postulated hypothesis that there exists a positive relationship between HbA1c levels and CVFD risk mainly driven by their interaction with lipid profiles [23]. These results highlight the need for gender-specific strategies in managing CVD and diabetes, particularly through interventions aimed at improving lipid profiles and blood pressure in women.

It was revealed that patients with poorly controlled diabetes have a higher risk of ischemic heart disease, coronary artery disease, and stroke compared to patients with better control of their diabetes. This type of association between glycemic control and the occurrence of CVD corroborates previous findings that HbA1c is an independent predictor for CVD [3]. Moreover, elevated cholesterol and triglyceride levels suggest that dyslipidemia plays a substantial role in the increased risk of CVD among diabetic patients. Interestingly, microvascular complications were higher among those with better glycemic control; hence, raising a question of whether intensive glycemic control might not be protective against these conditions. Previous studies have also highlighted that microvascular complications were more frequent among the group with well controlled glycemia compared to the group that was poorly controlled for glycemia as a result of a longer duration of diabetes among well controlled for glycemia [24], [25]. This finding is concord with other clinical trials that reflect difficulty in achieving optimal glycemic control with reduction of both microvascular and macrovascular complications [25], [26]. The findings of the current study suggest a strong association between CVD complexity with age, high HbA1c, high BMI, and elevated triglyceride levels. This underpins the utility of regular assessment of HbA1c and lipid profiles for management of blood sugar and for risk stratification of CVD in diabetic patients. Nevertheless, this current study has limitations that include patients already on anti-diabetes medications may have influenced the results. In addition, the current study was a cross-sectional study with small sample size, making it difficult to draw definitive conclusion about the effect of the observed associations and a further study with longitudinal design is required to establish a clearer cause-and-effect relationship between glycemic control and CVD outcomes.

V. CONCLUSION

In conclusion, this study reinforces the strong association between elevated HbA1c levels, disturbed lipid profiles, and increased cardiovascular risk in diabetic patients, particularly among women. The findings emphasize the importance of integrated care strategies that focus on strict glycemic control, lipid management, and blood pressure monitoring to reduce CVD risk in diabetic populations. Tailored interventions may be crucial in alleviating the burden of cardiovascular disease among individuals with diabetes.

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