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Original Article

Co-Relation Between Glycated Hemoglobin (HbA1c) and Dyslipidemia in Type II Diabetics Presenting in a Tertiary Care Hospital in Pakistan

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Abstract

Objective: Diabetes is a global disease that is affecting both developing and developed countries. According to a WHO survey (1994-1998), the overall prevalence of diabetes Mellitus is 11.47% in Pakistan. Based on a study done in Pakistan in 2015, the prevalence of dyslipidemia among people with diabetes was 95%. Both HbA1c and dyslipidemia lead to an increased risk for cardiovascular diseases. This study aims to identify the atherosclerotic disease risk factors among the Pakistani population to decrease morbidity and mortality. To determine the frequency of dyslipidemia among Type 2 Diabetic patients and compare dyslipidemia among Type 2 Diabetic patients with/without elevated Glycated hemoglobin (HbA1c).

Methods: A descriptive, cross-sectional study was performed at Internal Medicine Department, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, for Six months (Feb 02, 2020, till Jul 01, 2020). HbA1c levels, serum lipid profile, random and fasting blood sugar levels were tested. Non-probability consecutive sampling was done, and 100 patients were registered.

Results: Out of 100 patients, 47 were males and 53 females with a mean age of 47.85 ± 8.61. Sixty-nine diabetic patients with elevated HbA1c showed a positive relationship with total cholesterol and LDL-C level ($p<0.05$). In addition, patients with HbA1c higher than 7% showed a high risk and borderline dyslipidemia.

Conclusion: Elevated HbA1c, apart from being a glycemic index, is a good predictor of dyslipidemia. Therefore, patients with borderline or desirable lipid profile values with high HbA1c levels should start statin therapy or lifestyle modification to prevent cardiovascular diseases.

Keywords: Diabetes mellitus, Dyslipidemia, High Glycated Hemoglobin, uncontrolled diabetes.

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Introduction

Diabetes is a global disease that is affecting both developing and developed countries. According to the World Health Organization survey (1994-1998), the overall prevalence of diabetes mellitus is 11.47% in Pakistan. Based on a study done in Pakistan in 2015, the prevalence of dyslipidemia among diabetic males was 97.18%, while for females 87.15%, overall prevalence was 95%.[1]

Type II Diabetic patients with cardiovascular diseases were observed to have hypercholesterolemia and hyperlipidemia compared to those with type II diabetes who did not have cardiovascular diseases.[1]

Both HbA1c and dyslipidemia leads to an increased risk for cardiovascular diseases; the estimated risk of Cardio-Vascular Diseases has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic.[2]

A study conducted in India in 2013 concluded that HbA1c had a positive correlation with serum cholesterol, triglyceride, and LDL levels; however, it showed a negative correlation with HDL and that HbA1c can be used as a parameter envisage lipid profile in both genders.[3]

Another study in china in 2012 observed a significant increase in total cholesterol and LDL level with increasing HbA1c levels, whereas no significant relation was seen with triglyceride or HDL levels.[4]

Thi-Qar medical university conducted a similar study because HbA1c is now being observed as a predictor for dyslipidemia and cardiovascular disease risk factors. They concluded that strong relation was found between HbA1c and all components of lipid profile in diabetic patients, and HbA1c is a good predictor of hyperlipidemia in patients with diabetes.[5]

In 2015, a study in Riyad KSA concluded that there is an association between blood glucose & some lipid markers. and in 2017, a study conducted on the Afghani population concluded that HbA1c could be used as a predictor of dyslipidemia, and early detection of dyslipidemia can be used as a preventive measure for the development of cardio-vascular diseases in type II diabetic patients.[6]

Another study conducted in India in 2014 also indicated similar results, the usefulness of HbA1c as a marker for serum lipid profile for screening diabetic patients at high risk of developing cardiovascular diseases.[7]

The study conducted at the department of cardiology, Tehran heart center, in 2013 concluded that there is a strong relationship between Hba1c and cardiovascular diseases angiography proven and HbA1c can be used as a risk stratification in coronary artery disease severity.[8]

Previously studies have been conducted on dyslipidemia in diabetic patients and concluded that diabetes and dyslipidemia have a strong co-relation. However, recently it is known that HbA1c can be a good predictor of dyslipidemia and even if a patient has a normal lipid profile but elevated HbA1c.[9] preventive measures should be initiated to control unrecordable dyslipidemia, which will prevent cardiovascular diseases.[10] Studies have proven that both raised HbA1c and dyslipidemia have been independent factors in cardiovascular risk stratification. A strong association exists between coronary artery diseases with both dyslipidemia and raised HbA1c levels. However, there is limited data available for the Pakistani population in this regard. Hence, monitoring HbA1c could have additional benefits of identifying high-risk patients and decreasing morbidity and mortality from cardiovascular diseases. In the light of above, aim of present study was to determine the frequency of dyslipidemia among Type 2 Diabetic patients and to compare dyslipidemia among Type 2 Diabetic patients with/without elevated Glycated hemoglobin (HbA1c).

Methods

Six months (Feb 02, 2020, till Jul 01, 2020) descriptive cross-sectional study was conducted after ethical approval from the ethical review board of SZABMU at the Out-patient & In-patient Departments, General Medicine, Pakistan Institute of Medical Sciences, Islamabad. Non-probability consecutive sampling was done, and 100 patients were enrolled, keeping a 95% confidence interval.

Inclusion criterion

Follow-up and newly diagnosed (based on HbA1c, Fasting/random sugar levels) type II diabetic patients (35 - 65 years old), presenting to General Medicine Out & In-patient Departments, PIMS, Islamabad, with/without elevated levels of HbA1c.

Exclusion criterion

Patients having co-morbidities like type I Diabetes Mellitus, Gestational Diabetes, Familial Hypercholesterolemia, Chronic renal disease (KDIGO 2012, cut-off eGFR ≤89 ml/min/1.73m^2), iron deficiency anemia (AGA clinical guidelines for the management of anemia cut-off women <12g/dl and men <14g/dl), and those patients who were on lipid-lowering therapy were excluded from the study. The cause of exclusion of renal diseases and anemia was its probable effect on HbA1c results.

Data Collection Procedures

Patients were primed regarding the analysis after approval for involvement. After initial assessment & evaluation, inclusion criteria were applied.

Investigations including Complete Blood Count, Renal Function Tests, Pregnancy test (for women of child-bearing age), Serum Lipids, HbA1c, Fasting & Random blood sugars, via venous sampling were conducted at the onsite laboratory.

Patient biography and laboratory results were entered in the patient proforma.

Data Analysis Plan

Descriptive statistics employed in SPSS-21 for the analysis of qualitative and quantitative data. Quantitative data included patient age, HbA1c & Serum Lipids. Mean and SD analyzed for quantitative data. Qualitative data included patient gender, the severity of HbA1c, dyslipidemia. Percentage/frequency determined for each qualitative variable. Effect modifiers like age, gender, and hypertension controlled by stratification. Post-stratification Chi-square test was applied to compare Dyslipidemia with Normal & Elevated HbA1c. P-value ≤0.05 was considered significant.

Results

Out of 100 patients, 47 were men, and 53 were women. The majority of the patients, 47.0% were between age 35-45 years, 30.0% were between 46-55, and 23% between 56-65 years, evidently proving that younger age was more prone to have type II diabetes and dyslipidemia.

Half of the study population was hypertensive. More than two-thirds had elevated HbA1c. When lipid profile was evaluated, the bulk of the patients had cholesterol in the range of high risk, although patients have it borderline deranged. Most have triglycerides in the high-risk range. IN MOST CASES, the LDL range was desirable, whereas the HDL range was more pronounced in the high-risk and borderline categories.

Demographics and clinical features were stratified according to HbA1c to see any association. Proportionately, 45-55 year of diabetic patients were more likely to have elevated HbA1c levels; however, it was not statistically significant (p-value, 0.09). In addition, there was no difference in gender distribution and hypertension according to HbA1c findings (p-value, 0.80) and (p-value, 0.51), respectively.

The indices of lipid parameters were correlated with HbA1c findings. In this study, the high-risk range of total cholesterol was substantially associated with elevated HbA1c (p-value <0.001). Correspondingly, the high-risk range of HDL was also considerably associated with HbA1c elevation (p-value, 0.001). Additionally, TGs & LDL were observed similarly distributed according to qualitative findings of HbA1c in this study. Moreover, patients' demographic and clinical attributes were stratified according to lipid parameter ranges in terms of desirable, borderline, and high risk. It was witnessed that age, gender, and hypertension had no difference in total cholesterol ranges.

Tgs were found in borderline or high-risk range in more females than males; nevertheless, it was not statistically significant (p-value, 0.26). Likewise, hypertension was somewhat related to borderline deranged triglycerides as depicted in table 4. However, it was not statistically significant (p-value, 0.21). Most of the 35-45 years have desirable LDL levels though those between 46-55 years were found significantly associated with a high-risk LDL range (p-value, 0.05). Similarly, more males have a desirable LDL range, whereas females have a borderline or high-risk range of LDL; however, this difference was not statistically significant (p-value, 0.09) as presented in table 2.

Mean HbA1c Male = 8.3 ± 2.03

Table 1: *Distribution of Demographic and Clinical Characteristics (n=100)*

Patient characteristics	Frequency	Percentage (%)
Age Range		
35-45	47	47.0%
46-55	30	30.0%
56-65	23	23.0%
Gender		
Male	47	47.0%
Female	53	53.0%
Hypertension		
Yes	50	50.0%
No	50	50.0%
HbA1C		
< 7 (normal)	31	31.0%
> 7 (elevated)	69	69.0%
Total Cholesterol		
• Desirable	34	34.0%
• Borderline	30	30.0%
• High Risk	36	36.0%
Triglycerides		
• Desirable	5	5.0%
• Borderline	25	25.0%
• High Risk	70	70.0%
LDL Range		
• Desirable	71	71.0%
• Borderline	25	25.0%
• High Risk	4	4.0%
HDL Range		
• Desirable	32	32.0%
• Borderline	22	22.0%
• High Risk	46	46.0%

Table 2: *Stratification of Demographic & Clinical Characteristics According to LDL*

	LDL			p-value
	Desirable (n=71)	Borderline (n=25)	High Risk (n=4)	
Age (years)				
35-45	36 (50.7%)	10 (40.0%)	1 (25.0%)	0.05
46-55	22 (31.0%)	5 (20.0%)	3 (75.0%)	
56-65	13 (18.3%)	10 (40.0%)	0 (0.0%)	
Gender				
Male	37 (52.1%)	10 (40.0%)	0 (0.0%)	0.09
Female	34 (47.9%)	15 (60.0%)	4 (100.0%)	
Hypertension				
Yes	33 (46.5%)	15 (60.0%)	2 (50.0%)	0.35
No	38 (53.5%)	10 (40.0%)	2 (50.0%)	

Mean HbA1c Female = 7.9 ± 1.51

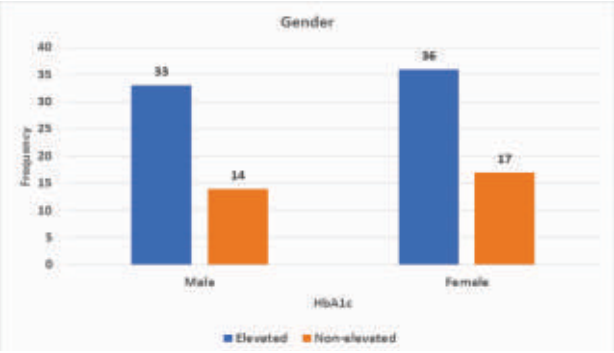

Figure I: *Distribution of HbA1c Findings According*

to Gender

When stratification was measured according to the HDL range, it was apparent that age and gender were similarly disseminated among the HDL range. There was a proportionate disparity in hypertension and HDL range. Surprisingly, hypertension was more prevalent in the desirable HDL range, and normotension was more prevalent with the borderline and high-risk HDL range; even so, this difference was not statistically significant, though it was close (p-value, 0.07)as shown in table 3.

Table 3: *Stratification of Demographic & Clinical Characteristics According to HDL*

	HDL			p-value
	Desirable (n=32)	Borderline (n=22)	High Risk (n=46)	
Age (years)				
35-45	11 (34.4%)	12 (54.5%)	24 (52.2%)	0.33
46-55	10 (31.2%)	7 (31.8%)	13 (28.3%)	
56-65	11 (34.4%)	3 (13.6%)	9 (19.6%)	
Gender				
Male	15 (46.9%)	10 (45.5%)	22 (47.8%)	0.98
Female	17 (53.1%)	12 (54.5%)	24 (52.2%)	
Hypertension				
Yes	21 (65.6%)	11 (50.0%)	18 (39.1%)	0.07
No	11 (34.4%)	11 (50.0%)	28 (60.9%)	

Discussion

West-china hospital concluded that raised hba1c had a direct relation with dyslipidemia. Patients having raised HbA1c had high LDL-C levels and Total cholesterol levels; however, HDL-C and serum triglyceride levels were not co-related,[4] in our study, we had similar results when hba1c was compared with total cholesterol and Ldl-c levels but along that raised hba1c also showed correlation with low HDL-C levels.

A study conducted in Saudi Arabia in 2014 at King Abdul Aziz Medical City evaluated the affiliation between high blood glucose levels, thyroxine, and blood lipid profile. Although they did not find any close link between high glucose and thyroxine levels, they found an association between high sugars and dyslipidemia. Since the association of dyslipidemia with high sugar level was incidental and thus individual parameters of lipid profile were not evaluated.[5] Similar to our study, they concluded an association between both mentioned parameters though statistical significance, whether present or not, was not observed.

Arshad Hussain, along with his colleagues, came up with similar results in afghani patients with a mean age of 51yrs; their study showed a positive co-relation between TC, TG, LDL-C, and LDL-C/HDL-C ratio. On the other hand, a correlation between hba1c and HDL-C was negative though statistically, it was insignificant. Thus, they concluded that glycosylated hemoglobin could be a strong predictor of dyslipidemia.[6] The outcomes were analogous to our research, and one reason could be the strong genetic linkage between the Afghani/Pakistani population and the ecological aspects affecting both inhabitants.

Indian and Pakistani residents reveal the same genetic background; they are economically, socially, & culturally strongly related to each other. A study conducted in India on people with type II diabetes showed a direct link of hba1c with Serum cholesterol, triglyceride, and LDL-C level. Thus, they clinched that HbA1c can be used as a strong marker to screen diabetic patients for dyslipidemia who have a high risk of developing cardiovascular diseases.[7] The results were statistically significant though the only difference they had from our study was a strong relation of hba1c with serum triglyceride levels, which was statistically insignificant. Multiple factors can be responsible for this deviation. One of them could be the sampling of lipid profiles, resulting in high serum triglyceride levels if not in the fasting state. However, the conclusion that hba1c can be used as a predictor for dyslipidemia was the same.

A study published in diabetes research clinical practice in 2013 evaluated hba1c levels in non-diabetic patients undergoing coronary artery angiography, they found that non-diabetic patients had high HbA1c levels and those having high hba1c had more severe coronary artery disease. The outcomes were statistically significant, and they recommended that along with other cardiac markers for cardiac evaluation, HbA1c can be a valuable marker to evaluate a patient's coronary artery disease extension and severity.[8] This study someway serves the intention our study conducted that dyslipidemia is a significant factor in effecting cardiovascular endpoint results and cardiovascular events. People having high HbA1c could have dyslipidemia which leads to severe coronary artery disease. Keeping this in opinion, patients having high HbA1c despite having coronary artery should take lipid-lowering therapy. Their lipid profile observed over a certain period could avert fatal/non-fatal cardiovascular events and reduce the incidence of stroke, ischemic heart diseases, myocardial infarctions, and atherosclerotic diseases with a significant number.

Conclusion

Pakistani population-based study established that dyslipidemia in diabetic patients was not correlated with gender or age but showed a considerable correlation with glycated haemoglobin.

When HbA1c was equated with serum lipids' parame-

ters, it was found that those having abnormal hba1c were more associated with levels of total cholesterol, serum LDL, and serum HDL. Furthermore, these parameters showed statistically significant co-relation whereas TGs showed a statistically insignificant positive co-relation with hba1c.

Elevated HbA1c, apart from being a glycemic index, is a good predictor of dyslipidemia. Patients with borderline or desirable lipid profile values with high HbA1c levels should start statin therapy along with lifestyle modification to prevent cardiovascular and atherosclerotic diseases. Risk factors identified can be followed up on an out-patient basis, improving patient mortality in the long run.

Conflict of interest

None

Funding Source

None

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