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Original Research Article

A study to evaluate the association of HBA1C and Cardiovascular functions among the diabetic and non-diabetic population of a rural setting

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Abstract

Introduction: Diabetes Mellitus (DM) has been progressively growing in prevalence over time, with overall annualised incidence rates per 1000 people rising from 3.0 in the 1970s to 5.5 in the first decade of the 2000s. This alteration resulted in an 83.3 percent rise in the incidence of T2DM, which was higher among males when compared with females.

Materials and Methods: This a prospective observational study undertaken at a rural tertiary care setting where two patient cohorts are made, one with diabetic patients and other with non-diabetic age and gender matched individuals. The study population (Cohort A) consisted of patients with type 2 diabetes attending the Medicine and Cardiology departments from January 2019 to February 2020. The Cohort B included age and gender matched non-diabetic individuals who are the relatives and attending staff of the patients and the working staff of the hospital.

Results and Discussion: HbA1c levels of 6.5 percent or higher in diabetics were linked to an elevated risk of cardiovascular disease. Glycosylation of haemoglobin may also affect RBC membrane lipid protein interactions, increasing internal viscosity, altering the viscoelastic properties of erythrocyte membranes and lowering RBC deformability.

Conclusion: HbA1c may be a valid predictor of cardiovascular mortality and morbidity in diabetics. The data of our study suggest that the healthcare professionals must appraise the values of HbA1c in assessing the cardiovascular risks and outcomes in the diabetes patients.

Keywords: Cardiovascular function, diabetes mellitus, glycosylated haemoglobin (HbA1c), medicine, rural setting

Introduction

Diabetes Mellitus (DM) has been progressively growing in prevalence over time, with overall annualised incidence rates per 1000 people rising from "3.0 in the 1970s to 5.5 in the first decade of the 2000s". This alteration resulted in a 83.3 percent rise in the incidence of T2DM, which was higher among males when compared with females [1, 2]. Among the patients with diabetes, cardiovascular disease (CVD) has been a leading cause of death and disability. DM can lower life expectancy by up to ten years and CVD is the leading cause of death in DM

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patients [3]. Diabetic individuals have a higher CVD prevalence rate than non-diabetic persons and the risk of CVD climbs continuously as fasting plasma glucose levels rise, even before they reach levels sufficient to diagnosis diabetes. Given the clinical burden that CVD problems impose on DM patients, there has been a greater emphasis on combining DM and CVD therapy. Glycaemic control remains the cornerstone of DM management [4, 5]. Although the relevance of strict glycaemic control for preventing microvascular complications and CVD in persons with Type 1 DM is well understood, its involvement in lowering cardiovascular risk in people with Type 2 DM is less evident [6]. As a result, biomarkers like haemoglobin A1c (HbA1c) may be effective in identifying those at risk of CVD and, in the long run, may help lessen the worldwide burden of CVD. There is a scarcity of data regarding association between the HbA1c levels and CVD risk among the patients with diabetes [7]. Diabetes will almost certainly be accompanied by an increase in cardiovascular disease (CVD). Several cardiovascular outcomes studies (CVOT) have been undertaken, suggesting that various anti-diabetic medications are linked to a lower risk of cardiovascular disease resulting in a good glycemic control combined with effective HBA1c monitoring could be a very effective way to reduce the risk of CVD in diabetics [8].

There are no studies from the Indian sub-continent which describe the relationship between HBA1C and CVD. As a result, we set out to investigate the link between "glycated haemoglobin A1c (HbA1c) levels and the risk of cardiovascular disease" in a rural diabetic community of India.

Materials and Methods

Study design: This a prospective observational study undertaken at a rural tertiary care setting where two patient cohorts are made, one with diabetic patients and other with non-diabetic age and gender matched individuals.

Study setting: This study is undertaken at a rural tertiary healthcare setting of Vadodara Region, Gujarat State after taking Ethical Committee Clearance from the institution (Sumandeep Vidyapeeth-Approval number: SV/19/26). The study population (Cohort A) consisted of patients with type 2 diabetes attending the Medicine and Cardiology departments from January 2019 to February 2020.

Data collection: The Cohort B included age and gender matched non-diabetic individuals who are the relatives and attending staff of the patients and the working staff of the hospital. Individuals with Chronic Heart diseases were excluded from the study. All participants were conducted questionnaire interview and health examination as a prescribed protocol. Each study participant was followed for the HBA1c levels and the cardiovascular status at the first visit, 1month, 3 months and 6 months of their first testing for HBA1c. The levels of HbA1c were measured by the immunoturbidimetric method, with a normal range of 4.5% to 5.6%, 5.7 to 6.5% as Pre-diabetes and HBA1c >6.5 are considered as People with Diabetes [9]. Each study participant's anthropometric measurements were taken, including standing height (cm), body weight (kg) and waist circumferences. An automatic sphygmomanometer was used to measure the systolic and diastolic blood pressures (SBP and DBP) at rest (Omron HEM-7120, Omron Healthcare, Kyoto, Japan). Participants had rested in a sitting position for at least five minutes prior to each assessment. If the first and second measures for either SBP or DBP differed by more than 10 mmHg, a third measurement was taken, and the average of the last two measurements was used for analysis. All of the HbA_{1c} values were recorded and further analysed. All the study participants were assessed for the cardiovascular function with the use of Cardiovascular Risk Assessment Questionnaire developed by Metagenics, Inc., California, USA [10]. This questionnaire included risk related to age (score range from 0 to 140),

cardiovascular history (score range from 0 to 250), CVD in family (score range from 0 to 45), healthy/unhealthy lifestyle (e.g. physical activity, smoking, passive smoking, alcohol abuse, and environment; score range from -35 to 150), stress and its management (score range from-19 to 330), sleep duration and its disorders (score range from 0 to 29), bowel toxicity (e.g. regularly experience lower abdominal pain, gas, bloating, diarrhea, constipation, straining when passing bowel motions, excessively smelly stools and/or a feeling that your bowels do not completely empty and taken the oral contraceptive pill and antibiotics in the last year; score range from 0 to 30), blood sugar and diabetes (score range from 0 to 110), infection and pain (score range from 0 to 60) and healthy/unhealthy nutrition (score range from -23 to 48). The higher score is associated with increased cardiovascular risk. Negative scores indicate a decreasing effect on cardiovascular risk (e.g., healthy lifestyle or nutrition). In this current study, Cronbach's alpha for total scale (internal consistency) was 0.76.

Data analysis

The data collected was entered into Microsoft Excel and stored for further analysis. Sums, averages and medians were used to describe the data. The primary outcome was a calculation of CVD prevalence rates among the T2DM patients. Individual variables had their weighted averages determined, where the simple averages and medians for patient characteristic were estimated.

Statistical analysis: The data was added to the Excel spreadsheet, which was used to run a descriptive analysis and calculate the mean and standard deviation (SD). All of the computations for the evaluation were completed using the GraphPad in Stat 3 programme (GraphPad software, Inc., California, USA). The statistical significance of the quantitative data in terms of mean distribution variations was examined using an unpaired Student's t-test. With a 95 percent confidence interval, a p value of less than 0.05 was considered statistically significant.

Results

The study comprised a total of 400 diabetic and non-diabetic patients, where the mean age was 64.2 years; Among the diabetic population, 42% were women and 77.6% had a significant family history of diabetes (Table 1).
The observed median HbA1c was 7.8% among the diabetics and 4.7% among the non-diabetics. Out of the total 400 patients with diabetes, 266 (66.5%) patients with a history of DM for more than a year had an raised "HbA1c ≥5.7%", with 54 (20.3%) of them having "HbA1c ≥6.5%". The HBA1c levels increased with the increasing age among both the study groups. Majority (92%) of the non-diabetic individuals fall under the low-risk status of CVD and most of the diabetics (57%) were observed to sustain the moderate CVD risk. (Table 2). 2 people from the diabetes group were found to have HBA1c > 10% and was associated with very high risk for CVD from the initial assessment.

Table 1: Clinico-demographic Characteristics of Study participants

Total number (800)	Diabetics (400)		Non-diabetics (400)	
HbA1C	<6.5% (Good control)	69 (17.3%)	<6.5% (Good control)	387 (96.8%)
	6.5-7.5 (Fair control)	219 (54.7%)	6.5-7.5 (Fair control)	12 (3%)
	>7.5 (Poor control)	112 (28%)	>7.5 (Poor control)	1 (0.2%)

Age (in yrs.)	<40	11 (2.8%)	12 (3%)	
	40-50	23 (5.8%%)	22 (5.5%)	
	50-60	156 (39%)	158 (39.5%)	
	60-70	177 (44.2%)	176 (44%)	
	>70	33 (8.2%)	32 (8%)	
Gender	Male (n=232; 58%)	Female (n=168; 42%)	Male (n=232; 58%)	Female (n=168; 42%)
Family History	Yes (n=310; 77.6%)	No (n=90; 22.4%)		

Table 2: Cardiovascular risk stratification among the study participants

Cardiovascular risk	Diabetics	Non-diabetics (n=400)
Low risk	152 (38%)	368 (92%)
Moderate risk	228 (57%)	30 (7.5%)
High risk	16 (4%)	2 (0.25%)
Very high risk	4 (1%)	None

Discussion

HbA1c levels of 6.5 percent or higher in diabetics were linked to an elevated risk of cardiovascular disease, which was in accordance with previous studies like Nichols *et al*. and Nishimura R *et al*. [11, 12]. Low HbA1c levels and non-diabetic individuals were observed to have low CVD risk. CVD is accountable for at least half of the mortality in people with T2DM, as previously stated by numerous studies. The most lethal disease within that term was coronary artery disease, followed by stroke. Straka *et al*. [13] followed 29,863 patients (5501 with T2DM and 24,362 without T2DM) over the course of a year and found similar results. They found that patients with T2DM had significantly increased rates of four of the six incident cardiovascular events. T2DM patients had a 10% higher risk of coronary artery disease, a 53% higher risk of MI, a 58% higher risk of stroke and a 112 percent higher risk of heart failure. As a result, T2DM is a significant risk factor for CVD and its complications. According to Sinning *et al*., the strongest link between HbA1c and cardiovascular risk was found among people over the age of 55, which is a similar finding brought out by our study [14, 15] Increased glucose levels and haemoglobin glycosylation are likely to affect RBC properties, reducing RBC flexibility and increasing their tendency to aggregate, resulting in increased blood viscosity [16]. Glycosylation of haemoglobin may also affect RBC membrane lipid protein interactions, increasing internal viscosity, altering the viscoelastic properties of erythrocyte membranes and lowering RBC deformability [17]. The increased blood viscosity could be one possible biological pathological mechanism by which fibrinogen and haematocrit increases promoting cardiovascular risk [18]. There's also additional evidence that glycosylation of haemoglobin reduces the relaxation of human mesenteric arteries caused by nitric oxide (NO) [19]. In rabbit aortic rings, haemoglobin glycosylation has been shown to affect NO binding with thiols, leading in reduced NO bioavailability and decreased vasodilation [20]. The production of reactive oxygen species is another way through which glycosylation of haemoglobin is thought to be vasoactive. Hypoxia and its associated systemic vascular vasodilatory adaptations and responses are aided by glycosylation of haemoglobin, which reduces its oxygen-carrying capacity [21, 22].

The limitations of this study include, because we only received data from adults 18 and older,

the findings of this study are limited to a specific patient population. As a result, our findings may not be applicable to children or teenagers. Furthermore, because this study only looked at T2DM, the results may not apply to T1DM or secondary diabetes, such as that caused by hemochromatosis or pancreatitis.

Conclusion

Among the people with known diabetes, high HbA1c levels were linked to a greater risk of CVD. As a result, HbA1c may be a valid predictor of cardiovascular mortality and morbidity in diabetics. The data of our study suggest that the healthcare professionals must appraise the values of HbA1c in assessing the cardiovascular risks and outcomes in the diabetes patients.

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