ROLE OF HBA1C AND HS-CRP IN TYPE 2 DIABETES MELLITUS WITH CARDIOVASCULAR DISEASES

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ABSTRACT

BACKGROUND

Important perspective studies on chronic complications of Diabetes Mellitus made it possible to establish with absolute certainty the role of glycated haemoglobin (HbA1c) as a marker of evaluation of long term glycemic control in diabetic patients and the strict relationship between the risk of chronic complications and HbA1c levels.

OBJECTIVE

This study was undertaken to assess the role of HbA1c in type 2 Diabetes Mellitus with cardiovascular disorders.

MATERIAL AND METHOD

This study was carried out in Department of Biochemistry, Katihar Medical College and Hospital, Bihar. Diabetic and non-diabetic subjects were selected from patients attending outdoor, indoor and ICU of Medicine Department and were investigated for HbA1c and hs-CRP.

RESULTS

The HbA1c was in normal range in non-diabetic subjects and significantly raised in diabetic patients. Among patients with cardiovascular complications, the HbA1c and hs-CRP were significantly raised indicating their positive correlation.

CONCLUSION

The lifestyle changes can dramatically reduce the incidence of diabetes and show the HbA1c and hs-CRP increase in both diabetic and non-diabetic individuals. Regardless of whether lifestyle changes are ultimately proven to reduce cardiovascular in our society, public health approaches to facilitate them urgently need to be implemented.

KEYWORDS

Diabetes Mellitus, hsCRP, HbA1c, Cardiovascular Disorders.

INTRODUCTION

Diabetes, description of which first appears 3000 years ago in the inscriptions of the Papyrus of Ebers in Egypt, is a metabolic disorder with inappropriate hyperglycemia either due to an absolute or relative deficiency of insulin secretion or reduction in the biologic effectiveness of insulin or both. The decreased uptake of glucose into muscle and adipose tissue leads to chronic extracellular hyperglycemia, which results in tissue damage and chronic vascular complications in both type 1 and 2 Diabetes Mellitus.[1] Previously, it was regarded as a relatively distinct disease entity, but in reality type 2 diabetes is often a much broader underlying disorders.[2,3]

This includes the metabolic syndrome (Sometimes called

syndrome X) a cluster of Cardiovascular Disease (CVD) risk factors that in addition to Impaired Glucose Tolerance (IGT) or diabetes includes hyperinsulinemia, dyslipidemia, hypertension, visceral obesity hypercoagulability and microalbuminuria.

The level of glycated hemoglobins in the blood is directly related to the average blood glucose levels over the lifespan of the haemoglobin in the circulation. Since the half life of red blood cells is about 120 days, a single determination of glycated haemoglobin reflects the average blood glucose level during the preceding 8 to 12 weeks.

The test is therefore a very good monitor for long-term (2 to 3 months) blood glucose control in patients with diabetes mellitus predicts risks for the developments and progression of diabetic complications. Tests of glycated haemoglobin are also inexpensive and can be done at any time of day. Moreover, randomized trials have clearly shown that decreasing the glycated hemoglobin level reduces these risks.[4,5] Elevated glycohemoglobin HbA1c is an established predictor for developing atherosclerosis beyond the risk associated with diagnosed diabetes.[6]

Epidemiological studies indicate that diabetes mellitus can accelerate atherosclerotic processes and increase the

incidence of cardiovascular events and strokes.[7] It has been demonstrated that inflammation plays an important role in atherosclerosis.[8] and in the pathogenetic mechanisms of some cardiovascular events.[9]

C-reactive protein was invented by Tillet and Francis in 1930 as a substance in the serum of patients with acute inflammation that reacted with the C-polysaccharide of Pneumococcus.[10] CRP is a plasma protein, an acute phase protein produced by the liver and by adipocytes.[11]

High concentrations of CRP mRNA have been demonstrated to be present in atherosclerotic plaques.[12] Two research groups revealed independently that CRP is produced by human artery smooth muscle cells of atherosclerotic lesions in response to inflammatory cytokines.[13,14] Taking all this evidence into account, locally produced CRP may actually participate directly in aspects of atherogenesis, promoting the development of cardiovascular complications.

Measurement of hs-CRP should be done twice, optimally 2 weeks apart, to provide a more stable estimate of level of this marker.

Changes in human behaviour and lifestyle over the last century have resulted in a dramatic increase in the incidence of diabetes worldwide. The diabetes epidemic relates particularly to type 2 diabetes and is taking place both in developed and developing nations.[2]

With this background of knowledge, we aim to study the role of HbA1c in type 2 diabetes and its cardiovascular complications.

MATERIALS AND METHODS

The present study was undertaken in the Department of Biochemistry, Katihar Medical College and Hospital [KMCH], Bihar. The study was started in December 2009 and completed in May 2011. The subjects for the study group were selected from patients attending the outdoor, indoor and ICU of Medicine Department of KMCH. The subjects for the control group were selected from healthy persons accompanying patients from the same region. All subjects were informed about the risks and benefits of the study. Written consents were taken before blood was drawn. The study was approved by the Institute Ethics Committee.

In the present study, 70 cases of diabetes type 2 with or without complications were selected from different age groups. The diagnosis of diabetes mellitus was made on the basis of history, physical examination and blood glucose levels. The patients with complications were selected on the basis of clinical findings. The patients with cardiovascular complications were tested for hs-CRP. All subjects were tested for HbA1c. The same number of healthy subjects (70 in number) was also tested for the above parameters. Blood was drawn with aseptic precautions from the antecubital vein after over-night fasting. Separate aliquots were prepared for estimation of blood glucose, HbA1c and hs-CRP using serum as the sample.

Quantitative determination of glucose in serum/plasma
Method- Glucose oxidase and peroxidase
Reference range-
Fasting: 70-110mg/dl
Postprandial: upto 140mg/dl
Determination of glycated haemoglobin (HbA1c)
Method – Ion exchange resin
Reference guidelines

Degree of glucose control, Total GHb, HbA1c
Normal (non-diabetic), <7% <6%
Near normo-glycemic, 7% to 8%, 6% to 7%
DCCT therapeutic goal, less than 7%
In good control, 8% to 9%, 7% to 8%
Actions suggested, 9% to 11%, 8% to 9%
Not in control, >11%, >9%
Estimation of High Sensitive C-Reactive Protien (hs-CRP)
Method : Sandwich ELISA
Reference Range :
<1mg/l = Low risk of CHD.
1-3mg/l = Intermediate risk of CHD.
>3mg/l = High risk of CHD.

DISCUSSION AND RESULT

The present study was carried out among 70 (n=70) cases of known diabetes mellitus, selected from different age group. Seventy cases of non-diabetic healthy individuals were selected as the control group. In the selection control group, (Healthy individuals) care had been taken to match the age with that of the test group (Diabetic patients). The diagnosis of diabetes mellitus was made on the basis of history, physical examination and the laboratory investigations. A fasting blood glucose level of ≥126mg/dl and/or a post-prandial glucose level of ≥200mg/dl were taken as the criteria to diagnose diabetes mellitus.

In the present study, it is depicted that (Table:1) diabetes mellitus affects both males and females with incidence among male is more (64.29%) than females (35.2%). This finding in present study is in accordance with a WHO report, which states that "In South–East Asia, an excess of male diabetics have been observed."[15]

The present study shows that the level of HbA1c was significantly raised among the diabetic patient (65.71%), patients had an HbA1c values of =7%, 24% of had HbA1c values of <7% when compared with their non–diabetic counter parts (Table: 2). The observations made by different workers using different sample sizes at different places in various previous studies are in agreement with the present study. Rabhar S. and his colleagues.[16] surveyed 1200 patients in Tehran and detected an abnormal band in two persons. On further inquiries, both of these individuals proved to be diabetic. Trivelli et al. (1971) showed a two-fold increase of HbA1c in diabetics over values found in healthy individuals.[17] Stratton IM et al. 2000: Jesudason DR et al. 2003: made the observation that "HbA1c is highly specific for identifying Diabetics in an ambulatory or in–patient setting."[18,19] Lanoe et al. (1972); Gonen et al. (1977); Graf et al. (1978); Ekkeles et al. (1978); Raheja et al. (1980); Shrivastava et al. (1984); Rohlfing CL, et al. (2002) and Nathan DM, et al. (2007) gave similar observations.[20,21,22,23,24,25,26,27]

The present study shows that the levels of HbA1c was significantly raised among diabetic patient (7.224±o.8940) when compared with their control. (Table 3).

In this study, the mean value of HbA1c±SEM among the cardiovascular was found to be 17.671±3.969, while the level in non-cardiovascular disorder was 17.314±6.371 (Table 4). When the means were compared and the P value was determined by using student 't' test it was found significant at the level of p<0.692.

This evidence provided up to this point clearly indicates that the level of HbA1c increases among the untreated diabetics with cardiovascular disorders.

India has the distinction of having the highest number of T2D individuals worldwide with a prevalence of 11.6% in urban populations.[28,29] Furthermore, Asian Indians are known to be at a high risk for T2D, CVD and metabolic syndrome.[30,31]

Hyperglycemia is known to stimulate the release of inflammatory cytokines from various cell types and can lead to the induction and secretion of acute-phase reactants by adipocytes. Inflammation has been the central orchestrator of atherosclerotic lesion formation, progression and eventual rupture and low-grade inflammation has been recognized as an important feature of cardiovascular disease. Therefore, markers of inflammation have been investigated for risk assessment of cardiovascular events. It is perceived that chronic low-grade inflammation as evidenced by elevated High Sensivity C-Reactive Protein (hsCRP) might potentially be a cause underlying the etiology and manifestation of type 2 diabetes (T2D), although the exact mechanisms are still not well understood.[32,33] Additionally, hsCRP has also emerged as a powerful predictor of Cardiovascular Disease (CVD).[34] However, hsCRP levels are known to vary among populations influenced by gender, age and obesity.[35]

The Table 5 displays the comparison of mean level of hs-CRP between cases suffering from diabetes mellitus and the control group. The level of hs-CRP was found to be significantly higher (P-value=0.000) in the cases suffering from diabetes mellitus (4.061±0.0876) than the controls (1.564±0.1242).

Both enhanced inflammation and hyperglycemia contribute to the development of atherosclerosis are found in patients with clinically advanced disease. Given the interrelation between inflammation, hyperglycemia, atherosclerosis may be speculated that HbA1c contribute to the cardiovascular risk.

CONCLUSION AND RECOMMENDATION

In present study, HbA1c was in normal range among the normal subjects and was significantly raised in diabetic patients as compared to their normal control. It was observed that among the patients with cardiovascular complications, the HbA1c was significantly increased indicating the positive correlation between cardiovascular complications.

As we know that lifestyle changes can dramatically reduce the incidence of diabetes and slow the HbA1c increase in both non–diabetic and diabetic individuals. Structural changes to our society that reduce caloric intake and increase physical activities today will lower HbA1c levels and reduce the societal rate of diabetes, consequences of diabetes tomorrow.

	Control Group	Cases of DM (%)
Male	40(57.1)	45(64.2)
Female	30(42.8)	25(35.2)
Total	70(100)	70(100)
Table 1: Distribution of Subjects according to Gender		

The present study constitutes a small number of sample for a very limited period of time, still have good results. Further study for a longer period and larger number of samples should be done.

	Cases of Diabetes Mellitus	Percentage
Hb1AC more than and equal 7%	46	65.7
Hb1AC less than 7%	24	34.2
Total	70	100
Table 2: Distribution of Cases of Diabetes Mellitus with HbA1C Level More Than Equal 7% and Less 7%		

	Comparison of Hb1AC Level (Mean±SD)	P value
Control	5.0086 ± 1.021	0.000
Cases of Diabetes Mellitus	7.2243 ± 0.894	
Table 3: Comparison of Means of HbA1C between the Cases Suffering from Diabetes Mellitus and Control Group		

	Comparison of HbA1C Level in Percentage (Mean±SD)	P value
With Cardiovascular disorder	17.671 ± 3.969	0.692
Without Cardiovascular disorder	17.314 ± 6.371	
Table 4: Comparison of Means of HbA1C among the Diabetic Patients between cases With or Without Cardiovascular Disorders		

	Comparison of hs-CRP Level (mg/L)
Diabetic	4.061 ± 0.733
Control	1.564 ± 1.039
P value	0.000
Table 5: Comparison of Means of hs-CRP between the Cases Suffering from Diabetes Mellitus and the Control Group	

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