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Prediction of Cardiac Risk Factors and Cardiac Events by HbAlc in Diabetes Mellitus.

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Abstract: The present study has been undertaken to compare the effect of HbAlc level (glycosylated haemoglobin) on the patients suffering from coronary artery disease (CAD) with and without diabetes. For the present study two hundred patients were selected who were admitted in hospitals with history of acute cardiac states (unstable angina diabetes, acute myocardial infarction, heart failure, cardiomyopathy). Patients were divided on the basis of diabetic mellitus into two groups - Group A (diabetics) and Group B (non diabetics). Patients were followed up for six month. Out of the 200 patients, 72 were diabetic (group A) whereas 128 were non- diabetic (group B). The mean value of HbAlc in group A was 8.6 ± 1.7% while in group B was 5.5 ± 0.4%. Risk factors like dyslipidemia, hypertension, previous history of heart disease and stable CAD like triple vessel disease were found more in group A than in group B. History of smoking, positive family history of heart disease, and angina as a presenting symptom were more in group B. Complications like heart failure and post infarction angina occurred significantly higher in patients with diabetes. In group A, unstable angina, ST elevation myocardial infarction, cardiac failure, accelerated hypertension, dilated cardiomyopathy and triple vessel disease were significantly higher in proportion of patients with poor glycemic control (HbA 1c ≥7%) compared to patients with HbA1c level < 7%. In group B, 92/128 (71.8%) patients had HbA1c levels ≥5.8%. Severity and complications of heart disease were significantly higher in diabetics and showed a significant correlation with HbA1c. A large number of non diabetics patients (71.8%) with acute cardiac states, had HbA1c values ≥5.8%.

Keywords: Coronary artery disease, Unstable angina, Acute myocardial infarction, Glycosylated haemoglobin , Diabetes mellitus Type II, Hyperglycaemia.

Introduction

Diabetes is a cardiometabolic disease with both microvascular and macrovascular complications. Macrovascular complications begin taking place long before the patient has overt diabetes (Halffner *et al*., 1990). Hyperglycemia is an independent risk factor for cardiovascular disease (Laakso, 1999). Hyperglycemia accelerates the process of atherosclerosis by the formation of glycated proteins and advanced glycation end products, which act by increasing the endothelial dysfunction (Brownlee, 1988). HbA1c could be considered a good marker of glycated proteins and its assay has been used as a measure of glycemic control in several landmark trials. The Framingham study has shown that the cardiovascular mortality is twice in diabetic men and four times in diabetic women when compared to their non-diabetic counterparts (Garcia *et al*., 1974). HbAlc levels of more than 7% are associated with a significant increase in the risk of cardiac events and deaths (Haffner *et al*., 1998). Interestingly, this correlation between higher HbAlc levels and increased cardiovascular morbidity occurs even before the diagnosis of clinical diabetes (Gerstein, 2004).

The present study was undertaken to find out the correlation between HbAlc levels and the severity of heart disease and complications in patients with history of admission for cardiac disease and acute cardiac states.

Material and Methods

This study was a retrospective analysis of follow up over a period of six months of patients admitted for acute cardiac state. All patients admitted with acute cardiac states were included in the study. Acute cardiac states included unstable angina (UA), acute myocardial infarction (AMI) both ST elevation myocardial infarction (STEMI) and non ST elevation myocardial infarction (NSTEMI), and heart failure (HF).

The patients were divided into group A (diabetics) and group B (non-diabetics). In patients without prior history of diabetes, a diagnosis of diabetes was made, if they had fasting blood sugar (FBS) ?140 mg/dl or random blood sugar (RBS) ≥200 mg/dl on two or more determinations along with an HbAlc of 7% or more. Those patients who required diet control or insulin while in the hospital for control of blood sugar values were also included in the diabetic group even when the HbA1c was < 7%. Patients with sepsis, aemoglobinopathy, anaemia, liver disorder, kidney disorder and hypothyroidism were excluded from the study. Those patients where HbAlc could not be obtained were also excluded from the study.

After a detailed review of history, Electrocardiogram (ECG) old clinical records, old investigation including HbAlc, lipid profile, cardiac enzymes, ECG and Echocardiogram were analysed in all patients. Coronary angiography findings were noted in all those who underwent the same, physical examination and investigation were repeated as required. Treatment was given as per standard protocol and guidelines of American College of Cardiology (Braunwald, 2000). The patients were followed up for six month events, complications like arrhythmias, cardiac failure, and cardiogenic shock were noted.

Statistical analyses were carried out using a computer based statistical analysis programme, SPSS (Statistical Program for Social Sciences) version 11.5. The Chi-square test (with correction wherever values in the cells were less than five) was used wherever comparisons were needed between the two groups, or between two categories in the same group. A p value < 0.05 was considered significant.

Results

Two hundred patients admitted with acute cardiac states were included in this study. There were 72 patients with diabetes (group A) and 128 patients without diabetes (group B).

The mean age of group A was 58.3 ± 12.0 years and that of group B was 60.4 ± 10.3 years. In group A, 40 (55.95%) cases developed the cardiac event within three years of diagnosis of diabetes. Interestingly, 32 patients were detected to have diabetes for the first time when they presented with an acute cardiac state.

Table 1 : Comparison of clinical profile of patients in group A and group B

Parameters	Group A		Group B		P value
	Number	%	Number	%	
Total number	72		128		
Mean age	58.3 ± 12.0		60.4 ± 10.3		0.48
Mean HbAlc	8.6 ± 1.7		5.5 ± 0.4		
Smoking	09	12.5	46	35.93	< 0.001
Hypertension	42	58.33	40	31.25	0.016
Previous myocardial infarction	36	50.0	32	25.0	0.001
Family history of heart disease	10	13.88	52	40.65	0.026
Angina	10	13.88	56	47.95	< 0.001
Orthopnoea	30	41.66	24	18.75	< 0.001
Pedal Oedema	27	37.5	18	14.06	<0.001
Triglyceridcs > 150mg/dl	30	41.66	24	18.75	0.004
HDL < 45mg/dl	34	47.22	28	28.87	0.018
Cardiomegaly	27	37.5	17	13.28	0.005
Triple vessel disease	32	44.44	10	7.81	0.004
Death	07	9.72	08	6.25	0.22

Table 2: Distribution of HbAlc in group A and group B

HbAlc	Group A (n=72)		HbA1c	Group B (n=128)	
(%)	No.	%	(%)	No.	%
<7	22	30.55	<5	42	32.81
7 - 9	22	30.15	5 - 5.5	64	50
9 -11	17	23.61	5.6 - 6	20	15.6
>11	11	15.27	>6	2	1.56

The risk factors, presenting symptoms, x-ray findings, echocardiography findings and complications in both the groups are presented in Table 1. Among the symptoms, angina was present in a significantly higher number of patients in group B, whereas orthopnoea and pedal oedema were found more in group A. Risk factors like hypertension and previous history of coronary artery disease (CAD) were more in group A, but smoking and positive family history of CAD were seen more in group B. Cardiomegaly was significantly more in group A than in group B.

The distribution of HbA1c in groups A and B is presented in Table 2. The mean HbAlc of group A was 8.6 ±1.7% and that of group B was 5.5 ± 0.4%.

Discussion

Diabetics develop CAD earlier, and have more extensive atherosclerosis (Goraya, 2002). Heart disease in patients with Diabetes Mellitus (DM) is different from that in non-diabetics. Several previous studies have shown that the prevalence of CAD is higher in patients with diabetes (Haffner, 1998 & Mohan *et al*., 2001). The present study results show significant differences in the risk factors, clinical presentation and complications of cardiovascular diseases between diabetics and non diabetics (Table 1). A significantly higher proportion of diabetics had additional cardiovascular risk factors like hypertension (58.33% vs 31.25%), hypertriglyceridemia (41.66% vs 18.75%), low HDL levels (47.22% vs 21.87%) and previous history of coronary artery disease (50% vs 25%) when compared with non-diabetics. Prospective studies done earlier indicate that all these cardiovascular risk factors continue to act as independent predictors of cardiovascular disease in patients with diabetes (Brezinka & Padmos, 1994).

Thirty two patients in this study were detected to have diabetes for the first time when they presented with an acute cardiac event. Majority of these patients (26/32, 81.25%) had HbA1c levels 7% indicating that these patients had pre-existing undiagnosed diabetes. Recent recommendations by ADA has included HbAlc ?6.5% as one of the criteria for diagnosis of Diabetes. In the rest hyperglycemia could represent stress hyperglycemia which is a common occurrence in patients admitted to the intensive care units with acute coronary syndromes. Stress hyperglycemia is defined as a transient elevation of blood glucose due to the stress of the illness. There is no consensus regarding the cut off value to define stress hyperglycemia as various studies have used different values ranging from an admission RBS 126mg/dl to 200 mg/dl. The blood sugar levels in stress hyperglycemia are usually between 140mg/dl to 300mg/dl. The blood sugar value was above 140mg/dl in some non-diabetic patient. Although an elevated HbAlc measured when hyperglycemia is first noted can be suggestive of hyperglycemia prior to hospitalization, a normal HbAlc concentration does not rule out the diagnosis of diabetes. Such patients need follow up to evaluate their diabetic status. Hyperglycemia in patients with Acute Myocardial Infarction (AMI) enhances the risk of mortality and morbidity whether or not patient has a prior diagnosis of diabetes. Stress hyperglycemia even in non-diabetics, is associated with many abnormalities usually seen in diabetics, like increased oxidative stress, inflammation and activation of stress responsive kinases (Keith, 2008) In fact earlier studies have shown even higher cardiovascular mortality and morbidity in patients with hyperglycemia in previously undiagnosed diabetes than in patients with known diabetes or normoglycemic subjects (Umpreizz, 2002)

Another important observation made in this study is a highly significant correlation between poorly controlled diabetes as indicated by HbAlc ?7% and the acute cardiac states.

It is well known that the macrovascular complications start taking place at lower blood sugar levels than the diagnostic cut off values for diabetics. Khaw *et al.,* (2004)found a continuous and significant relationship between HbAlc, cardiovascular events and all cause mortality, whereby persons with HbAlc< 5% had lowest rates of cardiovascular disease and mortality. They found a one-percentage increase in the HbAlc to be associated with a relative risk of death of 1.24 in men and 1.28 in women (Khaw *et al*., 2004). Selvin *et al*., (2004) suggested no risk of CAD in patients with HbAlc<4.6%. However, he further stated that for every 1 % increase in HbAlc over 4.6%, there was a 2.5 times risk of cardiovascular disease. The present study concludes significant differences in the clinical presentation, severity of disease and complications of cardiovascular disease between diabetics and non-diabetics. This study stresses the need for early diagnosis of diabetes, maintaining a tight glycemic control and screening for CAD in diabetes at much lower levels and early stage.

References

Braunwald E., Antman E., Beasley J.W. (2000): ACC AHA guidelines for the management of patients with unstable angina and Non-ST segment elevation myocardial infarction. A report of the American College of Cardiology / American Heart Association Task Force in Practice Guidelines (Committee on the management of Patients with Unstable Angina. J Am Coll. Cardiol; **36**,970-1062.

Brezinka V, Padmos I.(1994): Coronary heart disease risk factors in women. Eu Heart J;**15,**1571-84.

Brownlee M. (1988): Advanced glycosylation in diabetes and aging. Am Rev Med;**46,**223-4.

Garcia M.J, McNamara P.M., Gordon T., Kannel W.B. (1974): Morbidity and mortality in diabetes in the Framingham population. *Diabetes*;**23**,l05-116.

Gerstein H.C. (2004): Glycosylated Hemoglobin. Finally ready for prime time as a cardiovascular risk factor. *Ann Intern Med*;**141**,475-6.

Goraya T.Y., Leibson Cl., Palumbo P.S. (2002): Coronary atherosclerosis in diabetes mellitus. A population based study *J Am Coll Cardiol*;**40**, 946-53.

Haffner S.M., Lehtos, Ronnemaa T., Pyorala k. Laakso M. (1998): Mortality from coronary heart disease in subjects with type-II diabetes and in non diabetic subjects with an without prior myocardial infarction. *N Eng J Med*;**339**,229-34.

Halffner S.M., Stern M.P., Hazuda H.P. (1990):

Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes. *JAMA*;**263**,2893-8.

Keith A. (2008): Stress hyperglycemia and enhanced sensitivity to myocardial infarction. Current Hypertension reports; *Website*; **10**,78-84.

Khaw K.T., Wareham N., Bingham S. (2004): Association of haemoglobin Alc with cardiovascular diseases and mortality in adult: The European Prospective Investigation into cancer in Norfolk. *Ann Intern Med*; **141**,413-20.

Laakso M. (1999): Dyslipidemia, morbidity and mortality in non-insulin dependent diabetes mellitus: lipoprotein and coronary heart disease in Non-insulin Dependent Diabetes Mellitus. *J Diabetes Complication*;**11**,137-41.

Mohan V., Shanthirani C.S., Deepa R. (2001): Urban difference in the prevalence of the metabolic syndrome in Southern India. The Chennai urban Population Study (No-4) *Diabet Med*; **18**,280-7

Selvin E., Marinopoulos S. Berkenblit G. (2004): Meta-analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med*;**141**,421-31

Umpreizz G.E., Isaac S.D., Bazargan N. (2002): Hyperglycemia : An independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Endocrinology Metab*,**87**,978-982.