



GLYCOSLATED HAEMOGLOBIN AS A DIAGNOSTIC MARKER OF DIABETES MELLITUS IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

AIMS: This study was planned to assess the role of glycosylated hemoglobin as a diagnostic marker to diagnose and treat diabetes at earliest. It is meant to improve the prognosis in patients of acute myocardial infarction. As observed even in non diabetic patients of Acute Myocardial infarction admitted with hyperglycemic status. **METHODS:** This is hospital based cross-sectional study. 100 patients with acute myocardial infarction admitted to coronary care units, during October 2013 to September 2014 were studied. Patients during admission blood glucose $>140\text{mg/dl}$ with no past history of diabetes mellitus were included in the study. Serum blood glucose and HbA1c were estimated at admission. History and examination carried out. These patients were followed up after 15 days to assess their blood glucose. Their diabetic status was confirmed as per WHO criteria. Data were analyzed using SPSS-20 software. **RESULT:** Out of 100 patients, 84 patients had value of HbA1c in the diabetic range ($\geq 6.5\%$) and 16 patients had HbA1c in the non diabetic range ($< 6.5\%$). On follow up, out of 84 patients, 75 patients (89.28%) were confirmed to be diabetic according to the WHO criteria. Statistically study found highly significant ($p < 0.0001$). **CONCLUSIONS:** HbA1c estimation is useful tool and accurate interpretation of hyperglycemia following AMI. HbA1c estimation at the time of admission clearly differentiates stress induced hyperglycemia from hyperglycemia of undiagnosed diabetes mellitus. HbA1c is a more sensitive and specific diagnostic marker than blood glucose for diabetes mellitus in patients with MI.

Keywords: glycosylated haemoglobin, diabetes mellitus, myocardial infarction, hyperglycemia.

INTRODUCTION

Diabetes mellitus is a disease of antiquity known to mankind since past 3500 years. Ancient Indian scholar's *charak* and *sushruta* knew about it. Urine in diabetics was described as madhumeha. Now diabetes mellitus becomes the most common non communicable, life style associated disease worldwide. India and china are converting in to hub of diabetes [1]. Most dreadful part is large number of patients remains unrecognized.

It is of great concern because of the devastating effect of its complications. Diabetes mellitus has been recognized as a risk factor for coronary heart disease since ages [2]. Hyperglycemia is associated with large infarct size [3]. Mortality due to coronary heart disease is very high in diabetics [4]. Hence early diagnosis and control of diabetes mellitus is important. It is to improve the prognosis of patients with AMI and to prevent the adverse outcome. At the time of admission most of the patients of AMI have hyperglycemia, are associated with

increased risk of morbidity and mortality [5]. This hyperglycemia could simply be a marker of preexisting, not yet diagnosed diabetes, impaired glucose tolerance or may be stress induced hyperglycemia. Blood glucose estimation alone is insufficient, unreliable tool and oral glucose tolerance test is impractical.

This differentiation is important because any attempt to lower stress induced hyperglycemia may cause hypoglycemia leading to tachycardia and cause deleterious effects [6]. HbA1c estimation provides an average blood glucose level for a period of 8-12 weeks [7]. HbA1c proves useful for diagnosis of D.M. in AMI. Stress induced hyperglycemia is a confounding factor. HbA1c is unlikely to rise with stress induced acute hyperglycemia [8]. HbA1c concentration can be used to distinguish stress induced hyperglycemia from diabetes mellitus for early appropriate treatment to prevent morbidity and mortality.

MATERIALS AND METHODS

This study is carried out in Government NSCB Medical College, Jabalpur. Department of Pathology and ICCU. 100 M.I. patients admitted in ICCU during October 2013 to September 2014 fulfilling the inclusion criteria.

Inclusion criteria

1. Patients diagnosed AMI confirmed by electrocardiogram or cardiac marker (CPK-MB).
2. Patients not known or diagnosed as diabetic.
3. Patients whose admission glucose level found >140mg/dl

Exclusion criteria

1. Patients died of AMI and its complications during hospital stay.
2. Patients unavailable for follow up after 15 days.

Venous blood was taken at the time of admission for estimation of blood sugar and HbA1c before starting treatment. These patients were further followed up after 15 days. Their fasting blood sugar was estimated. Patients with HbA1c $\geq 6.5\%$ as cut off were analyzed for diabetes as per WHO criteria.⁹The majority of studies conducted included HbA1c $\geq 6.5\%$ as cut off for diabetic diagnosis as per American Diabetic Association and WHO. Patients with HbA1c $< 6.5\%$ were considered non diabetics and patients with $\geq 6.5\%$ were considered as diabetics.

Specimen collection and preparation

We need preferentially venous blood using EDTA anticoagulant. Reagents should be at room temperature. Dilute the sample with lysing reagent in the 1:100 ratios. Wait for minimum 3 minutes; take care to avoid the formation of foam. Erythrocytes are lysed by low osmotic pressure. Greenish-brown color develops as per the hemoglobin concentration of sample. HbA1c is determined immunoturbidometrically. The final result is expressed as percent HbA1c.

Method and Test principle

Test is based on immunoturbidometry performed by auto analyzer. It is based on interaction between antigen molecule (HbA1c) and HbA1c specific monoclonal antibodies coated on latex bead. This cross link reaction results in change in the solution turbidity. HbA1c was estimated by auto analyser Biosystem S.A. COD 22044, serum total cholesterol and HDL COD 21557, serum triglyceride and LDL COD 21528, CK-MB by Randox, RX CK3813.

Spurious result:

False high: Iron deficiency anemia, post splenectomy, drugs (aspirin, corticosteroid), high temperature, pH

False low: haemolytic conditions, chronic blood loss, blood transfusion, sickle cell anemia, chronic renal failure.

Advantages

HbA1c is stable after collection of sample. Their levels do not fall on storage prior to test. Sample can be obtained at any time. It requires no patient's preparation. Their levels do not vary between meals like blood sugar.

Statistical test applied

Statistical analyses were carried out by using SPSS 20 software. The results obtained are statistically analyzed. Sensitivity of the test was 98.6, specificity was 62.5, and positive predictive value 89.28, negative predictive value was 93.75. The results were considered significant with $p < 0.05$.

RESULTS AND DISCUSSION

Out of 100 patients, 84 patients had value of HbA1c in the diabetic range ($\geq 6.5\%$), Rest 16 patients had HbA1c ($< 6.5\%$) in non diabetic range. During follow up after 15 days, out of 84 patients, 75 patients (89.28%) were confirmed to be diabetic previously unrecognized cases of diabetes mellitus, come to light after HbA1c estimation. And only 9 patients (10.72%) were found to be non diabetic according to WHO criteria. Statistically this was highly significant ($p < 0.0001$). Rest 16 patients who were in stress induced hyperglycemia possibility to be considered as diabetic, HbA1c values prevented them to be treated for diabetes. Time also saved in preventing repeated testing of blood sugar. Time is critical in AMI patients which affect prognosis.

In present study male subjects were predominantly higher. Male to female ratio in diabetic is higher (4.5:1) as compared to ratio in non diabetics, which is comparable with studies done by Iqbal MJ et al [10].

Both rural and urban area in India are currently experiencing a great increase in lifestyle oriented diseases. Urban population have more number of diabetic patients but rural population is also at risk for development of diabetes mellitus. In this study number of diabetic patients are more (58.33%) in urban area as compared to rural area (41.67%) which was consistent with study of Baizayanti Baur [1], Dr. V.Mohan [12].

Diet rich in fiber and complex carbohydrate and restricted in fat improve control of blood glucose concentration and aid in good control of diabetes. In present study diabetes mellitus was found more amongst non vegetarians (94.1%) compared to vegetarian (78.8%), which was consistent with studies of Nizar Issa Alrabadi et al [13] and Shishir Nigam [14].

In AMI patients presenting complaints at the time of admission like chest pain, palpitation, and sweating was found more in diabetic subjects as compared to non diabetic, which was statistically significant.

In the present study modifiable risk factors like Smoking was found more common in diabetic patients (96.4%) than non diabetic patients (37.5%) which is in concurrence with the observation made by Iqbal MJ et al¹⁰

Habit of tobacco and alcohol intake was associated with increased incidence of diabetes which was consistent with study done by W.H. Linda [15]. In present study there was found significant association between diabetes and tobacco consumption ($\chi^2=3.97$, $p<0.05$) as well as alcohol consumption ($\chi^2=4.90$, $p<0.05$)

Obesity was seen in 30.9% of diabetic patients and 6.2% of non diabetic patients which is consistent with the findings of Iqbal M J et al¹⁰. Obesity and diabetes have several abnormalities in common like abnormal Carbohydrate metabolism, increased insulin resistance, high free fatty acid levels and high incidence of Hypertension. Increased level of cardiac enzyme parallel with severity of damage in M.I. which was consistent with that of study done by V. Peppel¹⁶ in present study also majority of cases (55%) was found to be associated with

increased level of cardiac enzyme (CK-MB) and majority of them was found to be in diabetic range. Statistically this was found to be significant ($\chi^2=6.93$, $p<0.05$)

In present study Dyslipidemia was found higher in diabetic subjects as compared to non diabetics, which was consistent with study of Ram Vinod Mahato [17].

The involvement of anterior wall was more M.I. patients supplied by left anterior descending branch of aorta. In present study also involvement of anterior wall was found in more than 50% cases. But this was not statistically significant.

In the present study mean age for diabetic patients was 58.76 years and mean age for non diabetic patients was 53.46 years. Diabetic patients were susceptible to AMI at an older age compared to non diabetics which was consistent with study of M.Sue.Kirkman [18].

Table 1: Association between HbA1c value and age, sex, dietary habit and habitat

Characteristics		HbA1c Value		χ^2 value	P value	95%confidence interval	
		<6.5%	>6.5%				
Age	<40years	3	1	10	<0	-	.
	>40years	13	83				
Sex	Male	8	68	7.	<0	-	-
	Female	8	16				
Habitat	Rural	11	35	3.	<0	.0	.
	Urban	5	49				
Dietary habit	Non veg.	2	32	3.	<0	-	-
	Veg.	14	52				

Table 2: Association between HbA1c, presenting complaints and family history of IHD

Characteristics		HbA1c Value		χ^2 value	P value	95%confidence interval	
		<6.5%	>6.5%				
Chest pain	Present	10	74	6.55	<0.05	-.503070	-.008834
	Absent	6	10				
Palpitation	Present	7	74	17.1	<0.0001	-.696199	-.190705
	Absent	9	10				
Sweating	Present	9	84	39.5	<0.0001	-.680573	-.194426
	Absent	7	0				
Family history of IHD	Present	0	16	3.63	=0.05	-.27445	-.106502
	Absent	16	68				

Table 3: Association between HbA1c, tobacco consumption and body mass index

Characteristics		HbA1c Value		χ^2 value	P value	95%confidence interval	
		<6.5%	>6.5%				
Tobacco chewing	Present	5	49	3.37	<0.05	-.521227	-.020438
	Absent	11	35				
Smoking	Present	6	54	4.02	<0.05	-.526258	-.009456
	Absent	10	30				
Alcohol intake	Present	2	35	4.90	<0.05	-.484993	-.098339
	Absent	14	49				
BMI	<25normal	15	58	4.16	<0.05	.092616	.401430
	>25	1	26				

Table 4: Association between HbA1c, serum lipid and cardiac enzyme level

Characteristics		HbA1c Value		χ ² value	P value	95%confidence interval	
		<6.5%	>6.5%				
Total cholesterol	<200mg/dl	10	37	3.97	<0.05	.103101	.521531
	>200mg/dl	1	25				
Triglyceride	<165mg/dl	10	44	4.08	<0.05	.188258	.414916
	>165mg/dl	0	19				
HDL	<60mg/dl	7	58	34.7	<0.0001	-.78580	-.28086
	>60mg/dl	8	0				
LDL	<130mg/dl	11	36	4.66	<0.05	.127290	.525714
	>130mg/dl	1	25				
CK-MB	<40IU/L	12	33	6.93	<0.001	.120658	.593627
	>40IU/L	4	51				

CONCLUSIONS

HbA1c estimation at the time of admission to ICCU clearly and quickly differentiates stress induced hyperglycemia in M.I. patients from hyperglycemia in undiagnosed diabetic patients with AMI.

HbA1c is more sensitive and specific diagnostic test for diabetes mellitus in patients with AMI than serum blood glucose. Prognosis in cases of AMI improves by early identification of diabetic and non diabetic cases by HbA1c evaluation and effective management.

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