

## ASSOCIATION BETWEEN GLYCOSYLATED HEMOGLOBIN AND LIPID PROFILE IN ACUTE MYOCARDIAL INFARCTION PATIENTS

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### ABSTRACT

*Patients with diabetes have an increased prevalence of lipid abnormality, contributing to their high risk of cardiovascular disease. This study is an attempt to evaluate the diagnostic value of glycosylated hemoglobin (HbA1c) for diabetes in acute myocardial patients and to assess the presence of dyslipidemia in them. 100 blood samples were collected from acute myocardial infarction patients at the time of admission to ICCU for blood sugar, HbA1c, and sera were analyzed for lipid profile panel test. Dyslipidemia was defined as per the National Cholesterol Education Programme Adult Treatment Panel guidelines. Diabetes was defined as per American diabetes Association and WHO. The statistical analysis was done by SPSS statistical package version 20. HbA1c demonstrate positive and significant correlation with total cholesterol (TC), triglyceride (TG), HDL, and LDL. So we concluded that dyslipidemia is higher in AMI patients with HbA1c >6.5 than those with HbA1c <6.5.*

### KEY WORDS

*glycosylated haemoglobin, diabetes mellitus, myocardial infarction, hyperglycemia, dyslipidemia, lipid profile.*

### INTRODUCTION

Diabetes mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defect in insulin secretion or action or both. Diabetes causes about 5% of all death globally each year. The chronic hyperglycemia is associated with damage of Heart, kidneys, nerves, blood vessels. 50% of patients with diabetes die of cardiovascular disease [1]. Most cases of acute myocardial infarction present with hyperglycemia due to release of catecholamine in response to stress. Hyperglycemia is associated with large infarct size [2]. 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 [3]. 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 [4].

HbA1c estimation provides an average blood glucose level for a period of 8-12 weeks. 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 [5]. HbA1c concentration can be used to distinguish stress induced hyperglycemia from diabetes mellitus for early appropriate treatment to prevent morbidity and mortality.

Insulin affects the production of apolipoprotein by liver. It regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in diabetes mellitus.

In Diabetic patients dyslipidemia is often unnoticed. Patients with diabetes and dyslipidemia both have increased risk of atherogenesis and cardiovascular disease (CVD) [6].

An early intervention to normalize lipid profile has been shown to reduce cardiovascular complication and mortality. Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic subjects [7]. The aim of this study was to find out association of HbA1c with serum lipid profile in acute myocardial infarction patient.



## 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. Sample for lipid profile was taken after a least 8 hour fasting. 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.

The majority of studies conducted included HbA1c  $\geq 6.5\%$  as cut off for diabetic diagnosis as per American Diabetic Association and WHO [8].

Patients with HbA1c <6.5% were considered non diabetics and patients with  $\geq 6.5\%$  were considered as diabetics. For serum lipid reference, National Cholesterol Education Programme Adult Treatment Panel 3 guideline was referred [9]. According to it hypercholesterolemia is defined as TC>200mg/dl, hypertriglyceridemia as TG>165mg/dl, high LDL when value >130mg/dl, and low HDL when value <60mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid value.

### **Specimen collection and preparation:**

We need preferentially venous blood using EDTA anticoagulant for HbA1c and in plain vial for lipid profile. 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 (bio system). 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 analyzer Biostem S.A. COD 22044, serum total cholesterol and HDL COD21557, serum triglyceride and LDL COD 21528, CK-MB by Randox ,RX CK3813.

*Spurious result:* The study has few limitations.

*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.

For serum lipid reference, National Cholesterol Education Programme Adult Treatment Panel 3 guideline was referred. According to it hypercholesterolemia is defined as TC>200mg/dl, hypertriglyceridemia as TG>165mg/dl, high LDL when value >130mg/dl, and low HDL when value <60mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid value. Value of HbA1c was given as percentage of total haemoglobin and values of all other parameters were given in mg/dl.

### **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

This is a hospital based cross sectional study, carried out in the setting of department of pathology and ICCU/ward, Department of Medicine NSCB Medical College and Hospital Jabalpur, in which 100 AMI patients admitted during October 2013 to September 2014, fulfilling the inclusion criteria were included.



**Table 1: Distribution of subjects according to their Age and HbA1c**

Age	HbA1c <6.5	HbA1c >6.5	Total
<40	3(75.0%)	1(25%)	4
40-59	7(14.9%)	40(85.1%)	47
>60	6(12.2%)	43(87.8%)	49

Table 1 shows about the age wise distribution of the cases. Out of 100 cases majority of cases were seen above age 40yrs. In 40-59 yr age cohort 47 cases were seen and out of these 40(85.1%) cases were found with increase HbA1c level, similarly in >60 yr age

group total 49 cases were seen, out of which 43(87.8%) cases were with increased HbA1c level. Statistically a significant association of increased age and increased HbA1c level was found ( $p<0.01$ ).

**Table 2: Distribution of subjects according to their Sex and HbA1c**

Sex	HbA1c<6.5	HbA1c >6.5	Total
Male	8(50%)	68(81.0%)	76
Female	8(50%)	16(19.0%)	24
Total	16	84	100

In this study male subject were predominantly higher and 76% cases male and 24% were female. In HbA1c >6.5 category total 84 cases were found out of these

81% cases were male and 19.0% cases were females. Statistically male subject were significantly higher in raised HbA1c category. ( $p<0.05$ )

**Table 4: Association between HbA1c, and serum lipid profile**

Characteristics		HbA1c Value		χ2 value	P value	95%confidence interval	
		<6.5%	>6.5%				
Total cholesterol	<200mg/dl	10	37	3.97	<0.05	.103101	.521531
		21.3%	78.7%				
	>200mg/dl	1	25	4.08	<0.05	.188258	.414916
		3.8%	96.2%				
Triglyceride	<165mg/dl	10	44	4.08	<0.05	.188258	.414916
		18.5%	81.5%				
	>165mg/dl	0	19	34.7	<0.0001	-.78580	-.28086
		0.0%	100.0%				
HDL	<60mg/dl	7	58	34.7	<0.0001	-.78580	-.28086
		10.8%	89.2%				
	>60mg/dl	8	0	4.66	<0.05	.127290	.525714
		100%	00.0%				
LDL	<130mg/dl	11	36	4.66	<0.05	.127290	.525714
		23.4%	76.6%				
	>130mg/dl	1	25	3.8%	96.2%		
		3.8%	96.2%				

In the present study lipid profile was done in 73 AMI patients only. In above table patients were classified into two groups as per their HbA1c value. Patients with HbA1c value >6.5% had significantly higher value of TC ( $p<0.05$ ), TG ( $p<0.05$ ), HDL ( $p<0.0001$ ), LDL ( $p<0.05$ )

Table No.4 shows 26 cases presented with hypercholesterolemia and out of these 96.2% cases found with increased HbA1c while 47 cases presented with normal cholesterol and out of these 78.7% had increased HbA1c. Statistically there is significant association between total cholesterol and HbA1c ( $p<0.05$ )

19 cases presented with triglyceridemia and out of these 100.0% cases found with increased HbA1c, while 54 cases have normal triglyceride and out these 81.5% cases had increased HbA1c. Statistically significant association seen between increased triglyceride level and HbA1c ( $p<0.05$ )

In present study 65 cases had abnormal HDL and out of these 89.2% cases found with increased HbA1c, while 8 cases have normal HDL and all these cases were having decreased HbA1c. Statistically highly significant association between HDL and HbA1c level seen ( $p<0.0001$ ).



Out of 73 cases, 26 cases presented with abnormal LDL and out of these 96.2% cases found with increased HbA1c, while 47 cases had normal LDL and 76.6% of these cases found with increased HbA1c. Statistically a significant association between LDL and HbA1c level was seen ( $p < 0.05\%$ ).

## DISCUSSION

Cardiovascular disease accounts for 70-75% of death in diabetic people with acute myocardial infarction being responsible for 30%[10]. Both type 1 and type 2 diabetic subjects are at increased risk of atherosclerotic disease, although the contributions of various cardiovascular risk factors differ between the two disease, several abnormalities such as hyperglycemia, insulin resistance, dyslipidemia, hypertension, procoagulant changes and endothelial dysfunction all appear to play important roles. In this study we found lipid profile more deranged in diabetic patients with AMI compared to non diabetic patients. Total Cholesterol  $>200$  mg/dl was found in 96.2% diabetic patients compare to only 3.8% in non diabetic patient. Studies done by Naseem A et al[11] and Iqbal MJ et al[12] also showed dyslipidemia more in diabetic patients compare to non diabetic patients. In the present study male subjects were predominantly higher. Male to female ratio in diabetic was higher (4.5:1) as compared to ratio in non diabetics, which is comparable with studies done by Naseem A et al[11] and Iqbal MJ et al [12].

## CONCLUSION

Dyslipidemia is higher in AMI patients with diabetes than in nondiabetics. Elevated HbA1c and Dyslipidemia are independent risk factor of CVD. Subjects with An elevated HbA1c along with dyslipidemia can be considered as very high risk group for CVD.

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