

Increased Non-Enzymatic Glycation of Plasma Proteins and Hemoglobin in Non-Diabetic Patients with Acute Myocardial Infarction (MI)

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ABSTRACT

Background: Glycation is known to play a key role in complications of many pathophysiological processes. The present study was carried out to assess whether there are abnormalities of non-enzymatic glycation of proteins and hemoglobin in acute Myocardial Infarction (MI) patients.

Methods: Eighteen acute Myocardial Infarction (MI) patients and 20 healthy controls were enrolled for the present study. Fasting plasma glucose, fructosamine, glycated hemoglobin were evaluated.

Results: A significant rise in the mean values of fructosamine and glycated hemoglobin was found in acute myocardial patients when compared with controls. When Pearson's correlation analysis was performed, no significant correlation was found between fasting plasma glucose with either fructosamine or glycated hemoglobin levels.

Conclusion: This data suggests an increased glycation of both plasma proteins and glycated hemoglobin in acute myocardial patients, which might be independent of prevailing glucose concentration.

Key words: Glycation, Fructosamine, Hemoglobin, Acute Myocardial Infarction (MI)

INTRODUCTION

Glycation of human proteins is currently of much experimental and clinical interest [1]. Glycation of hemoglobin and plasma proteins affords the clinicians an index of diabetes control [1], and glycation of other proteins is reported to be linked with late complications of diabetes mellitus and chronic renal failure [1]. Non-enzymatic glycation occurs when a schiff base is formed, following condensation of glucose and free amino group of an amino acid residue of a normal serum, structure or intercellular protein [1]. This Non-enzymatic modification of protein alters not only the structure, but also the biological properties of protein [2].

The two classical factors known to incite the glycation of proteins in vivo are glucose concentration and half life of the protein [1]. However, evidence in the literature has indicated increased glycated protein levels in some non-diabetic conditions [3,4]. We have also previously demonstrated increased circulating levels of glycated proteins in non-diabetic chronic renal failure, hyperthyroid, asthma, nephrotic syndrome and rheumatoid arthritis patients [5-10].

Recent report by Pu et al., has indicated that glycated albumin levels in type-2 diabetes can be used in the prediction of coronary artery disease [11]. Chowdhury et al., have reported an increased level of glycated hemoglobin (HbA1C) in non-diabetic acute Myocardial Infarction (MI) [12], yet to our knowledge no previous reports exist on the levels of glycated plasma protein levels in non-diabetic acute Myocardial Infarction (MI) patients. As glycation can cause deleterious effect on biological processes and is a risk marker for short-term mortality following acute Myocardial Infarction (MI) in non-diabetic patients [12], it was deemed pertinent to carry out this study.

METHODS

Eighteen consecutive non-diabetic patients who were admitted to the medical intensive care unit of JIPMER with a confirmed diagnosis of acute Myocardial Infarction (MI) and 20 healthy age-matched control subjects were enrolled in the study. The diagnosis of acute MI was made if patients had ischemic-type chest pain for ≥ 30 min with evidence of ST-segment elevation of ≥ 1 mm in two anatomically contiguous leads on the ECG or the appearance

of a new left bundle-branch block. Patients who had symptoms suggestive of acute MI but did not meet ECG diagnostic criteria, needed to have plasma creatinine kinase-MB levels that were more than twice the upper limit of normal. All participants gave written informed consent and this protocol was approved by the Institutional research committee and human ethics committee.

Overnight fasting blood samples were taken by venipuncture in tubes containing EDTA. The samples were collected within the first 24 hours of the onset of the symptom of MI. Whole blood was used for the estimation of glycated hemoglobin. Glycated hemoglobin was measured with ion-exchange micro column kits. Rest of the samples were centrifuged (2500 x g for 10 minutes at 4°C) and the plasma thus obtained were used for the estimation of fructosamine, glucose and creatinine kinase-MB. Plasma fructosamine was measured by p-indonitrotetrazolium violet kinetic method using Raichem kits (Haemagen Diagnostics, San Diego, CA) adopted to 550 Express Plus Analyzer (Ciba Corning Diagnostics, Oberlin, OH). Plasma glucose and creatinine kinase-MB were estimated, using commercially available kits, adapted to 550 express plus autoanalyzer.

All results are shown in mean \pm SD. The statistical significance of differences between groups was evaluated using Student's t-test. Correlation was assessed by Pearson correlation analysis. A p-value of 0.05 was selected as the point of minimal statistical significance.

RESULTS

Data for the acute Myocardial Infarction (MI) patients and healthy subjects are shown in [Table/Fig-1]. There was no statistically significant difference between the 2 groups with respect to age. The results showed that the fasting plasma glucose levels are increased in acute myocardial patients when compared with controls. The fructosamine levels were significantly higher in the patient group compared to controls. Similarly the levels of glycated hemoglobin were significantly increased in acute Myocardial Infarction (MI) patients when compared with the controls. Univariate analysis showed no significant correlation between plasma fasting glucose with either fructosamine or with glycated hemoglobin.

	Control (n = 20)	AMI patients (n = 30)
Fasting glucose (mg/dl)	82.50 ± 10.40	119.40 ± 11.5*
Glycated Hemoglobin (gm %)	5.47 ± 0.70	6.77 ± 0.63*
Fructosamine (nmol/ml)	2.90 ± 0.44	4.02 ± 0.47*

[Table/Fig-1]: Mean and S.D of fructosamine, glycated hemoglobin and fasting glucose in acute Myocardial Infarction (MI) patients and controls

* p < 0.05 compared to controls

DISCUSSION

Non-enzymatic glycation is a common posttranslational modification of protein in which the reducing sugars bind covalently to the free amino groups [1]. Among the various proteins that are known to undergo Non-enzymatic glycation in vivo, hemoglobin has been the most thoroughly investigated [13]. Determination of glycated hemoglobin in diabetic patients is currently acknowledged as the most reliable indicator for assessment of retrospective glycemic control and the planning of clinical management [1]. Furthermore, hemoglobin has been considered a model protein that has provided insights into the Non-enzymatic glycation of other more complex tissue proteins [13]. The concentration of Non-enzymatic glycation of protein including hemoglobin is reported to depend on the ambient concentration of glucose [1]. However, increased HbA_{1c} concentrations have been documented in many pathological conditions including acute Myocardial Infarction (MI) [4-7,12]. In the present study, we found an increased glycated hemoglobin level in acute MI patients who had no previous history of diabetes. In consent with this finding, Chowdhury et al., have previously reported an increased level of glycated hemoglobin (HbA_{1c}) in non-diabetic acute Myocardial Infarction (MI) [12].

Apart from the increased concentration of glycated hemoglobin, we have found that there is also an increase in fructosamine concentrations in acute Myocardial Infarction (MI) patients. To our knowledge, no study to date has attempted to clarify whether the levels of plasma glycated proteins are altered in acute Myocardial Infarction (MI) patients. Measurement of plasma fructosamine is accepted as an alternative method to evaluate glycemic control in diabetic patients. As albumin is the most abundant protein in plasma and contains multiple lysine residues, measurement of fructosamine mainly reflects glycated albumin [1] and have been advocated in adverse effects of vascular biological functions [14-16]. Previous studies have demonstrated that glycated albumin induces oxidative stress [14], enhances pro-inflammatory endothelial response to S100 A8/A9 [15], and promotes proliferation and migration of vascular smooth muscle cells [16], and thereby is said to be associated with atherosclerosis [11].

The mechanism(s) for higher fructosamine and glycated hemoglobin in AMI patients is difficult to entangle from the present study. Increased level of glycated hemoglobin has been reported in non-diabetic acute Myocardial Infarction (MI) patients [12]. A close association between oxidative stress and glycation has been reported previously [17-20]. We have also reported in our previous study, that lipid peroxides per se can enhance glycation of proteins [18]. So, it can be hypothesized that the oxidative milieu generally associated with Myocardial Infarction (MI) would be a reason for the enhanced glycation of circulating blood proteins in acute Myocardial Infarction (MI) patients.

CONCLUSION

In conclusion, the results from the present study provides evidence for the increase in both glycated hemoglobin and fructosamine levels in non-diabetic acute myocardial patients. Given the detrimental role of glycation in the development of cardiovascular complications, factors that can decrease these processes may help to alleviate or prevent the occurrence of such complications. Studies investigating potential avenues of such therapeutic interventions in hypertension are warranted.

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