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STUDY OF SERUM TOTAL SIALIC ACID LEVEL AND ITS CORRELATION WITH ATHEROGENIC INDEX IN CASES OF ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Sialic acid, an acylated derivative of nine carbon sugar neuraminic acid. Serum total sialic acid is a cardiovascular risk factor and associated with increased cardiovascular mortality. The present study was planned to explore the role of serum total sialic acid levels and its correlation with atherogenic index in acute myocardial infarction. It was a case controlled study conducted in the Department of Biochemistry, Pt B D Sharma PGIMS, Rohtak. 35 patients of myocardial infarction were placed in study group and 35 healthy volunteers in the control group. Serum Sialic acid was analyzed by Warren's TBA method. Serum total sialic acid levels were found to be significantly high in study group. A strong positive correlation was observed between atherogenic index and sialic acid levels in study group. Elevation in serum total sialic acid level might result either due to the cell damage after acute myocardial infarction or increase in sialidase activity.

KEY WORDS

Sialic acid, acute myocardial infarction, LDL cholesterol, atherogenic index.

INTRODUCTION

Serum sialic acid is N-acetyl Neuraminic acid. It is a protein bound carbohydrate. Clinically, neuraminic acid may be considered as an aldol condensation product of pyruvic acid with either D-glucosamine or D-mannosamine. The sialic acid is distributed in biological fluid as components of mucoprotein and mucolipids.[1] They are recognition markers for the sorting and distribution of proteins, regulate half-life of blood protein, variety of toxin neutralization, cellular adhesion. They mediate the interactions of cells with other cells as well as with molecules such as hormones.[2] In the last few years different workers have demonstrated that the concentration of sialic acid in human serum is abnormally high in tissue destruction, tissue proliferation, depolymerization or inflammation.[3] Raised level of serum sialic acid has been seen in malignancy, Diabetic mellitus, Coronary artery disease.[4]

Acute coronary insufficiency results when the balance between the oxygen requirement and blood supply to the myocardium is disturbed. Cessation of blood flow causes ultra structural changes, initiates inflammatory process and leading to irreversible cell damage which is known as myocardial infarction. Damage to the cell membrane results in the release of intracellular contents and some membrane components like sialic acid.[5] A recent epidemiological study showed that mortality from cardiovascular diseases was higher in population with high concentrations of sialic acid.[6] It has also been demonstrated that dyslipidemia, smoking, hypertension are important modifiable risk factors for cardiovascular disease and associated with high serum sialic acid.[7] Various studies indicate increased LDL desialyation is associated with increased peripheral atherosclerotic lesions. This in turn suggests a possible role of sialic acid in atherosclerosis and also its association with dyslipidemia. Hence, comparison of serum sialic acid levels with atherogenic index may be used as predictor of atherosclerosis.[8]

The present study was planned to explore the role of serum total sialic acid (TSA) levels and lipid profile in acute myocardial infarction and to correlate TSA levels with atherogenic index.

MATERIAL AND METHOD

It was a case controlled study conducted in the Department of Biochemistry and Department of Medicine, Pt B D Sharma PGIMS, Rohtak. Total 70 Subjects were enrolled in the study after taking written informed consent as per declaration of Helsinki. The study was approved by the Institutional Ethical Committee. Out of 70 subjects 35 patients of myocardial infarction, age 40-60 years admitted in accident and emergency medicine ward of Pt. B.D. Sharma PGIMS, Rohtak were placed in the study group. Only newly diagnosed and proven cases of acute myocardial infarction presenting for the first time with chest pain within 12 hours of onset of chest pain in which diagnosis is made by history, clinical examination, ECG changes and serum CKMB were included in the study. Patients with diabetes, renal failure, previous history of angina or MI, malignancy, autoimmune disease, acute infection, taking lipid lowering drugs or antioxidant supplements were excluded from the study. 35 healthy volunteers, age and sex matched were placed in the control group.

Method

All patients were thoroughly examined and blood sample was collected. Venous sample was collected at the time of enrollment in accident and emergency ward. During sample collection all precautions were followed as per CLSI guidelines.[9] Blood sample was collected in commercially available plain vial. Sample was allowed to clot and then centrifuged at 3000rpm for 5min. Serum was separated and analysed immediately. Samples collected were used for estimation of Blood urea, sugar, electrolytes and serum CKMB, AST, Sialic acid and Lipid profile.

Serum Sialic acid was analyzed by Warren's TBA method. Total sialic acid reacts with sodium metaperiodate to form beta formyl pyruvic acid. It reacts with thiobarbituric acid to form red chromaphore whose optical density is measured at 540nm.[10]

Serum lipid profile, AST, urea, sugar and electrolyte were analyzed on fully automated Random access analyzer (KONELAB 30, Thermo scientific) using commercially available kits of Randox laboratories. Atherogenic Index was calculated as total cholesterol– HDL cholesterol/ HDL cholesterol.

Serum CKMB is measured by semiautoanalyser (ERBACHEM) using commercially available kits of Siemens health care system.

Statistical Analysis

The levels of biochemical parameters in serum were compared between the study and control group by unpaired *t* test. The observed value for serum total sialic acid was correlated to the atherogenic index using Pearson's correlation coefficient. $P < 0.05$ was considered significant. The statistical analysis was carried out using SPSS version 18^{+}.

RESULT AND DISCUSSION

Acute myocardial infarction (AMI) is one of the most common diagnoses found in emergency wards of developing countries. The mortality rate of AMI is approximately 30%, approximately 1 of every 25 patients who survives the initial hospitalization dies in the first year after AMI.[11]

AMI generally occurs when coronary blood flow decreases abruptly after thrombotic occlusion of the artery at a site of vascular injury. This injury is produced or facilitated by factors such as cigarette smoking, hypertension, and lipid accumulation. In most cases, infarction occurs when an atherosclerotic plaque fissures, ruptures or ulcerates and when conditions (local or systemic) favour thrombogensis, so that a mural thrombus forms at the site of rupture and leads to coronary artery occlusion.[12]

We compared demographic profile of the subjects as shown in table 1. It has been observed that incidence of AMI is 80% in 50-60 year of age group as compared to 20% in 40-50 year of age group. It has also been seen that 88% of males develop AMI and 12% female suffered from AMI. This decreased incidence of AMI in females may be due to the beneficial effects of high estrogen. Blood pressure was significantly high in study group as compared to the control group. Thirteen subjects in study group were taking antihypertensive medication and 21 subjects were having history of smoking. In control group history of smoking is present in 13 subjects. These findings were in accordance with various studies which states that hypertension, smoking and dyslipidemia are important modifiable risk factor for AMI while age and sex are non modifiable risk factor.

TABLE 1
COMPARISON OF DEMOGRAPHIC PROFILE IN TWO GROUPS

Parameter		Control group (n= 35)	Study group (n=35)
Age	40-50 years	15	7
	50-60 years	20	28
Sex	Male	21	31
	Female	14	4
Blood pressure	Systolic BP	111±8.5	131±11.5
	Diastolic BP	78±4.8	88±6.2
Smoking		13	17

Early diagnosis of AMI is crucial for proper management. Patient's history of chest pain and ECG changes may not confirm the diagnosis of AMI. Therefore measurement of circulatory proteins and enzymes released from the necrotic myocardial tissue are useful in the diagnosis of AMI. We measured serum total sialic acid along with serum CKMB and AST levels within 12 hours of onset of chest pain as shown in Table-2.

TABLE 2
COMPARISONS OF BIOCHEMICAL CARDIAC MARKERS AT 12 HOURS

Parameters	Control group (Mean±SD)	Study group (Mean±SD)	p value
TSA (mg/dL)	40.2±4	58.5±6.7	0.001
CK-MB (U/L)	18.4±3.2	168±136	0.001
AST (IU/L)	25.2±8.4	44.8±16.1	0.001

We have observed that cardiac markers, serum CKMB and AST were significantly elevated in study group as compared to the control group. Serum total sialic acid levels were also found to be significantly high in study group as compared to the control group($p<0.001$).

Various studies documented raised sialic acid levels in AMI.[13,14] Elevation in serum total sialic acid level in the blood might result either from the shedding or secretion of sialic acid from the cell membrane surface, or releasing of cellular sialic acid from the cell into the bloodstream due to cell damage after myocardial infarction.[15] There is increase in the activity of sialidase enzyme in myocardial cell membrane surface. This enzyme causes hydrolytic release of α-glysidically bound sialyl residue of sialoglycoconjugates and sialooligosaccharides and causes increase in sialic acid concentration in AMI.[16] Hanson et al have demonstrated that increased plasma sialidase activity in these patients might be associated with clumps of desialylated erythrocytes that may alter blood flow in the capillaries.[17]

In another study by Lindberg et al have shown that sialic acid concentration increases with age in both men and women and this trend was absent in male smokers who from a younger age had a sialic acid concentration equal to that in older male smokers. They attributed the fact that in young men smoking initiates or aggravates atherosclerosis, which increases the sialic acid concentration. [18]

Gracheva E V et al in another study demonstrated Sialyltransferase activity in membrane preparations containing the Golgi

apparatus that were isolated from atherosclerotic and normal human aortic intima as well as in plasma of patients with documented atherosclerosis and healthy donors.They measured the transfer of *N*-acetylneuraminic acid (NeuAc) from CMP-NeuAc to asialofetuin. The asialofetuin sialyltransferase activity was found to be 2 times higher in the atherosclerotic intima as compared to the normal intima and 2-fold higher in patients' plasma than in that from healthy donors.[19]

Table 3 represents comparison of lipid profile and atherogenic index in two groups. Serum total cholesterol, triglyceride, LDL and VLDL cholesterol were significantly high in study group as compared to the control group. However, serum HDL cholesterol was comparable in both the groups. Atherogenic index were calculated from total cholesterol, HDL cholesterol. A significant rise in atherogenic index has been seen in study group as compared to the control group. A strong positive correlation was also observed between atherogenic index and sialic acid levels ($p<0.001$; r 0.617).

TABLE 3
COMPARISON OF LIPID PROFILE & ATHEROGENIC INDEX

Parameters	Controls group (Mean±SD)	Study group (Mean±SD)	p value
Total Cholesterol (mg/dL)	174±26.3	224.8±31.3	0.001
Triglyceride (mg/dL)	128.9±38.1	205±25.6	0.001
HDL (mg/dL)	37.65±6.0	35.6±5.7	NS
LDL (mg/dL)	108.4±21.1	148.7±28.4	0.001
VLDL (mg/dL)	25.9±8.3	43.4±11.8	0.001
Atherogenic Index	3.5±0.4	5.8±1.6	0.001

Hyperlipidemia has been proven to be an important modifiable risk factor for acute MI. Evidence suggests that oxidatively modified LDL contribute to the pathogenesis of atherosclerosis. The concentration of LDL correlates positively to the development of coronary heart disease.[20] In our study we also observed raised LDL cholesterol is positively correlated with the incidence of acute myocardial infarction and serum sialic acid. Dutt M et al reported that raised serum TSA levels as the earliest marker of raised atherogenic index. They suggested that increased destruction of tissues raised the serum sialic acid.[21]

It has been suggested that desialylation of LDL is an atherogenic modification taking place in the circulation, since sialic acid -poor LDL has been found in blood, especially in that of CAD patients. LDL with a low sialic acid content causes lipid deposition into cells and binds to arterial proteoglycans, It avidly internalizes in macrophage-foam cells. Thus, sialic acid -poor LDL could be one relevant factor leading to the development of CAD.[22] HDL cholesterol on the other hand is regarded as one of the most important protective factors against atherosclerosis. HDL's protective function has been attributed to its active participation in the reverse transport of cholesterol and correlates inversely to the development of coronary heart disease. However in our study HDL cholesterol levels are comparable in two groups.

Thus, serum total sialic acid level can be an important inflammatory marker of atherosclerosis. But about its specificity as cardiac marker and variation in its level according to different time point after AMI is yet to be studied in Indian population.

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