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Serum sialic acid, lipid profile and fibrinogen as markers of ST- elevated ECG in myocardial infarction.

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ABSTRACT

The aim of the study is to rule out the diagnosis by biomarkers approach in atherosclerosis which is main cause of cardiovascular disease. 80 patients with age group between 40-60 years complaining of chest pain, newly diagnosed as myocardial infarction with ECG of STEMI, admitted to casualty were selected as cases. 80 Healthy age matched persons were taken as controls. The results of cases were compared with controls which showed high significance for each parameter. There is a significant positive Correlation for Sialic acid with total cholesterol, TAG, LDL-C and Fibrinogen and negative correlation with HDL. Fibrinogen has significant positive correlation for Sialic acid, total cholesterol, TG and LDL-C. Of all the parameters Fibrinogen is the best marker. Sialic acid, Lipid profile and Fibrinogen together increase the diagnostic efficiency of cardiac biomarkers. These 3 parameters can be estimated on routine basis for the screening and evaluation of atherosclerosis. More over these are cost effective and has less technical effort in estimating them.

KEY WORDS: Atherosclerosis , Sialic acid, lipid profile, Fibrinogen, Myocardial infarction.

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Introduction:

Cardiovascular disease (CVD) is a serious health problem which causes substantial morbidity and mortality .It is now the most common cause of death worldwide. Before the year of 1900, infectious diseases and malnutrition were the most common causes of death throughout the world and CVD was responsible for <10% of all deaths. Today CVD accounts for ~30% of deaths worldwide [10]. In India it is expected to almost 2.03 million deaths by 2010 by CVD.

Cardiovascular diseases comprise the most prevalent serious disorders in industrialized nations and are a rapidly growing problem in developing nations. The growing prevalence of obesity, Type 2 Diabetes Mellitus, and Metabolic Syndrome which are important risk factors for atherosclerosis, now threatens to reverse the progress that has been made in the age-adjusted reduction of mortality of coronary heart disease. Also increasing the mortality rate of cardiovascular diseases among young adults [5]. There is another factor which contributes by

the environment in which a man works and that is stress [14].

Cardiovascular disease is mainly caused by atherosclerosis. Event of atherosclerosis is likely an inflammatory insult that occurs decades before the disease becomes clinically apparent [7]. Once initiated, atherosclerosis progresses as a result of a well-studied series of changes in the constituent cellular make-up of the vessel wall. Specific cytokine-mediated events in this cycle are required for lesional growth. Pathophysiology of atherosclerosis is a complicated process, governed by several risk factors.

Atherosclerosis of the coronary arteries commonly causes Myocardial infarction and angina pectoris. The spectrum of MI includes ST segment elevation and non ST elevation MI. ST segment elevation Myocardial infarction (STEMI) occurs when a coronary artery thrombus develops rapidly at a site of vascular injury, as a consequence blood flow decrease abruptly in an artery previously affected by atherosclerosis.

Some of biochemical changes concerned with diseases process are change in serum sialic acid, lipid profile and fibrinogen so an attempt has been made in the present study to show changes in Myocardial infarction caused due to atherosclerosis.

Sialic acid is the terminal sugar components of oligosaccharide chains of glycoproteins and glycolipids. Sialic acid is realeased from cell membrane during the process of atherosclerosis. So elevated silaic acid in coronary heart disease reflects the existence or activity of atherosclerotic process [17]. Sialic acid is a novel marker which in future may become an important parameter to assess the intensity of Myocardial infarction[12,4,11,17] and mortality.

Fibrinogen is circulating glycoprotein that acts at final step in coagulation response to vascular and tissue injury [6]. Fibrinogen is major contributor of increased blood viscosity, stimulates smooth muscle cell proliferation, migration and increases platelet agreeability .All of which may contribute to development of coronary heart disease. Fibrinogen is a marker of thrombogenesis [8, 21, 22, 24].

Among various lipoprotein fractions the protective effect of HDL and harmful effect of LDL have been well established. Triglycerides are proven atherogenic [19]. Hence this study is undertaken to assess the predictive value of these parameters in Myocardial infarction caused due to atherosclerosis.

Materials and methods

The study is conducted in the Department of Biochemistry, Osmania Medical College and Osmania general Hospital includes total 160 of which 80 patients newly diagnosed with Myocardial infarction admitted to casualty were selected as cases. 80 Healthy age and gender matched persons were taken as controls.

Basic information like age, weight, life style habits, and hypertension is taken from the individuals by questionnaire. Written consent is obtained from study subjects.

Inclusion Criteria: patients with first episode of MI with in 24 hrs of onset, ECG changes suggestive of STEMI, of both genders and age group between 40 – 60 yrs.

Exclusion Criteria: with non-STEMI ECG, H/O of Diabetes Mellitus, H/O of Liver Disorders, H/O of thyroid and Renal abnormalities, trauma and infections are excluded.

Blood is collected in vaccutainers and estimated for sialic acid, lipid profile, fibrinogen also basic investigations like blood sugar, blood urea, serum creatinine, bilirubin, ALT and serum electrolytes were done to rule out Diabetes Mellitus, Liver and Renal disease.

Sialic acid is done by Method Thiobarbituric acid assay (TBA) or warren assay and calculated from its molar extinction coefficient. Cholesterol, HDL, TG were analysed using Dade behring dimension a fully automated chemistry analyser where as LDL and VLDL was estimated indirectly using friedwald equation and fibrinogen was estimated as clot based method by biuret

reaction measured at 505nm using spectrophotometer.

S.No	Parameter	Mean ± S.D of controls	Mean ± S. D of cases	'p' values of Cases
1	Sialic acid	49.38±6.48	77.57 ±12.04	**<0.05**
2	Total cholestrol	173.96±24.68	264.10±34.44	**<0.05**
3	HDL-C	43.95±6. 99	31.70±3.64	**<0.05**
4	TAG	120.01±38.89	202.4±43.95	**<0.05**
5	VLDL-C	23.26±7.92	39.59±9.96	**<0.05**
6	LDL-C	105.85±24.44	192.86±35.1	**<0.05**
7	Fibrinogen	311.15±84.87	771.13±109.75	**<0.05**

Table 1: MEAN ± S.D, and 'p' values of Parameters in Controls and Cases

	Total cholesterol	HDL-C	TAG	VLDL-C	LDL-C	Fibrinogen
Sialic acid	0.875(**)	0.105	0.269(**)	0.186	0.809(**)	**0 .346(**)**
Fibrinogen	**0 .353(**)**	**o.018**	**0.207(*)**	**0.187**	**0.294(**)**	**1**

Table 2: Pearson Correlation values for sialic acid and fibrinogen with different parameters.
** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

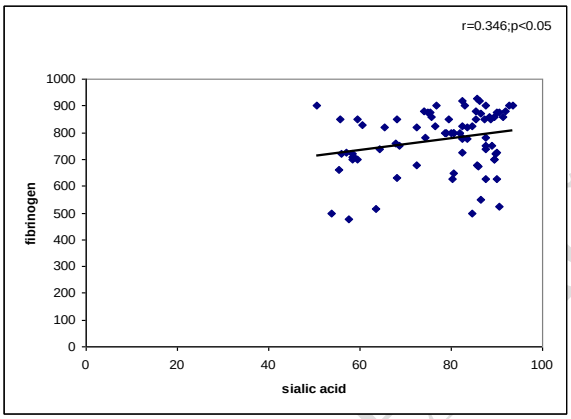
Results

The data was analysed by using SPSS 15.0 version and Microsoft Excel software. The results were expressed as Mean and Standard deviation (S.D). Independent sample't' test was used to assess the significance of difference of means between the cases and controls. P<0.05 is considered as significant. Specificity and sensitivity of the different parameters in diagnosing Myocardial infarction were with the "graph pad prism" software.

It is evident from the table-1 that sialic acid, total cholestrol, triglycerids, VLDL, HDL are significantly elevated in cases compared to controls except HDL-C which is statistically significantly fall in patients compared to normal healthy controls. High sialic acid in patients show the atherosclerotic changes associated with alteration in lipid parameters explains dyslipidaemia associated in myocardial infarction. Increased fibrinogen indicating thrombogenesis.

Parameter	Best Cut-Off Value	sensitivity	specificity
Sialic acid	58.34 mg/dl	90 %	91 %
Total cholestrol	206 mg/dl	87 %	87 %
HDL-C	34.5 mg/dl	77%	80%
TAG	146 mg/dl	96%	82 %
VLDL-C	29 mg/dl	92 %	85 %
LDL-C	151 mg/dl	85 %	97 %
Fibrinogen	472 mg/L	100 %	97 %

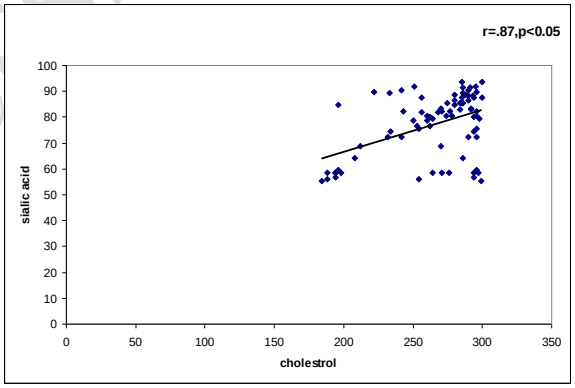
Table.3: Best Cut-Off Value, Sensitivity and Specificity of all parameters.



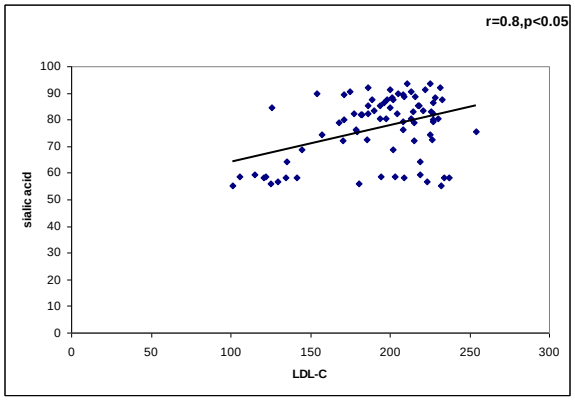
r = pearson correlation coefficient

Graph -1 Correlation between sialic acid and fibrinogen

Correlation study revealed (table-2) significantly positive correlation between sialic acid and fibrinogen and (graph-1) as platelet shedding of sialic acid increases its level in serum. Significantly positive correlation between sialic acid and total cholesterol (graph-2) also explains dyslipidemia associated with atherosclerosis. correlation between sialic acid and LDL-C showed significance(graph-3) explains that desialylation of LDL particles represents one of the first or the primary act of modification which is, apparently, a sufficient prerequisite for the development of atherogenic properties .Study showed negative correlation HDL –C which is not significant and also VLDL is insignificant.



Graph -2 Correlation between cholesterol and sialic acid



Graph -3 Correlation between LDL –C and sialic acid

In order to assess discriminatory capacity of various parameters in differentiating different study groups the sensitivities and specifications were calculated using best cut off values. The best cut off values was calculated by using Graph Pad Prism Software.

From Table-3 Fibrinogen has highest sensitivity and specificity. Other parameters follow in the order of Sialic acid, LDL-C,TAG,VLDL,HDL-C and total cholesterol.

Discussion

Cardiovascular diseases are mainly caused by atherosclerosis and the pathophysiology of atherosclerosis is a complicated process governed by several risk factors. Enormous progress in understanding this complicated process has been made in recent years and some new risk factors /markers have shown their relevance in this area. Present study was performed to investigate the association of these markers in a small group of cases those who already developed the Myocardial infarction due to atherosclerosis

Present study has statistically significant increase in Serum Sialic acid in cases compared to controls. [2, 21] The mechanistic aspects of the raised levels of sialic acid in cardiac patients have several possibilities, such as increase in acute phase reactants containing Sialic acid [9, 25]. Increased sialylation of serum proteins or reduction in desialylation of plasma glycoproteins.

There is significant increase in total cholesterol in cases compared to controls [13]. The reason for this is that all lipoproteins except HDL in blood are increased due to one or more major risk factors contributing to increase in total cholesterol resulting in atherosclerosis and its complications.

Study has significantly elevated levels of LDL-C in cases compared to controls [15]. Raised concentrations of LDL-C undergo oxidative modifications, rendering it more atherogenic. Oxidized LDL have enhanced uptake by macrophages, which contribute directly to foam cell formation, the hallmark of initial lesion .Ox-LDL may also adversely affect many other aspects of arterial wall metabolism and thus contribute further to the atherogenic process leading to MI.[16,23]

In this study TG and VLDL is significantly elevated as TAG is degraded by lipoprotein lipase to VLDL, which eventually turns into LDL contributing to its atherogenic property.

Present study show decreased HDL-C statistically significant. As major function of HDL-C cholesterol is to enhance reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues followed by esterification and delivering it to the liver eventual elimination from the body. Most importantly, HDL-C can inhibit oxidation of LDL-C, as well as the atherogenic effects of oxidised LDL-C[10] by virtue of its antioxidant property .So atheroprotective properties which is lost in atherosclerosis .[1,3,15].

A high plasma concentration of Fibrinogen suggests that Fibrinogen becomes elevated as a consequence of inflammatory processes.[24,26] in agreement with previous studies [8,28] P. which proved Influence of Plasma Fibrinogen Levels on the Incidence of Myocardial infarction.[20].

The present study shows statistically significant correlation between Sialic acid, fibrinogen and LDL-C. Similar correlation is observed in previous studies [18, 12]. The underlying mechanism is Sialic acid content of is shed into blood, raising levels of sialic acid in serum. Due to loss of charge imparted by sialic acid, platelets loss repulsiveness, tend to aggregate with each other and activation of coagulation cascade leading to increase in Fibrinogen levels. Loss of sialic acid from LDL accelerates the rate of internalization of the lipoprotein. Sialic acid which is released by these mechanisms increases its level in serum.

In present study there is significant correlation between Fibrinogen and LDL. It is in aggrement with previous studies [27]. Increased LDL peroxidation is associated with elevated plasma Fibrinogen level is reason for this.

In present study Fibrinogen is considered to be best marker in predicting atherosclerosis, has highest sensitivity of 100% and specificity of 97% .Other parameters also have sensitivity and specificity in following order sialic acid , LDL-C,TAG,VLDL,HDL-C

and total cholesterol. All the markers can be used in predicting atherosclerosis.

Conclusion

Cardiovascular diseases are mainly caused by atherosclerosis. Atherosclerosis actually involves an ongoing inflammatory response. Recent advances in basic science have established a fundamental role for inflammation in mediating all stages of this disease from initiation through progression and ultimately the thrombotic complications of atherosclerosis. These findings provide important links

Sialic acid, Fibrinogen and Lipid profile together increases diagnostic efficiency of biomarkers. In evaluation for screening atherosclerosis, these biomarkers can be estimated on a routine basis, as they are also cost effective and has less technical effort.

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