Evaluation of correlation between oxidative stress and abnormal lipid profile in coronary artery disease

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ABSTRACT

Background: Coronary artery disease (CAD) is the most common cause of sudden death, and death of men and women over 20 years of age. The aim of the study was to know if there is any linear correlation between oxidants and abnormal lipid profile parameters in CAD. **Materials and Methods:** The present study includes 42 known CAD cases (age = 41–75 years) and 33 age- and sex-matched healthy controls. Malondialdehyde (MDA), total cholesterol, high-density lipoprotein (HDL) cholesterol, and triacylglyceride were measured and low-density lipoprotein (LDL) cholesterol was calculated in both cases and controls, respectively. **Results:** MDA was significantly increased in cases than controls ($P = 0.0000001$). Total cholesterol was high in cases than controls ($P = 0.0000001$). HDL cholesterol was significantly decreased in cases than controls ($P = 0.0000001$). LDL cholesterol was high in cases than controls ($P = 0.0000001$). Triacylglyceride was high in cases than controls ($P = 0.0000001$). Insignificant positive correlation were observed between MDA and total cholesterol ($r = 0.258$), between MDA and LDL cholesterol ($r = 0.199$), and between MDA and HDL cholesterol ($r = 0.134$). Negative correlation was observed between MDA and triacylglyceride ($r = -0.314$). **Conclusion:** Increased oxidative stress and abnormal lipid profile were observed in CAD cases. Our study showed that statistically significant linear relationship could not be established between increased oxidative stress and abnormal lipid profile parameters, suggesting that increased oxidative stress and abnormal lipid profile are two independent risk factors in the pathomechanism of atherogenesis.

Key words: Abnormal lipid profile, atheromatous plaques, coronary artery, coronary artery disease, myocardium, oxidants

INTRODUCTION

Coronary artery disease (CAD or atherosclerotic heart disease) is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries[1] that supply the myocardium (the muscle of the heart) with oxygen and nutrients. CAD is the leading cause of death worldwide.[2]

Although the symptoms and signs of CAD are noted in the advanced state of disease, most individuals with CAD show no evidence of disease for decades as the disease progresses before the first onset of symptoms, often a "sudden" heart attack, finally arises. After decades of progression, some of these atheromatous plaques may rupture and (along with the activation of the blood clotting system) start limiting blood flow to the heart muscle. The disease is the most common cause of sudden death,[3] and is also the most common reason for death of men and women over 20 years of age. [4] According to present trends in the United States, half of healthy 40-year-old men will develop CAD in the future, and one in three healthy 40-year-old women.[5]

CAD is associated with smoking, diabetes, and hypertension.

A family history of early CAD is one of the less important predictors of CAD. Most of the familial associations of CAD are related to common dietary habits. Screening for CAD includes evaluating high-density and low-density lipoprotein (LDL) (cholesterol) levels and triglyceride levels. Despite much press, most of the alternative risk factors including homocysteine, C-reactive protein, lipoprotein (a), coronary calcium, and more sophisticated lipid analysis have added little if any additional value to the conventional risk factors of smoking, diabetes, and hypertension.

LDL particles can transport cholesterol into the artery wall, retained there by arterial proteoglycans and attract macrophages which engulf the LDL particles and start the formation of plaques, increased levels are associated with atherosclerosis. Over time, vulnerable plaques rupture, activate blood clotting, and produce arterial stenosis, which if severe enough results in heart attack, stroke, and peripheral vascular disease symptoms and major debilitating events.

In healthy individuals, about thirty percent of blood cholesterol is carried by HDL.[6] HDL particles are able to remove cholesterol from atheroma within arteries and transport it back to the liver for excretion or reutilization, which is the main reason why the cholesterol is carried within HDL particles.

The free radical reactions may have a primary role in the pathomechanism of atherogenesis.[7] Lipid peroxidation is the result of oxidative deterioration of polyunsaturated fatty acids. Very low-density lipoprotein, high-density lipoprotein (HDL), LDL are all the vehicles for peroxidation, it is the LDL which gets the maximum load. Oxidatively modified LDL (Ox-LDL) leads to generation of foam cells, main factor of atherosclerosis. Ox-LDL level gives better idea of atherogenic potential of an individual; quantitation of malondialdehyde (MDA) by thiobarbituric acid method is one of the commonly utilized indices of lipid peroxidation.

The aim of the present study was to investigate the relationship and degree of association between increased oxidative stress and abnormal lipid profile in CAD cases and comparing the same with healthy controls. So, correlation analysis was investigated.

MATERIALS AND METHODS

A total of 42 immediately survived myocardial infarction outpatients with CAD of both sex in the age group of 41 to 74 years (mean $\pm$ SD = 61.71429 $\pm$ 8.75210), attending cardiology department at Mamata medical college Hospital, Khammam, were included in the study. A total of 33 age- (mean $\pm$ SD = 59.24242 $\pm$ 9.57219) and sex-matched healthy

controls were included in the study. Persons with Diabetes mellitus, renal disease, and smokers were excluded from the study. Oxidative stress was assessed by measuring MDA, and dyslipidemia was assessed by measuring lipid profile parameters in all the subjects. Thiobarbituric acid reactive substances was estimated in plasma, described by K. Satoh[8] using MDA as reference standard, expressed as nmol/ml of plasma. Total cholesterol (CHOD-PAP-Method),[9-12] -HDL (HDL Precipitating method),[13-15] LDL (Friedwald formula), and triacylglycerol (TAG) (GPO-PAP Method)[9-12] were measured on Merck MicroLab 200 semiautoanalyzer in all the subjects.

Statistical analysis

Statistical analysis was done using SalStat statistical software and Minitab 15 English statistical software. Student t-test unpaired was used to compare the means between cases and controls at 5% level of significance. Equivalent nonparametric tests like Rank Sums test (unpaired samples) and Mann-Whitney U test (Unpaired samples) were also used to compare the means between cases and controls at 5% level of significance. Correlation analysis was calculated using Pearson's correlation coefficient and the nonparametric equivalent Spearman's rank correlation coefficient at 95% confidence of interval.

RESULT

In the present study, oxidative stress was assessed by measuring MDA and dyslipidemia was assessed by measuring lipid profile parameters in 42 immediately survived myocardial infarction outpatients with CAD and 33 healthy controls. Correlation analysis was investigated between oxidants and lipid profile parameters in CAD cases. MDA was significantly increased in cases (mean $\pm$ SD = 6.61429 $\pm$ 0.61891) than controls (mean $\pm$ SD = 3.07030 $\pm$ 0.44168) as P = 0.0000001. Total cholesterol was significantly high in cases (mean $\pm$ SD = 259.90476 $\pm$ 12.04020) than controls (mean $\pm$ SD = 177.48485 $\pm$ 11.11340) as P = 0.0000001. HDL cholesterol was significantly decreased in cases (mean $\pm$ SD = 34.80952 $\pm$ 3.95239) than controls (mean $\pm$ SD = 43.45455 $\pm$ 6.16487) as P = 0.0000001. LDL cholesterol was significantly high in cases (mean $\pm$ SD = 147.52381 $\pm$ 20.53817) than controls (mean $\pm$ SD = 107.09091 $\pm$ 6.10514) as P = 0.0000001. Finally, triacylglyceride was significantly high in cases (mean $\pm$ SD = 218.90476 $\pm$ 17.65912) than controls (mean $\pm$ SD = 130.48482 $\pm$ 13.02910) as P = 0.0000001 as shown in our Table 1.

Correlation analysis was calculated using Pearson's correlation coefficient and nonparametric equivalent Spearman's rank correlation coefficient. At 5% level of

Table 1: Showing the statistical analysis of data of MDA and lipid profile parameters

Variables	MDA nmol/ml	Total cholesterol mg/dl	HDL cholesterol mg/dl	LDL cholesterol mg/dl	Triglyceride mg/dl
Controls n = 33	3.07030±0.44168	177.48485±11.11340	43.45455±6.16487	107.09091±6.10514	130.48482±13.02910
Cases n = 42	6.61429±0.61891	259.90476±12.04020	34.80952±3.95239	147.52381±20.53817	218.90476±17.65912
t(73)-values	-27.785	-30.431	7.369	-10.922	-24.061
P-value	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001
Rank Sums test (unpaired samples)					
t value	-6.994	-6.994	5.198	-6.994	-6.994
P value	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001
Mann-Whitney U test (unpaired samples)					
z value	7.397	7.399	5.514	7.400	7.399
P value	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001

(Values are shown in mean ± SD) MDA - Malondialdehyde, HDL - High-density lipoprotein, LDL - Low-density lipoprotein

Table 2: Correlation analysis

Variables	MDA verses total cholesterol	MDA verses HDL cholesterol	MDA verses LDL cholesterol	MDA verses triglyceride
Pearson's correlation coefficient				
r(40) value	0.258	0.134	0.199	-0.314
t value	1.692	0.852	1.288	-2.092
P value	0.098346	0.399128	0.205302	0.042863
Spearman's rank correlation coefficient				
rho(40) value	0.078	0.225	0.222	-0.365
P value	0.624554	0.151929	0.156831	0.017452

MDA - Malondialdehyde, HDL - High-density lipoprotein, LDL - Low-density lipoprotein

significance, assuming that at least one of the variable is normally distributed, calculation of Pearson's correlation coefficient showed a statistically highly insignificant positive correlation between MDA and total cholesterol (r = 0.258) as $P = 0.098346$, between MDA and LDL cholesterol (r = 0.199) as $P = 0.205302$, and between MDA and HDL cholesterol (r = 0.134) as $P = 0.399128$. Significant negative correlation was observed between MDA and triacylglyceride (r = -0.314) as $P = 0.042863$ which was statistically significant as shown in our Table 2.

Calculation of correlation analysis by nonparametric equivalent Spearman's rank correlation coefficient also showed the same result as Pearson's correlation coefficient analysis, as shown in Table 2.

Correlation analysis was also represented graphically by scatter diagram. In all the scatter Figures 1-4, MDA values are taken on horizontal axis and lipid profile parameters values are taken on vertical axis. In all the scatter Figures 1,2,3, the points are scattered randomly around the arbitrary central linear line suggesting no statistically significant 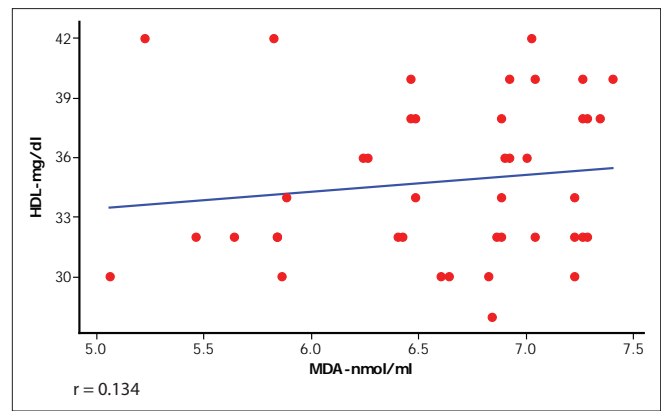linear relationship between increased oxidative stress and abnormal lipid profile. No linear relationship was observed between MDA and total cholesterol as shown in our scatter diagram one. Similarly, no linear relationship was observed between MDA and HDL cholesterol as shown in our scatter diagram two. Furthermore no linear relationship was observed between MDA and LDL cholesterol as shown Figure 3. In contrast to this, we have observed a statistically significant negative relationship between MDA and TAG, as shown in Figure 4.

CONCLUSION

Our study showed a significant increase in the oxidative stress in CAD cases than controls. Lipid profile was significantly abnormal in CAD case when compared with the controls. Increased total cholesterol, LDL, and TAG are well known atherogenic factors. Similarly, HDL less than 35 mg/dl is a known independent high-risk factor for arteriosclerosis. But in our study, both Pearson's correlation coefficient analysis and nonparametric equivalent Spearman's rank correlation coefficient analysis showed a statistically highly insignificant correlation between MDA level and each lipid profile parameter in CAD cases. Furthermore, the scatter
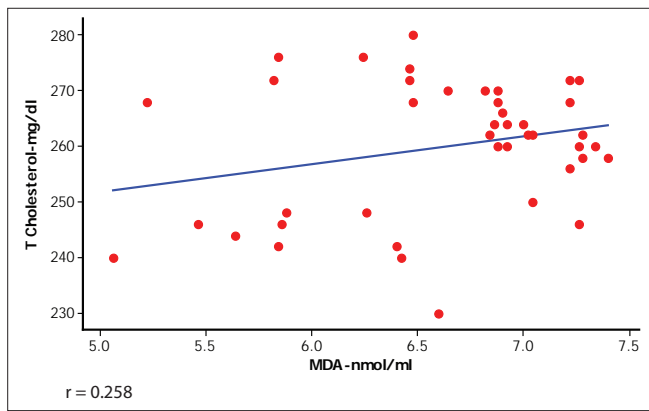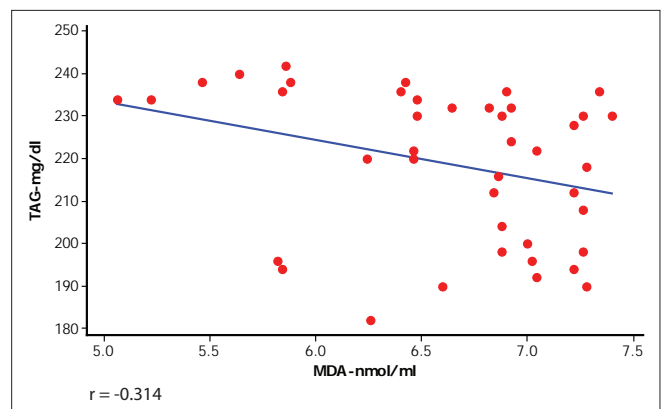
Figure 1: No linear relationship between MDA and total cholesterol

Figure 2: No linear relationship between MDA and HDL cholesterol
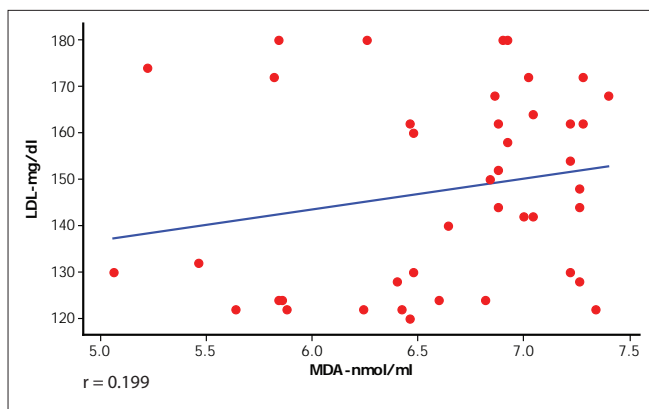
Figure 3: No linear relationship between MDA and LDL cholesterol

Figure 4: Negative linear relationship between MDA and TAG

diagrams between MDA and each lipid profile parameter also showed no correlation.

In our correlation coefficient analysis study, we could not establish a statistically significant linear relationship between increased oxidative stress and abnormal lipid profile parameters, except TAG which showed a significant negative correlation. This clearly suggests that increased oxidative stress and abnormal lipid profile are two independent risk factors in the pathomechanism of atherogenesis. The same study should be verified on a big sample size.

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