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Research Article

A COMPARATIVE STUDY OF NOVEL INFLAMMATORY MARKERS (HIGH SENSITIVITY C - REACTIVE PROTEIN AND LIPOPROTEIN A) AND LDL/HDL CHOLESTEROL RATIO IN ACUTE CORONARY SYNDROME AT TERTIARY CARE CENTRE IN CENTRAL INDIA

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A B S T R A C T

Background: In India, cardiovascular disease (CVD) is one of the leading causes of death. All subjects are not accurately predicted for risk of CVD by traditional risk factors. To improve the present risk prediction model, a search of novel biomarkers is required to recognize the risk of cardiovascular events. Novel biomarkers involved in inflammation cascade and developing atherosclerosis and coronary heart disease are of utmost importance. **Aims and Objectives:** To study high sensitivity C-reactive protein (hs-CRP), lipoprotein A and LDL/HDL cholesterol ratio in acute coronary syndrome (ACS) and its association with ACS severity. **Materials and Methods:** Eighty patients (aged 18-70 years of either sex) with ACS (diagnosed based on clinical history, clinical examination, electrocardiogram changes, and creatine phosphokinase-MB) were studied at a tertiary care hospital from 2017 to 2020. High Sensitivity C - reactive protein (hs-CRP), lipoprotein A, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were estimated from patients' blood samples, and the association was obtained. **Results:** Incidence of ACS was highest in 56-65 years (28.75%) male (85%) patients. The most common diagnosis was ST-elevation myocardial infarction (78.75%). The hs-CRP levels and lipoprotein A were increased in 49 and 44 patients out of 80, respectively. Patients with high hs-CRP (n=43 of 48; $p<0.0001$) and lipoprotein A (n=32 out of 48; $p=0.026$) at admission are prone for going into complications. **Conclusion:** hs-CRP and lipoprotein A levels obtained at admission in ACS patients can be used to identify patients who are likely to develop significant complications in the immediate in-hospital course and predict the prognosis.

INTRODUCTION

About one-fourth of the Indian mortality is due to coronary heart disease (CHD). India's age-standardized CHD death rate is much higher than the global average (272 vs. 235 per 100,000 population).[1] For the pathophysiology of CHD, inflammation is a significant contributing factor. Inflammatory processes also play an essential role in developing atherosclerosis.[2] Recent research has concentrated on novel biomarkers of inflammation to determine whether they might aid in risk stratification and identify patient groups who may benefit from specific treatment options.[3] Of these biomarkers, high sensitivity C-reactive protein (hs-CRP)[4], lipoprotein A[5], and low-density lipoprotein (LDL)/high-density lipoprotein (HDL) cholesterol ratio6have emerged as one of the most important novel inflammatory markers. The commercial availability of hs-CRP, lipoprotein A and LDL/HDL cholesterol ratio assays has made screening for this marker simple, reliable, and reproducible.[7] It can be used as a clinical guide to the diagnosis, management, and prognosis of CHD.[7]However, evidence on the usefulness of these novel biomarkers as a risk factor of the acute coronary syndrome (ACS) is scarce. Hence present study assessed the role of hs-CRP and lipid abnormalities as risk factors for ACS.

MATERIALS AND METHODS

A prospective observational study was performed on 80cases of ACS at the Department of Medicine, NSCB Medical College & Hospital, Jabalpur, from 2017 to 2020.

Patients were aged 18-70 years, and both sexes diagnosed as an ACS based on clinical history, clinical examination, electrocardiogram (ECG) changes, and creatine phosphokinase-MB (CPK-MB) were included. Patients with hematological malignancy, chronic heart failure, connective tissue disorders, cerebral stroke, pulmonary embolism within 6 months, therapy with steroids, immunosuppressant agents and non-steroidal anti-inflammatory drugs (excluding low dose aspirin), any inflammatory disease like systemic lupus erythematosus, rheumatoid arthritis, and pregnant females were excluded from the study. Written informed consent was taken from the cases after explaining the procedure. A detailed history was elicited from the patients, and general physical examination and systemic examination were carried out. With

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all aseptic precaution, a 6ml blood sample from the antecubital vein of ACS patient was taken in the non-EDTA vial; 2ml for hsCRP, 2ml for lipoprotein A and 2ml for LDL and HDL (obtained within 6 hours of admission). Fasting lipid profile was done with the ERBA XL300 autoanalyzer. Total cholesterol, Triglycerides, and HDL were estimated, and Friedwald's equation calculated LDL: LDL Cholesterol = Total cholesterol - Triglycerides/5 - HDL-C.

hs-CRP in serum was measured by turbidimetric immunoassay and carried out in a semi-automated analyzer-NEXGEN. Lipoprotein A was measured on the latex immunoturbidimetric assay and applied to COBAS MIRA (Roche).

Statistical method

Data was entered in MS Excel 2010 worksheet and exported in SPSS V22.0 for windows for statistical analysis. Categorized data were numerically coded and tabulated in frequency and percentage. Continuous variables were summarised in mean and standard deviation. Pearson's chi-square and Fisher's exact test were applied as appropriate. Statistically, analysis was performed using SPSS V22.0 for windows. The level of significance was assessed at 5%.

RESULTS

Maximum incidence of ACS was observed in the age group between 56-65 years [23(28.75%)], followed by 22(27.5%) in both 36-45 years and 46-55 years age group, and 10(12.5%) in 66-70 age group. The mean age was 53.11 years. Of the 80 patients, 85% (n=68) patients were males and 15% (12) were females. The mean age of incidence in males was 52.79 years and that for females 54.91 years. Out of the all 80 patients studied, 63(78.75%) had STEMI, 11(13.75%) suffered from NSTEMI, and 6 (7.5%) suffered from UA; of 63 STEMI, 55 were males and 8 females; of 11 NSTEMI, 9 were males and 2 females, and of 6 UA, 4 were male, and 2 were female. The most common risk factors were smoking [51 (63.8%)] followed by dyslipidemias [44 (55%)] and hypertension [33 (41.3). Alcoholism [15 (18.8%)] and diabetes mellitus [13(16.3%)] were other common risk factors.

Out of 63 patients who had STEMI, the distribution of lesions was as follows: Extensive anterior wall involvement was the most common type [31 (49.2%)] followed by inferior wall [19 (30.15%)], anteroseptal [11 (17.46%)] and anterolateral [2 (3.17%)]. Out of 80 patients, 48 (60%) developed complications. Left ventricular failure (LVF) was the most common complication seen in 75% (n=36), followed by cardiogenic shock (CS) in 10.42 % (n=5), atrioventricular block(AVB) in 6.25%(n=3), and bundle branch block(BBB) in 6.25%(n=3) patients and 2% (n=1) had ventricular tachycardia/ ventricular fibrillation (VT/VF).

In present study, 49(61.25%) patients had hs-CRP levels detectable (>3 mg/L), of that LDL/HDL ≥3 in 29(36.25%) of cases and <3 in 51(63.75%) cases(p=0.40).

Table 1 Post ACS complications concerning hs-CRP and Lipoprotein Alevels

Complications	hs-CRP		Lipoprotein	
	<3	≥3	<30	≥30
Left ventricular failure (n=36)	2	34	10	26
Cardiogenic shock (n=5)	1	4	3	2
Bundle branch block (n=3)	1	2	1	2
Atrioventricular block (n=3)	1	2	1	2
VT/VF (n=1)	0	1	1	0
Total (n=48)	5	43	16	32
P-value	<0.0001		0.026	

Table 2 Comparing hs-CRP and Lipoprotein A levels with ACS

Complications	Hs-CRP		Lipoprotein A	
	<3	≥3	<30	≥30
STEMI (n=63)	25	38	28	35
NSTEMI (n=11)	4	7	6	5
UA (n=2)	2	4	2	4
Total (n=80)	31	49	36	44
P-value	0.12		0.71	

In our study, 44(55%) patients had lipoprotein A levels detectable (≥30 mg/L), of that LDL/HDL ≥3 in 29(36.25%) of cases and <3 in 51(63.75%) cases (p=0.361).

Figure 1: Comparing hs-CRP level with complicatons

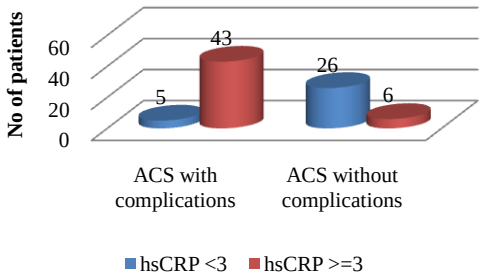
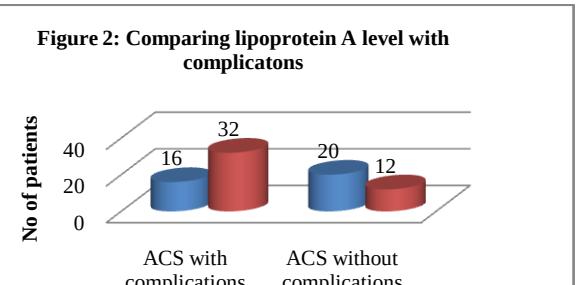


Figure 2: Comparing lipoprotein A level with complicatons



DISCUSSION

As a general guideline, novel risk markers should be physiologically plausible, quantifiable, and reproducible and should exhibit a robust and graded association with the disease. To be accepted in a clinical setting, the marker should be widely available and have an accurate assay with acceptable variability. A marker contributing to inflammation, atherosclerosis, and instability of atherosclerotic plaques should be considered. In the present study, hs-CRP levels and lipoprotein A levels obtained at admission in ACS patients can be used to identify patients who are likely to develop significant complications in the immediate in-hospital course and predict the prognosis.

In the present study mean age of occurrence of ACS was 53.11 years. In Suleiman *et al.*'s 8 study and Foussas *et al.*[9] study, the mean age was the seventh decade. In the Indian subcontinent, coronary artery diseases occur a decade earlier than the western population. So mean age of our patients is comparable to the studies mentioned above.

In our study, 80 patients were taken out of the majority were males (85%). This is nearly similar to Foussas *et al*. (79% males)[9] and Suleiman *et al*. (80% male)8study.

In our study, smoking was the most common risk factor (63.8%) for ACS. In the Foussas *et al*. 9study, smoking was observed in 57% of patients. In Suleiman *et al*.'s 8study, 40% of ACS patients were smokers. In Yusuf *et al*.'s study, 65.19% of patients were smokers.[10]

In our study, 55% of patients had lipid abnormalities. The most common lipid abnormalities were high triglycerides. In the Foussas *et al*.[9] study, 64.6% of patients had lipid abnormalities, and in Suleiman *et al*. [8] study, 41% of patients had dyslipidemias. Among 80 patients, LDL/HDL ratio was greater than 3 in 23 patients and less than 3 in 57 patients. So the ratio provides a significant ($p<0.05$) association with the incidence of myocardial infarction.

In our studies, 41.3% of patients had hypertension as the risk factor; this correlates with other studies. In the Singh *et al*. study, hypertension was seen in 33% of patients.[11]In the Foussas *et al*.[9] study, hypertension was seen in 51% of patients, and in Suleiman *et al*. 8study, hypertension was present in 53% of patients. In the "INTER HEART" study by Yusuf *et al*., hypertension was seen in only 19.3% of patients; however, they only considered the South Asian population.[10]

In our study, 78% of patients had ST-elevation myocardial infarction. A similar number of patients had STEMI in the Suleiman *et al*. study.[8]

In our study, 75% of patients had left ventricular failure followed by cardiogenic shock, which was present in 10.42% of patients. Bundle branch block and the atrioventricular block was present in 6.25% of patients, whereas the least common complication was ventricular tachycardia (2%). In Bahit *et al*.'s study[12], the prevalence of cardiogenic shock complicating MI varies between 5% and 15%, similar to our study.

In the present study, 61.25% of patients had raised levels (>3mg/dl) of hs-CRP. Out of 49 patients, 43 had complications, and 6 patients had no complications ($p<0.0001$). Behera *et al*. concluded that hs-CRP is a better and independent marker than Lp(a) in patients with CHD.[13]

In the present study, 55% of patients had raised levels (>30mg/dl). Out of 44 patients, 32 had complications, 12 patients had no complications, and 36 (45%) patients had lipoprotein A levels (< 30mg/dl), which was significantly high. Watts*et al*. reported that lipoprotein A is a powerful and independent risk factor for MI.[14]

Out of 63 STEMI patients, hsCRP levels were ≥3mg/L in 38 cases, out of 11 NSTEMI patients, hsCRP was elevated in 7 cases, and out of 6 UA patients, hsCRP was elevated in 4 cases ($p=0.12$) which was not significant may be because of small sample size. More STEMI patients have increased levels of hs CRP when compared to NSTEMI and UA. In Habib *et al*.'s study, it is concluded that patients with angiographically evaluated CAD have significantly higher hs-CRP levels than healthy individuals and are correlated with the presence & severity of CAD.[15]

Out of 80 patients, 44 (55%) patients had increased lipoprotein a levels, whereas they decreased in 36 (45%) patients. In Watts *et al*. study, in middle-aged men with familial hypercholesterolemia, the serum concentration of lipoprotein A is a powerful and independent risk factor for MI. [14]

In the present study, 29% of patients had LDL/HDL ratio >3, whereas 51% had LDL/HDL ratio <3. LDL/HDL cholesterol ratio >3 was present in 16 patients with hsCRP >3, whereas <3 the ratio was present in 33 patients with hsCRP >3, which was not statistically significant because of the small sample size. In the Thaned *et al*. study, 76 male and 24 female patients were found. hsCRP was elevated in 68 patients, out of which only 6 patients had LDL/HDL ratio >3 ($p<0.01$), and among 32 patients in whom hsCRP were not elevated, only 4 patients had LDL/HDL ratio >3.[16]

In our study, 44 (55%) patients had lipoprotein A levels detectable (> 30 mg/L); LDL/HDL ≥3 in29 (36.25%) of cases and <3 in 51(63.75%) cases ($p=0.361$). In the Cai *et al*. study, Lp(a) values were significantly associated with AMI risk in participants with normal LDL-C levels.[17]

In our study, lipoprotein A was elevated in 44 patients. Among them, 32met with complications, which is significant ($p=0.01$). In Mitsuda T *et al*.'s study, lipoprotein A levels at admission independently predict secondary vascular events in patients with STEMI.[18]Waldeyer *et al*. study Lp (a) as a marker of cardiovascular risk with a particular increase of the Lp (a)-associated risk for MCE and CVD events above the 66th and the 90th percentile.[19]

CONCLUSION

Plasma hsCRP and lipoprotein A levels on admission identify high-risk patients in the setting of the ACS. The LDL/HDL ratio was increased in less number of patients. So the raised hs-CRP level and lipoprotein A level are more significant with the ACS than the LDL/HDL ratio. Raised hsCRP levels and lipoprotein A levels are independent markers of adverse outcomes. Hence, hsCRP levels and lipoprotein A levels obtained at admission in ACS can be used to identify patients who are likely to develop significant complications in the immediate in-hospital course and predict the prognosis.

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