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LOW-DENSITY LIPOPROTEIN AND SERUM HIGH SENSITIVE C-REACTIVE PROTEIN IN SERUM AS DIAGNOSTIC MARKERS OF ACUTE CORONARY SYNDROME

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Abstract:

Background: *Acute coronary syndrome (ACS) remains the leading cause of mortality and morbidity worldwide. The level of lipoproteins and low-density cholesterol (LDL-C) is a major risk factor for the development of ACS and the pathogenesis of atherosclerosis. Atherosclerosis is a multi-stage disease characterized by low-grade chronic vascular inflammation that plays a role at every stage from onset, progression to plaque rupture, and then triggers ACS. Increasing the level of the highly sensitive C-reactive protein (hs-CRP) is a strong and independent prognostic factor for cardiovascular diseases.*

Aim: *The aim of the study was to evaluate the role of LDL-C and hs-CRP in the serum of patients with ACS.*

Place and Duration: *In the cardiology department of Sir Ganagaram Hospital Lahore for one-year duration from August 2019 to August 2020.*

Patients and Method: *The present study enrolled 45 patients with confirmed ACS and 30 apparently healthy people of the same age and gender as controls. The patients were divided into three subgroups, each of which included 15 patients: Subgroup A: STEMI (STEMI). Subgroup B: Non-ST segment elevation myocardial infarction (NSTEMI), Subgroup C: Unstable angina (UAP). All patients and controls were measured for low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol, triglycerides, highly sensitive CRP (hs-CRP), cardiac troponin I (cTnI) and creatine kinase-MB fraction (CK-MB), electrocardiography (EKG) and transthoracic echocardiography.*

Results: *In group I there was a very significant increase in the concentration of LDL-C and hs-CRP in the serum compared to group II ($p = 0.001$) and a significant increase in the concentration of LDL-C in the serum (($p < 0.05$) and a very significant increase in hs-CRP concentration ($P = 0.01$) in the STEMI and NSTEMI subgroups compared to the UAP subgroup and a very significant increase in serum LDL-C ($p = 0.005$) and serum hs-CRP ($p = 0.003$) in the UAP subgroup compared to group II. In all subgroups, a positive and significant correlation was also found between serum LDL-C level and both serum CK-MB and serum hsCRP.*

Conclusion: *Elevated serum levels of LDL and hs-CRP may serve as markers of disease severity, which helps in the assessment and treatment of patients with ACS.*

Keywords: *Acute coronary syndrome - lipid profile - Hs-CRP.*

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INTRODUCTION:

ACS remains the leading cause of mortality and morbidity worldwide, including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UAP). the presence of permanent high degree coronary obstruction due to increased myocardial oxygen and nutritional needs, for example, from exercise, emotional stress, or physiological stress, e.g., dehydration, blood loss, hypotension, infection, thyrotoxicosis, or surgery. The diagnosis of an acute myocardial infarction in this situation requires the detection of a typical increase in the biochemical markers of myocardial necrosis on the electrocardiogram, in addition to at least one of the following: ischemic symptoms, pathological Q wave development and ischemic ST segment changes.

ACS is mainly caused by atherosclerosis. Most cases of ACS occur as a result of disruption of a previously non-severe lesion (an atherosclerotic lesion that was previously hemodynamically insignificant but prone to rupture). Sensitive plaque is characterized by a large lipid pool, numerous inflammatory cells and a thin fibrous cap. The rupture of atherosclerotic plaque caused by dissolution of the fibrous cap is believed to be the main trigger of coronary thrombosis, and dissolution itself is due to the release of metalloproteinase (collagenase) from activated inflammatory cells. This event is followed by activation and aggregation of platelets, activation of the clotting pathway, and vasoconstriction. This process culminates in intraluminal coronary thrombosis and variable degrees of vessel occlusion. Distal embolization may occur. The severity and duration of coronary obstruction, the volume of the affected heart muscle, the level of heart demand, and the ability of the rest of the heart to compensate are the main determinants of the patient's clinical picture and outcome.

The five major groups of lipoproteins, which are ordered in size from largest to smallest, are chylomicrons, VLDL, IDL, LDL, and HDL. Low-density lipoprotein (LDL) enables the transport of a wide variety of fat molecules, including cholesterol, in the water around cells and in the aqueous bloodstream. Higher levels of B-type LDL particles are conducive to health problems and cardiovascular disease, and are often informally called bad cholesterol particles (as opposed to HDL particles, which are often referred to as good cholesterol or healthy cholesterol particles).

Inflammation plays a key role in initiating and promoting atherosclerotic lesions and can trigger ACS by inducing plaque instability. C-reactive protein (CRP) is a widely studied inflammatory factor, therefore its prognostic value in cardiovascular diseases has become increasingly important in recent years. Moreover, CRP is no longer considered only a marker but also appears as a mediator of atherosclerosis. Finally, it remains unresolved whether CRP is a potential therapeutic target or simply reflects an increased risk of an adverse outcome as a mock marker.

Objective:

Therefore, the aim of this study was to evaluate the role of LDL-C and hs-CRP in the serum of patients with ACS.

PATIENTS AND METHOD:

The present study involved 45 patients with ACS who were admitted in the cardiology department of Sir Ganagaram Hospital Lahore for one-year duration from August 2019 to August 2020 as group-I. These were 12 (26.7%) women and 33 (3.3%) of men aged 30 to 80 years. The remaining 30 apparently healthy subjects of the same age and gender were included in the study as healthy controls (group II). It was 9 (30%) women and 21 (70%) men aged 38 to 87 years. Prior to study initiation, approval was obtained from the ethics committee and informed consent from all participants.

Patients and controls were divided into the following groups and subgroups:

Patients from group I (45): were divided into three subgroups according to the conducted research and current guidelines:

a) STEMI as group (A) included 15 patients: 14 (93.3%) men and 1 (6.7%) woman. Their ages ranged from 30 to 80 years. With an average of 54.73 ± 12.81 years.

b) NSTEMI as group (B) included 15 patients: 10 (66.7%) men and 5 (33.3%) women: their age ranged from 40 to 76 years. with a mean of 58.2 ± 9.60 years.

c) UAP as group (C) included 15 patients: 9 (60%) men and 6 (40%) women. Their age ranged from 34 to 85 years, mean 56.33 ± 13.52 years.

II - healthy control group as group II: 9 (30%) women and 21 (70%) men aged 38-87 years. with an average of 55.16 ± 11.11 years.

A complete adult health interview and comprehensive physical examination were performed.

All participants of the study were subjected to:

1- Standard 12-lead electrocardiography (ECG).
2- Transesophageal echocardiography.
3- Chest radiography.

4- Laboratory tests: total cholesterol, triglycerides, LDL-C, HDL-C, total creatine kinase (CK), CK-MB, cardiac troponin I (cTnI) and serum hs-CRP.
Fasting (12-16 hours) 3 ml venous blood samples were collected from each patient, allowed to clot, and centrifuged at 1000 xg for 15 minutes. HDL-C was determined immediately and the remainder of the serum was stored at -20 ° C for the remainder of the study. The determination of total cholesterol and serum triglycerides was performed on a Hitachi 912 automated analyzer (Hitachi, Roche, Japan). The HDL fraction was measured with an automatic Hitachi analyzer as described by Primatesta and Poulter [9]. LDL-C was calculated according to Friedwald formula.
Total CK was determined by the kinetic UV method (Hartman et al., 1998) supplied by Intermedical (Intermedical sri, Vallaricca, Italy). Serum MB CK (CK-MB) isoenzyme was measured by an immunochemical-luminometric assay.

EXCLUSION CRITERIA:
Patients with chronic liver cell failure, chronic renal failure and diabetes were excluded.

Statistical analysis:
Data was collected, revised, coded and entered into the Social Science Statistical Package (SPSS) version 17 using the Chi-square test and / or Fisher's independent t-test, the Mann-Whitney test. Pearson and Spearman correlation coefficient.

RESULTS:
We found a highly significant increase in serum LDL-C (p = 0.001), serum hs-CRP (p = 0.001), and serum CK-MB (p = 0.001) in group I compared to group II. The serum concentration of cTn I increased in group I, as 30 (66.70%) patients were positive and the remaining 15 (33.30%) were negative compared to group II (Table 1).

Table (1): Comparison of laboratory parameters between groups I and II.

Parameters	Group I	Group II	P	Sig.
	Mean ± SD	Mean ± SD		
Age (years)	56.42±11.90	55.16±11.11	> 0.05	NS
LDL-C(mg/dl)	122.58±26.11	59.11±12.99	0.001	HS
CRP (mg/dl)	16.49±3.39	4.28±1.26	0.001	HS
CK-MB (U/L)	172.71±36.98	16.00±3.50	0.001	HS
Troponin I: :n,% Positive Negative	 30 (66.70%) 15 (33.30%)	 0 (0 %) 30 (100 %)		

We found a highly significant increase in the concentration of LDL-C and hs-CRP in the serum in the STEMI and NSTEMI subgroups (P = 0.001) compared to group II. Comparison of serum cTn I between the STEMI and NSTEMI subgroups showed that 15 (100%) patients were positive (Table 2, 3) compared to group II. In the UAP subgroup (p = 0.001), a very significant increase in the concentration of LDL-C and hs-CRP in the serum was found compared to group II. There was a non-significant difference in serum CK-MB in the UAP subgroup compared to the II group (P> 0.05). All patients in the UAP subgroup and group II had negative serum cTn I result (Table 4).

Table (2): Comparison of laboratory parameters between subgroup A versus group II.

Parameters	Subgroup A Mean ± SD	Group II Mean ± SD	p-value	Significant
LDL-C(mg/dl)	115.04±25.96	59.11±12.99	0.001	HS
CRP(mg/dl)	19.55±4.38	4.28±1.26	0.001	HS
CK-MB (U/L)	269.44±65.66	16.00±3.50	0.001	HS
Troponin I:n,% Positive Negative	 15 (100 %) 0 (0 %)	 0 (0 %) 30 (100%)		

Table (3): Comparison of laboratory parameters between subgroups B versus group II.

Parameters	Subgroup B Mean ± SD	Group II Mean ± SD	p-value	Significant
LDL-C(mg/dl)	142.23±41.72	59.11±12.99	0.001	HS
CRP (mg/dl)	17.08±4.02	4.28±1.26	0.001	HS
CK-MB (U/L)	213.27±51.74	16.00±3.50	0.001	HS
Troponin I:n,% Positive Negative	15(100 %) 0(0 %)	0 (0 %) 30 (100.0%)		

Table (4): Comparison of laboratory parameters between subgroup C versus group II.

Parameters	Subgroup C Mean ± SD	Group II Mean ± SD	p-value	Significant
LDL-C(mg/dl)	85.14 ± 15.95	59.11 ±12.99	0.005	HS
CRP (mg/dl)	12.37 ± 4.25	4.28 ±1.26	0.001	HS
CK-MB (U/L)	18.71 ± 2.87	16.00 ± 3.50	0.144	NS
Troponin I :n,% positive negative	0 (0 %) 15 (100%)	0 (0 %) 30 (100%)		

When comparing serum LDL-C, hs-CRP, and serum CK-MB levels in the STEMI and NSTEMI subgroups, non-significant differences were found (p = 0.095, 0.029, and 0.330, respectively). Comparison of serum cTn I between the STEMI and NSTEMI subgroups showed that all patients in the STEMI and NSTEMI subgroups were positive for serum cTn I (Table 5 and Fig. 1).

Table (5): Comparison of laboratory parameters between subgroup A versus group B.

Parameters	Subgroup A Mean ± SD	Subgroup B Mean ± SD	p-value	Significant
LDL-C(mg/dl)	115.04±25.96	142.23±41.72	0.095	N S
CRP(mg/dl)	19.55±4.38	17.08±4.02	0.029	N S
CK-MB (U/L)	269.44±65.66	213.27±51.74	0.330	N S
Troponin I:n,% positive negative	15 (100 %) 0 (0 %)	15(100 %) 0 (0 %)		

In the STEMI subgroup, a highly significant increase in serum LDL-C and hs-CRP was found (p = 0.024, 0.003 and 0.001, respectively). The comparison of serum cTn I between the STEMI subgroup showed that all patients in the STEMI subgroup (100%) were positive, and all patients in the UAP subgroup were negative (Table 6 and Fig. 1).

Table (6): Comparison of laboratory parameters between subgroup A versus subgroup C.

Parameters	Subgroup A Mean ± SD	Subgroup C Mean ± SD	p-value	Significant
LDL-C(mg/dl)	115.04±25.96	85.14±15.95	0.024	HS
CRP (mg/dl)	19.55±4.38	12.37±4.25	0.003	HS

CK-MB (U/L)	269.44±65.66	18.71±2.87	0.001	HS
Troponin I: n,% positive negative	15 (100 %) 0 (0 %)	0 (0%) 15 (100%)		

In the NSTEMI subgroup, there was a significant increase in serum LDL-C, hs-CRP and serum CK-MB levels (p = 0.046, 0.01, 0.001, respectively). In the NSTEMI subgroup, a very significant increase in serum cTn I concentration was found, as all patients (100%) were positive compared to the UAP subgroup, because all patients were negative (Table 7 and Fig. 1).

Table (7): Comparison of laboratory parameters between subgroups B versus subgroup C.

Parameters	Subgroup B Mean ± SD	Subgroup C Mean ± SD	p-value	Significant
LDL-C (mg/dl)	142.23 ± 41.72	85.14 ± 15.95	0.046	S
CRP (mg/dl)	17.08 ± 4.02	12.37 ± 4.35	0.010	HS
CK-MB (U/L)	213.27±51.74	18.71 ± 2.87	0.001	HS
Troponin I:n,% positive negative	15)100 %) 0 (0 %)	0 (0%) 15 (100%)		

Table (8): Correlation between serum LDL-C versus serum CK-MB and serum hs-CRP in all subgroups.

Parameters	LDL-C Subgroup A			LDL-C Subgroup B			LDL-C Subgroup C		
	R	pvalue	Sig	r	p-value	Sig	r	p-value	Sig
CK-MB (U/L)	0.643	0.010	S	0.847	0.001	HS	0.573	0.032	S
CRP(mg/dl)	0.956	0.001	HS	0.933	0.001	HS	0.968	0.001	HS

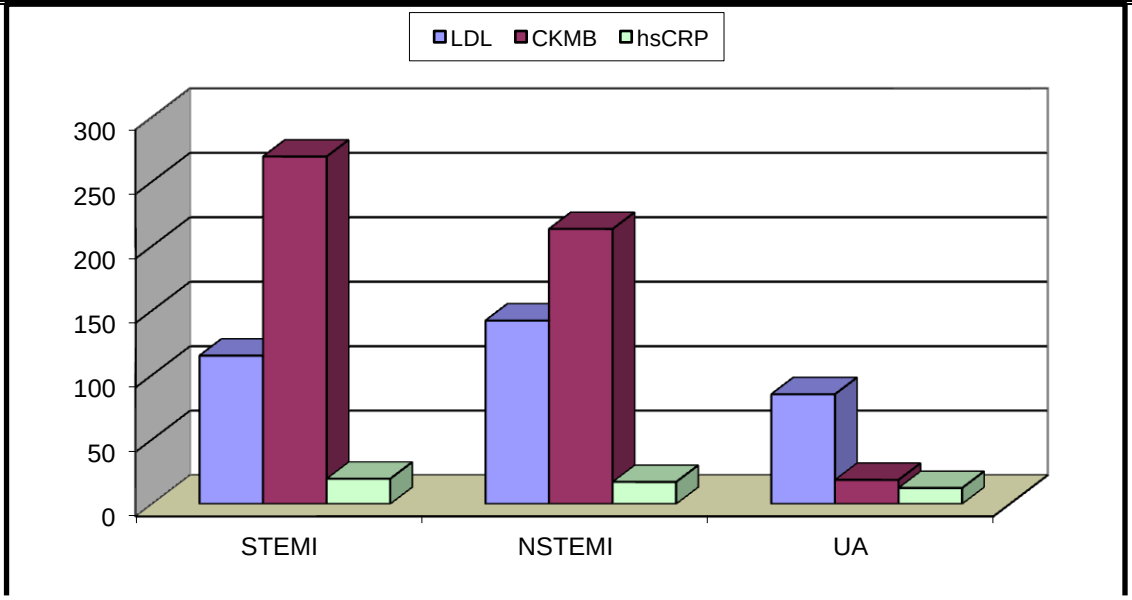

Figure (1): Comparison of serum LDL, serum CK-MB and serum hs-CRP in subgroups A, B and C.

DISCUSSION:

ACS is caused by an inflammatory response and plaque degradation, and is mainly caused by atherosclerosis. Elevated LDL-C levels showed a significant positive correlation with the severity of ACS and this observation suggests that elevated LDL-C levels are associated with instability of atherosclerotic plaques in the coronary arteries. Other studies found that the increase in CRP was associated with plaque rupture in patients with ACS. In the present study, we found a very significant increase in serum LDL-C concentration in patients with ACS compared to the control group, as well as a very significant increase in serum LDLC in patients with STEMI, NSTEMI and UAP compared to healthy controls. Krintus et al. Show a significant increase in serum LDL concentration in patients with ACS than in healthy subjects. In our study, the analysis of serum LDL-C concentration among patients with ACS showed no significant difference between patients with STEMI and NSTEMI and a very significant increase in both STEMI and NSTEMI compared to patients with UAP. These results were in agreement with Ehara and his colleagues; who show a significant increase in serum LDL concentration in the AMI group compared to the UAP group. The present study found a very significant increase in serum hs-CRP levels in patients with ACS compared to healthy controls. These results were in agreement with the result obtained by Krintus and his associates who found it; CRP levels in patients with ACS were 4 times higher than in healthy subjects. In our study, we found a very significant increase in serum hs-CRP levels in patients with STLMI, NSTEMI, and UAP by comparing each subgroup with a healthy control group. Hence, the assessment of diagnostic accuracy confirmed the very good ability of CRP to distinguish between cases and controls. There was also a non-significant difference in serum hs-CRP concentration in the case of STEMI compared to patients with NSTEMI. Serum hs-CRP levels showed a highly significant difference in STEMI and NSTEMI compared to each subgroup for UAP patients. These observations were consistent with the results of other investigators who found higher CRP levels in patients with myocardial infarction than in stable or unstable coronary artery disease. These results were also in agreement with Krintus and his colleague who showed that the highest levels of CRP were observed in patients with STEMI and NSTEMI than in patients with UA.

CRP levels are higher in patients with STEMI than in patients with NSTEMI, with a further and significant decrease in CRP in patients with UAP compared to STEMI and NSTEMI. Therefore, the observed variation in CRP levels between ACS types can be at least partially attributed to differences in the area of myocardial infarction. This can be explained by CRP, which has been found in atherosclerotic lesions and binds to LDL, is then taken up by macrophages without the need to modify it, and promotes inflammation by disrupting thromboregulation by inhibiting prostacyclin synthase expression, while potentially increasing the thromboxane A2 bioactivity present in atherosclerosis. . these changes then trigger platelet aggregation and smooth muscle contractions, which are prone to plaque rupture and thrombosis and the development of ACS.

CONCLUSION:

Elevated serum levels of LDL and hs-CRP can serve as markers of disease severity to assist in the evaluation and treatment of patients with ACS. Thus, more severe changes were associated with high serum LDL and serum hs-CRP levels.

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