CORRELATION OF SERUM LOW-DENSITY LIPOPROTEIN CHOLESTEROL WITH GRACE AND TIMI SCORES TO PREDICT 30 DAYSMORTALITY FOLLOWING ACUTE CORONARY SYNDROME

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ABSTRACT

Objective: To assess the relationship of serum LDL-C and HDL-C levels with Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) Scores to predict all-cause 30 days mortality following first onset Acute Coronary Syndrome (ACS).

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Inpatient departments of Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi, from Jan 2019 to Jun 2019.

Methodology: Ethical approval was taken from Institutional Ethical Review Board (IERB), AFIC/NIHD. Patients of any age and both genders who presented with chest pain and satisfied criteria for type 1 Myocardial Infarction (MI), as stated in 4th Universal Definition of MI, were included in study by non-probability consecutive sampling technique. Patients with a previous history of ischemic heart disease, Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Graft (CABG) surgery and patients taking lipids lowering medications over at least 3 months prior to admission were excluded. Both TIMI and GRACE scores for ST Elevation MI (STEMI) and Non-ST Elevation MI (NSTEMI) were calculated at time of admission. One non fasting blood sample was drawn for serum lipid levels from each patient within 24 hours of hospital admission and was analyzed using ROCHE cobas 6000 c501 analyzer. Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 25.

Results: Out of 236 patients, 210 were male and 26 were female. Minimum recorded age was 25 years and maximum 90 years. Subjects presented with NSTEMI seem older (65.5 ± 7.3 years) than the ones presented with STEMI (59.7 ± 12.5 years). Anterior wall MI was the most common presentation (35%). Hypertension was the most common (57.6%) risk factor noted for Coronary Artery Disease (CAD). Serum lipids had a higher trend among STEMI subjects than NSTEMI and a lower trend among deceased subjects, as compared to survivors, in both STEMI and NSTEMI groups. Negative correlations were recorded between LDL-C and GRACE score in STEMI group (-0.277) and between HDL-C and both GRACE and TIMI scores (-0.349 and -0.299, respectively) in NSTEMI group.

Conclusion: A significant paradoxical lower levels of serum lipids were found in deceased subjects who presented with ACS.

Keywords: Acute coronary syndrome, ACS, LDL, HDL, TIMI, GRACE.

INTRODUCTION

Plasma lipoprotein levels are recognized as independent risk factor for long-term cardiovascular (CV) events, with high levels of low-density lipoprotein cholesterol (LDL-C) associated with increased CV risk and high levels of high-density lipoprotein cholesterol (HDL-C) associated with decreased CV risk[1-4]. A direct relationship of serum lipids levels are present with atherosclerotic plaque formation and progression. Raised lipid levels also affect the process of thrombosis and thus the outcomes of an acute CV event[5].

There are studies available evaluating and linking relationship between in-hospital lipoprotein levels and in-hospital adverse CV outcomes following acute coronary syndrome (ACS),[6-8] however no study is available to correlate lipoproteins levels with established risk scoring systems to predict all cause in-hospital mortality.

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Global Registry for Acute Coronary Events (GRACE) and the Thrombolysis in Myocardial Infarction (TIMI) are the recommended risk scoring systems for clinical assessment and predicting prognosis among patients presenting with ACS[6-9].

This study assessed the relationship of GRACE and TIMI scores predicting all-cause 30 days mortality following acute myocardial infarction (AMI) with in-hospital plasma LDL-C and HDL-C levels after first onset ACS.

METHODOLOGY

It was a descriptive cross sectional study conducted at inpatient departments of Armed Forces institute of cardiology and National institute of heart diseases, Rawalpindi from 1st January 2019 to 30th June 2019. Ethical approval was taken from Institutional Ethical Review Board (IERB), AFIC/NIHD. Patients of any age and both genders who presented within 12 hours of onset of chest pain or within 12 to 24 hours of onset of chest pain having ongoing symptoms who satisfied criteria for type 1 Myocardial Infarction (MI), as stated in 4th Universal Definition of MI13, were included in study by non-probability consecutive sampling technique.

Patients with a previous history of ischemic heart disease, previous Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Graft (CABG) surgery and patients taking lipid lowering medications over at least 3 months prior to admission were excluded from study.

Informed written consent was taken from patients and/or patients' family. Risk factors assessment for CAD was done through detailed medical history and clinically relevant laboratory investigations.

Thrombolysis in Myocardial Infarction (TIMI) and GRACE scores for ST Elevation MI (STEMI) AND Non ST Elevation MI (NSTEMI) were calculated at time of admission for each patient by using specific variables (age, risk factors for CAD, aspirin use, angina episodes, heart rate, weight, time to treatment, systolic blood pressure, serum creatinine, Killip class, cardiac arrest at admission, elevated cardiac markers, and ST-segment deviation).

One non fasting blood sample was drawn from each patient within 24 hours of hospital admission. Serum lipids levels were analyzed using ROCHE cobas 6000 c501 analyzer.

Data obtained was converted into variables and analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Numerical variables were presented in the form of mean and standard deviation. Categorical variables were analyzed as frequency and percentages.Continuous variables were compared using one-way ANOVA. Correlation between serum lipids and GRACE and TIMI scores were known by using Pearson's correlation.

RESULTS

A total of 236 patients were included in our study. Minimum age recorded was 25 years and maximum 90 years. Male subjects were 210 while female were 26, with male to female ratio 8.1:1. Subjects who presented with NSTEMI were older (65.5 ± 7.3 year) than the ones presented with STEMI (59.7 ± 12.5 year). Anterior wall MI was the most common presentation followed by Inferior wall MI and NSTEMI (35%, 31% and 18.6%, respectively). Among the risk factors for CAD, hypertension was the most common (57.6%) followed by diabetes mellitus (37.3%), smoking (31.8%) and family history for ischemic heart disease (12.3%). Analysis of lipids revealed a higher trend among subjects presented with STEMI than NSTEMI (table-I).

Comparison of serum LDL-C, HDL-C and VLDL cholesterol between survivors and deceased subjects revealed a significant downward trend among deceased subjects in both STEMI and NSTEMI groups. Average recorded GRACE and TIMI scores were also higher among deceased subjects in both STEMI and NSTEMI groups (table-II).

A negative correlation was recorded between serum LDL-C and GRACE score in

STEMI group (-0.277), while NSTEMI group showed a negative correlation between HDL-C and both GRACE and TIMI scores (-0.349 and -0.299, respectively). A positive correlation was noted between LDL-C and TIMI (0.307) in STEMI and with GRACE and TIMI in NSTEMI arms (0.307 and 0.642, respectively). Also HDL-C was found in positive correlation with GRACE and TIMI in STEMI arm (0.439 and 0.613, respectively) (table-III).

Table-I: Clinical parameters comparison among GRACElow, intermediate and high-risk groups.

	Clinical Parameters		Low Risk	Intermediate Risk	High Risk	Total
STEMI	Age (Mean ± SD) years		46.18 ± 9.23	58.5 ± 9.1	67.8 ± 9.3	59.7 ± 12.5
	Gender	Male n (%)	43 (25%)	59 (34.3%)	70 (40.7%)	172 (100%)
		Female n (%)	1 (5%)	6 (30%)	13 (65%)	20 (100%)
	Diabetes mellitus n (%)		10 (15.6%)	22 (34.3%)	32 (50%)	64 (100%)
	Hypertension n (%)		19 (18.8%)	37 (36.6%)	45 (44%)	101 (100%)
	Current smoking n (%)		16 (25.4%)	21 (33.3%)	26 (41%)	63 (100%)
	Family history for ischemic heart disease n(%)		7 (41.2%)	10 (58.8%)	-	17 (100%)
	Type of STEMI	Anterior n (%)	21 (25.3%)	29 (34.9%)	33 (39.8%)	83 (100%)
		Anterolateral n (%)	7 (33.3%)	4 (19%)	10 (47.6%)	21 (100%)
		Lateral n (%)	3 (42.9%)	2 (28.5%)	2 (28.5%)	7 (100%)
		Inferior n (%)	13 (16%)	30 (37%)	38 (46.9%)	81 (100%)
	S. Cholesterol mg/dl (Mean ± SD)		189.1 ± 30.32	175 ± 44.9	167.91 ± 50	175.2 ± 45
	Triglycerides mg/dl (Mean ± SD)		193.75 ± 155	157.2 ± 88	148.9 ± 111.7	162 ± 117
	S. LDL-C mg/dL (Mean ± SD)		110.2 ± 23	106 ± 35	102.3 ± 40.8	105.6 ± 35.4
	S. HDL-C mg/dL (Mean ± SD)		40.6 ± 12.8	34.8 ± 8.7	37 ± 9.4	37.1 ± 10.2
	S. VLDL mg/dL (Mean ± SD)		38.5 ± 31	30.9 ± 17.5	28.2 ± 20.4	31.5 ± 22.7
NSTEMI	Age (Mean ± SD)		62.6 ± 8	59.8 ± 6.6	66.8 ± 9	65.5 ± 7.3
	Gender	Male n (%)	5 (17.5%)	5 (17.5%)	28 (73.6%)	38 (100%)
		Female n (%)	-	-	6 (100%)	6 (100%)
	Diabetes mellitus n (%)		2 (5.2%)	2 (5.2%)	20 (83.3%)	24 (100%)
	Hypertension n (%)		4 (10.5%)	5 (13.1%)	29 (76.3%)	38 (100%)
	Current Smoking n (%)		4 (33.3%)	2 (16.7%)	6 (50%)	12 (100%)
	Family history for ischemic heart disease n (%)		-	2 (16.7%)	10 (83.3%)	12 (100%)
	S. Cholesterol (Mean ± SD)		214 ± 50	178 ± 25.6	152 ± 42	162 ± 45.5
	Triglycerides (Mean ± SD)		192.8 ± 48.4	122.6 ± 30.5	145 ± 57	147.9 ± 55.8
	S. LDL-C (Mean ± SD)		136.8 ± 51.9	110 ± 15.5	91.4 ± 33.4	98.7 ± 36.8
	S. HDL-C (Mean ± SD)		38.8 ± 1.3	43.6 ± 16.3	34.5 ± 9.9	36 ± 10.5
	S. VLDL (Mean ± SD)		38.4 ± 9.6	24.4 ± 6	28.8 ± 11.2	29.4 ± 11

DISCUSSION

This study supports the concept of lipid paradox in patients presenting with ACS. A falling trend in mean serum LDL-C and HDL-C levels was noted in STEMI patients as we move from GRACE low to high risk group (table-I).

It seems an interesting finding that one of the major risk factors responsible for CAD actually falls during an acute coronary event, adopting a new role from being one of the causative factors to a prognostic marker. There are few possible, but not ascertained, explanations for it including LDL-C being an inverse acute phase reactant that falls at the time of ACS[14]. Grammer *et al*[15] while showing an association between large LDL particle with CV mortalities, had also shown their association with raised inflammatory

markers, suggesting alternative explanation for this finding. While another justification could be the nutritive value of serum cholesterol as lower risk of deaths are seen in malnourished patients when there are higher cholesterol levels[16,17].

A statistically significant lower LDL-C, HDL-C and VLDL cholesterol was found among deceased subjects as compared to survivors in both STEMI and NSTEMI groups (table-II).

There are number of limitations to this study. First, it is a single center study and number of subjects included might be not enough to make outcomes generalized to all patients presented with ACS. Secondly, inferences are based on single serum lipidssample drawn from each subject within 24 hours of admission, without considering the baseline levels. Further that, knowing the trend in serum lipids over the course of days during index hospital admission might be more useful to predict prognosis.

Table-II: Comparison between serum lipids and risk scores in survivals and deceased subjects.

	STEMI			NSTEMI		
	Survivals	**Deceased**	***p***	**Survivals**	**Deceased**	***p***
S. LDL-C mg/dL (Mean ± SD)	107.6 ± 34.75	83.62 ± 36.6	0.009	108.7 ± 32.9	64.6 ± 28.8	0.0004
S. HDL-C mg / dL (Mean ± SD)	37.76 ± 10.4	30.18 ± 4.6	0.004	38 ± 10.9	29.4 ± 5.2	0.02
S. VLDL mg/dL (Mean ± SD)	32.2 ± 23	24 ± 12	0.016	31.2 ± 11.5	23.2 ± 6.4	0.04
GRACE Score (average)	148	206	0.0001	152	200	<0.0001
TIMI Score (average)	3.7	7.2	<0.0001	3.8	5.8	<0.0001

Table-III: Corelation between LDL-C and HDL-C levels with GRACE and TIMI scores among deceased subjects.

	STEMI		NSTEMI	
	GRACE	**timi**	**grace**	**timi**
ldl-c	-0.277	0.307	0.309	0.642
hdl-c	0.439	0.613	-0.349	-0.299

Study reported by Cheng *et al*, shows significantly higher mortality rates in patients with LDL-C less than 62.5 mg/dL and triglyceride less than110 mg/dL who were admitted as case of ACS[18].

Study reported by Roe *et al*, has demonstrated low HDL-C level below 30 mg/dL in one-fifth of NSTEMI patients and was found to be related with greater risk for index hospital admission mortality[11].

While study reported by Acharjee *et al*., has shown a relationship between low HDL-C at admission with greater risk of in-hospital death and an extensive and severe CAD at coronary angiography[12].

Our study gives an account of negative correlation of HDL-C with GRACE and TIMI scores among deceased subjects who had NSTEMI, and a negative correlation of LDL-C and GRACE score in deceased subjects who had STEMI (table-III).

CONCLUSION

Significant paradoxical lower levels of serum lipids were found in deceased subjects who presented with ACS. A negative correlation was found between HDL-C levels and GRACE and TIMI scores among deceased subjects who had NSTEMI, while LDL-C was negatively correlated with GRACE score among deceased STEMI subjects.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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