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Original Article

Internal Medicine Section

Looking Beyond LDL-Cholesterol - A Study on Extended Lipid Profile in Indian Patients with Acute Coronary Syndrome

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ABSTRACT

Introduction: Assessment of dyslipidemia with only Total Cholesterol (TC), Triglyceride (TGL), Low- and High-Density Lipoprotein Cholesterol (LDL-C, HDL-C) levels, Standard Lipid Profile (SLP), leads to under-estimation of dyslipidemia as a risk factor in Acute Coronary Syndrome (ACS).

Aim: To assess whether extended lipid profile gives a better risk assessment in ACS patients.

Materials and Methods: In this single-centre, prospective, observational study of statin-naïve patients presenting with ACS, SLP and Extended Lipid Profile (ELP), consisting of TC/HDL-C ratio, non-HDL-C, apolipoprotein-B, apolipoprotein-A1 and their ratio, were studied at baseline and after high-intensity statin therapy. For continuous data, descriptive statistics mean±standard deviation and also 25th-75th percentile was reported. Number of patients and percentages were reported for categorical data. Pearson correlation coefficient was used to find the relationship between continuous variables.

Results: In the present study, 139 patients (mean age 55 years, range 21-88 years, 78% male) presented with ACS: ST-Elevation Myocardial Infarction (STEMI) 79%, non-STEMI 17%, Unstable Angina (UA) 4%. The ELP (barring non-HDL-C) showed more dyslipidemia than SLP. Dyslipidemia declined across the age spectrum from young to old and worsened across the ACS spectrum from UA to STEMI. High-intensity statin therapy reduced LDL-C significantly but not to target levels in most patients.

Conclusion: ELP is better able to identify dyslipidemic risk than SLP or LDL-C alone. Dyslipidemia is more prevalent in young and STEMI patients, suggesting a greater role as risk factor in them. Achievement of target LDL-C with statin therapy remains practically elusive in most patients.

Keywords: Apolipoprotein b, Apolipoprotein a1, Dyslipidemia, Myocardial infarction

INTRODUCTION

Cardiovascular disease is a major cause of morbidity and mortality in India and dyslipidemia is considered one of the major risk factors [1]. Traditionally this includes elevated Low Density Lipoprotein Cholesterol (LDL-C), reduced High Density Lipoprotein Cholesterol (HDL-C) and elevated Total Cholesterol (TC) and Triglyceride (TGL) levels. The mainstay of treatment of dyslipidemia is aimed at reducing LDL-C levels [2]. The current National Cholesterol Education Program Adult Treatment Panel-III guidelines recommend target LDL-C levels of <70 mg/dL for statin treatment in patients with Acute Coronary Syndrome (ACS) [3]. But despite achieving the target LDL-C goal of <70 mg/dL with high intensity statins, there still remains a risk for future coronary events [4]. This could be explained by other co-morbid conditions like diabetes mellitus, hypertension, smoking, physical inactivity and genetic predisposition to recurrent events. However, there could be dyslipidemic risk beyond what the standard lipid profile consisting of TC, TGL, LDL-C, and HDL-C portrays. An extended lipid profile that looks at other lipid parameters such as Non-High Density Lipoprotein Cholesterol (non-HDL-C), Apolipoprotein-A1 (Apo-A1) and Apolipoprotein-B (Apo-B) and ratios derived from lipid parameters (TC/HDL-C and Apo-B/Apo-A1) may better reflect the dyslipidemic riskfor coronary events [4].

This study is an effort in this direction where we studied the prevalence and pattern of atherogenic dyslipidemia using a wider range of parameters than the standard lipid profile in statin naïve Indian patients presenting with an acute coronary syndrome, as data with this regard is limited.

MATERIALS AND METHODS

This single-centre, prospective, observational study was conducted in the department of cardiology of a tertiary care teaching institute in India. The study protocol was approved by the institutional review and ethics board (letter no- 10790/17). Written informed consent was obtained from all patients, as well as postal address and mobile telephone number. The study was conducted over a 7-month period from April to October 2017. Follow-up of the patients was done after 11 to 18 months (14-months average), with each patient receiving a phone call, text message and post card when follow-up was due. The diagnosis of myocardial infarction (MI) was made based on the universal definition of the same [5].

Inclusion Criteria

Patients presenting to the Chest Pain Unit diagnosed as ACS, of more than 18 years of age, who were not on prior statin therapy, and with no contra-indications to high-intensity statin treatment, were included in the study.

Exclusion Criteria

Peri-procedural MI, pregnant women, inability to provide informed consent, patients with known history of thyroid, hepatic, or malignant disease and anemia were excluded.

All the patients presenting with acute coronary syndrome were given 80 mg atorvastatin loading dose, followed by 40 mg atorvastatin once daily. The patients were divided into 2 groups based on the follow-up obtained after statin therapy. Blood samples were taken within the first 24 hours of admission that included the standard lipid profile as well as Apo-B and Apo-A1 levels. Lipid profiles were measured using the cholesterol oxidase peroxidase method and apolipoprotein levels using the ELISA technique (Quantikine solid phase sandwich ELISA kit no- 1345/17). Non-HDL-C levels were obtained using the formula: Non-HDL-C=Total Cholesterol-HDL-C.

Lipid parameters were considered abnormal if the values fell outside the following threshold points: TC >200 mg/dL, TGL >150 mg/dL, HDL-C <35 mg/dL, LDL-C >100 mg/dL, non-HDL-C >130 mg/dL,

TC/HDL-C ratio >4, Apo-B >125 mg/dL and Apo-A1 <120 mg/dL Apo-B/Apo-A1 ratio >0.7 [6].

STATISTICAL ANALYSIS

For continuous data, descriptive statistics mean±standard deviation and also 25th-75th percentile was reported. Number of patients and percentages were reported for categorical data. Pearson correlation coefficient was used to find the relationship between continuous variables. For graphical representation, bar and scatter plots were used. All analyses were done using Statistical Package for Social Services software version 21.0 (Armonk, NY: IBM Corporation).

RESULTS

One hundred and thirty-nine patients with ACS were enrolled in this study. The clinical presentation of patients is shown in [Table/Fig-1]. There was a marked male preponderance (78%). The average age at presentation was 55 years with a wide range from 21 to 88 years. The most common presentation was ST-Elevation Myocardial Infarction (STEMI) seen in 79%, followed by Non-ST Elevation Myocardial Infarction (NSTEMI) seen in 17% and Unstable Angina (UA) seen in 4%. Younger males had a greater proportion of STEMI compared to older patients, the highest proportion (92%) being in males between 20 and 40 years of age [Table/Fig-2].

Age (years)	Men (n=109)			Women (n=30)		
	STEMI	NSTE-ACS	Total	STEMI	NSTE-ACS	Total
≤50	29 (88)	4 (12)	33 (100)	2 (67)	1 (33)	3 (100)
>50	59 (78)	17 (22)	76 (100)	19 (70)	8 (30)	27 (100)
Total	88 (81)	21 (19)	109 (100)	21 (70)	9 (30)	30 (100)

[Table/Fig-1]: Clinical presentation of patients (n = 139).
STEMI: ST-elevation myocardial infarction; NSTE-ACS: Non-ST-elevation acute coronary syndrome (includes both unstable angina and non-ST-elevation myocardial infarction); Data are number (percentage) unless specified otherwise

Age (years)	Men		
	STEMI	NSTE-ACS	Total
20-40	11 (92)	1 (8)	12 (100)
41-60	45 (80)	11 (20)	56 (100)
>60	32 (78)	9 (22)	41 (100)
Total	88 (81)	21 (19)	109 (100)

[Table/Fig-2]: Age specific acute coronary syndrome pattern in men.
STEMI: ST-elevation myocardial infarction; NSTE-ACS: Non-ST-elevation acute coronary syndrome (includes both unstable angina and non-ST-elevation myocardial infarction); Data are number (percentage) unless specified otherwise

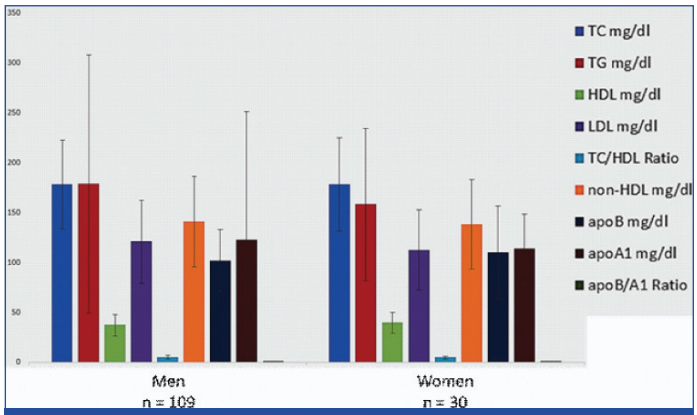
Females presenting with ACS were mostly above 50 years of age (post-menopausal), and had a higher proportion of non-ST elevation ACS (NSTE-ACS), which is the combination of UA and NSTEMI. [Table/Fig-3] shows baseline lipid profile patterns in men and women in the study. Both the standard and extended lipid profiles were not significantly different between both genders. This table also compares these parameters in patients who were re-assessed after statin therapy (Group 1) and those who were not (Group 2).

The prevalence of dyslipidemia using specific thresholds for each of the parameters in the standard and extended lipid profiles are depicted in [Table/Fig-4,5]. LDL-C showed the highest proportion of abnormality in the standard lipid profile (using a threshold value of 100 mg/dL). Non-HDL-C did not show as much dyslipidemia (threshold value 130 mg/dL). The rest of the extended lipid profile, however, showed greater prevalence of dyslipidemia than LDL-C, Apo-B (threshold value 125 mg/dL) showing the most dyslipidemia. Even when patients with low/normal LDL-C are selected, all the extended lipid profile parameters were able to detect dyslipidemia in a significant proportion of patients [Table/Fig-6].

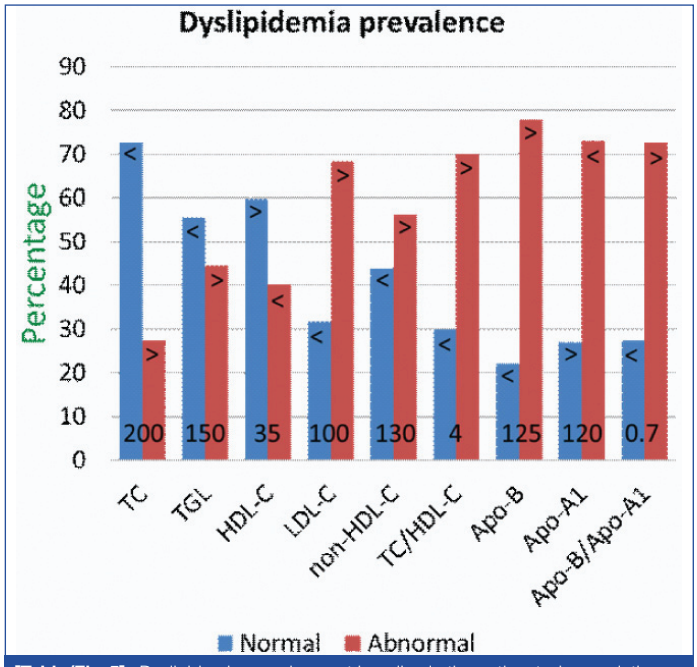
A striking feature seen in the standard lipid profile and in TC/HDL-C ratio, non-HDL-C and Apo-B patterns is the progressive reduction in dyslipidemia from the youngest age group (who had the worst

Variables	All patients (n=139)	Group 1 (n=53) (Follow-up obtained after statin therapy)	Group 2 (n=86) (No follow-up obtained)
Age (years)	57±12	57±12	57±12
Male sex	109 (78%)	44 (83%)	65 (76%)
STEMI	109 (79%)	42 (79%)	67 (78%)
Smoking	49 (35%)	22 (42%)	27 (31%)
Diabetes mellitus	71 (50%)	25 (47%)	46 (53%)
Systemic hypertension	67 (48%)	25 (47%)	42 (49%)
Total cholesterol (mg/dL)	175±45	179±90	178±48
Triglycerides (mg/dL)	178±119	162±79	181±138
LDL-cholesterol (mg/dL)	120±41	123±35	119±45
HDL-cholesterol (mg/dL)	38±11	39±12	37±9
TC/HDL-cholesterol ratio	4.99±1.63	4.98±1.57	5.04±1.69
non-HDL-cholesterol (mg/dL)	140±45	140±38	141±49
Apo-AI (mg/dL)	111±114	117±32	116±19
Apo-B (mg/dL)	104±35	107±37	102±34
Apo-B/Apo-A1 ratio	0.95±0.29	0.94±0.26	0.95±0.33

[Table/Fig-3]: Baseline characteristics of patients.
STEMI: ST-elevation myocardial infarction; LDL: Low density lipoprotein; HDL: High density lipoprotein; TC: Total cholesterol; Apo-A1: Apolipoprotein A1; Apo-B: Apolipoprotein B; Data are mean±standard deviation or number (percentage), There were no statistically significant differences between groups 1 and 2



[Table/Fig-4]: Standard and extended lipid profile parameters at baseline in men and women.



[Table/Fig-5]: Dyslipidemia prevalence at baseline in the entire study population.
Dyslipidemia prevalence at baseline in the entire study population (n=139) determined using different parameters; Numbers at the bottom of each bar represents the cut-off value (in mg/dL or ratio) used to differentiate normal (blue bars) from abnormal (red bars) values

Lipid parameter	LDL-C <100 mg/dL (n=42)	LDL-C <130 mg/dL (n=90)
Non-HDL-C >130 mg/dL	4 (10%)	34 (38%)
TC/HDL-C ratio >4	17 (40%)	54 (60%)
Apo-B >125 mg/dL	3 (7%)	11 (12%)
Apo-A1 <120 mg/dL	35 (83%)	73 (81%)
Apo-B/Apo-A1 ratio >0.7	26 (62%)	70 (78%)
Apo-B/Apo-A1 ratio >0.9	12 (9%)	41 (46%)

[Table/Fig-6]: Dyslipidemia detected by the ELP in patients with low/normal LDL-C. LDL-C: Low density lipoprotein cholesterol; non-HDL-C: Non-high density lipoprotein cholesterol; TC/HDL-C: Total cholesterol/high density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; Data are number (percentage)

dyslipidemia) to the oldest age group in each of these parameters [Table/Fig-7]. Apo-A1 values, on the other hand, declined (worsened) as age increased, and the Apo-B/Apo-A1 ratio consequently remained essentially unchanged.

Age group (years)	21-40		41-60		>60	
Number of patients	13		73		53	
TC (mg/dL)	187±42	(151-226)	180±45	(152-210)	174±45	(144-198)
TGL (mg/dL)	219±133	(118-320)	172±122	(108-194)	166±114	(93-206)
HDL-C (mg/dL)	36±10	(28-43)	37±12	(30-44)	39±10	(33-42)
LDL-C (mg/dL)	126±38	(99-157)	121±46	(92-149)	114±35	(92-136)
TC/HDL-Cratio	5.6±2	(3.7-6.8)	5±2	(4-6.4)	4.6±1.3	(3.7-5.5)
non-HDL-C (mg/dL)	151±43	(118-188)	143±46	(112-168)	135±43	(105-161)
Apo-B (mg/dL)	119±38	(83-161)	109 ±38	(84-125)	93±26	(72-110)
Apo-AI (mg/dL)	121±26	(104-142)	113 ±28	(96-122)	107±23	(92-119)
Apo-B/Apo-AI ratio	0.9±0.4	(0.7-1.1)	1±0.3	(0.8-1.1)	0.9±0.2	(0.7-1.1)

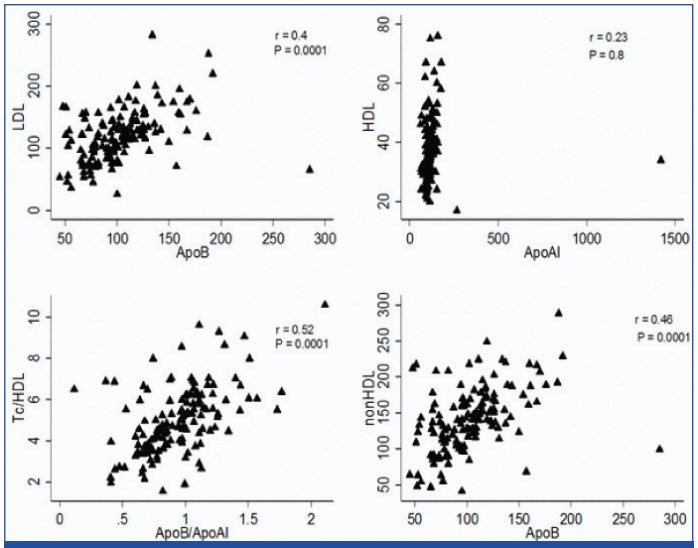
[Table/Fig-7]: Baseline lipid profiles according to age categories. TC: Total cholesterol; TGL: Triglyderides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; Data are mean±standard deviation (interquartile range); unless specified otherwise

[Table/Fig-8] shows the pattern of standard and extended lipid profile across the ACS spectrum from UA to STEMI. There was progressive worsening of all four standard lipid profile parameters as well as the TC/HDL-C ratio and non-HDL-C across the spectrum. The mean LDL levels rose from 98 mg/dL in the UA group to 115 mg/dL in the NSTEMI group and 121 mg/dL in the STEMI group. The apolipoprotein parameters however did not show this worsening trend.

	UA (n=6) Median (25^{th}, 75^{th})	NSTEMI (n=24) Mean (SD)	STEMI (n=109) Mean (SD)
ApoAI (mg/dL)	115.50 (106.75, 142.25)	108.96 (24.35)	108.0 (5)
ApoB (mg/dL)	70.5 (52.5, 115)	104.8 (39.7)	104.5 (33.5)
TGL (mg/dL)	74 (40.5, 189)	168.6 (86.5)	142.0 (35)
LDL (mg/dL)	82.5 (67.25, 138.25)	115.2 (46.9)	121.09 (39.9)
TC (mg/dL)	138.5 (123.25, 199.25)	177.2 (53.2)	179.4 (42.2)
HDL (mg/dL)	38.5 (32.75, 67)	40.1 (11.7)	36.9 (9.5)
TC/HDL	3.05 (2.5, 6.7)	4.7 (2.06)	5.09 (1.49)
Non HDL (mg/dL)	102 (66.75, 142)	37.08 (55)	142.5 (41.4)
ApoB/ApoAI	0.63 (0.49, 0.8)	0.99 (0.40)	(0.26)

[Table/Fig-8]: Baseline standard and extended lipid profile across ACS spectrum. TC: Total cholesterol; TGL: Triglyderides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; Data are mean±standard deviation (interquartile range), unless specified otherwise

Correlation between individual parameters in baseline standard and extended lipid profiles is shown in [Table/Fig-9]. Both LDL-C and non-HDL-C had moderate statistically significant correlation with Apo-B. The TC/HDL-C ratio and Apo-B/Apo-A1 ratio also had moderate statistically significant correlation with each other. However, the HDL-C with Apo-A1 correlation was surprisingly poor.



[Table/Fig-9]: Correlation of lipid profile parameter levels and ratios with corresponding apolipoprotein levels and ratios.

Effect of High-intensity Statins on Lipid Profile

In patients who were re-assessed after 11-18 months of high-intensity statin therapy (Group 1 in [Table/Fig-3], there was highly statistically significant improvement in three of the four standard lipid profile parameters as well as TC/HDL-C ratio and non-HDL-C [Table/Fig-10]. Changes seen in HDL-C and apolipoprotein parameters were however not significant. Group 1 patients (n=53), who came for follow-up, did not differ significantly in baseline

Statistic		Mean	SD	Median	IQR	p-value
TC (mg/dL)	Baseline	179	90	177	116-269	0.000*
	After	140	39	129	110-198	
	Change	39	51	46	6-73	
TGL (mg/dL)	Baseline	162	79	145	42-249	0.022*
	After	138	63	15	67-196	
	Change	24	74	130	-25-55	
HDL-C (mg/dL)	Baseline	39	12	37	17-67	0.081
	After	36	9	36	21-76	
	Change	3	11	1	-4-9	
LDL-C (mg/dL)	Baseline	123	35	45	26-220	0.000*
	After	92	39	84	26.5-288	
	Change	31	49	39	-0.5-68	
Non-HDL-C (mg/dL)	Baseline	140	38	143	41-220	0.000*
	After	104	39	99	32-149	
	Change	36	50	39	9-71	
TC/HDL-C ratio	Baseline	4.98	1.57	4.74	1.5-6.9	0.000*
	After	4.02	1.26	3.91	1.6-8	
	Change	0.96	1.54	0.96	-0.2-2.1	
Apo-B (mg/dL)	Baseline	107	37	102	54-159	0.41
	After	109	39	105	71-176	
	Change	-2	48	-3	-17-17	
Apo-AI (mg/dL)	Baseline	117	32	107	64-266	0.53
	After	116	19	115	85-283	
	Change	1	33	-4	-21-14	
Apo-B/Apo-AI ratio	Baseline	0.94	0.26	0.94	0.8-1.1	0.68
	After	0.92	0.37	0.90	0.7-1.1	
	Change	0.02	-0.11	0.04	-0.2-0.2	

[Table/Fig-10]: Change in lipid profile after statin therapy in all patients with follow-up (n=53). SD: Standard deviation; IQR: Interquartile range; TC: Total cholesterol; TGL: Triglycerides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; P values represent significance of difference in mean in each category; *statistically significant

characteristics from Group 2 patients (n=86), who did not return for follow-up; there were 10 interim deaths in the Group 2. As shown in [Table/Fig-11,12], in the 41-60 and >60 year age categories, significant improvement was seen at follow-up in TC, LDL-C, non-HDL-C and TC/HDL-C; the small number of patients in the 21-40 year age category probably led to the changes being insignificant in this category.

Age group 21-40 years (n=5)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
TC (mg/dL)	Baseline	171	43	157	134-214	0.14
	After	133	18	142	114-146	
	Change	38	10	46	6-73	
TGL (mg/dL)	Baseline	188	94	131	117-288	0.14
	After	145	39	114	127-185	
	Change	43	14	56	-1-103	
HDL-C (mg/dL)	Baseline	34	11	30	27-43	0.6
	After	31	5	33	27-34	
	Change	3	10	0	-3-10	
LDL-C (mg/dL)	Baseline	117	40	105	85-156	0.7
	After	106	34	94	82-136	
	Change	11	39	49	-52-70	
Age group 41-60 years (n=27)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
TC (mg/dL)	Baseline	182	36	188	167-210	0.001*
	After	138	49	131	117-164	
	Change	44	51	36	1-71	
TGL (mg/dL)	Baseline	154	57	150	102-194	0.29
	After	140	61	137	99-170	
	Change	14	63	13	-28-49	
HDL-C (mg/dL)	Baseline	38	13	36	28-45	0.43
	After	37	9	35	30-43	
	Change	1	11	1	-5-8	
LDL-C (mg/dL)	Baseline	125	39	129	101-148	0.002*
	After	91	38	83	67-106	
	Change	34	47	37	-2-69	
Age group >60 years (n=21)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
TC (mg/dL)	Baseline	177	43	175	159-198	0.01*
	After	139	46	126	111-146	
	Change	38	54	46	17-68	
TGL (mg/dL)	Baseline	166	99	145	94-211	0.36
	After	133	71	122	91-149	
	Change	33	92	15	-44-83	
HDL-C (mg/dL)	Baseline	40	11	38	33-44	0.19
	After	36	8	37	30-42	
	Change	4	13	2	-4-12	
LDL-C (mg/dL)	Baseline	122	29	119	99-137	0.02*
	After	91	42	83	59-102	
	Change	31	49	45	13-60	

[Table/Fig-11]: Change in standard lipid profile after statin therapy in different age categories.
SD: Standard deviation; IQR: Interquartile range; TC: Total cholesterol; TGL: Triglyderides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; p values represent significance of difference in mean in each category; *statistically significant

Age group 21-40 years (n=5)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
non-HDL-C (mg/dL)	Baseline	137	44	127	103-177	0.14
	After	102	19	107	83-119	
	Change	35	49	41	-6-70	
TC/HDL-C ratio	Baseline	5.5	2.4	5	3.8-7.4	0.14
	After	4.4	1.2	4.1	3.6-5.4	
	Change	1.1	1.5	0.9	0.3-2.4	
Apo-B (mg/dL)	Baseline	105	41	107	70-139	0.69
	After	115	13	112	103-128	
	Change	-10	35	-4	-44-21	
Apo-AI (mg/dL)	Baseline	116	26	111	93-142	0.35
	After	103	11	108	91-112	
	Change	13	31	7	-10-40	
Apo-B/Apo-AI ratio	Baseline	0.88	0.16	0.83	0.74-1.04	0.10
	After	0.91	0.19	0.96	0.71-1.08	
	Change	-0.03	0.25	-0.12	0.05-0.27	
Age group 41-60 years (n=27)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
non-HDL-C (mg/dL)	Baseline	140	39	143	111-167	0.002*
	After	104	39	99	79-126	
	Change	36	51	41	15-67	
TC/HDL-C ratio	Baseline	5.2	1.5	4.8	4.3-6.4	0.002*
	After	4.1	1.5	3.9	1.5-4.5	
	Change	1.1	1.5	0.9	-0.3-2.4	
Apo-B (mg/dL)	Baseline	115	44	106	95-134	0.98
	After	107	39	106	78-127	
	Change	8	50	-3	-13-21	
Apo-AI (mg/dL)	Baseline	118	38	107	96-134	0.39
	After	117	20	118	108-127	
	Change	1	40	-8	-26-18	
Apo-B/Apo-AI ratio	Baseline	0.99	0.26	0.97	0.8-1.1	0.5
	After	0.93	0.44	0.91	0.6-1	
	Change	0.06	0.43	0.04	0.2-0.7	
Age group >60 years (n=21)						
Statistic		**Mean**	**SD**	**Median**	**IQR**	**p-value**
non-HDL-C (mg/dL)	Baseline	137	41	129	115-159	0.01*
	After	103	42	92	76-109	
	Change	34	51	39	15-67	
TC/HDL-C ratio	Baseline	4.2	1.4	4.7	3.3-5.4	0.04*
	After	3.8	0.9	3.6	3-4.6	
	Change	0.8	1.5	1.1	-0.5-2.2	
Apo-B (mg/dL)	Baseline	99	21	97	82-110	0.41
	After	111	44	106	81-126	
	Change	-12	46	-3	-13-21	
Apo-AI (mg/dL)	Baseline	115	26	106	95-136	0.45
	After	118	19	115	101-136	
	Change	-3	23	-7	-21-10	
Apo-B/Apo-AI ratio	Baseline	0.89	0.25	0.89	0.69-1.05	2.09
	After	0.95	0.39	0.90	0.68-1.09	
	Change	-0.06	0.36	0.05	0.21-0.68	

[Table/Fig-12]: Change in extended lipid profile after statin therapy in different age categories.
SD: Standard deviation; IQR: Interquartile range; TC: Total cholesterol; TGL: Triglycerides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; Apo-B: Apolipoprotein B; Apo-A1: Apolipoprotein A1; p values represent significance of difference in mean in each category; *statistically significant

DISCUSSION

Dyslipidemia is a major risk factor for the development of coronary artery and cerebrovascular disease. Abnormal lipid levels contributed to the highest Population Attributable Risk (PAR) in both men and women in the INTERHEART study [7,8]. Consistent evidence from multiple genetic, epidemiological and clinical studies firmly

establishes that LDL-C causes atherosclerotic vascular disease [9]. However, LDL-C alone, or even the standard lipid profile, may be insufficient to adequately represent the dyslipidemic risk, and other lipid parameters need to be looked at. In this study we examined the patterns of atherogenic dyslipidemia prevalent in Indian patients presenting with ACS using the standard and an extended lipid profile, both at initial presentation and after statin therapy. A number of significant findings emerged, many of which corroborate with earlier studies, and some which may have important diagnostic and therapeutic implications.

The first is that the standard lipid profile is insufficient to expose the total dyslipidemic risk in patients. This is demonstrated by the fact that the proportion of patients with abnormality in several of the extended lipid profile parameters was more than the proportion with elevated LDL-C [Table/Fig-5] and that several of the extended lipid profile parameters were abnormal in patients with low/normal LDL-C. These findings corroborate earlier studies that have looked at extended lipid profile parameters. Liu et al demonstrated a strong association between non-HDL-C and cardiovascular risk, independent of the LDL-C levels [9]. Non-HDL-C, measures the cholesterol content present in all the atherogenic lipoproteins. It has also been shown to be a good risk predictor in patients with ACS. In the emerging risk factors collaboration, a combined data analysis from 68 studies, the authors report that non-HDL-C was the best predictor for coronary artery disease events and for strokes [10]. The Incremental Decrease in End Points through Aggressive Lipid Lowering (IDEAL) trial showed that elevated non-HDL-C and Apo-B levels were the best predictors of adverse cardiovascular outcomes in patients who were on lipid-lowering therapy, and when Apo-B or non-HDL-C was included in the regression model, LDL-C was not associated with poor outcomes [11].

In the current study, the apolipoprotein parameters and the TC/HDL-C ratio showed greater abnormality than non-HDL-C in ACS patients. Apo-B is the primary apolipoprotein of chylomicrons, very low-, intermediate- and low-density lipoprotein particles, whereas Apo-A1 constitutes approximately 70% of the apolipoprotein in HDL-C particles. Therefore Apo-B is reflective of total atherogenic potential whereas ApoA-1 reflects anti-atherogenic capabilities. High Apo-B/Apo-A1 ratio causes more cholesterol to be deposited in the arterial wall, promoting atherogenesis and increasing cardiovascular risk. High Apo-B/Apo-A1 ratio increased the risk of myocardial infarction in the AMORIS [12] and INTERHEART [8] studies. Apo-B/Apo-A1 ratio was found to be a better risk predictor than LDL-C in the prospective MONICA/KORA study [13]. Goswami et al also suggested that Apo-B/Apo-A1 ratio is a better discriminator of coronary artery disease risk in the atherosclerosis prone Indians [14]. Based on results from AMORIS and INTERHEART studies, patients can be risk stratified for the development of MI, based on Apo-B/Apo-A1 ratio: ratios of <0.3 (women) and 0.4 (men) as low risk; 0.3-0.6 (women) and 0.4-0.7 (men) as medium risk and 0.8-1.0 (women) and 0.9-1.1 (men) as high risk.

The second significant finding in our study was that young patients presenting with ACS had worse dyslipidemic status compared to older patients. There was a consistent pattern of improving lipid profile parameters across the age spectrum from young to old; only the apolipoproteins did not show this trend. This suggests that dyslipidemia may be a more important risk factor in the younger age groups, whereas the other risk factors (and age itself) may contribute more to the overall risk in older patients. This is of great importance, given the high prevalence of cardiovascular diseases and acute coronary syndromes in young Indiansand that this is an economically productive age group. Prabhakaran D et al., in their epidemiological report of cardiovascular disease, noted that four persons die of MI every two minutes in India and the age group is mainly between 30 and 50 [15]. This would make this age group a special target for urgent preventive and corrective measures to reduce the risk of a future coronary event.

Another interesting trend seen in our study was the worsening of lipid profile parameters through the ACS spectrum from UA to NSTEMI to STEMI [Table/Fig-8]. All standard and extended lipid profile parameters (excepting the apolipoprotein parameters) showed this trend which may indicate that the worse the dyslipidemia, the more likely the ACS will be a STEMI. This pattern is consistent with the earlier finding that young patients who have the worst dyslipidemia mostly present with STEMI.

A notable negative finding in this study was the lack of gender difference in lipid profile parameters [Table/Fig-4]. In a population based study from Greece, Kolovou GD et al., reported gender differences among dyslipidemic patients-higher TC, lower TGL and lower TC/HDL ratios among women [16]. The relatively small number of women, contributing less than one-fourth of our study group, may have contributed to this lack of demonstrable gender difference.

High-intensity statin therapy produced statistically highly significant improvements in lipid profile parameters [Table/Fig-10]; only HDL-C and the apolipoprotein parameters did not show significant change. However the LDL-C level achieved was still well above the desirable target of <70 mg/dL. The reasons for this include irregular intake of statin, reduction in dose by the patient or general practitioner and inadequacy of statin therapy alone in achieving target LDL-C levels. This shows the practical problems faced in risk reduction in the real world and the need for other lipid lowering therapies.

LIMITATION

There are several limitations to this study. It was a single-centre, hospital-based, observational study done in a tier-3 city with patients drawn from semi-urban background that may not be truly representative of the general population in India. The number of patients in some sub-groups, such as women and NSTE-ACS were small. Other lipid parameters that could contribute to dyslipidemic risk were not studied such as lipoprotein (a) and small dense LDL-C.

CONCLUSION

Dyslipidemia is an important risk factor in statin-naïve Indian patients who present with ACS. The extended lipid profile is better able to identify dyslipidemic risk than the standard lipid profile or LDL-C level alone. Dyslipidemia is more prevalent in young patients and those who present with STEMI, suggesting a greater role as a risk factor and indicating the need for more effective preventive measures in these patients. High-intensity statin therapy significantly improves lipid parameters in ACS patients, but achievement of target lipid levels remains practically elusive in most patients.

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