Original Article

DOI: 10.7860/JCDR/2014/8018.4694

Relationship of Lipid Profile and Serum Ferritin levels with Acute Myocardial Infarction

Biochemistry Section

SHIPRA[1], BHARAT KUMAR GUPTA[2], RANJAN SOLANKI[3], HIMANSHU PUNIA[4], VIBHUTI AGARWAL[5], JASKIRAN KAUR[6], ASHISH SHUKLA[7]

ABSTRACT

Introduction: National Health and Nutrition Examination Survey (NHANES III), 1988-1994, first time reported a significant, positive association in iron storage and heart disease risk. Thereafter several researchers have found an association between iron overload, serum ferritin (SF) and MI. No such Indian study was available in the literature and so we decided to find out the relation of lipid profile and Serum Ferritin with myocardial infarction (MI).

Materials and Methods: Fifty indian patients of AMI (study group) and fifty indian healthy volunteers (control group) were included for the present study. Lipid profile including TC, HDL-c, LDL-c, VLDL-c & TG and SF levels were estimated in all subjects.

Observations and Results: Mean ± SD of TC level was 250.64 ± 25.61, of HDL-c was 36.52 ± 2.86, of LDL-c was 165.69 ± 26.80, of VLDL-c was 42.35 ± 8.53 and of TG was 211.83 ± 42.65 in study group while these values were 174.46±47.68, 43.2±12.52, 98.37±41.13, 32.88±21.45 and 164.42±107.29 respectively in control group. All the parameters were found not only raised in patients of acute myocardial infarction (AMI) but were also statistically significant when compared with control group (p=<0.01).

Mean ± SD of SF levels was 268.43±30.17 ng/ml in study group and 110.96±56.5 ng/ml in control group; this level was found not only raised in patients of AMI but were also statistically significant when compared with control group (p=<0.01).

Conclusion: TC, LDL-c, VLDL-c, TG and SF levels were raised in patients of AMI and found to be statistically significant; while HDL-c levels were reduced in such patients and is also statistically significant. It can be concluded that there exists an association in lipid profile and SF with AMI therefore dyslipidemia and raised SF levels are the features of AMI.

Keywords: Acute myocardial infarction, Serum ferritin, Lipid profile, Indian population

INTRODUCTION

National Health and Nutrition Examination Survey (NHANES III), first time reported a significant positive association in iron storage and heart disease risk between 1988-1994. Several researchers, thereafter, have found and reported an association between iron overload, serum ferritin (SF) and acute myocardial infarction (MI) [1-4].

Literature has limited studies on serum ferritin levels and its relation with MI in Indian patients, and so we decided to undertake this study.

OBJECTIVES

- To estimate lipid profile and SF levels in indian patients of AMI in Meerut, India.
- To find out relationship of Lipid Profile and SF levels with Acute Myocardial Infarction.

MATERIALS AND METHODS

Patients reporting in Medicine and Emergency Department of Chhatrapati Shivaji Subharti Hospital, Subharti Medical College, Meerut between Jan. 2012 to June 2013, with the complaint of acute chest pain, were enrolled for the present study.

Ethical clearance was obtained from the Institutional Ethical Committee. Informed consent was taken from each individual patient / attendant.

Suspected or diagnosed patients of Diabetes Mellitus (DM), Neoplastic disease, Liver disease / Alcoholism and Primary / Secondary Hemochromatosis were not included.

Diagnosis of AMI was confirmed by standard procedures and investigations. Fifty AMI patients between 40-70 years of age constituted the study group. Control group included 50 healthy volunteers in same age. Both these groups were further divided into patients between 40-50, 50-60 and 60-70 years of age.

Lipid profile including TC, HDL-c, LDL-c, VLDL-c and TG levels were estimated in Vitros-250 auto analyser using readymade dry chemistry slides procured from Ortho- Clinical Diagnostics, Johnson and Johnson, USA. SF was estimated by ELFA on MINIVIDAS auto analyser (Biomerieux).

STATISTICAL ANALISIS

All the data so collected were duly recorded and was compiled; results and observations drawn and statistically analysed using Mean, Standard deviation, Annova, Unpaired Student t-test, Chi-square test and Z-test.

RESULTS AND OBSERVATIONS

Results and observations are given in [Table/Fig-1-7].

We observed that the levels of TC, LDL-c, VLDL-c, TG and SF were found raised while the levels of HDL-c were decreased in all three age groups in patients of AMI as compared with healthy controls. All these values were found statistically significant except values of TC, LDL-c, VLDL-c and TG that too only in 40-50 years.

Dyslipidaemia through was observed in all three age groups in AMI patients but it was significant only in 50-60 and 60-70 years age groups; while SF levels were found raised and significant in all three age groups.

DISCUSSION

The incidence of coronary artery disease (CAD) is alarmingly increasing in our country, Reddy and Yusuf concluded that 2.39 million people died of CAD in 1990 in India and hypothesized that the number may double by the year 2015 [2].

Group	Age Distibution	Mean±SD	t-value	p-value
Study Group	40-50 yrs, (n=8)	245.75 ±31.37	2.62	>0.01(N.SIG.)
	50-60yrs, (n=17)	255.64 ±26.21	9.46	<0.01(SIG.)
	60-70yrs, (n=25)	248.24±24.94	6.04	<0.01(SIG.)
	Total, (n=50)	250.646±25.61	9.95	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	183.70 ±61.00		
	50-60yrs, (n=22)	168.13 ±30.66		
	60-70yrs, (n=18)	177.05±54.08		
	Total, (n=50)	174.46±47.68		

[Table/Fig-1]: Total cholesterol levels in different groups and its statistical significance

Group	Age Distibution	Mean±SD	t-value	p-value
Study Group	40-50yrs, (n=8)	36.5 ±1.19	0.94	>0.01(N.SIG.)
	50-60yrs, (n=17)	37.94 ±2.34	3.75	<0.01(SIG.)
	60-70yrs, (n=25)	36.28±2.99	7.3	<0.01(SIG.)
	Total, (n=50)	36.52±2.86	3.51	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	42.9 ±19.59		
	50-60yrs, (n=22)	43.63 ±6.4		
	60-70yrs, (n=18)	42.83±14.08		
	Total, (n=50)	43.2±12.52		

[Table/Fig-2]: HDL-c levels in different groups and its statistical significance

Group	Age Distibution	Mean±SD	t-value	p-Value
Study Group	40-50yrs, (n=8)	162.87 ±30.26	2.61	>0.01(N.SIG.)
	50-60yrs, (n=17)	169.47 ±25.07	8.66	<0.01(SIG.)
	60-70yrs, (n=25)	163.08±27.59	5.69	<0.01(SIG.)
	Total, (n=50)	165.69±26.80	9.69	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	105 ±56.79		
	50-60yrs, (n=22)	93.22 ±29.58		
	60-70yrs, (n=18)	101.66±44.8		
	Total, (n=50)	98.37±41.13		

[Table/Fig-3]: LDL-c levels in different groups and its statistical significance

Group	Age Distibution	Mean±SD	t-Value	p-Value
Study Group	40-50yrs, (n=8)	40.5 ±8.56	1.60	>0.01(N.SIG.)
	50-60yrs, (n=17)	42.11 ±7.17	4.17	<0.01(SIG.)
	60-70yrs, (n=25)	42.04±9.64	4.11	<0.01(SIG.)
	Total, (n=50)	42.35±8.53	2.90	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	35 ±6.15		
	50-60yrs, (n=22)	31.72 ±7.85		
	60-70yrs, (n=18)	32.22±5.24		
	Total, (n=50)	32.88±21.45		

[Table/Fig-4]: VLDL-c levels in different groups and its statistical significance

Group	Age Distibution	Mean±SD	t-value	p-value
Study Group	40-50yrs, (n=8)	204.5 ±13.49	1.91	>0.01(N.SIG.)
	50-60yrs, (n=17)	212.47 ±15.41	3.55	<0.01(SIG.)
	60-70yrs, (n=25)	212.8±28.12	3.59	<0.01(SIG.)
	Total, (n=50)	211.83±42.65	2.90	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	177.1 ±38.95		
	50-60yrs, (n=22)	160.18 ±59.6		
	60-70yrs, (n=18)	158.61±70.04		
	Total, (n=50)	164.42±107.29		

[Table/Fig-5]: TG levels in different groups and its statistical significance

Lipid Profile abnormal level of reference (mg/dL)	No. of subjects with abnormal values in study group	No. of subjects with abnormal values in control group	Probable values of Z-score b/w two groups	p-values/ significance
TC>200	50(100%)	12(24%)	0.0000	p<0.01 (SIG.)
HDL-c <40(males)	31(62%)	14(28%)	0.0000	p<0.01 (SIG.)
HDL-c <50(females)	15(30%)	12(24%)	0.0000	p<0.01 (SIG.)
LDL-c >100	50(100%)	19(38%)	0.0000	p<0.01 (SIG.)
VLDL-c >35	40(80%)	10(20%)	0.0057	p<0.01 (SIG.)
TG>150	49(98%)	14(28%)	0.0050	p<0.01 (SIG.)

[Table/Fig-6]: Dyslipidemia in different groups

Group	Age Distibution	Mean±SD	t-Value	p-Value
Study Group	40-50yrs, (n=8)	267.75 ±31.7	4.91	<0.01(SIG.)
	50-60yrs, (n=17)	250.52 ±41.21	8.21	<0.01(SIG.)
	60-70yrs, (n=25)	264.16±31.87	14.99	<0.01(SIG.)
	Total, (n=50)	268.43±30.17	17.43	<0.01(SIG.)
Control Group	40-50yrs, (n=10)	125.4 ±76.39		
	50-60yrs, (n=22)	109.95 ±60.52		
	60-70yrs, (n=18)	104.16±37.99		
	Total, (n=50)	110.96±56.59		

[Table/Fig-7]: Serum ferritin levels in different groups and its statistical significance

In the last few decades there has been ever increasing awareness regarding the factors responsible for atherogenesis and CAD. Identification of various inflammatory markers like C-reactive protein (CRP), tumour-necrosis factor-α and free radical (FR) mediated injury has opened up new horizons for different aspects of control and management of epidemic of CAD. Umesh N Khot determined the prevalence of coronary heart disease (CHD) in cigarette smoking, DM, hyperlipidemia, and hypertension (HTN)—in a broad population of patients [3]. Sullivan postulated a link between tissue iron stores and the risk of ischemic heart disease (IHD), to explain the sex difference in IHD risk as early as in 1981[4].

In the present study, 100% patients with MI had borderline and high TC as compared to 24% subjects in control group; 62 % male and 30% female had low HDL-c levels in study group while 28% males & 24% females had low HDL-c in control group; 100% of patients with MI had above optimal LDL-c levels as compared to 19% subjects in control group; 80% of patients had higher VLDL-c levels as compared to 20% subjects in control group; and 98% patients had higher TG as compared to 28% in control group. We observed that TC, LDL-c, VLDL-c and TG levels are higher while HDL-c is lower in more patients of AMI in study group. Our finding were similar to that of Arun Kumar et al., who further observed that patients with chest pain and positive cardiac enzyme test were found to have significantly elevated levels of TC, TG, LDL-c and significantly reduced HDL-c levels when compared to the patients who experienced only chest pain and healthy controls [5].

Vincelj J, Bergovec M, et al., examined relationships between TC, LDL-c, HDL-c, TG and age, gender, and cigarette smoking in 190 patients aged 34-87 years with first AMI; control group in their study included 103 patients aged 29-90 years without a history of angina pectoris or AMI; they found high TC in 75% of patients with AMI v/s 48% in the control group ($p < 0.001$); patients with AMI had significantly higher TC and LDL-c levels than controls ($p < 0.0001$); HDL-c levels were significantly lower among patients with AMI than among the control group patients ($p < 0.0001$); TC and LDL-c was higher in patients with AMI up to 60-year-old, but lower

in patients older than 60 year and they suggested an influence of hyperlipoproteinemia upon development of MI, especially in younger patients [6]. These findings are in conformity with our findings.

Temelkova-Kurktschiev TS, Kurktschiev DP, 2009 et al reported that patients with hypercholesterolaemia, hypertriglyceridaemia and low HDL-c are established risk factors of macrovascular disease, which leads to stroke and MI and is the leading cause of death whose aim was to study and examine the prevalence and type of hyper/dyslipidaemia in patients with MI and HTN [7].

Tuomainen reported an association between increased body iron stores and excess risk of AMI. The concentration ratio of serum transferrin receptor (TfR) / ferritin was utilized as indicator of body iron stores [8]. Salonen, reported in the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) that the high stored iron level, as assessed by elevated SF concentration, is a risk factor for CAD [1]. On the other hand Bozzini's angiography based study could not support a role for biochemical or genetic markers of iron stores as predictors of the risk of CAD or its thrombotic complications [9].

Several studies have been conducted since then to assess this association of iron and AMI. Results of some studies have been in favour of ferritin being a risk factor for AMI (Klipstein-Grobusch et al.,) [10], while others have not (Ascherio et al.,) [11].

Several researchers have found significant association between iron overload and MI, Salonen JT et al., [1] suggested a link between iron overload and MI; while there are some others who does not support the link between iron storage and CHD like (Sempos CT) [12] (Sun Q) [13], or atherosclerosis (Moore M) [14]. Therefore, more evidences are required to establish the link between the MI/CHD/Atherosclerosis and level of stored iron (Kiechl S et al.,) [15] (Sempos CT) [12] (Danesh J) [16]. (Tuomainen TP) [8].

Serum ferritin levels were 268.43 ± 30.17 in AMI patients in the present study which are higher and statistically significant and these findings are in agreement with the findings of Silvia et al., [17], who estimated SF as 257.35 ± 76.34 µg/L in the MI patients and Bharathi BK & Shrikant chandrakar [18], who concluded that median serum ferritin levels were significantly associated higher in cases (325.5µg/L) of AMI as compared to controls (65.5µg/L) ($p<0.001$).

Bharathi BK and Shrikant chandrakar also concluded in their latest study on 30 AMI patients that there is strong and independent relationship of high SF with AMI and SF was significantly high in diabetics and smokers [18].

Frey GH, Krider DW, in their study found an association of high SF levels with excess risk of MI in men but later reviewed the clinical records of 298 male patients seen over a 10 year period in Southern West Virginia, in whom SF levels were obtained of the 32 patients who experienced an AMI, there were no significant statistical differences between their mean ferritin levels and the ferritin levels of the 266 patients with no MI. Only two of the 32 patients with MI showed an elevated SF level, so they concluded that the findings do not support the hypothesis that high SF levels are associated with MI [19].

Haidari reported that increased ferritin might be an independent predictor of premature CAD in male Iranian patients. Ferritin was higher in the male & female patients with MI than in the male & female subjects without MI [20]. Another study conducted by Silvia WD, Biswas S, Uthappa S et al., which involved 145 men (100 cases and 45 healthy control subjects) in the age group of 30-70 years. The hypothesis is that increased SF was related to increased chances of AMI along with the other risk factors like serum TC, HDL-c, LDL-c, VLDL-c and TG. Increased SF levels significantly ($p < 0.001$) correlated with an increase of other risk factors in Indian male patients with AMI. Significant direct correlation between SF levels and risk of AMI was observed [18].

LIMITATIONS

- Single sample was tested for lipid profile and serum ferritin levels.
- Sample size in the present study was small.
- Results were not compared with subjects having dyslipidemia but no chest pain and MI.

RECOMMENDATIONS

- Sample should be drawn serially at definite intervals in high risk patients and tested for lipid profile and serum ferritin levels.
- Large prospective studies in Indian population are needed to support the results of present study.
- A group including subjects having dyslipidaemia but no chest pain and MI in same age should also be included in the study and their levels of lipid profile and serum ferritin levels be compared with the existing groups.

CONCLUSION

TG, LDL-c, VLDL-c, TG and SF levels were raised in patients of AMI and found to be statistically significant; while HDL-c levels were reduced in such patients and is also statistically significant. It can be concluded that there exists a relationship in lipid profile and SF with AMI therefore dyslipidemia and raised SF levels are the features of AMI.

REFERENCES

[1] Salonen JT, Nyyssonen K, Korpela H, Tuomilehto J, et al. High Stored Iron Levels Are Associated With Excess Risk of Myocardial Infarction in Eastern Finnish Men. *Circulation.* 1992; 86:803-11.

[2] Reddy KS, Yousuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation.* 1998; 596-601.

[3] Umesh NK, Monica BK, Christopher TB, Shelly KT. Prevalence of Conventional Risk Factors in Patients with Coronary Heart Disease. *JAMA*. 2003;290(7):898-94.

[4] Sullivan JL, et al. Iron and the Sex Difference in Heart Disease Risk. *Lancet* 1981;1:1293-94.

[5] Arun Kumar and Brijesh Sathian, et al. Correlation between lipid profile and troponin I test results in patients with chest pain in Nepal. *Asian Pac J Trop Biomed.* 2013;3(6): 487–81.

[6] Vincelj J, Suci M, Bergovec M, Lajtman Z, Bergman-Markovi B, Bozikov V. Serum total, LDL, HDL cholesterol and triglycerides related to age, gender and cigarette smoking in patients with first acute myocardial infarction. *Collegium antropologicum.* 1997;21(2):517-24.

[7] Temelkova-Kurktschiev TS, Kurktschiev DP, Vladimirova-Kitova LG, Vaklinova I, Todorova BR, et al. Prevalence and type of dyslipidaemia in a population at risk for cardiovascular death in Bulgaria. *Journal of Diabetology*. 2009;51(2):26-22.

[8] Tuomainen TP , Punnonen K , Nyyssonen K , Salonen JT, et al. Association between body iron stores and the risk of acute myocardial infarction in men. *Circulation*. 1998;97:1461-66.

[9] Bozzini A, Corrocher R, et al. Biochemical and genetic markers of iron status and the risk of coronary artery disease. An angiography-based study. *Clin Chem.* 2002;48(4):622-28.

[10] Kerstin Klipstein-Grobusch, Johan F Koster, Diederick E Grobbee, Jan Lindemans, Heiner Boeing, Albert Hofman,and Jacqueline CM Witteman, et al. Serum ferritin and risk of myocardial infarction in the elderly. The Rotterdam Study. *Am j Clin nutr.* 1999;69:1231-36.

[11] Ascherio A, Willet WC, Rimm FB, et al. Dietary iron intake and risk of coronary disease among men. *Circulation.* 1994;89:969-74.

[12] Sempos CT, Looker AC, Gillum RF, McGee DL, et al. Serum Ferritin and Death from all Causes and Cardiovascular Disease. The NHANES II Mortality Study.*Ann Epidemiol* .2000;10:441-48.

[13] Sun Q, Ma J, Rifai N, Franco OH, Rexrode KM, Hu FB, et al. Excessive body iron stores are not associated with risk of coronary heart disease in women. *J Nutr.* 2008;138(12):2436-41.

[14] Moore M, Folsom AR, Barnes RW, Eckfeldt JH. No Association between Serum Ferritin and Asymptomatic Carotid Atherosclerosis. The Atherosclerosis Risk in Communities (ARIC) Study. *Am J Epidemiol.* 1995;141:719-13.

[15] Kiechl S, Aichner F, Gerstenbrand F, et al. Body iron stores and presence of carotid atherosclerosis. *result from the Bruneck Study. Arterioscler Thromb.* 1994;14:1625-30.

[16] Danesh J, Appleby P, et al. Coronary Heart Disease and Iron Status. *Circulation.* 1999; 99:852-54.

[17] Silvia WD, Biswas S, Uthappa S, Shetty P, et al. *Ferritin, a potent threat for acute myocardial infarction.* 2003; 51:947-50.
[18] Bharathi BK, Shrikant Chandrakar. Serum ferritin - a potential threat and risk factor for acute myocardial infarction. IJPBS. 2013;3(1):7-13.
[19] Frey GH, Krider DW, et al. Serum ferritin and myocardial infarct. *Med J.* 1994;90(1):13-15.
[20] Haidari M, javadi E, Sanati A, Hajilooi M, Ghanbili J, et al. Association of increased ferritin with premature coronary stenosis in men. *Clin Chem.* 2001;47 (9):1666-62.

PARTICULARS OF CONTRIBUTORS:
1. Post Graduate Student, Department of Biochemistry, Subharti Medical College, Swami Vivakan and Subharti University, Meerut, India.
2. Professor, Department of Biochemistry, Subharti Medical College, Swami Vivakan and Subharti University, Meerut, India.
3. Associate Professor, Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, India.
4. Reader, Department of Community Dentistry, Teerthankar Dental College, Moradabad, India.
5. Post Graduate Student, Department of Biochemistry, Subharti Medical College, Swami Vivakan and Subharti University, Meerut, India.
6. Assistant Professor, Department of Biochemistry, Subharti Medical College, Swami Vivakan and Subharti University, Meerut, India.
7. Assistant Professor, Department of Biochemistry, Subharti Medical College, Swami Vivakan and Subharti University, Meerut, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Shipra,
Post Graduate Student, Department of Biochemistry,
Subharti Medical College, Swami VivakanandSubharti University,
Bye Pass Road, Meerut- 250005, India
Phone : 919760036256, 919412701534, E-mail : bkgupta1951@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 28, 2013**
Date of Peer Review: **Nov 27, 2013**
Date of Acceptance: **Jun 20, 2014**
Date of Publishing: **Aug 20, 2014**