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SHORT TERM PROGNOSTIC VALUE OF SERUM FERRITIN ON ACUTE MYOCARDIAL INFARCTION

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Abstract

Background: Globally, coronary artery disease is a leading cause of mortality and morbidity. Elevated serum ferritin has been suggested to be associated with coronary artery disease especially myocardial infarction but the evidence remains tenuous, especially with regard to prognosis.

Methods: 50 patients of STEMI and 50 patients of NSTEMI were included in the study.A control group of 50 healthy persons was taken for comparision. Baseline characteristics, LV ejection fraction, Killip functional class and outcomes were compared across tertiles of serum ferritin.

Results: There was a significant correlation between serum ferritin and LV ejection fraction (p=0.01),Killip class(p=0.03) and mortality(p=0.03).

Conclusion: Raised serum ferritin is associated with worse outcome following myocardial infarction.

Introduction

A surfeit of total body iron is considered to have multiple deleterious effects. In myocardial tissue in particular, it is hypothesized to be causative of myocardial infarction especially in genetically vulnerable individuals. Excessive iron is converted intracellularly into hemosiderin, ferritin and free iron which in turn promotes free radical induced oxidative damage. Ferritin is the most accurate yardstick of total body iron as there is an intricate relationship between its intracellular and extracellular levels.

The connection between body iron and coronary artery disease was first noted by Jerome Sullivan in 1981.[1]While some studies have found a strong relationship between acute myocardial infarction (AMI) and ferritin, other studies have negated this connection. The conflicting results could be due to methodological variation in measuring iron stores or study design. Hence, the role of serum iron store (or its surrogate ferritin) in AMI is unclear.

Materials and Methods

100 patients of acute myocardial infarction (50 STEMI and 50 NSTEMI) were included in the study. 50 healthy patients of age 30 to 70 years were included in a control group for comparison. STEMI was diagnosed from typical chest pain associated with ST-segment elevation ≥0.1 mV in ≥2 contiguous precordial leads (for the diagnosis of anterior wall MI) as well as ≥0.1 mV in II, III, and aVF leads (for the diagnosis of inferior wall MI) except in v2, v3 where the following cut points apply: ≥0.2 mV in men ≥40 years, ≥0.25 mV in men <40 years, or ≥0.15 mV in women. NSTEMI was diagnosed from typical chest pain with raised troponin I values. All patients were subjected to routine investigations including haemogram, renal function test, lipid profile, liver function test and BNP. Serum ferritin analysis was done by chemiluminescence for all cases and controls.

The normal reference value of serum ferritin was 10-120 ng/ml .Patients were divided into three groups on the basis of serum ferritin (1st tertile:<120 ng/ml,2nd tertile:120 to 220 ng/ml and 3rd tertile:>220 ng/ml).

Results

The baseline characteristics of the three groups were analysed. There was no significant difference in the various baseline characteristics between the three tertiles.

Table 1:

Characteristic	Ferritin <120 ng/ml	120 -220 ng/ml	>220 ng/ml	P value
Age<60 years	20	18	20	0.22
Males	18	36	17	0.86
Smoking	12	8	6	0.27
DM	11	7	10	0.56
HTN	16	12	8	0.12
Dyslipidemia	16	14	10	0.38
Renal failure	2	1	0	0.77
Obesity	5	3	2	0.47

The type of ACS was also compared between the three groups. Out of 50 STEMI patients,12 belonged to first tertile,24 to second tertile and 14 to third tertile. Out of 50 NSTEMI patients,14 were in low ferritin,25 in intermediate and 11 in high ferritin group. There was no significant difference in distribution in the three tertiles (p=0.76).

Table 2:

TYPE OF ACS	Ferritin<120 ng/ml	120-220 ng/ml	>220 ng/ml
STEMI	12	24	14
NSTEMI	14	25	11

The LVEF was analysed across the tertiles by dividing it into four categories. In the first tertile,2 patients had EF less than 35%,12 had EF 35 to 45%,10 had EF 45 to 55% and 2 had EF more than 55%.In the second tertile, the corresponding numbers were 4,18,15 and 12.In the highest tertile, the distribution was 9,8,5 and 3.There was a significant difference between the 4 groups(p value:0.01).

Table 3

LVEF (in %)	Ferritin<120 ng/ml	120-220 ng/ml	>220 ng/ml
<35	2	4	9
35-45	12	18	8
45-55	10	15	5
>55	2	12	3

The functional status of patients (Killip class) was also compared across the groups .In the lowest tertile,10 patients each were in class II and class III but 4 were in class 1 and 2 in class IV. In the middle tertile,12 patients each were in class II and class III but 6 were in class I and 19 were in class IV. In the highest tertile,10 patients were in class III whereas 6 patients each were in class II and class III and 3 were in class IV. This was found to be significantly different with a p value of 0.03.

Table 4

Functional class	Ferritin<120 ng/ml	120-220 ng/ml	>220 ng/ml
Class I	4	6	6
Class II	10	12	6
Class III	10	12	10
Class IV	2	19	3

The in-hospital outcome was compared amongst the three groups. Recurrent angina showed a trend towards relation with ferritin (2 in first tertile,10 in second tertile and 8 in third tertile) but statistically not significant(p=0.09).Heart failure showed a similar pattern (4 in first tertile,6 in second tertile and 8 in third tertile) but p value of 0.1.Mortality was statistically strongly corelated with ferritin level (1 in first tertile,2 in second tertile and 5 in third tertile) with a p value of 0.03

Table 5:

OUTCOME	Ferritin<120 ng/ml	120-220 ng/ml	>220 ng/ml	P value
Recurrent angina	2	10	8	0.09
Heart failure	4	6	8	0.1
Death	1	2	5	0.03

Discussion

The present study shows that baseline clinical characteristics or type of MI had no relation with serum ferritin. However, raised ferritin is associated with worse NYHA class and lower ejection fraction. Also, mortality and raised serum ferritin show a statistically significant correlation.

Iron is an important element in multiple physiological processes in the body but excess iron is known to accelerate atherosclerosis.[2]Iron deficiency has been proven to be a frequent finding in heart failure worsening the outcome .Also, its correction leads to reduced morbidity and sense of well being. Hence, parenteral iron is indicated in HFref patients with iron deficiency (class IIa in ESC guidelines).[3]However, the importance of iron and ferritin in coronary artery disease remains to be elucidated.

Serum ferritin (>200 ug/l) has been found to increase the risk of MI by 5 times.[4]Serum ferritin levels could be a prime decisive factor of myocardial ischemic burden during periods of ischemia.[5]A raised ferritin level has been found to double the risk of AMI in males.[6]Dominguez-Rodriguez showed that reduced serum iron and ferritin is associated with adverse outcome in acute coronary syndrome.[7]A study on young patients of CAD revealed that ferritin was an independent discriminating factor for CAD in males with the highest quartile having an odds ratio of 1.62 compared to the lowest quartile.[8]Hoque et al found a significant corelation between serum ferritin and acute coronary syndrome($p<0.001$).[9]A recent metanalysis of 11 studies concluded that serum ferritin in AMI is higher than in controls.[10]

On the contrary, Frey concluded that there was no relation between MI and ferritin.[11]Similarly,Sempos et al negated any relation between serum ferritin and cardiovascular disorders or mortality.[12]Ascherio A also concluded that serum iron does not increase risk of CAD in men.[13]

The plausible mechanisms of the culpability of serum ferritin are many. There is a significant rise in ferritin concentration of monocytes when exposed to hydrocortisone. Stress which is an established risk factor for AMI could trigger this process.[12]Ferritin could act alongwith other traditional risk factors by promoting free radical generation which in turn causes LDL oxidation and plaque formation. This could also explain raised CRP levels in AMI.[14]A genetic component to causality has also been proposed. For example, persons with wild allele of tagSNP rs9366637 were more likely to suffer from CAD than mutant allele.[8]

Conclusion:

The current study shows that raised serum ferritin is associated with worse outcomes and increased mortality following AMI. Larger studies to further explore this relationship are in order.

References:

1. Sullivan JL. Iron and the sex difference in heart disease risk. Lancet 1981; 1:1293-4.
2. Pourmoghaddas A, Sanei H, Garakyaraghi M, et al. The relation between body iron store and ferritin,

and coronary artery disease. ARYA Atheroscler 2014;10:32–6

3. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure; The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129-200
4. Holay MP, Choudhary AA, Suryawanshi SD. Serum ferritin-a novel risk factor in acute myocardial infarction. Indian Heart J. 2012;64:173-177.
5. Yalta K.Sivri N.Yalta T.Yetkin E.Serum ferritin: a potential determinant of myocardial ischemic burden in the setting of ischemic conditions?.Int J Cardiol. 2011.
6. Salonen JT, Nyyssönen K, Korpela H, Tuomilehto J, Seppänen R, Salonen R. High stored iron levels are associated with excess risk of myocardial infarction in eastern Finnish men. Circulation. 1992;86:803-811.
7. Dominguez-Rodriguez A, Abreu-Gonzalez P. Quantification of serum ferritin in the acute coronary syndrome: a puzzle still to be resolved? Int J Cardiol. 2012;154(2):215
8. Haidari M, Javadi E, Sanati A, Hajilooi M, Ghanbili J. Association of increased ferritin with premature coronary stenosis in men. Clin Chem. 2001; 47(9): 1666-72
9. Hoque, Abu & Khan, HI & Chowdhury, Abdul & Ahmed, Md & Sabah, Khandker & Amin, Md & Mia, Md & Faruque, Chowdhury. (2018). Association of Serum Ferritin Level with Acute Coronary Syndrome. Bangladesh Heart Journal. 32. 89. 10.3329/bhj.v32i2.36094.
10. WEN, Shuang; YANG, Liu; HE, Lianping and LIU, Changwei. Serum ferritin levels is associated with acute myocardial infarction: a meta-analysis. Rev. Assoc. Med. Bras. [online]. 2020, vol.66, n.2 [cited 2021-01-01], pp.227-231.
11. Frey GH, Krider DW. Serum ferritin and myocardial infarct. W V Med J. 1994;90:13-15.
12. Sempos CT, Looker AC, Gillum RE, McGee DL, Vuong CV, Johnson CL. Serum ferritin and death from all causes and cardiovascular disease: the NHANES II Mortality Study. National Health and Nutrition Examination Study. Ann Epidemiol. 2000;10:441-448.
13. Ascherio A, Willett WC, Rimm EB, Giovannucci EL, Stampfer MJ. Dietary iron intake and risk of coronary disease among men. Circulation 1994;89:969-74
14. De Silva DM, Aust SD. Ferritin and ceruloplasmin in oxidative damage: review and recent findings. Can J Physiol Pharmacol, 1993;71:715-720.