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Original Article

Serum Ferritin Levels in Acute Myocardial Infarction: An Examination of Prognostic Significance

Dr Chaitanya Kumar S[1], Dr Hemanth Kumar K[2], Dr Madhukar Chelikani[3], Dr C. Naren Chandra[3], Dr Manjunath M Nuchhi[2], Kalakuntla Varshini Rao[3]

[1] Professor, Department of General medicine, Navodaya Medical College Hospital And Research Centre Raichur, Karnataka, 584103, India
[2] Final year post graduate, Department of General medicine, Navodaya Medical College Hospital and Research Centre Raichur, Karnataka, 584103, India
[3] 2nd Year Post Graduate, Department of General medicine, Navodaya Medical College Hospital and Research Centre Raichur, Karnataka, 584103, India

ABSTRACT

Background: Elevated serum ferritin levels have been associated with acute myocardial infarction (AMI), but its prognostic significance remains unclear. This study aimed to investigate the serum ferritin levels in patients with AMI and to explore its prognostic importance.
Methods: This study involved patients admitted to Navodaya Medical College Hospital and Research Centre, Raichur, with confirmed AMI, and age and gender-matched controls. Serum ferritin levels were measured at presentation and at a 4-week follow-up. Clinical features, co-morbidities, habits, and echocardiographic findings were also recorded.
Results: Serum ferritin levels were significantly elevated in patients with AMI at presentation (mean: 319.38, SD: 94.75) and at a 4-week follow-up (mean: 327.99, SD: 105.81) compared to controls ($p < 0.0001$). There was no significant difference in serum ferritin levels across different categories of left ventricular ejection fraction ($p = 0.762103$). The presence or absence of co-morbidities such as hypertension and diabetes, and habits like smoking and alcoholism, did not significantly influence serum ferritin levels.
Conclusion: Our study suggests that serum ferritin levels are significantly elevated in patients with AMI and these elevated levels persist even at a 4-week follow-up. However, these levels did not correlate with left ventricular ejection fraction or with the presence or absence of certain co-morbidities and habits. Future studies are needed to further explore these relationships and the potential prognostic role of serum ferritin in AMI.

Key Words: *Serum Ferritin, Acute Myocardial Infarction, Prognosis, Co-morbidities, Habits, Left Ventricular Ejection Fraction*

***Corresponding Author**
Dr Hemanth Kumar K
Final year post graduate, Department of General medicine, Navodaya Medical College Hospital and Research Centre Raichur, Karnataka, 584103, India

INTRODUCTION

Cardiovascular diseases are the leading cause of mortality globally as quoted by the World Health Organization (WHO) in the industrialized countries and is responsible for almost 45% of all deaths and also is associated with high morbidity, mortality and high rate of rehospitalization of the patients [1]. Myocardial infarction (MI) is defined pathologically as death of myocardial cell due to prolonged myocardial ischemia which is due to inadequate oxygen supply to myocardial cells [2].

It has become clear over the past 50 years that a cascade of thrombotic events following the atherosclerotic plaque rupture results in occlusion of coronary artery which in turn interrupts the blood supply and oxygen to myocardium resulting in infarction, which further leads to necrosis of myocardium ultimately leading to heart failure. Hence early treatment of myocardial ischemia is required to prevent necrosis which involves fibrinolysis, coronary artery bypass grafting, percutaneous coronary intervention, etc., to have a better improved outcome [3]. The rate of in-hospital mortality among patients with MI has decreased with the improved hospital care, but still acute myocardial infarction is a life-threatening disease worldwide and hence prompt revascularization with primary coronary intervention is critical [4].

Patients with acute MI present with intense chest pain which is more persistent and often accompanied by nausea, sweating, while 20-25% of the MI's are silent. The cardiac bio-markers like troponin I and T are highly specific for myocardial injury and is the preferred biochemical marker for diagnosis of acute myocardial infarction. Creatinine kinase is another biomarker widely used [5]. Over the past several years, many observational and epidemiological studies have identified new and potential factors for atherothrombotic vascular diseases. Levels of homocysteine, fibrinogen, infection and inflammation, atherogenic lipoprotein, elevated triglyceride and there is a strong evidence about oxidative free

radicals. Iron is a dietary constituent and a pre-oxidant and a high concentration of blood ferritin is considered as a potential novel risk factor for coronary heart disease (CHD) [6].

Metabolism of iron is important in order to maintain biological function and its disturbance leads to iron deficiency and iron deficiency is a prevalent co-morbidity in heart failure and is independently associated with mortality and reduced functional capacity [7]. The ability of iron to induce oxidative stress has been considered to be contributing to pathogenesis of coronary artery disease (CAD) and coronary heart disease is the leading cause of death in South Asian sub-continent. Dyslipidemia, physical inactivity, hyper-homocysteinemia, genetic, environmental and nutritional factors are associated with increased mortality [8].

Free iron is considered a catalyst of production of free radicals which has been implicated in ischemia of myocardial damage and peroxidation of lipid and free iron may accelerate progression of atherosclerosis and contribute to myocardial injury. Direct evidence of high stored concentration of iron increases the incidence of ischemic heart disease. Furthermore, serum ferritin was also observed to be one of the strongest indicators of presence and progression of carotid artery disease [9].

In order to understand the importance of serum ferritin levels among patients presenting with acute myocardial infarction, we undertook this study to find out the levels of serum ferritin among patients with acute MI and also to study the importance of serum ferritin levels as a prognostic factor for acute myocardial infarction.

AIMS AND OBJECTIVES

Aim:

"The aim of our study was to study the levels of serum ferritin in acute myocardial infarction and its prognostic importance"

Objectives:

1) To determine the levels of serum ferritin in acute myocardial infarction
2) To determine the prognostic importance of serum ferritin in acute myocardial infarction
3) To compare the relationship of serum ferritin with risk factors of acute myocardial infarction

MATERIALS AND METHODS

Myocardial infarction is a sudden episode and is associated with mortality if untreated promptly immediately. Our study aimed at determining the prognostic importance of serum ferritin in cases of acute myocardial infarction and also to compare the relationship between serum ferritin and other conventional risk factors of myocardial infarction.

Source of data:

The patients admitted in the general medicine wards of Navodaya Medical College Hospital and Research centre, Raichur with history of acute myocardial infarction were the source of our cases for data collection and the patients attending outpatient department (OPD) or admitted patients in department of general medicine with no present or past history of myocardial infarction were the control group for our study.

Study design:

The study design selected for our study was hospital-based Case-control study.

Study duration:

The study was carried out in the Navodaya Medical College Hospital and Research Centre, Raichur in the department of General Medicine for a duration of 18 months from 1st January 2021 to 31st July 2022.

Sample size and sampling method:

The sample size was calculated based on the formula used for sample size calculation for case-control studies,

$$n = \frac{2\,[(Z_{\alpha/2} + Z_{1-\beta})^2]\ x\ (\sigma)^2}{(m_1 - m_2)^2}$$

Where,

$Z_{\alpha/2}$ is confidence interval at 95% which is 1.96
$Z_{1-\beta}$ is power at 80% which is 0.84
σ is standard deviation = 34.88 (difference between cases and controls [15]
m1 is 170.21 (Serum ferritin mean among cases [15]
m2 is 149.42 (Serum ferritin mean among controls [15]
$m_1 - m_2$ is the mean difference (170.21 – 149.42 = 20.79)

With a design effect of 2 and by substituting the values in the above formula, the sample size obtained was 88, which was rounded off to 100.

So, finally the sample size was estimated to be 100 cases and 100 controls and they were selected based on simple random sampling technique.

Sampling procedure:

All the patients admitted in the medicine ward in Navodaya Medical College Hospital and Research Centre, Raichur fulfilling the inclusion and exclusion criteria were selected for our study after obtaining an informed written consent from them. The patients were recruited until our sample size was attained in the given duration of time for our study.

The cases were recruited once they are assessed by clinical examination, ECG and troponin I investigation. The controls were matched with gender and age and will be recruited irrespective of presence of risk factors like hypertension, diabetes, history of smoking etc. The controls were randomly selected from the subjects attending the OPD for minor ailments or routine medical check-up or the subjects accompanying the patients or amongst the office working staff from various departments in the institution. It was ensured that the subjects enrolled for the study in the control group did not have any evidence of acute myocardial infarction and coronary heart disease in the past or in the present, which was assured based on clinical examination and ECG findings.

Once recruited, the subjects and their attenders were explained in details about our study and the following investigations were done:

1) Complete blood hemogram (CBC)
2) Electrocardiography (ECG)
3) Troponin I
4) Serum ferritin
5) Random blood sugar (RBS)
6) Glycosylated hemoglobin (HbA1c)

A detailed history was taken from the patients related to their co-morbidities like diabetes, hypertension, dyslipidaemia, also their history of smoking, alcohol consumption etc. Serum ferritin levels was assessed on the day of admission and also after 4 weeks.

Inclusion criteria:

1. All diagnosed acute myocardial infarction cases which fulfils any of the following two criteria:

- Chest pain of duration less than 12 hours
- ST elevation in the ECG of more than 1 mm in at least two consecutive leads
- Elevated value of troponin I
- Presumably new onset bundle-branch block

2. Age of the cases and controls more than 18 years

Exclusion criteria:

1) Cases with high ferritin levels like haemochromatosis, liver diseases. Tuberculosis, chronic inflammatory diseases and those patients on iron therapy.
2) Control group patients with past or present history of acute myocardial infarction or any coronary heart diseases.

Ethical clearance:

Ethical clearance was obtained from institutional ethics committee, Navodaya Medical College Hospital and Research Centre, Raichur on

Data analysis plan:

The data collected from the patients were coded and entered into MS Excel sheet and master chart was prepared. The data was presented as rates, ratios and proportions. The data were presented in pie charts, bar diagram and associations were presented with line diagram. The association between the desired variables were established using chi-square test, t-test and ANOVA test. The association was considered statistically significant if the p value was found to be less than 0.05. EPI info software was used for the statistical analysis.

RESULTS

Table 1: Demographic and Clinical Characteristics of Cases and Controls

		Cases		Controls		
		Number	**Percentage**	**Number**	**Percentage**	**p-value**
Age	**<40 years**	5	5%	18	18%	**0.169**
	41 to 50 years	18	18%	26	26%	

	51 to 60 years	35	35%	31	31%	
	61 to 70 years	34	34%	21	21%	
	>71 years	8	8%	4	4%	
Sex	**Male**	78	78%	71	71%	**0.632**
	Female	22	22%	29	29%	
History of co-morbidities	**Hypertension**	65	65%	35	35%	**0.239**
	Diabetes Mellitus	67	67%	33	33%	
History of habits	**Smoking**	55	55%	45	45%	**0.146**
	Alcohol consumption	57	57%	43	43%	

The table above presents the demographic and clinical characteristics of the study participants, divided into cases and controls. The p-values for each characteristic indicate the statistical significance of the difference between the two groups.

A total of 100 cases and 100 controls were included in the study. Age distribution across both groups was varied, with the highest concentration of participants being in the age range of 51-60 years for cases (35%) and 41-50 years for controls (26%). The age distribution between the cases and controls was not statistically significant ($p = 0.169$).

The study included more males than females in both groups, with 78% male participants in the case group and 71% in the control group. The gender distribution was also not statistically significant between the two groups ($p = 0.632$).

In terms of co-morbidities, hypertension and diabetes mellitus were more prevalent in the cases (65% and 67% respectively) compared to the controls (35% and 33% respectively). However, these differences were not statistically significant ($p = 0.239$).

In terms of habits, more cases reported smoking and alcohol consumption (55% and 57% respectively) compared to controls (45% and 43% respectively). Again, these differences were not statistically significant ($p = 0.146$).

In conclusion, the cases and controls appear to be well matched in terms of age and sex. However, the cases had higher, but not statistically significant, prevalence of hypertension, diabetes mellitus, smoking, and alcohol consumption. These findings suggest that while these risk factors are more common in the cases, the differences were not statistically significant in this sample.

Table 2: Duration of Risk Factors in Cases

Duration	**Smoking (n=55)**		**Alcoholism (n=57)**		**Hypertension (n=65)**		**Diabetes (n=67)**	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
<10 years	10	18%	15	26%	18	28%	24	36%
11 to 20 years	25	46%	32	56%	34	52%	33	49%
>21 years	20	36%	10	18%	13	20%	10	15%

Table 2 illustrates the duration of the four risk factors - smoking, alcoholism, hypertension, and diabetes - among the case group.

Among those who reported smoking (n=55), 18% had been smoking for less than 10 years, 46% for 11 to 20 years, and 36% for more than 21 years. The prevalence of smoking was highest in the 11 to 20 year duration category.

For participants reporting alcoholism (n=57), 26% had a history of alcohol consumption for less than 10 years, 56% for 11 to 20 years, and 18% for more than 21 years. Like smoking, alcoholism was most prevalent in the 11 to 20 year duration category.

Regarding hypertension (n=65), 28% had been diagnosed with the condition for less than 10 years, 52% for 11 to 20 years, and 20% for more than 21 years. Again, the majority of participants had a history of hypertension for 11 to 20 years.

Lastly, among participants with diabetes (n=67), 36% had been diagnosed with the disease for less than 10 years, 49% for 11 to 20 years, and 15% for more than 21 years. Unlike the other risk factors, the prevalence of diabetes was distributed more evenly across the duration categories, with the highest prevalence in the 11 to 20 year duration category.

These findings suggest that the majority of cases with smoking, alcoholism, and hypertension have a history of these risk factors in the 11 to 20 year duration category. For diabetes, the distribution is more evenly spread across the duration categories. Further studies could explore the potential links between the duration of these risk factors and serum ferritin levels in acute myocardial infarction.

Table 3: Presence of Signs and Symptoms in Cases

		Present		Absent	
		Number	**Percentage**	**Number**	**Percentage**
Signs and symptoms	**H/o chest pain**	88	88%	12	12%
	ECG Abnormality	95	95%	5	5%
	Echo RWMA	95	95%	5	5%
	Troponin positive	100	100%	0	0

		Cases		Controls		
		Number	**Percentage**	**Number**	**Percentage**	
Pulse rate	**<60 bpm**	0	0	0	0	**0.001**
	61 to 100 bpm	1	1%	100	100%	
	101 to 120 bpm	94	94%	0	0	
Systolic Blood pressure	**<120 mmHg**	20	20%	100	100%	**0.001**
	121 to 140 mmHg	15	15%	0	0	
	141 to 160 mmHg	30	30%	0	0	
	>161 mmHg	35	35%	0	0	
Diastolic Blood pressure	**<80 mmHg**	26	26%	100	100%	**0.001**
	81 to 90 mmHg	43	43%	0	0	
	91 to 100 mmHg	27	27%	0	0	
	>101 mmHg	4	4%	0	0	
Haemoglobin	**<11 gm%**	18	18%	0	0	**0.003**
	>11 gm%	82	82%	100	100%	

Table 3 shows the presence and absence of various signs and symptoms in the case group, which consists of patients diagnosed with acute myocardial infarction.

The presence of a history of chest pain was reported in 88% of cases, while 12% of cases did not report such a history. This indicates that the majority of cases experienced chest pain as a symptom before the acute myocardial infarction event.

An ECG (Electrocardiogram) abnormality was detected in 95% of the cases, with only 5% of cases showing no ECG abnormalities. This suggests that ECG abnormalities are a common finding in acute myocardial infarction patients in this sample.

Echo RWMA (Regional Wall Motion Abnormality), a sign of abnormal motion or thickening of the heart wall segments, was present in 95% of cases, while it was absent in 5% of cases. This high prevalence of RWMA indicates a significant association with acute myocardial infarction in this sample.

Finally, all cases (100%) were troponin positive, reinforcing that troponin is a critical and sensitive biomarker for the diagnosis of acute myocardial infarction. No case was reported as troponin negative.

These results highlight the importance of these signs and symptoms in diagnosing acute myocardial infarction. Further studies could help understand the correlation between these signs and symptoms and serum ferritin levels in acute myocardial infarction patients.

Table 4: Comparison of Serum Ferritin Levels between Cases and Controls at Presentation and 4-Week Follow-up

Serum ferritin levels	Cases		Controls		t test value
	Mean	SD	Mean	SD	(p value)
At presentation/first visit	319.38	94.75	183.78	44.17	-12.97 (<0.0001) *
At 4-week follow-up	327.99	105.81	186.14	41.91	-12.46 (<0.0001) *

Table 4 presents the comparison of serum ferritin levels between the cases and controls at presentation/first visit and at the 4-week follow-up.

At presentation/first visit, the mean serum ferritin level in the cases was significantly higher (319.38 ng/mL; SD = 94.75) than in the controls (183.78 ng/mL; SD = 44.17). The t-test value was -12.97, indicating a highly statistically significant difference ($p < 0.0001$) between the two groups.

At the 4-week follow-up, the mean serum ferritin level in the cases remained significantly higher (327.99 ng/mL; SD = 105.81) than in the controls (186.14 ng/mL; SD = 41.91). The t-test value was -12.46, again indicating a highly statistically significant difference ($p < 0.0001$) between the two groups.

These results suggest that serum ferritin levels are significantly elevated in patients with acute myocardial infarction both at the time of presentation and at a 4-week follow-up, indicating its potential as a prognostic marker. Further studies could be valuable to investigate the role of serum ferritin in the pathophysiology and prognosis of acute myocardial infarction.

Table 5: Comparison of Serum Ferritin Levels among Different LVEF Categories

Echo findings	Serum ferritin levels		ANOVA test value
	Mean	SD	(p value)
LVEF <40% (n=33)	325.15	85.58	**0.27244 (0.762103) NS**
LVEF 40 – 50% (n=38)	322.74	105.08	
LVEF 50 – 60% (n=29)	308.41	94.46	

Table 5 compares the mean serum ferritin levels among three different categories of left ventricular ejection fraction (LVEF) in the case group.

The group with LVEF less than 40% (n=33) had a mean serum ferritin level of 325.15 ng/mL (SD = 85.58). For the group with LVEF between 40% and 50% (n=38), the mean serum ferritin level was 322.74 ng/mL (SD = 105.08). Lastly, for the group with LVEF between 50% and 60% (n=29), the mean serum ferritin level was 308.41 ng/mL (SD = 94.46).

An analysis of variance (ANOVA) was conducted to test for a statistically significant difference in serum ferritin levels among the three LVEF groups. The ANOVA test value was 0.27244, with a corresponding p-value of 0.762103. This result is not statistically significant (NS), indicating that there is no significant difference in the serum ferritin levels among the three different LVEF categories in this sample.

These findings suggest that in this sample, the severity of left ventricular dysfunction, as measured by LVEF, does not appear to significantly influence serum ferritin levels in patients with acute myocardial infarction.

Table 6: Comparison of Serum Ferritin Levels Based on Presence or Absence of Co-morbidities and Habits

Co-morbidities		Serum ferritin levels		t test value
		Mean	SD	(p value)
Hypertension	**Present (n=65)**	307.2	101.04	**1.778 (0.0785) NS**
	Absent (n=35)	342	76.83	
Diabetes	**Present (n=67)**	317.52	93.71	**0.280 (0.7804) NS**
	Absent (n=33)	323.15	96.73	
History of habits		**Serum ferritin levels**		**t test value**
		Mean	**SD**	**(p value)**
Smoking	**Present (n=55)**	320.16	87.19	**-0.091 (0.9274) NS**
	Absent (n=45)	318.42	103.23	
Alcoholism	**Present (n=57)**	314.4	91.17	**0.606 (0.5458) NS**

	Absent (n=43)	325.98	98.91	

Table 6 provides a comparison of mean serum ferritin levels based on the presence or absence of co-morbidities (hypertension and diabetes) and habits (smoking and alcoholism) in the case group.

For participants with hypertension (n=65), the mean serum ferritin level was 307.2 ng/mL (SD = 101.04). For those without hypertension (n=35), the mean serum ferritin level was higher at 342 ng/mL (SD = 76.83). However, the t-test value of 1.778 with a corresponding p-value of 0.0785 indicates no statistically significant difference in serum ferritin levels between the two groups.

Similarly, for participants with diabetes (n=67), the mean serum ferritin level was 317.52 ng/mL (SD = 93.71). For those without diabetes (n=33), the mean serum ferritin level was slightly higher at 323.15 ng/mL (SD = 96.73). Again, the t-test value of 0.280 with a corresponding p-value of 0.7804 suggests no statistically significant difference in serum ferritin levels between the two groups.

For the presence of the habit of smoking (n=55), the mean serum ferritin level was 320.16 ng/mL (SD = 87.19), while for non-smokers (n=45), the mean serum ferritin level was slightly lower at 318.42 ng/mL (SD = 103.23). The t-test value of -0.091 with a corresponding p-value of 0.9274 suggests no statistically significant difference in serum ferritin levels based on the presence or absence of smoking.

Lastly, for participants with alcoholism (n=57), the mean serum ferritin level was 314.4 ng/mL (SD = 91.17). For those without alcoholism (n=43), the mean serum ferritin level was higher at 325.98 ng/mL (SD = 98.91). The t-test value of 0.606 with a corresponding p-value of 0.5458 indicates no statistically significant difference in serum ferritin levels based on the presence or absence of alcoholism.

These results suggest that in this sample, the presence or absence of hypertension, diabetes, smoking, and alcoholism does not significantly affect serum ferritin levels in patients with acute myocardial infarction.

DISCUSSION

This study aimed to investigate the levels of serum ferritin in patients with acute myocardial infarction and to explore its prognostic significance. Our results showed that serum ferritin levels were significantly elevated in patients with acute myocardial infarction at both presentation and at a 4-week follow-up, compared to controls ($p < 0.0001$). There was no significant difference in serum ferritin levels across different categories of left ventricular ejection fraction (LVEF) ($p = 0.762103$). Additionally, the presence or absence of co-morbidities such as hypertension and diabetes, and habits like smoking and alcoholism, did not significantly influence serum ferritin levels.

These findings align with previous research that has suggested a relationship between elevated serum ferritin levels and acute myocardial infarction. For instance, a study by Tuomainen et al. found that men with higher serum ferritin levels had a significantly increased risk of acute myocardial infarction [10]. Furthermore, Klipstein-Grobusch et al. reported that high serum ferritin levels were associated with an increased risk of myocardial infarction in women [11]. However, our study extends these findings by demonstrating that these elevated levels persist even at a 4-week follow-up.

Interestingly, our findings did not indicate a significant correlation between serum ferritin levels and LVEF. This contradicts some previous studies. For example, Anand et al. reported a significant association between high serum ferritin levels and reduced LVEF in patients with heart failure [12]. The discrepancies between our findings and those of Anand et al. might be due to differences in study populations, sample sizes, or methods of assessing LVEF.

We also found no significant relationship between serum ferritin levels and the presence or absence of co-morbidities like hypertension and diabetes, and habits like smoking and alcoholism. These findings contrast with previous research. For instance, a study by Ford et al. found that serum ferritin levels were significantly higher in diabetic patients compared to non-diabetic patients [13]. Additionally, Sullivan suggested that iron overload due to excessive alcohol consumption could lead to elevated serum ferritin levels [14]. However, our study did not support these associations. This discrepancy could be due to differences in the sample size, population characteristics, or methods of assessing and categorizing these risk factors.

Our study has some limitations. The sample size was relatively small, which might limit the generalizability of our findings. Additionally, we did not assess other potential confounders, such as dietary habits, physical activity levels, or genetic factors, that might influence serum ferritin levels.

CONCLUSION

In conclusion, our study provides compelling evidence that serum ferritin levels are significantly elevated in patients with acute myocardial infarction, and these elevated levels persist even at a 4-week follow-up. Despite these associations, serum ferritin levels did not correlate with left ventricular ejection fraction or with the presence or absence of certain co-

morbidities and habits, such as hypertension, diabetes, smoking, and alcoholism. These findings indicate that serum ferritin could potentially serve as a marker of acute myocardial infarction, but its role in prognosis remains uncertain. Future research with larger sample sizes and more comprehensive assessments of potential confounders are needed to further elucidate the complex relationships between serum ferritin, acute myocardial infarction, and associated risk factors.

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