ORIGINAL RESEARCH

A Case control study on the Association of Serum Ferritin levels with Acute Myocardial Infarction

Vadiga Ramana Kumar[1], Atul Pundlik Ramteke[2], Guguloth Prem Kumar[3]

[1,2&3]Senior Resident, Department of General Medicine/Hospital, Suryapet Telangana, India

ABSTRACT

Background: To evaluate the serum ferritin levels in patients with acute myocardial infarction. To inspect normal healthy individuals with non-cardiac chest pain for serum ferritin levels. To distinguish ferritin levels persisting in both the study population. Comparing serum ferritin levels to the probability of developing acute myocardial infarction. To study relevance of serum ferritin level to acute myocardial infarction.

Material and Methods: A case controlled study was held by Department of General Medicine, Government General Hospital, Suryapet, Telangana, India from December 2021 to September 2022. The study consisted of male patients with myocardial infarction for determining the association of serum ferritin to acute myocardial infarction.

Results: The statistical analysis data for the evaluation of study details for different diagnostic test between cases and control group and determines significance between them. Comorbidities associated with cases and control shows that evidence of diabetes mellitus. The comparison of ferritin and lipid profile no significance existed. On differentiating ferritin administrated value to that of day 3 shows statistical significance. While comparing ferritin and glycaemic control, correlation prevailed. A mixed results were obtained from performed study that proved insufficient to correlated ferritin with myocardial infarction.

Conclusion: The study contradicted the hypothesis. Neither of the tested iron biomarkers confirmed the iron hypothesis, based on the meta-analysis. These finding suggest that the evidence is not robust enough to support the connection among iron and cardiovascular disease. This discrepancy in results could be due to the study's use of different iron markers. Despite the large amount of data that has been published to far, the importance of iron in CVD is still up for debate.

Keywords: ECG, Ferritin, Myocardial infarction, Haemoglobin, Lipid profile.

Corresponding Author: Dr. Vadiga Ramana Kumar, Senior Resident, Department of General Medicine/Hospital, Suryapet Telangana, India.

INTRODUCTION

A mobilised form of iron, ferritin is an intracellular globular protein with a multi-subunit protein shell called apoferritin enclosing a core of up to 4500 ferric ions. A molecule or chemical fragment that contains one or more free radicals has a separate existence and has unpaired electrons in its outer orbit.[1,2] Typically, oxidative processes ensure that all of the molecular oxygen is used. Complete oxygen reduction, which is uncommon in most cases. The production of free radicals is crucial to both health and illness. Free radicals from oxygen encourage the oxidation of lipids, which causes the production of atherosclerosis. The connection between the titres of autoantibodies supports this against the development of carotid atherosclerosis and oxidatively modified LDL3,4,5.[2,3] Free iron catalyses the

creation of free radicals, which creates powerful oxidants may raise the risk of atherosclerosis, oxidation of lipids, and cardiovascular disease. By ferrireductase or ascorbic acid, ferrous iron is converted from ferric iron, and then DMT-1 transports the iron to the enterocytes in the villus of the intestinal lumen.[4,5] Through an interaction between IRP-1 and the IRE of DMT-1, the amount of intracellular iron controls the expression of DMT-1 within these cells. Therefore, the amount of iron absorbed from the intestinal lumen depends on the iron concentration in enterocytes.[5,6] Based on the present data, the intracellular iron level of enterocytes is influenced by the interaction between the HFE protein and transferrin receptors (TfR) on the basolateral surface of crypt cells. The TfR interacts with cells which have HFE protein expressed on their surface, lowering the TfR's affinity for transferrin. The interaction between transferrin and TfR is a key mechanism for iron uptake into cells. Intracellular iron levels are inversely associated with TfR expression.[6] The normal entry of iron into the crypt cell of the villus and the control of iron absorption depends on the connection of HFE with TfR.[7] Iron is primarily absorbed from the intestines and stored in the liver. Iron is deposited in other parenchymal tissues, such as the spleen and the acinar cells of the erythrocyte, when its capacity is surpassed. The most significant protein in the body that stores iron is ferritin. Very little iron is naturally present in normal serum. The amount of iron in the body and the concentration of iron in the blood are connected. It is helpful for figuring out the body's iron stores. During the course of treatment, it is helpful.[7,8] Oxygen supply and demand are out of balance, which results in myocardial ischaemia. Myocardial supply is affected by the aortic diastolic pressure, the degree of coronary artery obstruction, the tone of the coronary vessels distal to the obstruction, and the sufficiency of collateral blood flow.[8] Your myocardial oxygen supply is restricted when one of the following circumstances occurs: Obstructive atherosclerotic lesion-induced coronary artery disease, platelet aggregation, thrombosis, rupture, subintimal haemorrhage, plaque, and a lesion of atherosclerosis that has already spasmed, Spasms that develop suddenly, Coronary artery embolism, particularly in atrial fibrillation patients (AF) and Myxoma of the left atrium or mitral valve failure, Paroxysmal supraventricular tachycardia causes a shortening of the diastole, Coronary artery disease in lupus nephritis and other collagen illnesses, Aorto-arteritis, Kawasaki illness, and polyarthritis nodosa.[9,10] The left coronary artery originates from the pulmonary artery that is abnormal, Severe anaemia and carbon monoxide poisoning, The coronary ostia narrows, similar to syphilitic aortitis, Thyroid problems, Myocardial bridges. This investigation has been performed to focus on the method in order to iron levels and myocardial infarctions are linked. There are several contradictory results about the link between high amounts of stored iron and Myocardial infarction rates rising.[10]

MATERIALS & METHODS

The study consisted of 50 cases and 50 controls which were conducted from December 2021 to September 2022. It considered the components like clinical history and duration from onset of symptoms in patients. ECG, Cardiac specific enzymes, Serum ferritin levels by ECLIA on day 1 of presentation and repeat ferritin levels on day 3, or at discharge in cases, Routine lab investigations and Echo were the parameters involved for evaluation of association of serum ferritin to acute myocardial infarction.

Inclusion Criteria:

Male Patients presenting with acute myocardial infarction satisfying the following criteria:

1. ST elevation Myocardial Infarction.
2. Non ST elevation myocardial infarction with elevated cardiac enzymes.

Control: Age matched healthy male subjects, with non-cardiac chest pain;

Exclusion Criteria:

All female patients Subjects with:

1. Neoplastic and liver diseases
2. Primary and secondary haemochromatosis
3. Alcohol abuse
4. Chronic kidney disease
5. Clinical history suggestive of inflammation or infection.

RESULTS

Of the total 94 clinically suspected dengue cases, 23 serum samples were positive for dengue infection .7 serum samples were positive for Dengue NS1 antigen ELISA , 4 for Dengue IgM ELISA and 12 for both NS1 Antigen + IgM Antibody .

Table No. 1: Mean Age of Cases and Controls:

	Age (years)				
Group	**N**	**Mean**	**Std. Deviation**	**t- value**	**P value**
Cases	50	58.80	8.0458	0.097	0.923
Controls	50	58.60	12.7103		

Table No. 2: Diagnosis

		Group		**Total**
		Cases	**Control**	
AAA	Count	0	1	1
	%	.0%	2.0%	1.0%
AG	Count	0	2	2
	%	.0%	4.0%	2.0%
APD	Count	0	3	3
	%	.0%	6.0%	3.0%
ALMI	Count	4	0	4
	%	8.0%	.0%	4.0%
AWMI	Count	17	0	17
	%	34.0%	.0%	17.0%
BPH	Count	0	6	6
	%	.0%	12.0%	6.0%
CC	Count	0	2	2
	%	.0%	4.0%	2.0%
Cellulitis	Count	0	1	1
	%	.0%	2.0%	1.0%
Depression	Count	0	1	1
	%	.0%	2.0%	1.0%
F.U. O	Count	0	1	1
	%	.0%	2.0%	1.0%
LRTI	Count	0	2	1
	%	.0%	4.0%	1.0%
H. A	Count	0	2	2
	%	.0%	4.0%	2.0%
HTN	Count	0	3	3
	%	.0%	6.0%	3.0%

IBS	Count	0	2	2
	%	.0%	4.0%	2.0%
IVDP	Count	0	7	
	%	.0%	14%	7%
IWMI	Count	25	0	25
	%	50.0%	.0%	25.0%
LWMI	Count	4	0	4
	%	8.0%	.0%	4.0%
MD	Count	0	1	1
	%	.0%	2.0%	1.0%
Pleurisy	Count	0	2	2
	%	.0%	4%	2.0%
Seizure	Count	0	6	6
	%	.0%	12%	6.0%
UC	Count	0	1	1
	%	.0%	2.0%	1.0%
TIA	Count	0	5	5
	%	.0%	10%	5%
Tonsillitis	Count	0	1	1
	%	.0%	2%	1%
UTI	Count	0	1	1
	%	.0%	2%	1%
TOTAL	COUNT	50	50	100
	%	100%	100%	100%

Table No 3: Chi-Square test

	Chi-Square Test			
	Value	df	Asymp. Sig. (2 sided)	
Pearson Chi-Square	84.98	88		.571

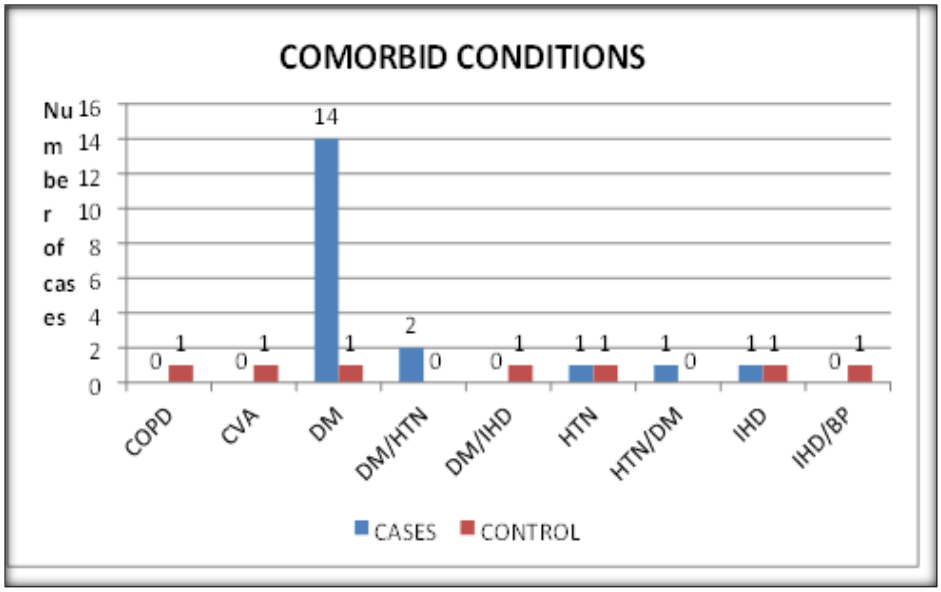

Figure No. 1 Comparison of different comorbidity conditions

Table No. 4: Comorbidity conditions

Comorbid Conditions					**Total**
			Group		
			Cases	**Control**	
		Count	23	35	58
		%	54.8%	83.3%	69.0%
	COPD	Count	0	1	1
		%	.0%	2.4%	1.2%
	CVA	Count	0	1	15
		%	.0%	2.4%	1.2%
	DM	Count	14	1	15
		%	33.3%	2.4%	17.9%
	DM/HTN	Count	2	0	2
	DM/IHD	Count	0	1	1
		%	0%	2.4%	1.2%
	HTN	Count	1	1	2
		%	2.4%	2.4%	2.4%
	HTN/DM	Count	1	0	1
		%	2.4%	.0%	1.2%
	IHD	Count	1	1	2
		%	2.4%	2.4%	2.4%
	IHD/BP	Count	0	1	1
		%	.0%	2.4%	1.2%
	TOTAL	COUNT	50	50	100
		%	100%	100%	100%

Table No 5: Chi-Square test

	Chi-Square Tests		
	Value	df	Asymp.Sig.(2-sided)
Pearson Chi-Square	41.58	28	.047 (Sign.)

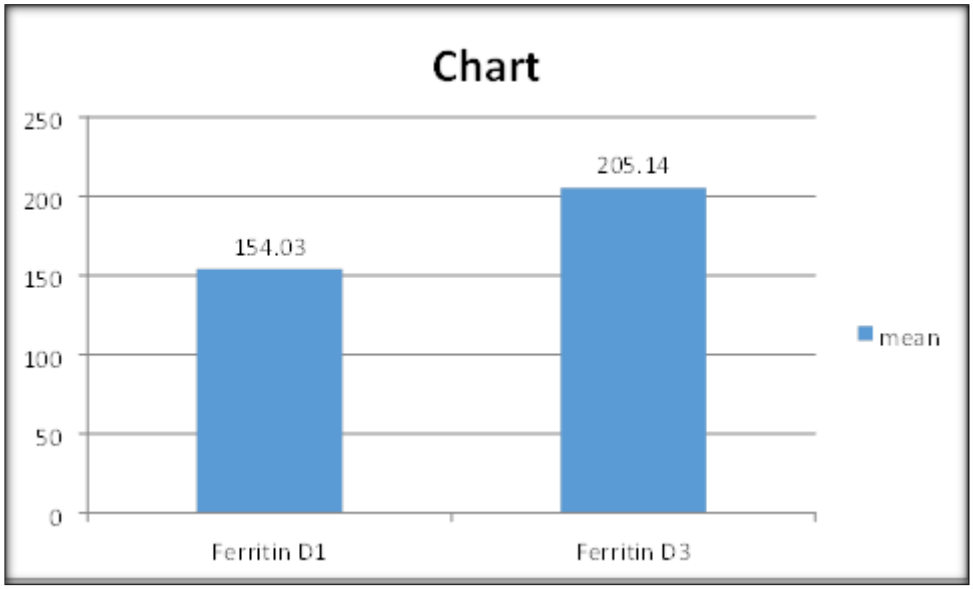

Figure No 2: Comparison of Ferritin D1 and Ferritin D3

Table No 6: Comparison of correlation of Ferritin with Lipid Profile

		Descriptive Statistics			
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation mn**
TC	50	99.4	273.0	161.974	42.6990
TG	50	59.0	288.0	108.444	45.7240
LDL	50	47.0	207.3	96.644	35.4648
VLDL	50	11.80	57.60	24.3128	11.09995
HDL	50	28.6	67.2	38.694	7.5060
TC/HDL	50	2.82	7.48	4.1954	.87670

Table No 7: Correlation between ferritin and lipid profile

Correlations							
Group			**TC**	**TG**	**LDL**	**VLDL**	**HDL**
CASE	Ferritin Dl	R	0.07932	-0.02246	-0.01538	0.04892	0.08628
		P	0.584	0.877	0.9156	0.7358	0.5513
		N	50	50	50	50	50

Table No 8: Comparison of Ferritin levels on admission and on day 3 -Cases

	Paired Samples Statistics				
Group		**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**
	Ferritin Dl	154.032	50	109.9610	15.5508
	Ferritin D3	205.139	50	110.4321	15.6174

Table No 9: Paired samples t test

	Paired Samples Test				
Group		**Paired Differences**		**T**	**Sig. (2-tailed)**
		Mean	Std. Deviation	-5.695	.000
	Ferritin D1 & Ferritin D3	-51.1076	-0.4718		

Table No 10: Comparison of Ferritin levels in Cases and Controls

		Ferritin		**K**		
	Group	**N**	**Mean**	**Std. Deviation**	**T**	**p-value**
Ferritin Dl	Cases	50	154.0322	109.9610	0.953	0.345
	Controls	50	138.7422	60.08422		

Table No 11: Correlations of ferritin levels with glycohemoglobin and haemoglobin

		Correlations		
Group-Cases			**Hb**	**Glyco Hb**
	Ferritin Dl	Pearson Correlation	.195	.485
		Sig. (2-tailed)	.175	0.012 (sign.)
		N	50	26

DISCUSSION

In this investigation, which included 50 cases and 50 controls, there was no significant difference in serum ferritin levels between patients and controls. Patients who visit the Governament General Hospital, Suryapet are the subjects of this study. Venous samples from patients who have undergone an acute myocardial infarction are taken and processed on days one and three. This indicated that larger amounts of stored iron in these two categories may be the cause of the increased incidence of heart illness in men and postmenopausal women compared to premenopausal women. The following findings lend support to this theory: (1) myocardial failure in individuals with iron storage diseases; (2) the build-up of stored iron in men after adolescence as a function of age; and (3) the accumulation of stored iron in women after menopause to levels comparable to men and roughly proportional to the increased risk. After three blood donations per year, a man's serum ferritin level reaches that of a young woman in menstruation.[11,12] Contrarily to a previous study, the results point to a possible inverse link between iron stores and cardiovascular and total mortality. The likelihood of an association between body iron status and the risk of coronary heart disease was strengthened by a three-year Finnish study that connected rising dietary iron and ferritin levels to an increased risk of myocardial infarction. A significant risk factor for acute myocardial infarction is a high blood ferritin level.[13] Males with blood LDL cholesterol levels of at least 5.0 mmol/l (193 mg/dl) had a larger correlation with this than other men. Additionally, a higher risk of sickness was connected to dietary iron intake. According to the study, larger iron stores are associated with a higher risk of acute myocardial infarction.[13,14] The risk of MI is associated with the highest tertile of ferritin was particularly pronounced in subjects who were current or former smokers, as well as in those who had diabetes or hypercholesterolemia, suggesting that serum ferritin may negatively affect the risk of ischemic heart disease in the elderly when combined with other risk factors.[15,16] A study to support the premise that serum ferritin levels are related to all-cause mortality or that serum ferritin levels are related to an increased risk of CVD, CHD, or MI death was earlier done. Men with iron levels in the top quartiles were found to have an inverse risk of MI. The researchers got to the conclusion that lower risk of first Ml was associated with iron levels in the higher normal range.[16,17] The iron theory proposed by Sullivan received little support from studies, and received even less opposition. There is no solid evidence to support the idea that iron is a CVD risk factor, according to research summarising the major conclusions of the most significant epidemiological studies published in the previous 32 years. In our study, the only group of men with diabetes who showed a correlation between greater ferritin levels and the risk of myocardial infarction was males. These results provide credence to the idea that iron only negatively affects coronary risk when there is oxidative stress coming from other sources. Free metal ions have the ability to catalyse the formation of the highly reactive hydroxyl radical from superoxide and hydrogen peroxide. Body iron is so tightly bound that it's possible there isn't any free iron in vivo under normal circumstances.[17,18] The release of iron from ferritin can be triggered by oxidative stress. Therefore, the occurrence of earlier oxidative stress may be required for the development of the detrimental effects linked to increased iron storage. Our inquiry is restricted by the absence of baseline ferritin levels, the small sample population, and the lack of further follow-up. Furthermore, no individual studies have been done to determine how other risk factors like smoking, hyperlipidaemia, and diabetes affect ferritin levels.[18,19] Therefore, the idea that iron is connected to CVD is not supported by any strong data. According to our research, ferritin behaves like an acute phase reactant everywhere other than where uncontrolled diabetes is present, where ferritin levels are high. The meta-analysis showed no support for the iron hypothesis in any of the investigated iron biomarkers.[19,20] These results suggest that the idea that iron is related to

cardiovascular disease is not well supported by the available evidence. The fact that the study used various iron markers may be the cause of this disparity in results. The significance of iron in CVD is still up for debate despite the vast number of research that has been published so far.

CONCLUSION

To conclude the study no evidence was found to suggest the hypothesis that iron may be associated with Coronary Vascular Disease.

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