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RESEARCH ARTICLE

Serum ferritin levels in patients with Acute Myocardial Infarction – A Prospective controlled study.

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Abstract

Background: Various studies showed statistically significant association of high serum ferritin and AMI while some authors did not find any significant association of high ferritin and AMI. The main objective of our study was to compare the ferritin levels in cases and controls, in order to assess the relationship of serum ferritin with AMI, in both univariate and multivariate analysis, after controlling for established conventional risk factors (like diabetes mellitus, hypertension, lipids, body mass index, smoking, and alcohol intake).

Materials and methods: The present study was undertaken in the Department of General Medicine, S.V.S Medical College and Hospital, Mahabubnagar during 1-8-2010 and 31-7-2014. A total of 150 patients age, sex and Hemoglobin matched, were recruited from S.V.S Medical College and hospital for the present study of which 75 subjects constituted the control group called as the group A and remaining 75 subjects constituted the study group called as group B. the above cases were recruited irrespective of presence of any risk factors like hypertension, diabetes, smoking and alcohol.

Results and observations: The age of the patients varied form a minimum age of 30 yrs to a maximum of 70 years. The mean age of the patients in group A was 51.74 and the mean age in group b was 52.24, the mean age in two groups were not significantly different from each other $t = 0.265$, $p > 0.05$. The mean values for Total cholesterol, triglycerides, LDL, ferritin are significant higher in group B compared to group A $p < 0.001$. The mean value of HDL is significantly lower in group B compared to group A $p < 0.001$. Serum ferritin was significantly higher in the study group and when compared with other markers of myocardial injury this as significantly elevated as CPK, LDL and SGOT.

Conclusions: The univariate and multivariate analysis with serum lipids, diabetes, hypertension, smoking and alcoholism and obesity showed and independent risk factor and in the presence of other risk factors the risk estimated to be much higher.

Introduction:-

JL Sullivian (1981) was first to observe ferritin association with coronary heart disease (CHD) [1]. Over the past several years, observational and epidemiological studies have identified a host of new and potential risk factors for atherothrombotic vascular diseases. In this growing list of new and emerging risk factors, the entities like elevated blood levels of homocysteine, fibrinogen, inflammation and infection, atherogenic lipoprotein, elevated triglyceride, and number of genetic polymorphism are of particular interest. Apart from these, there is strong evidence that oxidative free radicals have a role in the development of degenerative diseases including CHD [2 and 3]. Oxidative free radicals increase the peroxidation of low-density lipoprotein (LDL), thereby increasing its uptake by macrophages with increased foam cell formation and atherosclerosis [4 and 5]. Iron, a dietary constituent, is a pre-oxidant and a high concentration of blood ferritin, which measures stored iron, is a potential novel risk factor for CHD. Free iron which acts as a catalyst for the production of free radicals has been implicated in lipid peroxidation and atherosclerosis leading to myocardial infarction (MI) [3]. Serum ferritin concentrations are directly proportional to intracellular ferritin concentration and considered to be the best clinical measure of body iron stores and most feasible to use in epidemiological studies [6]. Subsequently, results of the various studies showed statistically significant association of high serum ferritin and AMI [7 – 15]. However, some authors did not find any significant association of high ferritin and AMI [16 – 20].

Aims and objectives of the study: The main objective of our study was to compare the ferritin levels in cases and controls, in order to assess the relationship of serum ferritin with AMI, in both univariate and multivariate analysis, after controlling for established conventional risk factors (like diabetes mellitus [DM], hypertension [HTN], lipids, body mass index [BMI], smoking, and alcohol intake).

Materials and methods:-

The present study was undertaken in the Department of General Medicine, S.V.S Medical College and Hospital, Mahabubnagar during 1-8-2010 and 31-7-2014. A total of 150 patients age, sex and Hemoglobin matched, were recruited from S.V.S Medical College and hospital for the present study of which 75 subjects constituted the control group called as the group A and remaining 75 subjects constituted the study group called as group B. the above cases were recruited irrespective of presence of any risk factors like hypertension, diabetes, smoking and alcohol. The group A comprised of Controls that were selected randomly from subjects attending outpatient department of hospital for minor ailments, subjects accompanying patients or amongst office working staff from various departments. Controls were selected irrespective of presence of any risk factors like hypertension, diabetes, smoking and alcohol but without having Acute Myocardial Infarction in the present or past or any evidence of CHD. All the controls were screened by clinical examination and normal ECG. Group B comprised of cases of Acute Myocardial Infarction admitted into the Coronary Care Unit at S.V.S Medical College and hospital. Serum lipid profile, hemogram, serum ferritin and cardiac markers viz. serum CPK, LDH, SGOT were analyzed in all subjects. The results were expressed in mg/dl for Total Cholesterol, HDL, LDL, Triglycerides results for hemoglobin was expressed in gm/dl and serum ferritin in µg/L. BMI was measured in both the groups and results were expressed in kg/m^2.History of presence of any risk factors like smoking, alcohol, hypertension, diabetes was taken and tabulated in the master sheet data. The data was analyzed using SPSS software version 17.0. Appropriate statistical tests were used to determine the role of various parameters in AMI. Descriptive results are expressed as mean and SD of various parameters in different groups. Probability value (p value) was used to determine the level of significance p value < 0.05 was considered as significant, p value < 0.01 was considered as highly significant.

Results and observations:-

The age of the patients varied form a minimum age of 30 yrs to a maximum of 70 years. The mean age of the patients in group A was 51.74 and the mean age in group b was 52.24, the mean age in two groups were not significantly different from each other $t = 0.265$, $p > 0.05$.

Table I: Distribution of subjects by Age group

Age group in years	Group A		Group B	
	Number	%	Number	%
30 – 40	11	14.67	6	8
41 – 50	22	29.33	26	34.67
51 – 60	25	33.33	36	48
61 – 70	17	22.67	7	9.33
Total	**75**	**100**	**75**	**100**
Mean± SD	**51.74 ± 10.75**		**52.24 ± 8.16**	

T = 0.265, p = 0.791

Among the total 75 patients in group A 59 were males (78.67%) and 16 were females (21.33%) compared to group B where 61 were males (81.33%) and 14 were females (18.67%).There was no significant difference observed in the sex distribution of subjects among three groups, Chi square value was 0.167 and significance (p) > 0.05.

Table II: Gender wise distribution of subjects among the groups

Sex	Group A		Group B	
	Number	%	Number	%
Male	59	78.67	61	81.33
Female	16	21.33	14	18.67
Total	**75**	**100**	**75**	**100**

$\chi^2 = 0.167$ p = 0.683

The mean BMI was significantly more in group B compared to group A (p < 0.001). 49.33 % of subjects in group A had a BMI between 21 – 25, 36 % had a BMI between 15 – 20, 14.67% had BMI between 26 – 30, compared to group A where 58.67 % subjects had a BMI between 21 – 25, 30.67% had BMI between 26 – 30 10.67 % had a BMI between 15 – 20.

Table III: Distribution of subjects according to BMI in different groups

BMI	Group A		Group B	
	Number	%	Number	%
15 – 20	27	36	8	10.67
21 – 25	37	49.33	44	58.67
26 – 30	11	14.67	23	30.67
Total	**75**	**100**	**75**	**100**
Mean± SD	**22.04 ± 2.68**		**24.14 ± 2.41**	

t value = 5.05 p value = <0.001

The mean values for Total cholesterol, triglycerides, LDL, ferritin are significant higher in group B compared to group A p < 0.001. The mean value of HDL is significantly lower in group B compared to group A p < 0.001. There was no statistical difference in the hemoglobin value between groups t 0.527, p > 0.05.

Table IV:Mean ± SD values of studied parameters in controls and patients with AMI.

PARAMETER	Group A		Group B		t value	p value
	MEAN	SD	MEAN	SD		
Total Cholesterol	170.4	23.7	209.04	16.87	11.48	<0.001
Triglyceride	128.3	34.43	164.5	41.9	5.78	<0.001
HDL	48.3	5.9	40.5	6.6	7.56	<0.001
LDL	96.4	23.4	135.5	19.04	11.21	<0.001
Hb %	11.97	1.19	12.07	1.15	0.527	0.59
Ferritin	112.52	33.28	216.54	42.85	9.26	<0.001

Table – V: Role of Smoking as a risk factor

Smoking	Group A		Group B		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	18	24	31	41.33	5.12	0.024
Absent	57	76	44	58.67		

Group A comprised of 24% cases who gave a positive history of smoking compared to 41.33 % in group B. there was a significantly higher number of smokers in patients who were admitted with acute myocardial infarction (χ^2 = 5.12) (p = 0.024).

Table – VI: Role of Alcohol as a risk factor

Alcohol	Group A		Group B		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	18	24	25	33.33	1.597	0.206
Absent	57	76	50	66.67		

Group A comprised of 24% cases who gave a positive history of chronic alcoholism compared to 33.33 % in group B. there was no statistical significance in consumption of alcoholics in patients leading to admission with acute myocardial infarction (χ^2 = 1.597) (p > 0.05).

Table – VII: Role of Hypertension as a risk factor

HTN	Group A		Group B		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	7	9.33	19	25.33	6.7	0.01
Absent	68	90.67	56	74.67		

Group A comprised of 9.33 % cases who had a positive history of hypertension compared to 25.33 % in group B. there was a significantly higher number of hypertensive patients who were admitted with acute myocardial infarction (χ^2 = 6.7) (p = 0.01).

Table VIII: Incidence of diabetes mellitus amongst the present subjects

Diabetes mellitus	Group A		Group B		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	4	5.33	32	42.67	26.65	< 0.001
Absent	71	94.67	43	57.33		

Group A comprised of 5.33 % cases who had a positive history of diabetes compared to 42.67 % in group B. there was a significantly higher number of diabetic patients who were admitted with acute myocardial infarction (χ^2 = 26.65) (p < 0.001).

Table IX. Comparison of the patients according to the blocked vessels

	Single vessel disease (20) Group B 1	**Double vessel disease (34) Group B 2**	**Triple vessel disease (21) Group B 3**
Serum Ferritin levels (Mean in mg/dL)	218.22	209.78	218.66

Table X. The values of serum ferritin and cardiac markers

Parameter	Group A (Control)	Group B (AMI Cases)	'p' value
Serum ferritin (Mean in $\mu g/L$)	112.52	216.54	< 0.001
Serum CPK (Mean IU/L)	128.34	404.84	< 0.001
Serum SGOT (Mean IU/L)	26.46	124.36	< 0.001
Serum LDH (Mean IU/L)	46.58	398.44	< 0.001

Table XI: Association of acute myocardial infarction with high serum ferritin and high serum cardiac markers

Parameter	Group A (Control)	Group B (AMI Cases)	Total	'p' value
Serum ferritin ≥200µg/L <200µg/L	 16 59	 65 10	 81 69	X^2 -16.48 O.R -12.69 C. I -7.36-69.8 P < 0.001
Serum CPK ≥ 200(IU/L) < 200(IU/L)	 5 70	 72 3	 77 73	X^2 -18.63 O.R -14.46 C. I -3.42-45.6 P < 0.001
Serum SGOT ≥40(IU/L) <40(IU/L)	 8 67	 62 13	 70 80	X^2-14.12 O.R - 9.62 C. I -2.48-30.02 P < 0.001
Serum LDH ≥300(IU/L) <300(IU/L)	 6 69	 61 14	 67 83	X^2 -14.92 O.R -10.08 C. I -3.2 - 30.0 P < 0.001

TABLE-3: **Comparison of conventional risk factors for myocardial infarction in cases and controls**

	Group A (Control)	Group B (AMI Cases)	Total	'p' value
Diabetes mellitus Present Absent	75 4 71	75 32 43	150 36 114	X2 -8.148 O.R -4.75 C. I -1.58-14.25 P < 0.005
Hypertension Present Absent	75 6 69	75 19 56	150 25 125	X2 -10 O.R -6 C. I -2.08-17.29 P < 0.005
Smoking Present Absent	75 18 57	75 31 44	150 49 111	X2 - 19.29 O.R -13.14 C. I -3.84-45.01 P < 0.001
Alcohol Present Absent	75 18 57	75 25 50	150 43 107	X2 -10.13 O.R -6.14 C. I -1.07-21.74 P < 0.005
BMI < 25 kg/M^2 >25 kg/M^2	75 11 64	75 23 52	150 34 116	X2 - 19.29 O.R -13.14 C. I -3.74-54.01 P < 0.001

Table Comparison of serum lipids for myocardial infarction in cases and controls

Parameter	Group A (Control)	Group B (AMI Cases)	Total	Significance
Serum cholesterol < 200 mg > 200 mg	 52 23	 24 51	 76 74	X^2 – 10.33 OR – 6.55 CI - 1.97-21.74 'p' - <0.05
Serum triglyceride <150 mg/dL >150 mg/dL	 64 11	 12 63	 76 74	X^2 – 13.82 OR – 7.8 CI - 2.45-25.9 'p' - <0.05
Serum LDL <130 mg/dL >130 mg/dL	 71 4	 13 52	 84 56	X^2 – 11.6 OR – 7.91 CI - 2.24-25.1 'p' - <0.05
Serum HDL >40 mg/dL <40 mg/dL	 44 31	 28 47	 72 78	X^2 – 7.2 OR – 5.46 CI - 1.41- 13.1 'p' < 0.05

Table XII. The association of ferritin and coronary artery disease after adjusting for age, diabetes, hypertension, dyslipidemia and smoking

	OR (95% of CI)	**Significance 'p' value**
Serum ferritin	1.005 (1.008 to 1.012)	0.045
Serum ferritin > 200 mg	4.56 (1.32 to 10.82)	0.001

OR – odds ratio; CI – confidence interval

Discussion:-

This case control study of 150 Indian subjects (75 AMI cases and 75 control individuals) showed a significant elevation in serum ferritin levels in AMI group. When adjusted for age, diabetes, hypertension, dyslipidemias and smoking showed a strong association of serum ferritin level and myocardial ischemic disease; but we could not find any difference in ferritin levels with severity of the disease. Similarly, the evidence of an association of elevated serum ferritin and increased risk of AMI came from various authors, [7 -15, 21 and 22] which is similar to our findings. But few studies did not reveal any significant elevation in serum ferritin levels [16 -20]. MONICA AMI study [23] found elevated ferritin levels in Finnish population. Rotterdam study also showed elevated serum ferritin in ischemic heart disease. Klipstein and his colleagues [24] concluded that elevated serum ferritin concentration was associated with increased risk of myocardial infarction in the elderly population of Ommoord, Netherland. This study demonstrated the more the elevation in ferritin levels the more is the risk i.e. a risk of 2.2 in patients with ferritin levels below 200 μg/L to a risk of 7.41 in the group with serum ferritin ≥ 200 μg/L [24]. This case control study revealed that excess serum ferritin is associated with acute myocardial infarction. In addition, findings showed that the risk of high serum ferritin persisted when other risk factors such as age, hypertension, diabetes, hyperlipidemia, high LDL-C, and smoking were adjusted in the model. Results indicated that people with CAD and serum ferritin concentration ≥ 200 ng/ml had a four-fold higher risk of atherosclerosis than healthy men. Therefore, elevated serum ferritin level may have an independent adverse effect on the incidence of atherosclerosis in patients with CAD. No significant statistical difference was seen in patients with single vessel, double vessels, and triple vessels disease regarding serum ferritin. A review article suggested strong epidemiological evidence is available that iron is an important factor in processing of atherosclerosis [31]. Many studies suggested that elevated serum ferritin increased the risk of atherosclerosis in the presence of other risk factors. Ferritin can act as a catalyzer in the production of oxygen free radicals and lipid peroxidation and play a role in the formation of oxidized LDL [28 and 31].

In conclusion, high stored iron concentration, as assessed by serum ferritin, was associated with the increased risk of CAD, while the number of injured vessels in these patients did not have any association with the progression of disease. In addition, it should be noted that high stored iron concentration was a strong and independent risk factor

in the incident of atherosclerosis. Ferritin levels did not show any significant changes in AMI with one, double and triple vessel disease. Serum ferritin levels can be used another biochemical marker for diagnosing AMI along with serum CPK, LDH and SGOT. The specificity and sensitivity of the same is to be determined by further studies.

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Conflicts:-

Authors have no conflicts of interest.

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