



ASSOCIATION BETWEEN SERUM FERRITIN AND HYPERTENSION IN PATIENTS ATTENDING TERTIARY CARE HOSPITAL.

Biochemistry

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ABSTRACT

Background: Ferritin is the major iron storage protein of our body and a diagnostic tool in the evaluation of iron status. Excessive iron storage increases the risk of vascular disease. Serum Ferritin is also referred as acute phase reactant. High ferritin values were found associated with increased risk of hypertension.

Materials and Methods: This cross-sectional study was conducted among 42 hypertensives (study group) and 42 normotensives (control group) attending the medical OPD in a tertiary care centre at south Tamil Nadu between August -October 2020. Serum ferritin was measured using Chemiluminescent immunoassay method in human serum using the Access Immunoassay systems – Beckman Coulter.

Results: Serum ferritin values were abnormal (elevated) among 25(58%) patients in study group ($P < 0.001$) with a mean serum ferritin value of 341.374 ± 191.8572 . Pearson Correlation coefficient = +0.526, P value < 0.001 Regression P value < 0.001

Conclusion: This study shows that elevated ferritin level was strongly associated with hypertension.

KEYWORDS

Hypertension, Ferritin, Inflammation

INTRODUCTION:

Iron is an essential element of our human body. Serum ferritin is the storage form of iron. Body iron is a strong pro-oxidant which causes oxidative tissue damage. Iron plays an important role in maintaining physiological homeostasis in the body; however, excess iron can lead to free radical damage, resulting in tissue damage¹. In addition, serum ferritin is known to reflect systemic inflammation as an acute phase reaction and several studies have shown that inadequately elevated iron stores may adversely affect health outcomes^{2,4}.

Increased serum ferritin plays an important role in metabolic risk factors such as Type 2 Diabetes, Insulin resistance, hypertension and dyslipidemia. The relationship between body iron store and blood pressure (BP) status has not been well established. Heme iron intake, which is exclusively provided by red meat, poultry, and fish, is positively associated with increased BP⁵. It was recently reported that erythropoietin was closely associated with iron or ferritin metabolism and can increase oxidative stress leading to the accentuation of hypertension^{6,7}. Hypertension (HTN) is an important health concern as it is a major risk factor for variety of cardiovascular diseases which includes stroke, atherosclerosis, Type 2 Diabetes Mellitus, coronary heart disease and renal disease. Currently it affects 26% of adults worldwide and its prevalence is predicted to increase to 29% by 2025⁸.

Inflammation plays an important contribution in the pathogenesis of atherosclerosis and its subsequent complications. Recently published data also suggest that chronic inflammation could be an independent risk factor for high blood pressure. Hence it has been decided to find the association between serum ferritin and hypertension in patients attending a tertiary care hospital

AIM & OBJECTIVE:

To study the association between serum ferritin and hypertension among patients attending the medical OPD at a tertiary care centre in south Tamil Nadu.

MATERIALS AND METHODS:

A cross sectional study was conducted to study the association between serum ferritin and hypertension among hypertensive patients attending medical outpatient department of a tertiary care centre in south Tamil Nadu. The study was conducted after getting approval from the Institutional ethics committee. Only eligible and willing participants were included in the study after getting their written informed consent. The total study duration was two months and the study was conducted between August- October 2020. Patients with systemic illness other than hypertension, those who were not willing to participate, pregnant

and lactating women were excluded from the study. A total of 84 subjects which included 42 hypertensives and 42 normotensives (bystanders of patients attending various departments of the tertiary care centre who were not hypertensives and without any other comorbidities) were enrolled in the study.

Serum ferritin was measured using Chemiluminescent Immunoassay method in human serum using the Access Immunoassay Systems-Beckman coulter. Body mass index (BMI) and Blood pressure were also measured during the visit. Basic demographic details along with BMI, Serum ferritin values were entered in a pre structured proforma.

STATISTICAL ANALYSIS:

The Data collected were entered in excel sheets and analysed using SPSS software version 23. Basic demographic details were analysed using descriptive statistics and expressed as percentages. Body mass index and Blood pressure measurements between the groups were analysed using independent sample T test and serum ferritin levels between the groups were analysed using Chi-square test and the results were represented as tables and figures.

RESULTS:

A total of 84 patients were enrolled in the study. Out of total 84 participants, 42(50%) were male and remaining 42(50%) were female. Among the control group, 6(14%) patients belong to less than 40 yrs, 27(64%) were between 41-60 yrs age group and 9(22%) were above 60 years of age, whereas in the study group, it was 2(5%), 25(60%) and 15(35%) respectively and the P value was 0.348 which was not significant. The Mean age of control and study group was 50.85 and 56.67 (yrs) with no statistical significance ($P = 0.190$).

Table No.1 Sex Distribution

AGE GROUP	SEX		
	MALE (%)	FEMALE (%)	
21-40 years	2 (5%)	6 (15%)	CHI SQUARE Test P value = 0.348
41-60 years	28 (67%)	24 (57%)	
>60 years	12 (28%)	12 (28%)	
Total	42	42	84

Table No.2 Basic Demographic Details

Parameter	Control group (Mean $\pm$ SD)	Study group (Mean $\pm$ SD)	Statistics
Age (years)	50.85 $\pm$ 12.483	56.67 $\pm$ 10.672	Chi square test P = 0.190
BMI (kg/m ²)	25.951 $\pm$ 2.9562	27.417 $\pm$ 3.3162	Independent sample T test P = 0.035

SBP (mmHg)	106.59± 10.395	153.44 ± 11.541	Independent sample T test P < 0.001
DBP (mmHg)	72.44 ± 5.823	93.72 ± 6.181	Independent sample T test P < 0.001

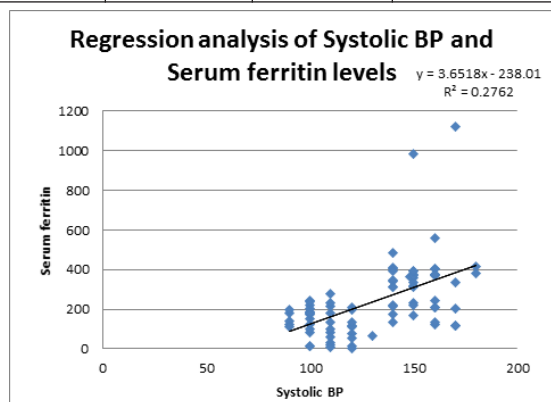


Fig No.1 Regression Analysis

Pearson Correlation coefficient = +0.526, P value < 0.001 Regression P value < 0.001

A simple linear regression was calculated to predict Serum ferritin levels based on systolic BP. A significant regression equation was found ($F(1,82) = 31.289$, $p < 0.001$), with an R^2 of 0.276. Participants predicted serum ferritin level is $-238.014 + 3.652$ (systolic BP). $\mu\text{g/L}$ when the systolic BP is measured in mmHg. Participants' serum ferritin levels increased 3.652 for each mmHg of systolic BP.

Table No. 3 Comparison Of Serum Ferritin Between Groups

SERUM FERRITIN LEVELS (μG/L)	No. of patients		CHI SQUARE TEST
	CONTROL GROUP (%)	STUDY GROUP (%)	
NORMAL	42(100%)	17(40.47%)	P<0.001
ELEVATED	0(0%)	25(59.526%)	

Serum ferritin was abnormal (elevated) among 25(59.52%) patients in study group while it was normal among all participants in control group ($p < 0.001$). The mean serum ferritin value was 131.227 in control group and 341.374 in study group respectively.

DISCUSSION:

This cross sectional study was conducted to study the association between serum ferritin and hypertension. Among the study participants, 50% were female with majority between 41-60 yrs of age group. This is in accordance with a study conducted by Dong Hoon Lee et al⁹. Comparison of Body Mass Index (BMI) between groups in the study was statistically insignificant. According to a study conducted by Stephanie De Loach et al, very weak association of BMI with Blood pressure was found¹⁰. Also in the study by Howard D. Sasso et al, it was found that BMI was an important confounder for its association with systemic hypertension¹¹. Serum ferritin values were elevated among 25(58%) patients in study group ($P < 0.001$) with a mean serum ferritin value of 341.374 ± 191.8572 .

Some studies have reported that significant associations were found between hypertension and serum ferritin level in men¹²⁻¹⁵. Two studies were cross-sectional studies^{12,14}, and others were longitudinal studies^{13,15}. According to another study, 7104 healthy Korean men who visited a health center were surveyed to assess the incidence of hypertension from 2005 to 2010. Also elevated serum ferritin level was found to be independently associated with the incidental risk for hypertension¹⁵.

In this study a strong association between serum ferritin and hypertension was found. Iron accumulation promotes increased free radicals and oxidative stress which leads to cell and tissue damage. Oxygen radicals play an important role in atherosclerosis by accelerating lipid peroxidation. Iron also directly reacts with primed platelets via a Fenton-like reaction resulting in activation and subsequent aggregation of platelets. This can increase the risk of ischemic stroke.

A cross-sectional study was conducted using serum ferritin as an

indicator of iron stores and it shows that serum ferritin levels and the prevalence of hyperferritinemia were increased in men with hypertension compared with normotensive healthy individuals¹⁶. However, Pilar et al. found that baseline hemoglobin and ferritin concentrations were not associated with changes in BP or incidental hypertension after 5.4 years of follow-up in another study¹⁷. Both iron deficiency and iron overload might contribute to the production of reactive oxygen species, increasing oxidative stress and inflammation which could have deleterious effect on endothelial function, ultimately could result in increase in blood pressure.

This study has some limitations. Small sample size and sampling method adopted were among them. A prospective large scale study with long term follow up shall assess the causal relationship between hypertension and ferritin.

CONCLUSION:

This study shows that elevated ferritin level was strongly associated with hypertension. Hence, serum ferritin can also be used as an additional indicator to evaluate hypertension on high variant blood pressure checks

Conflict of Interest: None declared

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REFERENCES:

- Naito Y, Hirotsu S, Sawada H, Akahori H, Tsujino T, Masuyama T. Dietary iron restriction prevents hypertensive cardiovascular remodeling in Dahl salt-sensitive rats. *Hypertension* 2011; 57:497-504.
- Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med*. 1999;340:448-54.
- Kalantar-Zadeh K, Don BR, Rodriguez RA, Humphreys MH. Serum ferritin is a marker of morbidity and mortality in hemodialysis patients. *Am J Kidney Dis*. 2001;37:564-72.
- Kalender B, Mutlu B, Ersöz M, Kalkan A, Yilmaz A. The effects of acute phase proteins on serum albumin, transferrin and haemoglobin in haemodialysis patients. *Int J Clin Pract*. 2002;56:505-8.
- Galan P, Vergnaud AC, Tzoulaki I, Buyck JF, Blacher J, Czernichow S, Hercberg S. Low total and nonheme iron intakes are associated with a greater risk of hypertension. *J Nutr* 2010; 140:75-80.
- Rancourt ME, Rodrigue ME, Agharazii M, Lariviere R, Lebel M. Role of oxidative stress in erythropoietin-induced hypertension in uremic rats. *Am J Hypertens* 2010; 23:314-320.
- Vaziri ND. Role of oxidative stress in the pathogenesis of erythropoietin-induced hypertension. *Am J Hypertens* 2010; 23:226-227.
- Monaster SH, Ahmad MK, Braik AG. Comparison between strain and strain rate in hypertensive patients with and without left ventricular hypertrophy: a speckle-tracking study. *Menoufia Med J* 2014; 27:322-328.
- Association between serum ferritin and hypertension according to the working type in Korean men: the fifth Korean National Health and nutrition examination survey 2010-2012 - Dong-Hoon Lee¹, Seong-Kyu Kang^{1,2*}, Won-Jun Choi^{1,2}, Kyeong Min Kwak¹, Dukyung Kang¹, Sang Ha Lee¹ and Jun-Hyung Lee¹. *Annals of Occupational and Environmental Medicine* (2018) 30:40 <https://doi.org/10.1186/s40557-018-0251-y>
- Stephanie DeLoach, Yonghong Huan, Scott W. Keith. Relationship of blood pressure and obesity with inflammatory cytokines among African Americans. *Therapeutic Advances in Cardiovascular Disease* (2011) 5(3) 149-157 DOI: 10.1177/1753944711408757
- Howard D. Sesso, ScD, MPH; Monik C. Jimenez, ScD, SM; Lu Wang, MD, PhD; Paul M. Ridker, MD, MPH; Julie E. Buring, ScD; J. Michael Gaziano, MD, MPH Plasma Inflammatory Markers and the Risk of Developing Hypertension in Men. *Journal of the American Heart Association* DOI: 10.1161/JAHA.115.001802
- Choi B, Yeum KJ, Park SJ, Kim KN, Joo NS. Elevated serum ferritin and mercury concentrations are associated with hypertension; analysis of the fourth and fifth Korea national health and nutrition examination survey (KNHANES IV-2, 3, 2008-2009 and V-1, 2010). *Environ Toxicol*. 2015;30:101-8.
- Kim MK, Baek KH, Song K-H, Kang MI, Choi JH, Bae JC, et al. Increased serum ferritin predicts the development of hypertension among middle-aged men. *Am J Hypertens*. 2012;25:492-7.
- Piperno A, Trombini P, Gelosa M, Mauri V, Pecci V, Vergani A, et al. Increased serum ferritin is common in men with essential hypertension. *J Hypertens*. 2002;20:1513-8.
- Ryoo JH, Kim SY, Oh CM, Park SK, Kim E, Park SJ, et al. The incidental relationship between serum ferritin levels and hypertension. *Int J Cardiol*. 2015;183:258-62.
- Piperno A, Trombini P, Gelosa M, Mauri V, Pecci V, Vergani A, Salvioni A, Mariani R, Mancina G. Increased serum ferritin is common in men with essential hypertension. *J Hypertens* 2002; 20:1513-1518.
- Galan P, Vergnaud AC, Tzoulaki I, Buyck JF, Blacher J, Czernichow S, Hercberg S. Low total and nonheme iron intakes are associated with a greater risk of hypertension. *J Nutr* 2010; 140:75-80.