Original Research Article

Patterns of Iron Biomarkers among Hypertensive Individuals in Yenagoa, Bayelsa State, Nigeria.

ABSTRACT

Aims: This research aims to evaluate the patterns of iron biomarkers among hypertensive subjects in Yenagoa, Bayelsa State, Nigeria.
Study Design: The investigation is a cross-sectional comparative study.
Place and Duration of Study: Department of Internal Medicine (Cardiology Unit), Niger Delta University Teaching Hospital (NDUTH) in OkolobiriYenagoa, Bayelsa State, Nigeria, between July 2023 and December 2023.
Methodology: The research involved 246 consenting participants: 74 normotensive individuals and 172 hypertensive patients. Serum iron, ferritin, transferrin, and total iron-binding capacity were measured using spectrophotometricmethod.
Results: A significant increase in serum ferritin level was observed among female hypertensive subjects compared to their normotensive counterparts ($p<0.05$). Additionally, when the age groups were matched, the hypertensive group exhibited significantly elevated serum ferritin levels compared to the normotensive controls ($p<0.05$). We found increased transferrin levels in hypertensive male individuals in the present study ($p<0.05$). Also, a significant transferrin increase was observed across the age groups of hypertensive individuals compared to the control group ($p<0.05$).
Conclusion: The above findings suggest that hypertensive patients are prone to abnormal iron metabolism. The notable elevation in certain iron status markers underscores the importance of including iron biomarker assessments as part of the clinical evaluation in hypertensive individuals.

Keywords: Hypertension, iron markers, serum ferritin, transferrin, cardiovascular disease.

1.INTRODUCTION

Hypertension is a chronic disease of public health importance. Hypertension, often known as raised blood pressure, is characterized by a consistent blood pressure measurement of 140/90mmHg or higher [1]. According to a 2022 study from the World Health Organization [2], over one billion adults between the ages of 30 and 79 have hypertension, and this health issue is becoming more prevalent in low- and middle-income countries. The prevalence of hypertension worldwide has had a twofold increase in the last thirty years, impacting around 1.3 billion

individuals in 2019 [3]. This trend is expected to persist due to the expansion and ageing of populations, and age-adjusted hypertension was more prevalent in males than in females [3,4]. Schutte et al [5] reported a rising prevalence of hypertension in Caribbean countries, with some countries exceeding a 45% rate. Hypertension prevalence in Nigeria exhibits considerable variation, spanning from 8% to 46.4%, contingent upon factors such as the study's target population, method of measurement, and hypertension threshold [6,7]. The prevalence rates are comparable in urban areas (8.1%-42.0%) and rural areas (13.5%-46.4%), in addition to gender (7.9%-50.2% vs. 3.5%-68.8%) [7]. Previous studies reported that high blood pressure was responsible for the fatalities of 10.9 million individuals, or 19.2% of all deaths, 92% of these were attributable to cardiovascular disease (CVD), which comprises stroke, heart attack, and heart failure [8,9]. Bovet et al [3] discovered that, except for high-income countries, the aggregate illness burdens attributable to high blood pressure increased from 1990 to 2019 in the majority of regions. Studies or reports from several locations in Nigeria indicate that hypertension is a major risk factor for stroke, heart failure, ischemic heart disease, and renal failure [6, 9].

The biological activities of iron, a transition metal, are crucial. The iron that mediates the transport of oxygen in mammals is mostly found in haemoglobin, which is a component of red blood cells. Myoglobin, found in skeletal muscle cells, also contains substantial amounts of iron [10,11,12]. For various metalloproteins to function, other cell types necessitate lower amounts of iron [13]. One of iron's most important functions is to keep the body's physiological homeostasis levels stable. On the other hand, tissue damage can occur when iron levels are too high because free radicals are produced [14,15,16,17]. An important biomarker for determining iron status and diagnosing iron insufficiency is ferritin, one of the proteins crucial for maintaining iron homeostasis. It has been reported that hypertensive men had higher ferritin values than normotensive healthy subjects, according to a cross-sectional study that used serum ferritin level as an indicator of iron storage [17]. Several cardiometabolic diseases, including diabetes, metabolic syndrome, dyslipidemia, and hypertension, have been linked to iron overload. Atherosclerotic plaque development and instability are two examples of organ injury that can result from an imbalance in lipid and iron metabolism [18,19].

However, studies assessing body iron status—specifically transferrin, ferritin, total iron-binding capacity (TIBC), and serum iron—among hypertensive individuals are scarce worldwide. To the best of our knowledge, no such study has been conducted in Yenagoa, Nigeria. This research aims to evaluate the patterns of iron biomarkers among hypertensive subjects in this region.

2.MATERIALS AND METHODS

2.1 Study Population and Research Design

The investigation is a cross-sectional comparative study. The participants in this research were individuals with hypertension who were attending the cardiology clinic of the Niger Delta University Teaching Hospital (NDUTH) in OkolobiriYenagoa, Bayelsa State, Nigeria.
The Niger Delta University Teaching Hospital (NDUTH) in Okolobiri, Yenagoa, is the sole teaching hospital situated in Bayelsa State, Nigeria, on the outskirts of Yenagoa. It serves as a referral centre for patients from both private and public hospitals in Bayelsa State and nearby areas in Rivers State. Hypertensive subjects who sought cardiologist care at the cardiology clinic, within the study time frame were recruited into this research.

The study included hypertensive individuals aged 31 to 60 years who were on antihypertensive medications and had consistently high blood pressure readings, with systolic pressure greater than 140 mmHg and diastolic pressure above 90 mmHg. The control group comprised healthy individuals within the same age range, with blood pressure readings below 140 mmHg systolic and 90 mmHg diastolic.Participants were excluded if they were taking steroids or other medications that could affect the parameters under investigation. Additionally, subjects with comorbid conditions, such as chronic liver or kidney diseases, were not included in the study.

2.2 Data and Sample Collection

The investigator and trained research assistants administered a questionnaire to each participant, ensuring that it was understood by all. The questionnaire gathered demographic information from the participants, and a physical examination was conducted, which involved measuring the participant's body weight with a Fullmedi adult weighing scale, (FM-S120, Full Medical Co., Ltd, China) and height using a standard wall meter rule. The body mass index (BMI) of each participant was calculated by dividing their weight in kilograms by the square of their height in meters. Participants were only included in the study if they met the inclusion criteria and supplied their informed consent.After 5 minutes of rest, the systolic and diastolic blood pressures (SBP and DBP) of the subject were determined manually using a functional mercury sphygmomanometer fitted with a cuff of the appropriate size.Five (5) milliliters of blood were taken by peripheral venipuncture from all participants who consented in a plain bottle, and another in an EDTA bottle (gently mixed) for packed cell volume. Samples were immediately transported for analysis in a cold chamber of about 2^0C to 8^0 C temperature range.

2.3 Laboratory Analysis

Markers of iron status were assessed using a Contecsemi-auto Biochemistry analyzer (BC300, Contec Medical Systems Co., Ltd. UK), ferritin was assessed using Fine care Ferritin Rapid Quantitative test kit (Guangzhou Wondfo Biotech Co., Ltd, China) while iron, transferrin, and total iron binding capacity were assayed using Biosystems test kit (BioSystems, Spain),all by spectrophotometric method.

2.4 Data Analysis.

Data collected from the clinic and laboratory were entered into an Excel spreadsheet (2019) and analyzed using the Statistical Package for the Social Sciences (SPSS 24.0). Mean comparisons were conducted using ANOVA at a 95% confidence level, with group differences considered statistically significant at $p<0.05$. A pre-test was conducted with ten hypertensive subjects from the hospital's medical outpatient department to evaluate the instrument's applicability, the quality of the information obtained, and the appropriateness and comprehension of the respondents.

3. RESULTS

Table 1 presents the sociodemographic characteristics of the study population. The hypertensive group comprised 69 males (40.1%) and 103 females (59.9%), while the control group, consisting of normotensive individuals, included 31 males (41.9%) and 43 females (58.1%). In both groups,

females slightly outnumbered males. Participants ranged in age from 31 to 60 years. Among the control subjects, the largest age group was 31–40 years (41.9%), followed by 51–60 years (32.4%), with the smallest proportion being those aged 41–50 years (25.7%). In the hypertensive group, the largest age group was 41–50 years (43.0%), followed by 51–60 years (34.9%), with the smallest proportion being those aged 31–40 years (22.1%). Regarding educational attainment, 83.8% of the control group had tertiary education, while 16.2% had secondary education, and none had only primary education.

Table 2 presents the mean values (± standard deviation) for each variable in the two groups, along with the p-values indicating the significance of the differences between them. Both the control (normotensive) and experimental (hypertensive) groups were within the same age range (45.15±8.08 vs. 45.97±6.71 years, $p > 0.05$). However, systolic and diastolic blood pressure were significantly higher in the hypertensive group compared to the control group. Specifically, systolic blood pressure was notably lower in the control group (113.27±9.65 mmHg) compared to the hypertensive group (133.84±22.15 mmHg; $p < 0.05$). Similarly, diastolic blood pressure was 83.46±14.65 mmHg in the hypertensive group, whereas it was 74.92±8.24 mmHg in the control group ($p < 0.05$) significant difference was observed between the two groups on mean arterial pressure: 98.57 16.18mmHg for the experimental group versus 86.42 8.14 for the control group ($p <0.05$).

Table 3: illustrates the means (± standard deviation) for each variable in the two groups, as well as the p-values for the group differences.Pack cell volume was slightly higher among hypertensive individuals when compared with the normotensive group. Serum ferritin and transferrin were both higher in the hypertensive group than in the control group. Serum ferritin was lower in the control group (189±154.05 ng/ml) compared to the hypertensive group (210.65±169.95 ng/ml, $p>0.05$). similarly, the serum transferrin (mg/dl) of the control group was 360.27±50.92, while it was 373.66±56.88 in the hypertensive group ($p>0.05$). Also, there was a statistically significant difference observed between the two groups on serum iron for the control group 37.20±39.96 vs 26.84±23.53 for the hypertensive group ($p<0.05$). In addition, the table shows that the total iron binding capacity (TIBC) for the control group was 69.17±45.84 versus the hypertensive group's 59.63±37.58 ($p>0.05$)

Table 4 illustrates the age-based variations in iron status parameters among the study population. A statistically significant increase in ferritin levels was observed in the hypertensive group compared to the control group within the 31-40 and 51-60 age brackets (164.58±199.94 vs. 187.04±117.52, $p<0.05$) and (210.85±123.36 vs. 255.91±223.65, $p<0.05$), respectively. However, in the 41-50 age bracket, ferritin levels decreased in hypertensive subjects compared to their normotensive counterparts. Similarly, transferrin levels were significantly higher in the hypertensive group compared to the control group across all age brackets. Additionally, serum iron levels were significantly lower in hypertensive individuals compared to the control group, while total iron-binding capacity (TIBC) showed a pattern similar to ferritin across the various age groups

Table 1: Social demographic distribution of the study population

Variables	**Normotensive n(%)**	**Hypertensive n(%)**
Sex		
Male	31(41.9)	69(40.1)

Female	43(58.1)	103(59.9)
Total	**74 (100)**	**172 (100)**
Age(Yrs)		
31-40	31(41.9)	38(22.1)
41-50	19(25.7)	74(43.0)
51-60	24(32.4)	60(34.9)
Tribe		
Ijaw	70(94.6)	148(86.0)
Others	4(5.4)	24(14.0)
Educational Level		
Primary	0(0.0)	18(10.5)
Secondary	12(16.2)	35(20.3)
Tertiary	62(83.8)	119(69.2)

Table 2: Age, and blood pressure parameters characteristics of hypertensive subjects and control.

Parameters	**Normotensive n=74**	**Hypertensive n=172**	**Z Test significant (p<0.05)**
Age (Yrs)	45.15±8.08	45.97±6.71	0.412
Systolic blood pressure (mmHg)	113.27±9.65	133.84±22.15	0.001
Diastolic blood pressure (mmHg)	74.92±8.24	83.46±14.65	0.001
Mean arterial pressure (mmHg)	86.42±8.14	98.57±16.18	0.001

Table3: Iron status parameters characteristics of the study population.

Parameters	**Normotensive subjects n=74**	**Hypertensive subjects n=172**	**Z Test significant (p<0.05)**
Packed cell volume (%)	39.54±4.83	39.59±4.08	0.90
Ferritin (ng/ml)	189.89±154.05	210.65±169.95	0.40
Transferrin (mg/dl)	360.27±50.92	373.66±56.88	0.08
Serum iron (µmol/L)	37.20±39.96	26.84±23.53	0.01
Total iron binding capacity (µmol/L)	69.17±45.84	59.63±37.58	0.10

Table 4: Age-based variation in iron status parameters of the study population

		Ferritin (ng/ml)	**Transferrin (mg/dl**	**Serum Iron (µmol/L)**	**TIBC (µmol/L**
31 – 40Yrs	Normotensive	164.58±199.94	371.13±59.18	36.31±37.19	67.89±34.37

	(n=31)				
	Hypertensive (n=38)	187.04±117.52[a]	392.50±55.47[a]	24.31±21.67[a]	79.72±55.09[a]
	Normotensive (n=19)	204.70±90.87	359.74±13.76	45.65±43.08	91.90±66.34
41 – 50Yrs	Hypertensive (n=74)	186.07±132.83[a]	375.14±58.03[a]	33.28±29.53[a]	54.30±31.41[a]
	Normotensive (n=24)	210.85±123.36	346.67±56.21	31.64±41.47	52.82±31.25
51 – 60Yrs	Hypertensive (n=60)	255.91±223.65[a]	359.90±53.44[a]	20.53±11.56[a]	53.48±32.91[a]

Results are given as mean± standard deviation**.** [a]=Significant at p<0.05 when hypertensive group values are compared to those of normotensive groups across the age ranges.

Table 5: Gender-based variations in iron status parameters of the study subjects

Parameters	**MALE**		**FEMALE**	
	Normotensive (n=31)	**Hypertensive (n=69)**	**Normotensive (n=43)**	**Hypertensive (n=103)**
Ferritin (ng/dl)	293.40±158.05	259.50±202.77	115.26±98.97	177.92±135.34[a]
Transferrin (mg/dl)	331.45±29.37	371.72±60.94[a]	381.05±53.25	374.95±54.26
Serum Iron (µmol/L)	21.10±14.66	23.22±17.62	48.80±47.89	29.28±26.57[a]
TIBC (µmol/L)	78.99±62.62	51.56±35.06[a]	62.09±27.01	65.04±41.64

Results are given as mean ± standard deviation**.** [a=] Significant at p<0.05 when hypertensive male/female values are compared to those of normotensive males/females.

Table 5 highlights the gender-based variations in iron parameters among the study subjects. Ferritin levels were significantly higher in female hypertensives compared to female normotensives (177.92±135.34 vs. 115.26±98.97, p<0.05), while no statistically significant difference was observed among males. Transferrin levels were lower in male normotensives compared to male hypertensives (331.45±29.37 vs. 371.72±60.94, p<0.05). Additionally, the total iron-binding capacity (TIBC) was higher in male normotensives than in male hypertensives (78.99±62.62 vs. 51.56±35.06, p<0.05). Among female subjects, serum iron levels were significantly higher in the control group compared to the hypertensive group (48.80±47.89 vs. 29.28±26.57, p<0.05).

4. DISCUSSIONS

Hypertension continues to be a major global public health concern. Elevated serum ferritin and other iron status biomarkers can contribute to the generation of free radicals and lipid peroxidation, which are associated with an increased risk of cardiovascular disease—a major cause of morbidity and mortality worldwide. The present study evaluated iron status markers in

hypertensive individuals in Yenagoa, Bayelsa State, Nigeria. The study included 246 consenting participants: 74 normotensive individuals and 172 hypertensive patients.The largest age group in the study was 41–50 years old, comprising 43.0% of the participants, followed by the 51–60 age group at 34.9%. The average age of the experimental group was 46.0 years, consistent with findings by Kim et al. [17], who reported a similar average age among hypertensive individuals. The study also had a higher proportion of female respondents (59.9%), aligning with previous research by Choi et al. [20]. Additionally, the study found a statistically significant increase in BMI among the hypertensive group compared to the control group ($p<0.05$), highlighting obesity as a significant risk factor for hypertension. Therefore, maintaining a normal BMI through lifestyle changes aimed at weight loss is strongly recommended to reduce the risk of developing hypertension and cardiovascular disease.

Data from this study showed an upward trend in serum ferritin levels in the hypertension group relative to the normotensive group. A significant increase in ferritin levels was observed in the age groups of 31-40 and 51-60 years when comparing the hypertensive group to the normotensive group ($p<0.05$). Female hypertension participants had a significantly higher amount of ferritin compared to normotensive females ($p<0.05$). This discovery confirmed previous research linking high levels of serum ferritin with hypertension and a higher likelihood of cardiovascular disease. A noteworthy correlation was identified by Choi et al [20] between serum ferritin concentrations and the incidence of hypertension among both males ($p=0.029$) and females ($p<0.001$). However, ferritin concentration was not found to be statistically significant for male hypertension participants compared to normotensive males ($p>0.05$). This differs from previous findings [17, 21]. The cause of this discrepancy in the present study is unknown. The difference in alcohol use between normotensive and hypertension men may explain this finding, as normotensive persons tend to consume alcohol in excess while hypertensive individuals are typically encouraged to reduce their alcohol intake [22].

Ferritin is a crucial protein that plays a major role in controlling the balance of iron in the body. It is commonly used as a biomarker to monitor iron levels and detect iron insufficiency. Ferritin, an acute phase protein, reflects both body iron stores and systemic inflammation. Excessive iron exposure in humans can lead to metabolic and cardiovascular disorders [21, 23]. Reactive oxygen species (ROS) generation causes endothelial dysfunction by disrupting the balance between nitric oxide (NO) and reactive oxygen species (ROS), leading to heightened vasoconstriction, oxidation, inflammation, thrombosis, and proliferation in the arterial wall [24, 25]. The subsequent narrowing of blood vessels, restructuring of the vascular system, and subsequent rise in blood pressure (hypertension) are caused by increased resistance to blood flow [16, 26, 27]. Iron can increase inflammation by generating free radicals that cause oxidation of proteins and DNA, as well as lipid peroxidation, particularly in adipose tissue [27]. This can lead to insulin resistance in adipocytes, muscle, and hepatocytes [28, 29, 30]. In the present study, we found a significant increase in serum ferritin among hypertensive individuals. Therefore, we suggest that elevated serum ferritin is associated with an increased risk of hypertension. This finding may be a target for therapeutic intervention and management of these patients.

We found increased transferrin levels in hypertensive male individuals in the present study. Also, a significant transferrin increase was observed across the age groups of hypertensive individuals compared to the control group ($p<0.05$). The transport of iron is aided by transport protein

referred to as transferrin. Approximately one-third of transferrin in healthy individuals is bound to iron, while the remaining portion acts as a buffer to prevent the buildup of redox-active and dangerous non-transferrin-bound iron [31,32]. Transferrin level is usually elevated in an iron-deficient state [33,34]. A previous study showed iron deficiency as a prevalent coexisting condition in some patients with stable heart failure,irrespective of left ventricular function [35,36]. Iron appears to be a "double-edged sword" in the body. Therefore, both iron deficiency and iron overload might lead to the generation of reactive oxygen species (ROS) [17,32], leading to an increase in oxidative stress, and inflammation and could impact negatively on endothelial function, which could result in hypertension.

Iron is an essential component in numerous biological processes due to its ability to transition between Fe2+ and Fe3+ valence states, which permits it to either donate or receive electrons [37]. The control group showed a higher level of serum iron compared to the hypertension group. Normotensive individuals have significantly higher iron levels than the experimental group, with a p-value of 0.01. The reason for this finding in our present study is not known. However, as earlier noted, abnormal metabolism of iron whether at a higher or deficient level might result in free radical generation which could have deleterious effects on endothelial physiology, causing vascular resistance and leading ultimately to elevated blood pressure [17, 32].

A total iron-binding capacity (TIBC) test is essential for detecting iron-deficient anaemias or other iron metabolism disorders. Total iron-binding capacity refers to the total serum iron and unsaturated iron-binding capacity [31, 32, 38]. Our data showed a higher TIBC value in a male normotensive group than that of the male hypertensive subjects. However, we found a higher trend in TIBC in the hypertensive group compared to the normotensive individuals. Raised total iron-binding capacity values are likely to be found in most individuals with iron deficiency [17]. This suggests that iron deficiency is most probably associated with hypertension as indicated in the present study.

5. CONCLUSION

Elevated iron markers, including ferritin and transferrin, were observed among hypertensive patients receiving medical care at a tertiary hospital in Yenagoa, southern Nigeria. This study highlights abnormal iron metabolism as a potential risk factor for hypertension and cardiovascular disease. These findings have important implications for hypertension management in Nigeria, across Africa, and beyond. Consequently, iron status markers should be included as part of the routine evaluation for hypertensive patients.

Ethical Approval

The research design and protocol were approved by the Ethics Committee Board of the Niger Delta University Teaching Hospital (Protocol number: NDUTH/REC/2023/040821).

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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REFERENCES

1. Ibrahim MH, Albertino D., Hypertension in The Developing Countries. The Lancet; 2012, 380 (9841): p611-619.
2. World Health Organization. A global brief on hypertension: silent killer, global public health crisis: World Health Day 2013. World Health Organization; 2013. https://iris.who.int/handle/10665/79059
3. Bovet P, Schutte AE, Banatvala N, Burnier M. Hypertension: burden, epidemiology and priority interventions. In Noncommunicable diseases 2023;58-65.Routledge. https://www.taylorfrancis.com

4. Ostchega Y, Fryar CD, Nwankwo T, Nguyen DT. Hypertension prevalence among adults aged 18 and over: United States, 2017–2018. 2020. https://stacks.cdc.gov/view/cdc/87559

5. Schutte AE, Jafar TH, Poulter NR, Damasceno A, Khan NA, Nilsson PM. et al. Addressing global disparities in blood pressure control: perspectives of the International Society of Hypertension. Cardiovascular research. 2023; 119(2):381-409.

6. Adeloye D, Owolabi EO, Ojji DB, Auta A, Dewan MT, Olanrewaju TO. et al. Prevalence, awareness, treatment, and control of hypertension in Nigeria in 1995 and 2020: A systematic analysis of current evidence. The Journal of clinical hypertension.2021;23(5):963-77. https://doi.org/10.1111/jch.14220
7. Odili AN, Chori BS, Danladi B, Nwakile PC, Okoye IC, Abdullahi U. et al. Prevalence, awareness, treatment and control of hypertension in Nigeria: data from a nationwide survey 2017. Global heart. 2020;15(1).

8. Eziuzo CI, Chinko BC, Dapper DV. Comparative assessment of some white blood cell and platelet parameters among normotensive and hypertensive subjects in Port Harcourt, Nigeria. Nigerian Medical Journal. 2017; 58(4):131-7. DOI: 10.4103/nmj.NMJ_25_17

9. Ogah OS, Okpechi I, Chukwuonye II, Akinyemi JO, Onwubere BJ, Falase AO. et al. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: A review. World journal of cardiology. 2012;4(12):327. https://doi.org/10.4330/wjc.v4.i12.327
10. Galaris D, Barbouti A, Pantopoulos K. Iron homeostasis and oxidative stress: An intimate relationship. Biochimica et BiophysicaActa (BBA)-Molecular Cell Research. 2019;1866(12):118535.. https://doi.org/10.1016/j.bbamcr.2019.118535
11. Ganz T. Systemic iron homeostasis. Physiological reviews. 2013;93(4):1721-41. https://doi.org/10.1152/physrev.00008.2013
12. Nemeth E, Ganz T. Hepcidin and iron in health and disease. Annual review of medicine. 2023;74(1):261-77. https://doi.org/10.1146/annurev-med-043021-032816
13. Fillebeen C, Charlebois E, Wagner J, Katsarou A, Mui J, Vali H. et al. Transferrin receptor 1 controls systemic iron homeostasis by fine-tuning hepcidin expression to hepatocellular iron load. Blood, The Journal of the American Society of Hematology. 2019;133(4):344-55.. https://doi.org/10.1182/blood-2018-05-850404
14. Han M, Guan L, Ren Y, Zhao Y, Liu D, Zhang D. et al. Dietary iron intake and risk of death due to cardiovascular diseases: A systematic review and dose-response meta-analysis of prospective cohort studies. Asia Pacific journal of clinical nutrition. 2020;29(2):309-21. https://doi.org/10.6133/apjcn.202007_29(2).0014
15. Vinchi F, Porto G, Simmelbauer A, Altamura S, Passos ST, Garbowski M. et al. Atherosclerosis is aggravated by iron overload and ameliorated by dietary and pharmacological iron restriction. European heart journal. 2020 Jul 21;41(28):2681-95. https://doi.org/10.1093/eurheartj/ehz112
16. Sawada H, Hao H, Naito Y, Oboshi M, Hirotani S, Mitsuno M. et al. Aortic iron overload with oxidative stress and inflammation in human and murine abdominal aortic aneurysm. Arteriosclerosis, thrombosis, and vascular biology. 2015;35(6):1507-14.https://doi.org/10.1161/ATVBAHA.115.305586

17. Kim MK, Baek KH, Song KH, Kang MI, Choi JH, Bae JC. et al. Increased serum ferritin predicts the development of hypertension among middle-aged men. American journal of hypertension. 2012;25(4):492-7.
18. Olesnevich ME, Kuczmarski MF, Mason M, Fang C, Zonderman AB, Evans MK. Serum ferritin levels associated with increased risk for developing CHD in a low-income urban population–Corrigendum. Public Health Nutrition. 2012;15(6):1138-.
19. Zhou B, Ren H, Zhou X, Yuan G. Associations of iron status with apolipoproteins and lipid ratios: a cross-sectional study from the China Health and Nutrition Survey. Lipids in Health and Disease. 2020;19:1-2. https://doi.org/10.1186/s12944-020-01312-9
20. 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). Environmental toxicology. 2015;30(1):101-8. DOI 10.1002 /tox.21899.
21. Lee DH, Kang SK, Choi WJ, Kwak KM, Kang D, Lee SH, Lee JH. 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. Annals of occupational and environmental medicine. 2018;30:1-7.
22. Ali N, Ferrao K, Mehta KJ. Liver iron loading in alcohol-associated liver disease. The American journal of pathology. 2023;193(10):1427-39. https://doi.org/10.1016/j.ajpath.2022.08.010
23. Li G, Yu W, Yang H, Wang X, Ma T, Luo X. Relationship between serum ferritin level and dyslipidemia in US adults based on data from the national health and nutrition examination surveys 2017to2020. Nutrients. 2023;15(8):1878. https://doi.org/10.3390/nu15081878
24. Briones AM, Touyz RM. Oxidative stress and hypertension: current concepts. Current hypertension reports. 2010;12:135-42. https://doi.org/10.1007/s11906-010-0100-z
25. Gallo G, Volpe M, Savoia C. Endothelial dysfunction in hypertension: current concepts and clinical implications. Frontiers in medicine. 2022;8:798958.
26. Ambrosino P, Bachetti T, D'Anna SE, Galloway B, Bianco A, D'Agnano V. et al. Mechanisms and clinical implications of endothelial dysfunction in arterial hypertension. Journal of cardiovascular development and disease. 2022;9(5):136. https://doi.org/10.3390/jcdd9050136
27. Leiva E, Mujica V, Sepúlveda P, Guzmán L, Núñez S, Orrego R. et al. High levels of iron status and oxidative stress in patients with metabolic syndrome. Biological trace element research. 2013; 151:1-8.
28. Piperno A, Trombini P, Gelosa M, Mauri V, Pecci V, Vergani A. et al. Increased serum ferritin is common in men with essential hypertension. Journal of hypertension. 2002;20(8):1513-8.
29. Amponsah-Offeh, M., Diaba-Nuhoho, P., Speier, S. and Morawietz, H., Oxidative stress, antioxidants and hypertension. Antioxidants, 2023;12(2):281. https://doi.org/10.3390/antiox12020281
30. Ryoo JH, Kim SY, Oh CM, Park SK, Kim E, Park SJ. et al. The incidental relationship between serum ferritin levels and hypertension. International journal of cardiology. 2015;183:258-62. https://doi.org/10.1016/j.ijcard.2014.10.152

31. Brissot P, Ropert M, Le Lan C, Loréal O. Non-transferrin bound iron: a key role in iron overload and iron toxicity. Biochimica et BiophysicaActa (BBA)-General Subjects. 2012;1820(3):403-10. https://doi.org/10.1016/j.bbagen.2011.07.014

32. 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. The Journal of nutrition. 2010;140(1):75-80.https://doi.org/10.3945/jn.109.114082

33. Galaris D, Barbouti A, Pantopoulos K. Iron homeostasis and oxidative stress: An intimate relationship. Biochimica et BiophysicaActa (BBA)-Molecular Cell Research. 2019;1866(12):118535.https://doi.org/10.1016/j.bbamcr.2019.118535
34. Ganz T. Systemic iron homeostasis. Physiological reviews. 2013;93(4):1721-41. https://doi.org/10.1152/physrev.00008.2013
35. Hughes CM, Woodside JV, McGartland C, Roberts MJ, Nicholls DP, McKeown PP. Nutritional intake and oxidative stress in chronic heart failure. Nutrition, Metabolism and Cardiovascular Diseases. 2012;22(4):376-82. https://doi.org/10.1016/j.numecd.2010.08.006
36. Loncar G, Obradovic D, Thiele H, von Haehling S, Lainscak M. Iron deficiency in heart failure. ESC heart failure. 2021;8(4):2368-79. https://doi.org/10.1002/ehf2.13265
37. Jomova K, Valko M. Importance of iron chelation in free radical-induced oxidative stress and human disease. Current pharmaceutical design. 2011;17(31):3460-73. https://doi.org/10.2174/138161211798072463
38. Faruqi A, Zubair M, Mukkamalla SK. Iron-Binding Capacity. InStatPearls [Internet] 2024. StatPearls Publishing.