Al-Salam Journal for Medical Science
Journal Homepage: http://journal.alsalam.edu.iq/index.php/ajbms
E-ISSN: 2959-5398, P-ISSN: 2958-0870

Iraqi patients suffering from valvular heart diseases' serum iron levels

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DOI: https://doi.org/10.55145/ajbms.2025.4.1.008
Received June 2024; Accepted August 2024; Available online September 2024

ABSTRACT: Valve heart disease (VHD), caused by a heart valve becoming too narrow (valvular stenosis) or not closing adequately (valvular insufficiency), is one of the heart illnesses that causes the most morbidity and mortality. The study included ninety participants, who were divided into three groups: Thirty people in excellent health, thirty patients with aortic valve disease (atrioventricular valve group: 14 men, 16 females), and thirty patients with mitral valve disease (mitral valve group: 13 males, 17 females). group C, the control group, consisted of 16 men and 14 women. Serum UIBC decreased significantly ($P < 0.001$) while serum ferritin, transferrin saturation, and iron increased significantly ($P < 0.001$) when the patient groups were compared to group C. Conversely, there were no statistically significant changes ($P>0.05$) seen in the concentrations of transferrin and TIBC in the serum between the two patient groups and the control group. Moreover, no appreciable variations were noted in the concentrations of iron, TIBC, UIBC, transferrin, transferrin saturation, or ferritin between the AV and MV groups.

Keywords: valvular heart disease, Iron ,Ferritin ,TIBC,UIBC, Transferrin

1. INTRODUCTION

At a prevalence of 2.5% in the US, valve heart disease (VHD) is a serious health issue that primarily affects the elderly. Congenital abnormalities or acquired pathology are the causes of VHD [1]. Aortic valve sclerosis (AVSc), a mild thickening of the valve, develops into calcific aortic valve disease (CAVD), which results in a major restriction of the valve's mobility, known as aortic valve stenosis (AVS). CAVD is becoming more common in the elderly and is on the verge of becoming an epidemic. The subclinical form of aortic sclerosis affects about one-third of adults over 65[2]. With a significant section of the global population aging, it is anticipated that acquired forms of VHD will become more common [3].

In the crust of the Earth, iron is thought to be the second most common metal. Although it is only found in minute levels, iron is a vital trace element for human health [75–80% of total iron is located in hemoglobin's heme group, and myoglobin contains a moderate quantity of iron. Iron is an essential component of many enzymes and is involved in a wide range of biological processes [4]. Ferritin and hemosiderin are the primary forms of iron storage in humans, and they are found mostly in the liver, spleen, and bone marrow [5]. In mammals, ferritin is mostly present in the cytosol, with a little amount being found in plasma [6] in addition to trace amounts seen in human serum, which is raised in iron overload and inflammatory conditions [7]. Transferrin (Tf), a glycoprotein with a very high affinity for ferric iron, binds the majority of the iron in blood plasma and transports it to other organs [8]. Therefore, in order for ferrous ions (Fe^{+2}) to bind to transferrin, they must be oxidized to ferric ions (Fe^{+3}). Several coppers oxidases mediate this oxidation process [9].

On the other hand, because iron can exchange electrons between ferrous and ferric forms, an excess of iron can be hazardous [10]. This exchange may result in reactive oxygen species through the Fenton and Haber-Weiss processes, which may cause OS and the oxidation of organic biomolecules. Diseases including cancer, cardiovascular disease, and neurological disorders are primarily caused by this mechanism [9].

According to epidemiological research on CVD, having high iron reserves increases the chance of developing metabolic and cardiovascular problems [[11]. In summary, the presence of iron in macrophages and foam cells increases the risk of developing atherosclerotic plaques. Hepcidin can further exacerbate plaque instability by blocking the export of iron from intraregional macrophages, which might result in ischemia episodes [12].

2. MATERIAL AND METHODS

2.1 Chemicals

In this investigation, only extremely pure grades of chemicals were employed.

2.2 Subjects

There were ninety participants in the study.Three groups were formed from the groupings. There were 33 patients in the first (AV) group—17 men and 16 women. There were also (27 patients, 10 male and 17 female) in the second group (MV). Their BMIs range from 28.99 to 4.02 kg/m2, and their ages range from 53.81 to 10.01 years. The control group, designated as Group 3 (C), consists of thirty persons in good health, sixteen of whom are male and fourteen of whom are female. Their BMI is 28.35 ± 3.79 kg/m2, and they are 46.63 ± 8.79 years old. The patient samples came from the Ibn Al-bitar Center for Cardiac Surgery in Baghdad, Iraq.Those with kidney problems, diabetes, or hypertension were excluded from the AV or MV groups.

2.3 Blood samples

Venous blood samples totaling ten milliliters were taken from the patient and control groups, collected in a plane tube, and left to stand at room temperature for ten minutes. After that, the sera were divided into aliquots and kept at -20 °C until they were needed. To separate the sera, the blood samples were centrifuged for 10 minutes at 4000 r.p.m.

2.4 Iron

The Ran dox kit was used to measure the iron assay in serum. Utilizing the colorimetric approach, absorbance was measured at (595 nm)to determine the results.

2.5 Ferritin

Ferritin levels were determined by solid phase enzyme-linked immunosorbent assay (ELISA) with a commercially available CALBIOTECH kit. Check the absorbance at 450 nm.

2.6 TIBC

The Randox kit was utilized to measure the TIBC test in serum. The colorimetric approach was used to determine the results.

2.7 Determination of UIBC

The following equation was used to determine the UIBC:
UIBC (µg/dl) = TIBC (µg/dl) – Iron conc. (µg/dl)

2.8 Determination of Transferrin

The transferrin was indirectly estimated using the following equation [13]:
Transferrin (µg /dl) = 0.7 x TIBC (µg/dl)

3. STATISTICAL ANALYSIS

The SPSS program (version 21) was used to conduct the statistical analysis. The data were statistically compared between the study groups using a one-way ANOVA, and the findings were shown as mean ± SD. This technique was considered to have occurred because it was significant at $p<0.05$ and extremely significant at $p<0.001$.

4. RESULTS

The study participants, AV, MV, and C, had mean ± SD ages of 55.5±13.3, 53.81±10.0, and 46.63±8.79 years, respectively (Table 1), indicating a significant age difference ($p<0.05$) between the patient (AV & MV) and control groups.

Table 1 indicates that no significant variations in BMI were found across the analyzed groups ($p>0.05$).

Table 1. - The age, gender and BMI of AV, MV and C groups

Groups	n	Age (years)	Gender		BMI (Kg/m²)
			Male No. (%)	Female No. (%)	
C	30	46.63±8.79	16 (53.3%)	14 (46.6%)	28.35±3.79
AV	33	55.50±13.3[a*]	17 (51.5%)	16 (48.4%)	28.73±6.26
MV	27	53.81±10.0[a*]	10 (37.0%)	17 (70.8%)	28.99±4.02

* significant at p<0.05, ** highly significant at p<0.001; [a] compared to control, [b] compared between AV & MV

The findings displayed in Figure (1) demonstrate that the patient groups' (AV and MV) serum iron concentrations were significantly higher (p<0.001) than the C group's.However, no discernible variations in iron concentration were found between the AV and MV groups (p>0.05). Upon analysis of the iron levels in each group, it was shown that the female MV group had a substantial drop (p<0.05) in contrast to the male group, although no significant changes were observed in the C or AV groups.

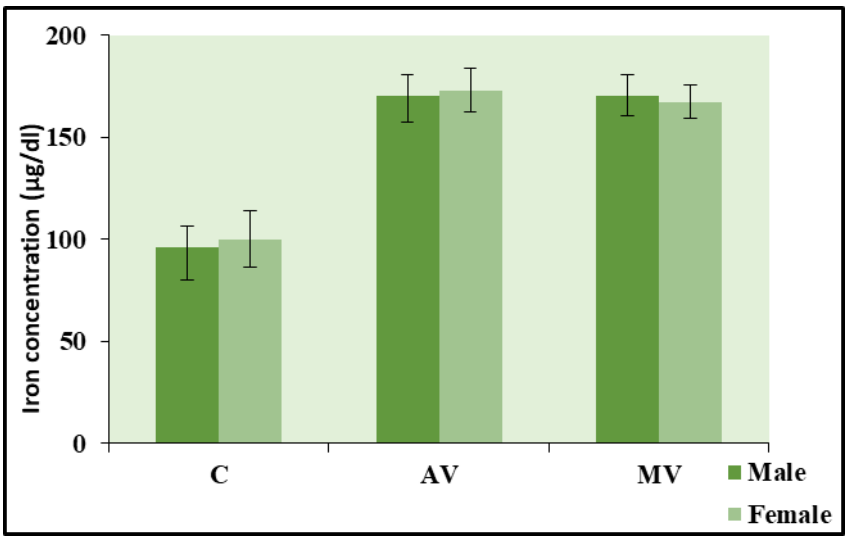

FIGURE 1. - Mean values ± SD of serum Fe concentration in patients and control groups

The difference is significant at * p<0.05 and highly significant at *p<0.001
a: significant difference between C and AV
b: significant difference between C and MV
c: significant difference between male and female in the same group

Table 2 indicates that there were no statistically significant variations in the TIBC levels of the patient groups (AV and MV) when compared to the C group (p>0.05) or within AV and MV. In every group under study, there were no appreciable variations between male and female participants.

Table 2. - Average values ± standard deviation of the iron status metrics for the patient and control cohorts.

Parameters	Groups						p-value		
	C n=30		AV n=33		MV n = 27				
	M (n=16)	F (n=14)	M (n=17)	F (n=16)	M (n=10)	F (n=17)	AV&C	MV&C	AV&MV
TIBC (µg/dl)	326.0±3 6.6	323.0±3 0.12	314.5±3 6.69	321.1±4 0.7	322.9±3 3.47	325.7±3 6.99	0.830↔	1.000↔	0.847↔
UIBC (µg/dl)	229.8±3 9.19	222.9±3 6.73	144.0±3 5.87	148.2±3 9.25	148.0±3 7.49	158.4±4 0.42	0.000↓	0.000↓	0.773↔
Transferrin (µg/dl)	228.2±2 5.62	226.1±2 1.09	220.2±2 5.68	224.7±2 8.49	226.0±2 3.43	228.0±2 5.89	0.830↔	1.000↔	0.847↔
Transferrin Saturation (%)	29.84±5 .86	31.33±5 .66	54.80±7 .06	54.58±7 .18	54.78±7 .37	52.09±7 .29	0.000↑	0.000↑	0.763↔

The difference is significant at $p<0.05$ and highly significant at $p<0.001$.

↑ Significant increase, ↓ Significant decrease, ↔ Non-significant

Table 2 UIBC results show that the AV and MV groups fall significantly when compared to the C group ($p<0.001$), although there are no significant changes between the Aortic valve AV and Mitral valve MV patient groups ($p>0.05$). Furthermore, in none of the study groups were there statistically significant variations in UIBC between the sexes.

These results show that the serum transferrin levels of the patient groups (AV and MV) and the C group do not differ significantly ($p>0.05$). The serum transferrin saturation of the Aortic valve AV and Mitral valve MV groups is significantly higher than that of the C group ($p<0.001$), despite the fact that there are no discernible differences between the two groups. Meanwhile, there were no appreciable differences observed between the male and female participants in the study groups

Figure (2) displays the serum ferritin concentrations for each group. The Aortic valve AV and mitral valve MV groups did not substantially differ in the interim ($p>0.05$), however the patient groups show a statistically significant increase ($p<0.001$) compared to the control group. The substantial drop in female ferritin levels in the AV and MV groups relative to the male group is also illustrated in Figure 2.

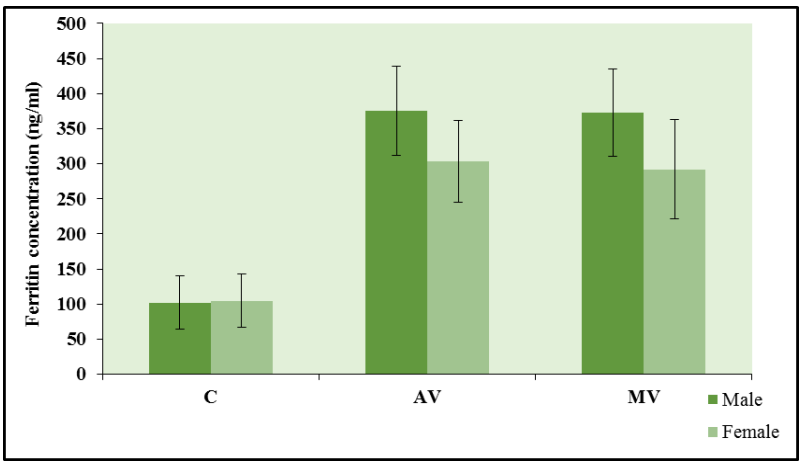

FIGURE2. - Mean values ± SD of serum Ferritin concentration in patients and control groups

The difference is significant at * $p<0.05$ and highly significant at *$p<0.001$
a: significant difference between C and AV
b: significant difference between C and MV
c: significant difference between male and female in the same group

5. DISCUSSION

It has been established that iron excess increases the risk of heart failure, CAD, and atherosclerosis as CAD progresses. An augmented OS is thought to be the mechanism tying iron excess and higher cardiovascular risk [14]. Through the Fenton and Haber-Weiss reactions, ferrous iron (Fe+2) catalyzes a range of free-radical oxidative processes that encourage the production of hydroxyl radicals from superoxide and hydrogen peroxide [15]. Thus, too much iron raises the creation of ROS, which results in tissue damage "organ" failure, and cell death [16].

Our analysis of the observed iron parameters revealed that, in comparison to healthy individuals, VHD patients had higher serum iron, ferritin, transferrin saturation, and UIBC, but there were no differences in serum TIBC and transferrin levels between the patient group and the healthy control. Iron overload is evident in VHD patients based on elevated ferritin content and transferrin saturation. [17].

When these results are compared to other research on various forms of CVD, Chopra et al. found that Indian patients with CAD had significantly lower TIBC and significantly higher blood iron and ferritin levels than normal healthy controls [17]. Another study by Pourmoghaddas et al. found that Iranian patients with CAD had higher ferritin levels but no appreciable changes in their serum iron, TIBC, or transferrin saturation [18].

Furthermore, our findings concur with a study by Eftek hari et al. that discovered elevated levels of ferritin and serum iron in Iranian patients with cardiovascular disease [19]. Furthermore, Iqbal et al. reported a noteworthy rise in ferritin levels in Acute Myocardial Infarction [AMI] in a Pakistani population [20]. According to Siva Raman et al., individuals with AMI had substantially higher serum iron levels and % transferrin saturation as compared to the control group [21].

Furthermore, the current study's findings are in line with those of a prior investigation that found that Iranian MI patients had significantly higher serum iron and ferritin levels than healthy subjects, while female patients had significantly lower levels of both substances. Essentially, a woman's serum ferritin levels differ in her body during her pre-menstrual, menstrual, and post-menstrual phases. Serum ferritin levels are often greater in men than in women [22].

Increasing bodily iron reserves, or ferritin levels, have been linked to an increased risk of cardiovascular disease (CVD), according to numerous research [22]. The most commonly employed marker of bodily iron storage in biochemical investigations is serum ferritin, a type of intracellular protein that controls the homeostasis of serum iron. Consequently, the method via which the body's high iron status may be raising the risk of VHD. Increased oxidative damage through increased production of reactive oxygen species (ROS), enhanced reperfusion injury and atherogenic properties, increased proliferation of vascular smooth muscle cells, or a combination of these factors along with other heart disease risk factors like inflammation and hypertension could be the cause [23].

6. CONCLUSION

According to the results obtained from the current study, we found a significant increase in Iron, Transferrin Saturation and Ferritin while a significant decrease in UIBC. "Therefore, adding ferritin to current or upcoming clinical models for risk classification may improve diagnostic performance by identifying individuals at high risk who may benefit from more frequent monitoring. Lastly, new research directions are opened by the question of whether various strategies to lower ferritin serum levels might lower the mortality risk of heart failure".

FUNDING

None

ACKNOWLEDGEMENT

I extend my thanks and appreciation to Ibn Al-Bitar Specialized Hospital for Cardiology for providing everything required to complete the research.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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