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Serum Ferritin and Hemoglobin Levels in Female Cardiovascular Patients of District Peshawar; A Hospital Based Study

Huma[1], Faridullah Shah[2], Mohammad Hashir Ahmad[2], Attaullah Khan[3], Mudassir Ahmad Khan[2], Zahoor Ahmed[2],

[1]Department of Nutrition Rehman Medical Institute, Peshawar, KPK, Pakistan.
[2]Department of Biochemistry, Rehman Medical College, Peshawar, KPK, Pakistan.
[3]Department of Medicine, Peshawar Institute of Medical Science, Peshawar, KPK, Pakistan.
[4]Department of Biochemistry, Khyber Medical College, Peshawar, KPK, Pakistan

Correspondence: *Dr. Zahoor Ahmed*
zakhan70@yahoo.co.uk

Abstract

Objective: The study was conducted to assess iron and hemoglobin levels of female cardiovascular patients.
Material and Methods: Total eighty-six subjects including equal number of patients and controls were enrolled for the present study fulfilling the predefined selection criteria. About 5 mL blood sample was collected for each subject for determination of serum ferritin hemoglobin concentration. A 24-hr dietary recall method was used for estimation of dietary energy, carbohydrate, protein, fat and iron intake of subjects.
Result: The results showed non-significant difference ($p>0.05$) in the mean weight, height and body mass index between the cases and controls. The same results were noted for the biochemical parameters including serum ferritin and hemoglobin concentration. However significant ($p<0.05$) results were obtained for BP. Demographic and socio-economic status demonstrates that both cases and controls had large family sizes between 10-13 members with non-significant difference.
Conclusion: Logistic regression did not reveal any relationship between CVD patients and iron status indicators, rather age and BMI were the only independent variables associated significantly with CVD.
Key Words: Ferritin, CVD, Hb, RMI, KMC, Dietary Iron

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Introduction

Cardiovascular disease (CVD) is a broad term used to describe a range of diseases that affect heart or blood vessels. The various disorders that fall under this include coronary artery disease, heart attack, heart failure, high blood pressure and stroke.[1] The causes related to the development of heart disease vary among different regions and situations. Increasing age, sex and positive family history are modifiable risk factors while the remaining modifiable risk factors are an unhealthy diet, lack of exercise, being obesity, hypertension, hyperlipidemia, diabetes mellitus and smoking.[2] CVD is the leading cause of death and a No. 1 killer in United State (US), responsible for 40% of all deaths[3] with estimated cost of $ 400 billion/year[4]. The prevalence increases with advancing age and varies within racial, ethnic, geographic, and socio-demographic groups. Among the 71.3 million adults with one or more forms of CVD, the most prevalent conditions are hypertension or high blood pressure (65 million), coronary heart diseases (13.2 million), stroke (5.5 million), heart failure (5 million), and congenital heart defects (1 million).[5] It has been estimated that within the next 20 years, about 1.3 million people per year will be affected by heart disease in Africa[6]. While National Health Survey of Pakistan revealed that 12% of adult mortality is due to ischemic heart disease.[7]

A number of factors have been responsible for increasing prevalence of CVD among them iron is considered to be a potential risk factor during infection[8]. Iron available to the body through diet transferred into hemoglobin or myoglobin or stored as a ferritin in liver, spleen and bone marrow.[9] It is estimated

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that about 67% of body iron is present as hemoglobin and myoglobin. Hemoglobin, which is present in red blood cells, is essential for transferring oxygen from the lungs via the blood to the tissues. Normal value of hemoglobin for adult male is ≥13g/dL and for adult female pregnant women is ≥ 11g/dL and non-pregnant women is ≥12g/dL.[10] A deficiency of iron can lead to anemia which limits oxygen delivery to cells, resulting in anemia, irritability, fatigue, tachycardia, sore or swollen tongue, speleenomegaly, and development of pica; a condition to desire to eat a peculiar substance such as dirt or ice. Causes of iron deficiency are diets low in iron, body changes, gastrointestinal tract abnormalities and blood loss[11]. Measurement of serum ferritin in blood is an indicator of iron store in the body, which ranges between 20–300 ng/mL for male and 10–212 ng/mL for female.[12] Free ferritin is a risk factor for cardiovascular and other chronic diseases. Ferritin must bind with protein to prevent cellular damages.[13] Iron has been suggested to play a role in the development of CVD through its pro-oxidant properties and iron also help to catalyze reactions that lead to produce too many free radicals that may damage the coronary arteries.[14] Serum iron plays an important role in the oxidation of low density lipoprotein cholesterol (LDL-c), it induces inflammatory reactions and it is positively related to coronary heart disease.[15] Iron is a pro-oxidant nutrient that can contribute to the development of atherosclerosis**.** Higher iron levels were linked with higher levels of body mass index, total cholesterol, triacylglycerol, glucose and diastolic blood pressure, on the whole, CVD risk factors; especially those relating to glucose and lipid metabolism are linked with iron status in women.[16]

Iron deficiency a major contributing factor for the anemia is one of the major nutritional deficiencies affecting, about 43 to 47% of rural and 35–41% of urban women between 15–44 years being anemic in Pakistan.[17] The prevalence of iron deficiency in low socio-economic status with poor hygiene and sanitation increases women's vulnerability to impaired physical productivity and increase cardiovascular diseases or morbidity[18]. Despite the fact that CVD made up 16.70 million (24%) of total global deaths.[19]

Keeping in view the importance of CVD and iron deficiency in women as a public health issue, the present study was designed to assess the iron status of female suffering from cardiovascular diseases and attendants as controls seeking Rehman Medical Institute (RMI), Peshawar for consultation and treatment.

Materials and Methods

A case-control study was carried out during March 2017 and February 2018 in the outpatients department (OPD) of the Cardiology Department, Rehman Medicinal Institute (RMI), Peshawar, KPK, Pakistan in collaboration with Khyber Medical college, Peshawar, in which forty three (n=50) females served as patients whereas same number of females were selected from the general population as controls. The study was approved from Ethical Review Committee of the hospital. The inclusion criteria set for selection of patients was those females having age 40 to 60 years visiting the Cardiology Department, RMI with complaints of myocardial infarction (MI). The disease was assessed and confirmed by clinical and laboratory investigations. The control subjects were all those females belonging to the same socioeconomic and age group enjoying good health without any complaint of CVDs, All the relevant information viz. age, weight, height, income, family size, blood pressure, physical inactivity, personal and family history of cardiac disease, were taken from study population and recorded on standard proforma. A 24-hours dietary recall was filled from cases and controls. Approximately 5 mL blood sample from anticubical vein was drawn from each subject for the determination of hemoglobin (Hb) and ferritin concentration. The serum was separated and transferred into the micro tubes for the transportation to the Department of Human Nutrition Laboratory where serum was analyzed for different parameters. Hb concentration of all the study populations was determined by using the Hemocue analyzer[20], while serum ferritin was determined on ELISA method[21]. The data was analyzed for any statistical significance using EPi-Info statistical programme. Student's T-test was used to compare the mean difference of serum ferritin, Hb and anthropometric indicators.

Results

General characteristics of study population are expressed in Table I. It is evident from the table that the mean age of patients were significantly higher (p<0.006) when compared with normal healthy individuals who served as controls. Similar trend of result was observed while comparing systolic blood pressure (SBP) of patient with control (p<0.011). Non-significant results were obtained regarding the BMI and diastolic blood pressure (SBP).

Table I: General Characteristics of Study Population

Variable	Cases (n=50)	Controls (n=50)	*p-value*
Age (Years)	50.4±7.10[a]	45.2±6.0[b]	0.006
Systolic BP (mm/Hg)	132.47±20.94[a]	123.02±11.45[b]	0.011
Diastolic BP(mm/Hg)	86.16±14.68[a]	83.79±10.51[a]	0.391
Weight (Kg)	65.8±16.0[a]	68.1±10.80[a]	0.428
Height (Cm)	153.30±4.30[a]	152.44±4.4o[a]	0.365
BMI (Kg/m^2)	27.3±6.03[a]	29.2±4.68[a]	0.160

The description of various parameters of the study population is depicted in Table II. The mean±SD serum ferritin level of patients and controls were found to be 53.75±23.93 ng/dL and 41.39±20.79 ng/dL respectively with no significant difference between two groups when compared for serum ferritin. The same results were obtained for Hb when compared with normal healthy individuals. It is further revealed that prevalence of iron deficiency for patients was higher (n=18; 41.86%) than controls

Table II: Pattern of Serum Ferritin and Hemoglobin in Patients and Controls					
Groups	**Variable**	**Cases**	**Controls**	***p-value***	**Total**
Overall	Ferritin(ng/dL)	53.75±23.93 (n=43)	41.39 ± 20.79 (n=43)	0.217	47.57±21.28 (n=86)
	Hemoglobin (g/dL)	13.52±2.18 (n=43)	13.14 ± 1.18 (n=43)	0.525	13.33±2.00 (n=86)
ID (n=30)	Ferritin (ng/dL)	2.39±3.41 (n=18)	4.55 ± 3.49 (n=12)	0.106	3.25±3.55 (n=30)
	Hemoglobin (g/dL)	12.68±2.34 (n=18)	13.36 ± 1.86 (n=12)	0.373	12.95±2.09 (n=30)
NID (n=56)	Ferritin (ng/dL)	90.74±83.34 (n=25)	55.65 ± 77.86 (n=31)	0.113	71.32±81.57 (n=56)
	Hemoglobin (g/dL)	13.81±2.24 (n=25)	14.56 ± 2.89 (n=31)	0.243	14.19±2.60 (n=56)
Anemic (n=17)	Hemoglobin ((g/dL)	14.13±1.96 (n=25)	13.96 ± 1.82 (n=31)	0.041	13.54±1.94 (n=56)
	Ferritin (ng/dL)	15.40±16.97 (n=8)	43.92 ± 51.09 (n=9)	0.145	30.49±40.58 (n=17)
Non-anemic (n=69)	Hemoglobin (g/dL))	10.20±1.66 (n=8)	10.62 ±0.65 (n=9)	0.516	10.42±1.2 (n=17)
	Ferritin (ng/dL)	62.52±82.63 (n=35)	40.72±74.60 (n=34)	0.253	51.80±78.96 (n=69)
IDA (n=7)	Hemoglobin (g/dL)	14.28±1.45 (35)	13.81+1.37 (n=34)	0.169	14.05±1.42 (n=69)
	Ferritin (ng/dL)	4.06±5.20 (n=5)	3.90±5.44 (n=2)	0.907	4.02±4.79 (n=7)
IDNA (n=23)	Ferritin (ng/dL)	1.74±2.40 (n=13)	4.68±3.39 (n=13)	0.033	3.02±3.17 (n=23)
	Hemoglobin (g/dL)	13.78±1.04 (n=13)	13.92±1.43 (n=13)	0.803	13.84±1.20 (n=23)
NIDA (n=10)	Ferritin ng/dL)	34.29±9.40 (n=3)	55.36±52.80 (n=7)	0.344	49.04±44.54 (n=10)
	Hemoglobin (g/dL)	10.87±1.4 (n=3)	10.64±0.67 (n=7)	0.770	10.7±0.78 (n=10)
NIDNA (n=46)	Ferritin (ng/dL)	98.43±86.09 (n=22)	55.74±84.73 (n=24)	0.097	76.16±87.14 (n=46)
	Hemoglobin (g/dL)	14.58±1.60 (n=22)	13.77±1.37 (n=24)	0.073	14.15±1.52 (n=46)

Values are expressed as mean+SD
ID=Iron deficient NID= Non iron deficient
IDA= Iron deficiency anemia IDNA= Iron deficient non-anemia
NIDA=Non iron deficiency anemic NIDNA= Non Iron deficient non-anemic

(n=12; 27.91%) respectively. A small difference in iron status parameters between cases and controls suggests their lack of sensitivity and specificity to CVDs. The mean higher ferritin value of the CVD patients may be attributed to infection and haemochromatosis. Ferritin being an acute phase protein the level of which tends to raise in infection, however, its response to chronic diseases including MI is under controversy.

Table III shows the results of dietary intake of patients and controls. The mean caloric intake of patients was 699.07±69.77 Kcal/day and that of controls it was 949.23±70.86 Kcal/day respectively. The mean carbohydrate intake of patients and controls were found to be 107.17±51.72 g/day and 141.77±50.51 g/day respectively. Similarly, the mean fat intake of both the study groups was found to be lower than the recommended fat intake. The overall dietary intake results show that patients had significantly lower ($p<0.05$)

Table III: Dietary Habits of Patients Suffering from CVD and Controls			
Variables	**Cases (n=43)**	**Control (n=43)**	**Total (n=86)**
Energy (Kcal/day)	699±269.77[a]	949±275.86[b]	824.16±298.98
Proteins (gm/day)	31.86±10.86[a]	41.76±17.34[b]	36.81±15.22
Carbohydrates (gm/day)	107±51.72[a]	141.7±750.51[b]	124.47±53.72
Fats (gm/day)	23.84±21.18[a]	33.35±12.00[b]	28.60±17.77
Iron (mg/day)	8.63±5.44[a]	10.11±4.44[b]	09.37±4.99

Mean in each row with similar letters are not significantly different ($p>0.05$).

Discussion

The probable reason for relatively lower systolic and diastolic blood pressure values of CVD patients may be attributed to the time of taking patient's blood pressure which was taken after MI during convalescent stage in the intensive cardiac care unit (ICCU). These patients were hypertensive but after treatment with beta-blockers and vasodilatation, their BP could have dropped. These results are somewhat contrary to those of Swada *et al*., who reported that both systolic and diastolic blood pressures were associated with increased risk of cardiovascular diseases.[22] Non-significant difference in mean BMI between cases and controls is also not in line with the general perception that obesity is one of the risk factors for cardiovascular diseases. The present BMI results are also different than those of Girotra and coworkers who reported a significant correlation between age, general obesity and central obesity as cardiovascular risk factors.[23, 24] The difference in influence of BMI as risk factor to CVDs among the different studies could be due to differences in age, gender, and ethnicity, severity of obesity and CVD diseases. It may also possible that Pakistani women with lower BMI could be vulnerable to CVDs or it may be less sensitive in presence of other CVD risk factors in Pakistani women. The BMI results obtained in the present study are in conformity with those of Srikanthan and collegues.[25]

Ferritin has also been recognized as pro-oxidant that cause cellular damage.[12] The present results of serum ferritin are in accordance with those of Sempose *et al*., and Friedrich *et al.,* who also reported non-significant association between serum ferritin and mortality among CVD patients.[26-27] Conversely, Alissa and colleagues have reported a significant correlation between serum ferritin and coronary risk factors[28]. The present ferritin results do not support the hypothesis that serum ferritin levels increase the risk of CVDs. However, the present results of Hb are in close agreement with those of Micheal and Nielson (2008) who reported that most of the CVD patients had normal Hb levels.[29] The results suggest that iron status indicators are either insensitive to CVD or CVD does not affect iron status indicators to make a difference between cases and controls. These results are in conformity with those of Galan *et al*., (2006) who reported insignificant association between iron status and CVD.[30]

The recommended dietary caloric intake for the age group between 40-60 years is 2210 Kcal/day[31], which means that both patients and controls were receiving below 50% of the recommended dietary caloric intake. The mean lower caloric intake of cases than controls may be ascribed to their hospitalization and anorexia while impaired caloric intake of controls could be due to their unusual dietary practices in the hospital as they were the attendant of the patients and were away from their homes. The study suggests that cases and controls failed to consume the recommended macronutrient intake during hospitalization period. The study also emphasizes the importance of administering enteral and parenteral nutrition during hospitalization of cardiovascular disease.

Generally, South Asians and Africans have large family sizes and number of children compared to European and others from developed countries and more than 50% of the world population is inhabitant of Asia and Africa[32]. The education level of the subjects presents a very pathetic situation which could be one of the contributing factors toward under development, political and social unrest of the country. The results on literacy rate and education level of the studied subjects are somewhat different from those of Qamar (2000) who reported that 58% females were illiterate and had the education level of below secondary school education in Pakistan. The difference in literacy rates and level of female education between different research studies in Pakistan is attributed to difference in socio-economic conditions of the areas as well as in location where the studies have been conducted.[33] The higher employment rate in the hospitalized patients and their attendants was expected due to their relatively higher socio-economic group as poor and low income group of the population do not attend the hospital due to its high medical cost. However, the results of the present study may be different from the community based or public hospital based retrospective studies as this study was limited only to the affluent private hospital where medical care facilities have been qualitatively superior to those of other hospitals. The present results are somewhat different than those of Alexender *et al*., (2009) who reported that parental SES, childhood and early life factors and inequalities in health services contribute to elevated CVD risk in people of low SES despite living in developed countries.[34]

Conclusion

It was concluded from the study that age, systolic blood pressure, BMI were significantly associated with cardiovascular disease. It was further concluded that higher ferritin value of the patients may be due to infection and haemochromatosis and had normal haemoglobin levels. It is recommended that individuals should take regular exercise, control obesity, high BP and diabetes. It is further emphasized on importance of administering enteral and parenteral nutrition during hospitalization. Avoid stress, negative habits, fried/junk food and soft drink and increase consumption of fresh fruits, vegetables and complex carbohydrate.

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