Original Article

INCREASED SERUM IRON ASSOCIATED WITH CORONARY HEART DISEASE AMONG NIGERIAN ADULTS

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ABSTRACT

Objective: To examine the concentrations of serum iron and some risk factors of coronary heart disease in Nigerians with evidence of Coronary Heart Disease.

Methodology: The concentration of serum iron, the plasma cholesterol level, the hip-waist ratio and body mass index of 70 patients with evidence of CHD seen at a Cardiology Unit of a Specialist Hospital in Ibadan and 70 healthy subjects selected randomly were determined. Subjects were grouped into four age categories and three socioeconomic classes (high, middle and low).

Results: The age of the subjects ranged from 31-70 years with the mean of 53.6±11.0 years and 50.1±10.5 years for patients and controls respectively. The mean serum iron and plasma cholesterol levels were significantly higher among patients than controls irrespective of age and sex (p<0.05). No correlation was found between serum iron and the variables; plasma cholesterol level, age, body mass index (BMI) and hip-waist ratio.

Conclusion: Significantly higher serum iron levels found in patients with evidence of CHD appears to support the hypothesis that there is a potential association between iron status and CHD.

KEY WORDS: Serum iron, Plasma Cholesterol, Coronary heart disease, Body mass index, Hip-waist ratio.

INTRODUCTION

Coronary heart disease is one of the leading causes of death in most industrialized countries of the world and it is now also considered as a prominent health problem in developing countries.[1] An independent relationship between coronary heart disease and the level of serum iron status as a risk factor was reported from Finland by Salonen et al.[2] Sullivan speculated that maximum protection exists among iron deficient subjects since iron status affects the modification of LDL cholesterol and myocardial reperfusion injury.[3] More recent studies have shown that men with moderately elevated ferritin level have a significantly worse coronary artery disease risk profile than men with lower level.[4-6] Conflicting epidemiological evidence has also emerged as regard the role of iron, a lipid peroxidation catalyst, in coronary heart disease. In two different studies of coronary angiography in different centres in Brazil, no significant independent relationship between angiographic findings and serum ferritin level in patients with myocardial infarction were found.[7,8] Some studies[9,10] also described equivocal relationship between iron status and serum lipid levels.

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Coronary heart disease was previously reported to be relatively uncommon among Nigerians in spite of high prevalence of hypertension.[11] A study reported an evidence of increasing occlusive coronary heart disease in Nigerians especially among elderly affluent and hypertensive patients exposed to Western diets and habit.[12] A similar trend has been reported in other developing countries where their diets and lifestyles appear similar to those of the developed countries.[13,14]

The contribution of iron status to the rising incidence of coronary events in Nigerians is not known. Many individuals use iron containing medications because of the relationship between anaemia and iron intake. It is necessary to examine the serum iron status and some risk factors of coronary heart disease among Nigerians owing to its increasing public health significance. Therefore, this study was carried out to evaluate the hypothesis that an association exist between high serum iron level and coronary heart disease (CHD).

PATIENTS AND METHODS

Subjects: Seventy consecutive patients with diagnosis of coronary heart disease (CHD) seen at the Cardiology Clinic of Ring Road Hospital, Ibadan, Nigeria were enrolled in the study. The diagnosis of coronary heart disease was made based on the history, clinical examination and electrocardiography. Informed consent was obtained from each subject. Those who had other chronic diseases, infections, bleeding disorders and anaemia were excluded. Seventy healthy adults, who were specifically free from any symptom related to heart disease, were also enrolled as the control group.
Collection of Data: Data was collected by personal interview using a structured questionnaire with emphasis on features (clinical and laboratory) related to coronary heart disease (CHD). Subjects were grouped into four age categories and three socioeconomic classes (high, middle and low) as described previously.[15]
Sample Collection: Five millilitres of venous blood samples were collected from all subjects after an overnight fast to avoid dietary effect and diurnal variation on serum iron. The samples were separated into storage bottles within 30minutes after collection.

Laboratory Analysis: Serum iron concentrations were determined by the method of Garcic[16] using chemical kits supplied by Human (Human Diagnostica, Germany). Cholesterol was determined by the enzymatic method of Allain et al[17] using chemical kits also supplied by Human (Human Diagnostica, Germany). Humatrol, quality control samples (Human Diagnostica, Germany) were used for quality assessment.

Statistical Analysis: The data were analysed on computer using SPSS for Windows 11.0[18] As a result of the skewed distribution of the data on serum iron concentration the values were log-transformed before determination of the mean values (Geometric mean) and subsequent statistical tests. StudentÒ *t* test and ANOVA were used to compare the means of the continuous variables depending on the number of categories. Pearson correlation coefficient was used to evaluate the correlation of serum iron with plasma cholesterol, age, body mass index and hip to waist ratio. Values were expressed as mean ± SD (standard deviation) and/or 95% Confidence Interval. The level of significance was set at 5% ($p < 0.05$).

RESULTS

The characteristics of the study subjects are described in Table-I. Of the 70 patients, there were 40 (57.1%) women and 30 (42.9%) men while the control subjects consisted of 36 (51.5%) women and 34 (48.5%) men. The age

Table-I: Characteristics of the Study Subjects

Characteristics	Patients n=70	Control n=70
Sex, n (%)		
Female	40 (57.1)	36 (51.4)
Male	30 (42.9)	34 (48.6)
Age (years)		
Range	32-70	31-70
Mean ± SD	53.6±11.0	50.1±10.5
Social Class, n (%)		
High	16 (45.7)	14 (40.0)
Middle	13 (37.1)	13 (37.1)
Low	6 (17.2)	8 (22.9)

of the subjects ranged from 31-70 years with the mean of 53.6±11.0 years and 50.1±10.5 years for patients and controls respectively (p = 0.181). Nearly half (45.7%) of the patients belong to the high socioeconomic class; the middle class were 37.1% while the low socioeconomic class constituted 17.2% of the patients.

The mean serum iron levels in patients and controls in the four age groups according to gender are shown in Table-II. A higher mean serum iron value was obtained from the patients in all age group compared with corresponding control subjects. There was progressive increase in mean serum iron level as age increases in patients. The average serum iron concentrations in male and female patients were 41.1µmol/l (CI, 18.2-59.5) and 32.1µmol/l (CI, 22.8-45.3) respectively. Both male and female patients had higher mean serum iron values than their control counterparts (p = 0.006 and p = 0.004 respectively).

Table-III shows the mean serum iron concentration of the patients and control subjects according to their socioeconomic class. Serum iron level was highest in the high socioeconomic class but there was no significant relationship between iron level and socioeconomic class in patients (p = 0.188) and in control (p = 0.107).

The mean values of serum iron concentration, plasma cholesterol concentration, body mass index (BMI) and hip to waist ratio are as shown in Table-IV. The mean serum iron level was significantly higher in patients, 35.7±0.4µmol/l than the control group, 15.6±0.2µmol/l (t = 5.163; p=0.001). Plasma cholesterol level of 8.3±2.2mmol/l obtained in patients was significantly higher than 5.0±0.7mmol/l obtained in their control counterparts (t = 8.458; p = 0.001). The average BMI

Table-II: Serum Iron Concentration by Sex and Age in Patients and Control Subjects

Age (years)	Patients		Control	
	Male *Mean (CI)	Female *Mean (CI)	Male *Mean (CI)	Female *Mean (CI)
31 – 40	29.9 (28.6-31.8)	28.0 (13.6-58.5)	17.3 (13.6-21.9)	11.6 (6.6-31.2)
41 – 50	32.8 (5.2-71.1)	34.4 (11.5-103.3)	12.9 (7.8-21.4)	17.3 (6.9-43.5)
51 - 60	42.4 (17.7-101.6)	40.4 (25.1-64.9)	16.5 (14.3-21.4)	15.4 (15.3-20.8)
61 – 70	48.2 (23.6-98.5)	19.9 (9.0-130.4)	18.6 (15.2-19.2)	17.5 (9.6-31.9)
All Subjects	41.1 (18.2-59.5)	32.1 (22.8-45.3)	15.7 (12.7-19.3)	15.6 (13.0-18.6)

Patients vs. control, P < 0.05   *Geometric Mean (ìmol/l) CI – Confidence Interval

was significantly higher in patients (29.6±6.1kg/m^2) than controls (24.8±2.2kg/m^2); p=0.001. The mean value of the hip-waist ratio for patients, (1.15±0.08) was not significantly different from the value of 1.11±0.09 obtained in control group (t = 0.736; p=0.477). The correlation of serum iron with age, body mass index and hip-waist ratio are as shown in Table-V. There was no significant correlation between serum iron and each of age, BMI, hip-waist ratio and plasma cholesterol level as dependent factors among patients; p = 0.305, 0.730, 0.180 and 0.428 respectively. Similarly, there was no correlation between serum iron and each of age, BMI, hip-waist ratio and plasma cholesterol; p = 0.237, 0.868, 0.927 and 0.180 in control subjects.

DISCUSSION

In recent years, a substantial body of evidence has suggested that iron as a prooxidant might be involved in the pathogenesis of atherosclerosis.[19-21] The present study reveals a significantly higher serum iron level in patients with evidence of coronary heart disease than

Table-III: Comparisons of Serum Iron Concentration by Social Class in Patients and Controls

Social Class	Patients				Control			
	*Mean	95% CI	F	P	*Mean	95% CI	F	p
High	51.0	23.2-111.6	1.763	0.188	19.7	13.8-28.2	2.403	0.107
Middle	27.7	16.9-45.4			13.8	11.2-17.1		
Low	38.3	28.6-51.4			15.3	12.6-18.6		

*Geometric Mean in micromole per litre (µmol/l)   CI – Confidence Interval

Table-IV: Comparison of Serum Iron Concentration, Plasma Cholesterol, Body Mass Index
and Hip-Waist Ratio in Patients and Control Subjects

	PatientsMean (CI)	ControlsMean (CI)	t- values	P
*Serum Iron (μmol/dl)	35.7 (24.0 -112.7)	15.6 (6.8-39.9)	5.163	0.000
Plasma Total Cholesterol (mmol/l)	8.3 (5.6-14.5)	5.0 (3.6-6.4)	8.458	0.000
Body Mass Index (kg/m²)	29.6 (27.5-31.7)	24.8 (24.0-25.6)	4.329	0.000
Hip-Waist ratio	1.15 (1.07-1.10)	1.11 (1.07-1.05)	0.736	0.477

Values are expressed as Geometric Mean (Confidence interval)

control subjects, irrespective of their age, sex or socioeconomic level. This finding supports with the levels reported by Tuomainen et al[5] and Milman et al.[10] Although, serum iron measurement is not the best index of body iron store, the finding from this study suggests that increased iron may play a prominent role in evolution of atherosclerosis in Nigerians. The range and mean iron levels obtained in all age groups also compare favourably with the values reported by Sigurd.[22] The contrary reports by some investigators[8,9,23-25] who found a rather low iron level in coronary heart disease patients could be largely a result of the vast biological and measurement variability in methods used in assessing body iron. Variability was minimised in our study by stringent use of control and good laboratory practice.

Almost half of the patients in this study belonged to the high socioeconomic class. Ogunowo et al[12] had earlier reported evidence of increasing frequency of occlusive coronary heart disease among the elderly affluent Nigerians in the high socioeconomic class. A similar trend has been reported in other developing countries where diet and lifestyle are becoming closer to those of developed countries.[13,14] The occurrence of coronary heart disease in the low and middle income groups in

Nigerians is also not unexpected. The explanations for this might be due to increasing average life expectancy and the rapidly changing unhealthy life style with regards to diet, smoking habit and alcohol consumption.

The pattern of decreasing value of serum iron with increasing age reported by Magnusson et al[26] was not observed in this study, rather there was increasing serum iron level as age increases up to the end of sixth decade in both male and female groups. This discrepancy may be explained by variability in diet. The well known occurrence of higher serum iron level in male than female subjects was however upheld in this study. This difference has been attributed to the regular iron loss that accompanies menstruation in women.[27]

An interesting finding was that mean serum iron level was lowest in the middle class. It might be interesting to know if there is increased exposure of subjects to infections and worm infestations across the socioeconomic classes. Infestation and recurrent bacterial infection have been identified as one of the major causes of iron deficiency among Nigerians in the low socio-economic class.[28] If these factors are ruled out, it follows that there may be the need to classify subjects according to socioeconomic class in establishing normal ranges of serum iron.

Larsson et al[29] in a report showed that the distribution of fat deposits might be a better indicator of cardiovascular disease and death than the degree of adiposity measured by hip-waist ratio. The values of hip-waist ratio obtained in the present study showed no significant difference between patients with CHD and healthy individuals. This observation probably support the findings earlier reported.[29]

Table-V: Correlations of Serum Iron Concentration
with Age, Body Mass Index and Hip-Waist ratio

	Patients		Controls	
	Correlation coefficient (r)	P	Correlation coefficient (r)	p
Age (years)	0.179	0.305	0.205	0.237
Body mass index (kg/m²)	-0.061	0.730	0.029	0.868
Hip- Waist ratio	-0.232	0.180	0.016	0.927
Plasma Total Cholesterol	0.0331	0.428	-0.232	0.180

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CONCLUSION

The present study suggests that high serum iron concentration occurs in CHD patients in Ibadan. No statistically significant associations exist between the level of serum iron and age, body mass index, hip-waist ratio and plasma cholesterol. These results appear to support a possible role of increase body iron in the development of coronary heart disease in Nigerians.

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