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Association Risk Factors of Coronary Artery Disease with Total Iron Binding and Serum Ferritin Capacity in Men at Tikrit City

ABSTRACT:

Background Many international studies have discussed the important of serum ferritin and other iron status as a risk marker in coronary artery disease(CAD).

Aim: is to assess the effect of serum iron, total iron binding capacity(TIBC) , and serum ferritin on coronary artery disease (CAD) and their relationship with other risk factors.

Patients and Methods a case control study carried out from November 2016 and for 3 months duration enrolled on 96 male with age over 35 years,48 healthy men without (CAD) as control and other 48patients attending in Tikrit teaching hospital suffering of (CAD).All participants were assessed physically examination like blood pressers measurement, Wight and height. Then, the blood collected after 14 hours for measurement lipid profile , serum ferritin, serum iron, and total iron binding capacity (TIBC).Data analyses done include, t-test , chi-square test, and one-way ANOVA.

Results revealed that significant difference was found among the controls and CAD patients regarding the occurrence of BMI, blood presser(Systolic and diastolic) and fasting blood sugar were high significant in CAD patients as compared to normal healthy controls. However, significant differences was not observed in age groups. Regarding to Lipid profile(TG ,LDL-C and HDL-C). LDL-C and TG were high significant in CAD patients as compared to normal participants controls, while HDL-C was low significant in CAD patients as compared to normal healthy controls. About iron state ,it is evident that significant with Hemoglobin and TIBC at level $p < 0.05$. No significant differences of serum ferritin were observed between CAD patients and controls, while become significant when associated with other risk factors like obesity, hypertension, diabetes mellitus, and low LDL-C, but not with other parameters such as high TG , low HDL-C,high LDL-C, low TIBC,smoking and low exercise.

Conclusion: Study concluded that serum ferritin might serve as risk factor for coronary artery disease when associated with other risk factors like obesity, hypertension, diabetes mellitus,and hyperlipidemia.

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Introduction

Coronary artery disease, were previously called ischemic heart disease (IHD),(1)is a group of diseases that includes: stable angina, unstable angina, myocardial infarction, and sudden death.(2)It is include the group of cardiovascular diseases of which it is the most common type(3

Iron is important for many physiological processes whereas, iron overload has been known as a progressive factor of atherosclerosis(4).The production of free radicals, and to enhance lipid peroxidation by depressing the levels of antioxidants in plasma; thus, it leads to increase the risk of ischemic cardiovascular events.(5,6).Other study show a possible association between body iron status and risk of coronary artery disease (CAD) has been found to be controversial risk factors (7).

Aim of the study is to assess the effect of the serum ferritin, serum iron and total iron binding capacity (TIBC) in the causation of coronary artery

disease and their relationship with other risk factors.

Patients and Methods

A case-control study,was don on **Patients** attending in Tikrit teaching hospital with IHD and admitted in the Cardiac care unit ,with age over 35 years,the study start from November 2016 and for 3 months duration.

The diagnosis of CAD was depend on history of ischemic chest pain, positive troponin-I test, and electrocardiogram [ECG] . Diagnosed of diabetes mellitus ,when fasting blood glucose was >126 mg/dl. Patient with hypertension when systolic blood pressure was >140 mm Hg and diastolic blood pressure was >90 mm Hg or history reported use of antihypertensive drugs. Demographic data, any concurrent illness history, and information of medication, smoking, diabetes, hypertension etc were collected by interviews or from the case notes of the patients.

Anthropometric assessments included measurement of body weight and height.

Height of the participants with bare foot was determined by measuring tape, and body mass index (BMI) was calculated by dividing weight (kg) by squared height (m²).

The patients deal as dyslipidemia, when had total cholesterol (TC) level of >220 mg/dl or triglyceride (TG) >200 mg/ dl, high density lipoprotein (HDL-C) levels <45 mg/ dl, in female while <50 in male

We excluded individuals with an acute or chronic inflammatory disease, such as viral or liver disease, inflammatory bowel disease (IBD), gastric ulcer, cancer, rheumatoid arthritis, those who took iron and vitamin supplements. In addition, patients with thalassemia and hemochromatosis were excluded from the study. The biochemical parameters measurement included.

The blood samples were taken after 12-14 hours of fasting for measuring hematologic indexes, fasting blood sugar, and serum lipid profile by standard clinical laboratory procedure. Serum lipids, including triglycerides (TG), total cholesterol (TC), high-density

lipoprotein cholesterol (HDL-c) using enzymatic methods, and low density lipoprotein cholesterol (LDL-c), were calculated according to the Friedewald et al. formula (6). Serum ferritin concentration was determined by enzyme-linked immunoassay (Ideal Company). The CVs were 2.8%, 4.0%, and 10.4% for ferritin concentrations of 389, 139, and 27 mg/l, respectively. Serum iron and TIBC were determined by photometry with an eppendorf patient oriented system (EPOS) Chemistry Analyzer.

Statistical analysis was done by using T-test were used to compare case and control groups. For considering the differences in the variables in the patients, one-way ANOVA was employed. The logistic regression was used to estimate the incidence of CAD as dependent variable and serum ferritin as independent variable, adjusted for age, hypertension, diabetes, hyperlipidemia, and smoking. Numerical values were expressed as mean \pm standard deviation. P-values of 0.05 or less were considered as statistically significant.

Results

The present study included (96) men were evaluated; they were divided into individuals with CAD (48) and individuals without CAD as control (48).

(Table 1) : Significant difference was found among the controls and CAD patients regarding the occurrence of BMI (24.4 ± 1.1 kg/m² versus 29.4 ± 1.5 kg/m², $p < 0.05$) levels in patients than controls.

Systolic and diastolic blood pressure were high significant in CAD patients as compared to normal healthy controls. (148 ± 8 mmHg versus 115 ± 3.5 mmHg, $p < 0.5$) (95 ± 1.2 , 71 ± 5 mmHg, $p < 0.05$) respectively. About FBS it was found high significant in CAD patients as compared to control (143 ± 9 mg/dl versus 111 ± 7 mg/dl, $p < 0.5$). However, significant differences was not observed in age groups. **Table(2)** clarifies the Mean \pm SD of Lipid profile (LDL-C, HDL-C and TG) in case and control groups. LDL-C and TG were significantly higher in CHD patients as compared to healthy participants. (140 ± 5.3 mg/dl

versus 105 ± 9.1 mg/dl, $p < 0.05$), (189.1 ± 36.2 mg/dl versus 152.40 ± 40.45 mg/dl, $p < 0.05$) respectively, while HDL-C was low significant in CAD patients as compared to normal healthy controls. (33 ± 4.4 mg/dl versus 43.8 ± 8.3 mg/dl, $p < 0.05$) respectively.

Table(3) illustrates the Mean \pm SD of iron state in case and control groups. It is evident that serum ferritin was not significant. While significant with hemoglobin at level $p < 0.05$ (Hb in CAD was 14.2 mg/dL while 11.1 mg/dL). In concern to TIBC the study showed that significant correlation between Control group (301.7 ± 29.3) and Case group (221.5 ± 81.2) when $p < 0.05$.

In regarding to serum iron, it is found significant correlation between control group and case group, which become higher in case group 193.53 ± 66.485 mg/dL than control group 133 ± 51 mg/dL.

Table(4) show compares between serum ferritin in CAD associated other risk factors and Control groups, the risk factors include diabetes mellitus, hypertension, smoking high TG

,lowHDL-C,highLDL-C, low TIBCand 147±87mmHg153.6102 mg/dl, low exercise. 135±85.87 mg/dl, respectively).

The study revealed serum ferritin become significant when associated with other risk factors like obesity, hypertension, diabetes mellitus, and high LDL-C (127.9±62.8 kg/m², exercise. Furthermore, lack of a significant statistical difference in the other parameters such as high TG , low HDL-C, low TIBC,smoking and low exercise.

Table(1)show compares between serum ferritin associated other risk factors in CAD and Control groups.

Characteristic	Control group n=48 (Mean±SD)	Case group n=48 (Mean±SD)	P-value
Age (years)	51±4.2	57±3.8	NS
BMI(kg/m ²)	24.4±1.1	29.4±1.5	<0.05
Systolic blood pressure	115±3.5	148±8	<0.05
Diastolic blood pressure	71±5	95±1.2	<0.05
	111±7	143±9	<0.05

BMI=body mass index, FBS=fasting blood sugar, n=number, NS=Not Significant

Table(2)show characteristics of Lipid profile in case and control groups .

Lipid profile	Control group n=48 (Mean±SD)	Case group n=48 (Mean±SD)	P-value
LDL-C (mg/dl)	105±9.1	140±5.3	<0.05
HDL-C (mg/dl)	43.8±8.3	33±4.4	<0.05
TG(mg/dl)	152.40 ±40.45	189.1 ±36.2	<0.05

LDL-C = low density lipoprotein cholesterol, HDL-C= high-density lipoprotein cholesterol, TG= triglycerides

Iron state	Control group n=48 (Mean±SD)	Case group n=48 (Mean±SD)	P-value
Serum Ferritin (mg/dl)	87±26	147±106	NS
Hemoglobin (g/dL)	11.1	14.2	<0.05
TIBC (mg/dl)	301.7±29.3	221.5±81.2	<0.05
Serum Iron(mg/dl)	133±51	193.53±66.485	<0.05

Table(3)show characteristics of Iron state in case and control groups, TIBC= total iron binding capacity,

Table(4)show compares between serum ferritin associated other risk factors and Control groups in CAD

Serum ferritin in CAD group			Serum ferritin in Control group		P value
Associated other risk factors	Number (%)	(Mean±SD)	Number (%)	(Mean±SD)	
DM	20(42%)	153.6102	48(100%)	87±26	<0.05
HT	28(58%)	147±87	48(100%)	87±26	<0.05
Smoking	26(54%)	126±71.1	48(100%)	87±26	NS
Over w.t	34(71%)	127.9±62.8	48(100%)	87±26	<0.05
H.Chol(mg/dl)	16(33%)	135.7±65.4	48(100%)	87±26	<0.05
H.TG(mg/dl)	12(25%)	128.1±98.6	48(100%)	87±26	NS
L.HDL-C(mg/dl)	32(67%)	146.2±121	48(100%)	87±26	NS
H.LDL-C(mg/dl)	40(83%)	135±85.87	48(100%)	87±26	<0.05
L.TIBC (mg/dL)	46(96%)	97.2±2.9	48(100%)	87±26	NS
L.exersise	18(38%)	124.4±145.6	48(100%)	87±2	NS

DM=diabetes mallets , w.t=wight,H=high,L=low

Discussion

Serum ferritin concentrations are good index to intracellular ferritin concentrations; therefore, it is considered to be the good evidence of iron stores. This case-control study revealed that serum ferritin is not associated directly with atherosclerosis and CAD (Table 1). Armaganijan and Batlouni, like in this study suggested that serum ferritin and other organic iron not indicators as a risk factors or a risk markers for coronary atherosclerosis and serum iron levels were increase in those without atherosclerosis.(9).

This is agree with Auer *et al.* study showed that higher ferritin concentrations was not associated with an increased extent of coronary atherosclerosis in patients who referred for coronary angiography.(10)

This come paralled with ObioraEgbuch.*et al* study show that a higher serum ferritin level was not associated with an increased risk of incident CAD events or incident stroke, and may not be an independent

predictor of Incident CAD or stroke in blacks. (11)

whereas, other studies Ali Pourmoghaddas. *et al.*,(12) study revealed that excess serum ferritin is associated with atherosclerosis in Iranian males with coronary artery disease.

Also Haidari *et al.* concluded that high serum ferritin, is a good and independent risk factor for premature coronary artery disease in the male (13).

In addition, findings showed (TABLE 4) that the risk of serum ferritin become valuable when other risk factor present such as hypertension, diabetes, hypercholesterolemia, high LDL-c, and obesity were adjusted in the model. Ferritin can act as a catalyzer in the formation of oxygen free radicals and lipid peroxidation and important in the formation of oxidized LDL.(14-16). Oxidation of LDL get the accumulation of lipids in endothelial and smooth cells, and prevents macrophages from going out the arterial wall. Thus, these lead to promote the atherosclerosis lesion.(17-19)

Obesity was significant among CAD (TABLE 1) and still significant (TABLE 4) because obesity affects the cardiovascular system directly and indirectly. Many studies revealed that body mass index (BMI) was associated with CAD risk factors or adverse events. (20-22)

A numerous studies reported a good link between iron metabolism and obesity. This is due to inflammatory process related to obesity and or due to co morbidities. (24), the possible biological interaction of serum ferritin and BMI with CAD risk, a study provided evidence of additive interaction. It concluded that overweight get increase the level of serum ferritin. This result provided potential evidence that increase iron body to the risk of CAD found to be strong significant among overweight. (25)

Hyperlipidemia is the major risk factor for atherosclerosis. Small dense LDL (sdLDL) LDL-C, VLDL-C, chylomicron remnants, Lipoprotein(a), and oxidized LDL are pro-atherogenic and HDLs are non-atherogenic material. Those with

smaller denser LDLs are more liable to oxidation, and get strong affinity to the extracellular matrix. Delayed clearance of triglyceride-rich lipoproteins results in the production of sdLDL which is related with resistance to insulin and postprandial hypercholesterolemia. HDL had a significant attributed in the reverse transportation of cholesterol as well as having antioxidative and anti-inflammatory effects. HDL dysfunction of is an independent pro-atherogenic effect. In addition, low HDL-C is a sign of the metabolic hyperlipidemia (31-33).

As show in table (1) Triglycerides was significant increase among CAD due to arterial stiffness has been increasingly recognized as a strong predictor of cardiovascular disease and atherosclerotic disease and this come parallel with result of the study by wang *et al* (34) and other study (35) revealed that Triglycerides are a predictive factor for arterial stiffness .

conclusion:

Study concluded that serum ferritin might serve as risk factor for coronary

artery disease when associated with other risk factors like obesity, hypertension, diabetes mellitus, and hyperlipidemia.

Recommendation:

1-It is important to estimate serum ferritin like other risk marker in coronary artery disease management.

2- Emerging evidence suggests that avoid iron therapy in old age may enhance CAD .

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