Original Article

Risk of coronary artery disease and its association with high serum Ferritin

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Abstract

Coronary artery disease (CAD) is one of the major causes of death in India. Various factors contribute for atherogenesis. In the present study serum ferritin association was studied in CAD patients and control subjects. Significantly higher levels of serum ferritin were reported in CAD patients [45.37(±54.43)] than controls in [123.43(± 148.65)]. Association of serum ferritin has been observed in CAD patients with other co morbidities like type 2 diabetes and hypertension. A significant correlation has been noted between serum ferritin and fasting blood sugar (FBS), Glycosylated haemoglobin (HbA1c). **Conclusion:** The present study observed that serum ferritin levels were increased in CAD patients but it has also been noted that a significant correlation of serum ferritin levels was observed with glucose profile.

Keywords: Ferritin, CAD and additional risk factors of CAD, inflammation.

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INTRODUCTION

Coronary artery disease (CAD) is the most common cause of deaths in developed countries. CAD is responsible for more than one third of the deaths in individuals over the age of 35 years[1-3]. In 2013 CAD was the most common cause of death globally, resulting in 8.14 million deaths (16.8%) up from 5.74 million deaths (12%) in 1990. Risk of death in young age has increased between 1980 and 2010 especially in the developing world due to changing life styles, work patterns and sleeping deficits which mainly leads to stress[5]. Indians are predisposed to CAD through their genetic pattern[6]. Overall India is becoming the burning capital for type 2 diabetes, hypertension which leads to metabolic syndrome as an effect of fast urbanization[7]. Inflammation is a very widespread and complicated mechanism; various pro and anti inflammatory mediators play an intricate role in various inflammatory cascades[8]. Inflammation has been identified as a key subclinical feature where molecular events of inflammatory cascade which starts much early; even before the appearance of the clinical symptoms. A significant increase in variety of inflammatory mediators like IL-6, TNF –α have been observed in obese, type 2 diabetic and CAD patients in Indian population[9-12]. Body iron is mainly stored in the form of Ferritin. It consists of soluble protein (apo ferritin) and an inner layer of ferric hydrophosphate. Iron status of the body can be evaluated by screening serum

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Ferritin and it is especially important for detecting iron deficiency. Ferritin acts as a buffer against iron deficiency and iron overload. According to some researchers higher serum ferritin levels are not associated iron overload but it is due to destruction of the cells. Free iron is the culprit as it catalyses free radical formation, hence it is tightly bound to transport and storage proteins. The serum concentrates of ferritin are directly proportional to intracellular concentrations. Hence, it is the best indicator of body iron stores[13,14]. The man role of ferritin is to store iron but excess storage can produce harmful effects as iron has a potential to participate in free radical generation and might increase the oxidative stress[15]. Further it has been observed that serum ferritin concentration was found to be associated with dyslipidemia and abdominal adiposity[16]. While some studies supported ferritin as an acute phase reactant and thus may be increased in inflammation[17]. According to some researchers high ferritin in circulation is just a marker of cell destruction but they supported its inflammatory nature. Contradicting results keep it as a question of debate as the actual role of ferritin in inflammation is still an unresolved question. The aim of this study is to evaluate the association of serum ferritin concentrations and cardiovascular risk factors.

METHODS

In the present study 109 CAD patients and 107 controls were enrolled. The present study was carried out at Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai. Patients were recruited from outpatient department (OPD) & Indoor patient department (IPD). Written informed consent was obtained from all study participants. The study has been approved by the Institutional Ethics Committee.

Inclusion Criteria

Coronary Artery disease (unstable angina, stable angina, Non ST elevation, Myocardial infarction & ST elevation Myocardial infarction) proved by history, clinical examination, blood investigations, Electrocardiogram, Echocardiography & Coronary Angiography. Healthy Controls > 20 yrs of age are included. Age and sex matched healthy individuals without clinical evidence of coronary artery disease and with normal ECG constituted the control group.

Exclusion Criteria

Pregnant women, patients < 20 years of age, with Congenital Heart disease, acute or chronic infection, chronic liver and kidney disease. Fasting venous blood samples were collected from CAD patients and controls. Routine biochemical tests were performed on autoanalyser. Ferritin levels were estimated on Flash Chemiluminescence.

RESULTS

The mean serum ferritin concentration of the CAD group [123.43 (± 148.65) ng/ml] was significantly higher than controls [45.37 (±54.43)]. It was observed that serum ferritin concentrations were high in CAD patients with type 2 diabetes. No significant difference has been noted in Body mass index (BMI) [23.68(±3.26)/ 24.70(±3.59)] cholesterol [177.05(±39.45)/ 175.12(±51.37)], triglycerides [124.02(±47.08)/ 142.91(±69.78)] levels in two groups (controls/CAD). However, Fasting blood glucose and insulin, HbA1c were significantly high in CAD group compared to Controls. Lower levels of HDL has been observed CAD patient than control. No significant difference in other parameters of lipid profile has been noted between CAD and controls.

Table 1: Clinical and Biochemical Characteristics of study subjects

Variables	Controls (n=109)	CAD (n=107)	P value
Age	44.22(± 12.8)	55.79(± 10.8)	NS
Males %	48.2	51.8	-
Females %	54.5	45.5	-
BMI	23.68(±3.26)	24.70(±3.59)	NS
FBS (mg%)	96.37 (±28.36)	127.66(±55.49)	0.000
HbA1c (mg%)	5.72 (±1.43)	7.09 (±1.77)	0.000
Insulin	9.64 (±6.00)	12.39 (±8.84)	0.004
Triglycerides (mg%)	124.02(±47.08)	142.91(±69.78)	NS
Total cholesterol (mg%)	177.05(±39.45)	175.12(±51.37)	NS
LDL (mg%)	107.54(±35.70)	109.24(±41.81)	NS
HDL (mg%)	45.68 (±12.12)	39.07(±14.05)	0.001
Ferritin ng/mL	45.37(±54.43)	123.43(± 148.65)	0.000

Further it has been observed that out of 107 CAD patients, 43 showed high ferritin levels, while only 06 subjects out of 109 controls, showed very high serum ferritin.

Table 2: Circulatory levels of Ferritin in CAD and Controls

Ferritin levels (ng/dl)	Controls (n=109)	%	CAD (n=107)	%	Total
1-20	35	71.4%	14	28.6%	49
21-60	37	54.4%	31	45.6%	68
61-100	14	50%	14	50%	28
100-200	06	20%	24	80%	30
200-300	00	00	11	100%	11
>300	00	00	08	100%	08

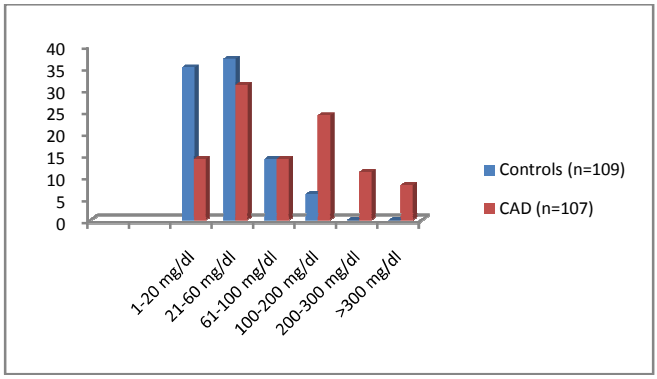

Figure 1: Camparison of Serum ferritin in CAD and Controls

Table 3: Correlation of Glucose profile with circulatory ferritin levels

Variable	Pearson's coefficient	Significance
FBS/ Ferritin	0.205	0.004*
HbA1c/ Ferritin	0.306	0.000*
Insulin/ Ferritin	0.056	>0.005

In the present study significantly higher levels of ferritin were observed in CAD patients with type 2 diabetes with abnormal glucose homeostasis. Pearson's correlation showed a significant association of ferritin levels with fasting blood glucose and glycosylated hemoglobin (HbA1c) concentrations. Fasting insulin didn't show any significant correlation with serum ferritin levels.

DISCUSSION

This present study showed a significant variation in serum ferritin levels among the study groups (CAD and controls). Further the study reported that significantly high ferritin levels were observed in CAD patients (with diabetes) than CAD patients (without diabetes). In CAD patients (with diabetes) a significant correlation has been observed between fasting blood glucose, glycosylated Hemoglobin (HbA1c) and circulatory concentration of ferritin; which suggests an important role of ferritin in pathophysiology of diabetes. Ferritin is an acute phase reactant protein and its levels shown to be elevated in chronic inflammation even when iron levels were completely normal[13]. The exact role of iron in induction of diabetes in not known clearly. High levels of ferritin were reported and the researchers have postulated three mechanisms for the development of diabetes -1) Insulin deficiency 2) Insulin resistance and 3) Hepatic dysfunction[18,20,22]. While High ferritin and its association with CAD have been reported by various studies and concluded, ferritin as a strong indicator of presence of atherosclerosis which is known as an advance stage of inflammation[17,24,25]. Iron-induced lipid peroxidation has been identified as a crucial feature involved in the early stages of atherogenesis[19,24]. Ferritin has been linked with imminent inflammation due to the strong oxidative capacity of iron. The ability of Iron in participation of free radical generation is high and due to high levels of Ferritin in circulation, more iron will be readily made available for promoting oxidative stress. Generating oxygen species, oxidizing lipoproteins and activation of platelets are the abilities of body iron that cause atherosclerosis[21,23]. Hence excessive iron in circulation is capable of stimulating atherogenesis as it generates free radicals, which stimulate lipid peroxidation, LDL oxidation, and endothelial damage[15,23]. In 2012 Khali et al reported the involvement of high ferritin levels with risk of plaque formation in CAD[25].

CONCLUSION

In conclusion, the current observation supported the hypothesis that ferritin is associated with incidence of CAD and showed a significant increase in its circulatory levels with presence of additional factors like type 2

diabetes as it plays a pathogenic role in diabetes and its related complications like CAD.

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