

Comparison of Serum Ferritin Levels in Healthy Individuals and Patients with Ischemic Heart Disease

SOBIA IMTIAZ, M ZAMIR AHMAD, RUBINA BASHIR, MOHSIN ALI, MUHAMMAD YASIR

ABSTRACT

Background: Development of ischemic heart disease (IHD) has been associated with higher body iron stores. The lower incidence of coronary heart disease (CHD) in premenopausal women as compared with men of the same ages and with postmenopausal women has been related to the lower body iron stores in the former group.

Objective: To compare serum ferritin levels of healthy individuals and patients with IHD.

Methods: A total of 137 subjects were included in the study, 47 healthy individuals with no history of IHD as controls and 90 patients of IHD. We compared serum ferritin levels of healthy men and male patients with IHD, healthy premenopausal women and premenopausal women with IHD, healthy postmenopausal women and postmenopausal women with IHD.

Results: Serum ferritin levels of IHD patients were significantly higher than healthy controls in all the three groups. Moreover, serum ferritin levels of IHD patients were suggestive of higher iron stores.

Conclusion Ischemic heart disease patients have higher iron stores than healthy individuals.

Key words Acute myocardial infarction, Coronary heart disease, Ischemic heart disease,

INTRODUCTION

Sullivan proposed the iron hypothesis in 1981. He associated the development of IHD to higher body iron stores. The lower incidence of CHD in premenopausal women as compared with men of the same ages and with postmenopausal women was related to the lower body iron stores in the former group¹. Many epidemiological studies have been carried out to test the iron hypothesis and serum ferritin concentration has been the most widely used indicator of the iron status in these studies. However, inconsistent results have emerged from the epidemiological studies linking iron status and the risk of CVD and there are both supportive and non-supportive studies².

Objective: To compare serum ferritin levels of healthy individuals and patients with IHD. In order to minimize the differences originating from factors like gender and menopausal status, we compared serum ferritin levels of healthy men and male patients with IHD, healthy premenopausal women and premenopausal women with IHD, healthy postmenopausal women and postmenopausal women with IHD.

MATERIALS AND METHODS

It is an analytical cross-sectional study which was conducted at University of Health Sciences (UHS) in

Department of Biochemistry, LM&DC, AIMC, UHS, Lahore

Department of Cardiology, PIC, Lahore

Correspondence to Dr. Sobia Imtiaz, Assistant Professor Email:

dr_mohsinali@yahoo.com

collaboration with Punjab Institute of Cardiology (PIC), Lahore. A total of 137 subjects were included in the study, 47 healthy individuals (40-60 years, both sexes) with no history of IHD as controls and 90 patients of IHD (40-60 years, both sexes). Ninety diagnosed patients of acute myocardial infarction (within first 48 hours of AMI) admitted to different wards of PIC were selected as patients. Diagnosis of AMI was based on typical history, suggestive ECG changes and serum cardiac biomarkers. Forty seven healthy individuals with no history of IHD were selected as controls. The subjects in each group were included in the study as they came and were categorized according to gender and menopausal status afterwards. As ferritin is an acute-phase protein and may become elevated in acute and chronic inflammatory conditions, malignancies and severe liver diseases, subjects suffering from these conditions were excluded^{3,4,5}. Selected subjects were informed about the study and consent was obtained. Relevant history was recorded in proformas. Venous blood samples were collected after overnight fast (i.e., 12-14 hours fast) between 8:00 am to 9:00 am. As a biphasic circadian rhythm has been reported for serum ferritin, specimens were drawn at nearly the same time of morning for each subject.⁶ Blood was allowed to clot and serum was separated by centrifugation. Serum was transferred to labelled aliquots and stored at -20°C. Human Ferritin Enzyme Immunoassay Test Kit (BIOCHECK, INC.) was used for the quantitative determination of human ferritin concentration in the serum samples.

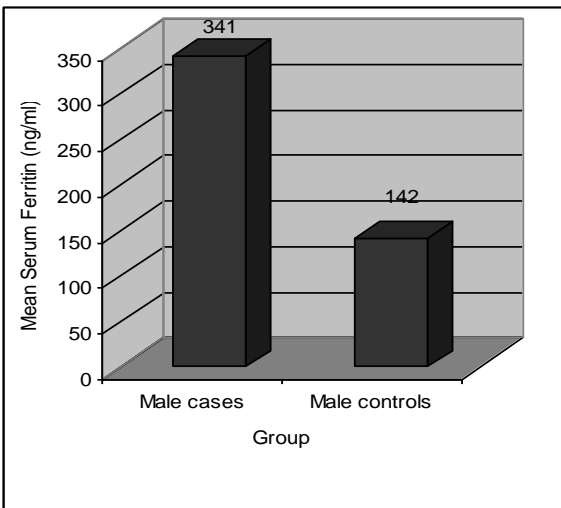
We compared serum ferritin levels of healthy men and male patients with IHD, healthy premenopausal women and premenopausal women with IHD, healthy postmenopausal women and postmenopausal women with IHD.

The data was entered and analyzed using SPSS (16.0). Independent sample t test was applied to observe group mean differences. A p-value of <0.05 was considered as statistically significant.

RESULTS

Out of 90 IHD patients, 63 (70%) were male and 27 (30%) were female. Out of 47 controls, 18 (38%) were male and 29 (62%) were female. Out of 27 female IHD patients, 19 (70%) were postmenopausal and 08 (30%) were premenopausal. Out of 29 female controls 12 (41%) were postmenopausal and 17 (59%) were premenopausal. Range of serum ferritin concentration in male IHD patients and male controls was 24-1054 ng/ml and 01-736 ng/ml respectively. Significant difference was observed between serum ferritin concentration of male IHD patients and male controls (340.56 ± 266.95 vs. 142.17 ± 181.09 ng/ml, $p < 0.05$) showing that male IHD patients have a mean serum ferritin concentration higher than male controls (Figure 1).

Fig. 1: Differences in serum ferritin of male IHD patients and male controls



Range of serum ferritin concentration in premenopausal IHD patients and premenopausal controls was 56-478 ng/ml and 02-180 ng/ml respectively. Significant difference was observed between serum ferritin concentration of premenopausal IHD patients and premenopausal controls (197.25 ± 143.30 vs. 30.59 ± 50.74 ng/ml, $p < 0.05$) showing that premenopausal IHD patients

have a mean serum ferritin concentration higher than premenopausal controls (Figure 2).

Range of serum ferritin concentration in postmenopausal IHD patients and postmenopausal controls was 36-802 ng/ml and 05-476 ng/ml respectively. Significant difference was also observed between serum ferritin concentration of postmenopausal IHD patients and postmenopausal controls (271.63 ± 243.45 vs. 75.50 ± 128.64 ng/ml, $p < 0.05$) showing that postmenopausal IHD patients have a mean serum ferritin concentration higher than postmenopausal controls (Figure 3)

Fig. 2: Differences in serum ferritin of premenopausal IHD patients and premenopausal controls

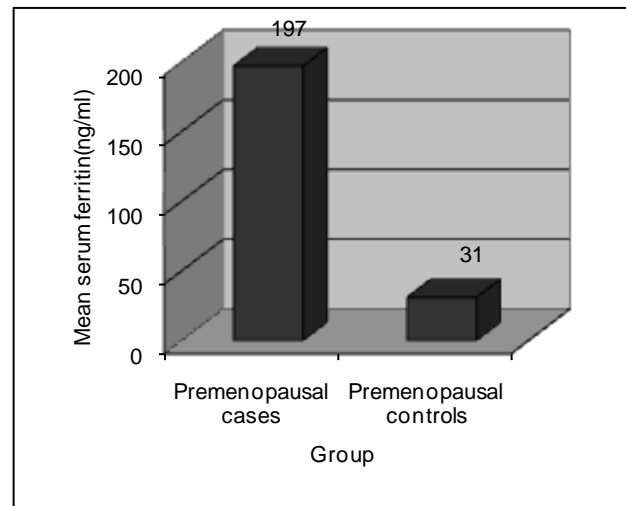
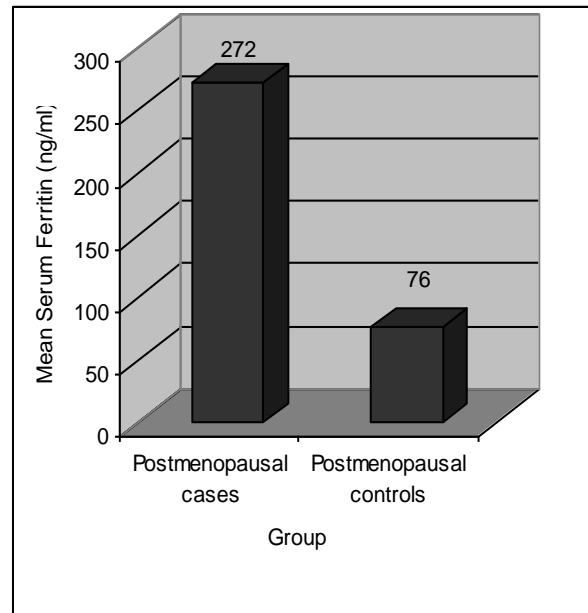


Fig. 3: Differences in serum ferritin of postmenopausal IHD patients and postmenopausal controls



DISCUSSION

Ferritin is the major iron storage compound and a readily available source of iron for metabolic requirements. It is a large multimeric protein found in nearly all cells of the body.⁴ Highest concentrations are found in the reticuloendothelial cells of spleen, liver and bone marrow and parenchymal liver cells.³ Initially, ferritin was thought to be exclusively an intracellular protein, with no measurable quantities in serum. In 1972, a sensitive radioimmunoassay for ferritin was developed and it was found to be a normal constituent of serum.⁷

Concentration of the small proportion of ferritin that is found in the blood correlates closely to the size of body iron stores.^{3,4,5,8} Serum ferritin concentration is a non-invasive measurable indicator of body iron stores and 65 mg increase in body iron stores is reflected by an increase of 1 µg/L in serum ferritin.^{3,9} Reference range of serum ferritin is 10-120 µg/L for females and 20-250 µg/L for males.⁴ High iron stores have been defined as serum ferritin concentration >300 µg/L in men and >200 µg/L in women¹⁰.

Male IHD patients had higher mean serum ferritin than male controls. Similarly, premenopausal IHD patients had higher mean serum ferritin than premenopausal controls. Moreover, postmenopausal IHD patients had higher mean serum ferritin than postmenopausal controls.

Mean serum ferritin concentration of male IHD patients was >300 µg/L suggesting high iron stores whereas mean serum ferritin concentration of male controls was within normal range. Mean serum ferritin concentration of premenopausal IHD patients was very close to iron overload cut-off value suggested by Fleming et al. whereas mean serum ferritin concentration of premenopausal controls was within normal range. Moreover, mean serum ferritin concentration of postmenopausal IHD patients was >200 µg/L suggesting high iron stores and mean serum ferritin concentration of post menopausal controls was within normal range.

These findings suggest that relative iron depletion offers protection against IHD and support Sullivan's hypothesis that the development of IHD might be related to acquisition of body iron stores.¹ Moreover, our results are in agreement with findings of Salonen et al. and Klipstein-Grobusch et al. who have reported that higher serum ferritin is associated with the higher risk of MI.^{11,12} Kiechl et al. have also reported that iron-deficient men and women constitute a low-risk group whereas subjects with prominent iron stores face a high-risk burden of carotid atherosclerosis¹³.

CONCLUSION

We conclude that IHD patients have higher iron stores, as indicated by higher serum ferritin, than healthy controls.

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