

Comparison of serum ferritin levels between newly diagnosed and clinical follow-up patients with metabolic syndrome

Yeni tanı ve klinik takip altındaki metabolik sendromlu hastalarda serum ferritin düzeylerinin karşılaştırılması

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Abstract

Background: The purpose of this study was to compare serum ferritin levels between newly diagnosed and clinical follow-up patients with metabolic syndrome.

Methods: Fifty-one newly diagnosed patients with metabolic syndrome according to the NCEP ATP III criteria were compared 179 patients with metabolic syndrome who have receiving conventional insulin resistance therapy.

Results: Ferritin and HOMA-IR levels in newly diagnosed patients with metabolic syndrome were significantly higher than clinical follow-up patients with metabolic syndrome (both $p < 0.01$).

Conclusions: Our study demonstrated that newly diagnosed metabolic syndrome patients had higher ferritin levels compared to clinical follow-up patients, and higher ferritin levels were associated with metabolic syndrome.

Key words: Ferritin, metabolic syndrome, insulin resistance

Özet

Amaç: Bu çalışmada yeni tanı ve klinik takip altındaki metabolik sendromlu hastalarda serum ferritin düzeylerinin karşılaştırılmasını amaçladık.

Materyal ve metod: NCEP ATP III kriterlerine göre yeni metabolik sendrom tanısı konan 51 hasta ile konvansiyonel insülin direnci tedavisi alan metabolik sendrom tanılı 179 hastada serum ferritin düzeyleri karşılaştırıldı.

Bulgular: Serum ferritin ve HOMA-IR düzeyleri yeni metabolik sendrom tanısı alanlarda, tedavi alan diğer metabolik sendromlu hastalara göre anlamlı yüksek tespit edildi (her ikisi için $p < 0.01$).

Sonuç: Bu çalışma yeni tanı almış metabolik sendromlu hastalarda ferritin düzeylerinin klinik takip altındaki hastalara göre daha yüksek olduğunu ve yüksek ferritin düzeylerinin metabolik sendrom ile ilişkili olduğunu göstermiştir.

Anahtar kelimeler: Ferritin, metabolik sendrom, insülin direnci

Introduction

The metabolic syndrome (MetS), clinically defined by the Adult Treatment Panel III (ATPIII), affects ~25 % of western adults (1, 2). The MetS is closely linked to insulin resistance and implies an increased cardiovascular risk (3, 4). Accumulating evidence suggests a link between body iron excess and insulin

metabolism (5). Prospective studies in apparently healthy men and women have shown that elevated serum ferritin levels independently predicted incident type 2 diabetes (7, 8). Further, higher ferritin levels have been associated with the MetS and insulin resistance (6, 9–11). Although based on these relationships between MetS and ferritin levels mentioned above, the pathogenesis of this

association is still unclear. Beyond these studies, we aimed to compare iron stores, measured by serum ferritin levels, between newly diagnosed patients with MetS and clinical follow-up MetS patients.

Materials and methods

Prior to subject recruitment, the study protocol was reviewed and approved by the hospital ethics committee, in accordance with the ethical principles for human investigations, as outlined by the Second Declaration of Helsinki. Fifty-one newly diagnosed patients with MetS according to the NCEP ATP III criteria were compared with 179 MetS patients who have received insulin resistance therapy such as metformin or/and pioglitazone. We identified MetS subjects according to ATP III because of three or more of the following: 1) fasting glucose ≥ 110 mg/dl or antidiabetes medication, 2) hypertension (blood pressure $\geq 135/85$ mmHg or medication), 3) triglycerides ≥ 150 mg/dl, 4) HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women, and 5) obesity (BMI ≥ 27 kg/m² instead of waist circumference, due to unavailability of waist circumference measurement in all subjects). We excluded patients who had any condition affecting the specificity of serum ferritin as an indicator of body iron stores: 1) recent acute illness and/or history of any overt chronic inflammatory disease; 2) cirrhosis, chronic hepatitis 3) heavy drinkers (> 60 g alcohol/day); and 4) neoplastic disease.

Blood pressure was measured in a supine position after 5 min of rest; waist circumference (the smallest circumference between the lower rib and the iliac crests), weight, and height were measured in lightly clad participants, and the BMI was calculated. Ferritin was measured in frozen serum samples by immunonephelometry and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5.

The data were analyzed using SPSS version 13.0 for Windows (SPSS Inc. Chicago, Illinois). A *Student t* test was used for the comparison of continuous variables. Analyses were also conducted to determine whether there was an association between ferritin and MetS. A *p* value of < 0.05 was considered significant.

Results

The clinical characteristics of patients were shown on

table 1 and 2. Ferritin levels were 212.19 ± 97.67 ng/ml (30-400 ng/ml) in newly diagnosed male subjects with MetS and were significantly higher than those 51 control clinical follow-up male subjects with MetS (ferritin: 124.83 ± 86.33 ng/ml) ($p < 0.01$). In the same way, mean ferritin levels were significantly higher in female MetS subjects (ferritin: 185.23 ± 79.81 ng/ml) (13-150 ng/ml) than those 128 control female subjects (ferritin: 80.30 ± 38.38 ng/ml) ($p < 0.001$) (Figure 1). Besides, HOMA-IR levels were found 3.75 ± 2.33 in newly diagnosed male subjects with MetS and were significantly higher than those control male subjects (HOMA-IR: 3.21 ± 1.15) ($p < 0.01$); also, HOMA-IR levels were significantly higher in female MetS subjects (HOMA-IR: 3.79 ± 1.94) than those control female subjects (HOMA-IR: 3.34 ± 1.21) ($p < 0.01$).

Discussion

To the best of our knowledge this is the first study that compared the ferritin levels between newly diagnosed and clinical follow-up MetS patients.

Studies have shown an association between serum ferritin and MetS feature (6, 10, 12-14). The MetS carries a well known increased risk for cardiovascular disease, however whether hyperferritinemia entails an additional risk or not is unknown (15, 16). In cross-sectional studies, elevated ferritin levels have been associated with hypertension (15), dyslipidemia (16, 17), elevated fasting insulin and blood glucose (9), and central adiposity (18). Although the mechanisms for the potential effect of iron on the risk of MetS are unclear, it has been hypothesized that elevated iron stores may interfere with hepatic insulin extraction leading to peripheral hyperinsulinemia (19, 20). Others have suggested that iron is a transition metal capable of causing oxidative tissue damage by catalyzing the formation of free radicals, which contribute to the development of insulin resistance (21, 22). Also iron overload may contribute to insulin resistance through mechanisms related to both reduced extraction of insulin and impaired insulin secretion (23). However, serum ferritin is an acute-phase reactant and may be artificially elevated in the presence of inflammation (24). We attempted to minimize this potential source of confounding by adjusting for CRP and by excluding those individuals with suspected inflammation, infection, liver and neoplastic diseases in sensitivity analyses.

Increasing evidence suggests that serum ferritin, a good indicator of body iron stores, is positively associated with MetS (6, 25). Ferritin and transferrin were shown to

independently predict hyperglycemia in a 3-year follow-up of our French cohort, Data from an Epidemiological Study on the Insulin Resistance Syndrome (26). Furthermore, it has been recently documented in a Japanese population that serum ferritin is associated with visceral fat area and subcutaneous fat area (27). Additionally, serum ferritin has been shown to be a significant predictor of carotid atherosclerosis progression and it is associated with an increased risk of ischemic stroke (28, 29). Therefore, high iron stores might be considered as an adjunctive risk factor for the development of ischemic stroke in persons with MetS. These studies clearly defined the relationship between serum ferritin and MetS. In our study, we aimed to show the relationship at a different point of view. If the ferritin is a risk factor of MetS, we thought that ferritin levels should be significantly lower in clinical follow-up patients, and our study showed that those patients who met the criteria for the MetS according to the ATPIII had slightly higher ferritin than

the rest of the patients who have been treated with MetS. Also we determined that HOMA-IR score levels was significantly lower than newly diagnosed MetS patients and these findings showed that insulin resistance treatment plays role to decrease ferritin levels in MetS patients.

In conclusion, the present study suggests that ferritin elevation in our patients is a marker of the MetS and serum ferritin should be added to routine evaluation of MetS patients; this would help identify a subgroup of individuals at risk for iron-related tissue damage. Induction and maintenance of a state of iron depletion should be evaluated as a practical modality in the treatment of MetS. The direct pathogenic mechanism, however, remains unknown. Further studies are needed to obtain evidence concerning the association between serum ferritin levels and the MetS.

Table 1: Newly diagnosed patients with metabolic syndrome

	Male (n=23)	Female (n=28)
Age, years	47.61±10.95	54.43±10.38
Waist circumference, cm	103.35±7.20	101.36±10.14
Systolic blood pressure, mmHg	150.87±23.53	154.46±26.19
Diastolic blood pressure, mmHg	93.04±9.62	94.64±15.59
Glucose, mg/dl	119.30±40.30	116.93±54.35
Triglyceride level, mg/dl	196.48±76.29	186.61±59.21
HDL level, mg/dl	39.22±7.15	43.79±9.68
HOMA-IR	3.75±2.33	3.79±1.94

Table 2: Clinical follow-up patients with metabolic syndrome

	Male (n=51)	Female (n=128)
Age, years	52.18±8.32	57.12±9.35
Waist circumference, cm	101.42±8.11	99.48±8.56
Systolic blood pressure, mmHg	140.87±18.42	145.14±21.13
Diastolic blood pressure, mmHg	88.12±7.34	91.72±14.28
Glucose, mg/dl	102.40±35.40	98.55±44.23
Triglyceride level, mg/dl	155.14±46.54	164.37±66.22
HDL level, mg/dl	43.22±8.24	46.79±8.36
HOMA-IR	3.21±1.15	3.34±1.21

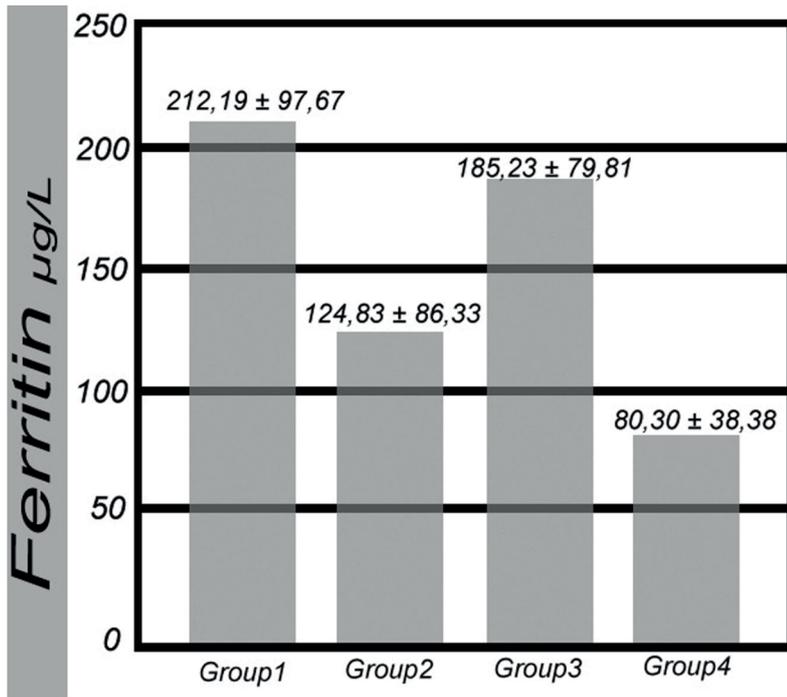


Figure 1: Graph demonstrating the ferritin levels among groups
 Group 1: The male newly diagnosed patients with metabolic syndrome
 Group 2: Control group-male
 Group 3: The female newly diagnosed patients with metabolic syndrome
 Group 4: Control group-female

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