

SERUM FERRITIN IN TYPE 2 DIABETES MELLITUS AND ITS RELATIONSHIP WITH HbA1c

F. Sharifi* and Sh. Sazandeh

Department of Endocrinology, School of Medicine, Zanzan University of Medical Sciences, Zanzan, Iran

Abstract- Diabetes mellitus (DM) type 2 is one of the most common endocrine disorders affecting more than 135 million people in the world. The etiology of the disease is not fully understood, but recently subclinical hemochromatosis has been considered as one of the probable causes of DM. This study was carried out to examine the relationship between serum ferritin as a marker of iron overload with DM and HbA1c. This study was conducted on 97 patients with type 2 DM who were referred to Zanzan Diabetes Clinic. Ninety-four normal age-matched individuals were included in the study as the control group. Ferritin, hemoglobin, HbA1c, and fasting blood sugar were measured in blood samples. Exclusion criteria included anemia, or any other disease or drug that could affect ferritin levels. Results were analyzed statistically by Chi-square test, t-test and Pearson regression coefficient test. One hundred ninety-one cases including 97 diabetics (37 males and 60 females) and 94 normal individuals were studied. There were no significant differences between the two groups regarding age, hemoglobin and body mass index. Mean serum ferritin was significantly higher in diabetics than in the control group (101 ± 73 mg/ml vs. 43.5 ± 42 mg/ml, $p < 0.001$). There was no correlation between serum ferritin and HbA1c in diabetic patients of either sex. Ferritin levels in patients with DM is high, but not related to levels of HbA1c and blood glucose control.

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Key words: Diabetes mellitus, ferritin, HbA1c

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent endocrine disorders in the world (1). Although type 2 DM is more common than type 1, its pathogenesis is less well understood. Nevertheless both beta cell defects and insulin resistance are present in overt DM (1). The relation between the beta cell abnormality and insulin resistance is not resolved. Kaye and Fedstate (1993) have reported the possibility for a link between subclinical hemochromatosis and type 2 DM (2). The probable role of ferritin as an iron overload marker in pancreatic damage or peripheral insulin resistance is not clear (3). This study was performed in order to

find a link between serum ferritin and DM and also HbA1c as a blood glucose control marker in diabetic patients.

MATERIALS AND METHODS

This study was carried out in a group of diabetic patients who had been referred to Zanzan Diabetes Clinic, and a normal control group. From June 2001, all patients with type 2 DM who had been referred to this clinic were enrolled in the study. Patients with a history of ketoacidosis and other diabetic complications, were excluded from the study. Our criteria for the diagnosis of anemia were based on clinical examination and a hemoglobin level of less than 12 g/dl. The control group consisted of individuals who had been referred to the laboratory center for routine checkup with no history of any medical disorder. They had fasting blood sugar levels of less than 110 mg/dl and hemoglobin levels of more

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***Corresponding Author:**

F. Sharifi, Department of Endocrinology, School of Medicine, Zanzan University of Medical Sciences, Zanzan, Iran
Fax: +98 241 29665

than 12 g/dl. They did not have a history of medication use, and were matched with the diabetic group regarding age and sex. One standard questionnaire was completed for each subject, which included their personal data, drug usage, disease history and physical examination. Weight and height were measured by a standard device and body mass index (BMI) was calculated based on weight / (height)² formula. The blood sugar was measured after 12 h of fasting by orthotoluodene method, HbA1c by ion exchange (DSS), and ferritin by RIA in the same laboratory center. Results were analyzed with SPSS software and t-test was used for quantitative variables, Chi-square test for qualitative variables and Pearson's regression for correlation between variables.

RESULTS

One hundred one cases, including 97 diabetics (37 males and 60 females) and 94 normal subjects as control group were examined. Mean age for diabetic group was 42±3 y and for control group was 39±2.9 years. The mean ±SD level for BMI in diabetics was 26.9 ±4.5 kg/m² and for control group was 24.2±3 kg/m². There wasn't any significant difference between the two groups for age and body mass index. The mean level of hemoglobin in diabetics (13.7±1.5 g/dl) was not different from those of normal controls (13.4 ±1.1g/dl) statistically. The mean serum ferritin in diabetics was significantly higher than normal group (101.5±73 vs. 43.5±41.8 µg/ml, $P<0.001$) (Fig. 1).

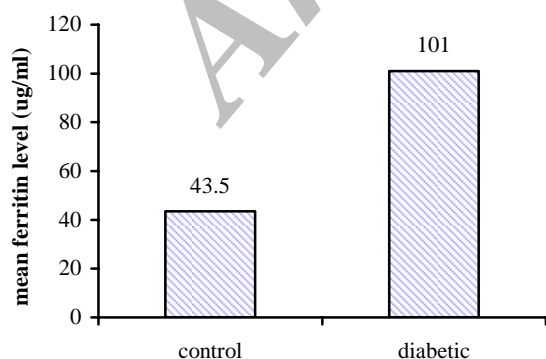


Fig. 1. Comparison between diabetic and normal cases regarding their ferritin levels

The ferritin levels were not significantly different in male and female diabetics (123±97 vs. 94.4±64 µg/ml, respectively). Diabetic patients were divided into three groups based on their HbA1c: good control was defined as HbA1c of <7% (28 cases, 29%), moderate control as HbA1c of 7-9% (38 cases, 39%), and poor control as HbA1c levels of more than 9% (31 cases, 32%).

The mean ferritin level was 103±95.3 µg/ml in the first group, 113±77.5 µg/ml in the second, and 96.5±66 µg/ml in the third. There were no significant differences between these three groups regarding ferritin levels (Fig. 2).

Statistical analysis showed that there was no significant correlation between serum ferritin and HbA1c ($r=0.23$), BMI ($r=0.1$) and FBS ($r=0.004$) in diabetic patients. No correlation was found between ferritin level and age either (Fig. 3).

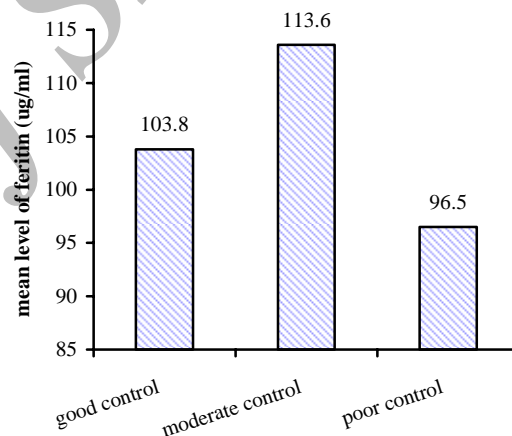


Fig. 2. Serum ferritin levels in three different conditions of blood glucose in diabetic patients

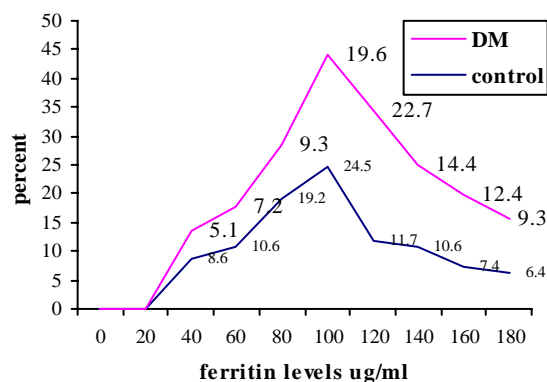


Fig. 3. Ferritin levels in diabetics and control group

DISCUSSION

The results of this survey showed that serum ferritin in diabetic patients is significantly higher than non-diabetics, but its level has no correlation with blood sugar or HbA1c in diabetic patients.

Ferritin has been known as an index for body iron stores and also as an inflammatory marker. In some epidemiological studies serum ferritin was the second strongest determinant of blood glucose (after BMI) in regression models and the third strongest determinant of serum insulin (after BMI and age) (4). Its concentration also correlated positively with plasma triglycerides and apolipoprotein B concentrations, and negatively with HDL2 cholesterol (5). We hypothesized that serum ferritin could be a marker of insulin resistance. The probable correlation between ferritin and DM was considered first in 1993 by Kay et al. (6), after which other studies were focused on this subject. In 1999 a survey by Ford and his colleagues in United States on 9486 diabetic adults determined high levels of ferritin in diabetics (7). Another study by Kwant (8) on the prevalence of C282Y mutation of hemochromatosis gene, determined the higher prevalence of this mutation in type 2 DM, that could be considered as an evidence for some relationship between these two disorders. Fernandez in 1998 studied the relationship between serum ferritin and the results of glucose tolerance test and insulin sensitivity in healthy subjects (5). In this study the correlation between serum ferritin and diastolic blood pressure, HDL, glucose area under the curve and insulin sensitivity suggest that serum ferritin could be a marker of insulin resistance. Such results have also been reported by Kim et al. (4). They suggest that serum ferritin may also be an independent determinant of poor metabolic control in diabetic patients, but our data didn't confirm this suggestion. This difference can be due to our exclusion criteria such as anemia and severe diabetic complications that had not been considered in other studies.

There are different theories regarding the role of ferritin in DM. Pancreatic damage due to some degree of subclinical hemochromatosis has been considered at least in some cases of diabetes (6). Others has determined ferritin just as a marker of

pancreatic inflammation, and some have referred to it as a marker for insulin resistance as mentioned above.

Fernandez et al, studied the effect of ferritin reduction by blood letting on insulin sensitivity and HbA1c levels in diabetic patients (9). In this study the positive effect of ferritin reduction on blood glucose control was used for confirmation of the probable role of ferritin in DM pathogenesis but, the use of blood letting may affect total hemoglobin level and HbA1c as well, so the use of HbA1c as a marker of blood glucose control has not been appropriate. Recently some studies have investigated the effect of chelator agents such as Desferal on the control of diabetes mellitus (10). There are different results in this regard. Some studies have determined a higher level of ferritin in people who are high risk for atherosclerosis (11). Since insulin resistance has been considered as the basic factor in the pathogenesis of atherosclerosis (12) higher ferritin in atherosclerotic patients can be due to insulin resistance.

In conclusion, ferritin is higher in diabetics than in controls. There isn't any correlation between serum ferritin and blood glucose control in diabetics. So, it seems that ferritin may have a role in the pathogenesis of type 2 DM. We propose that more studies need to be performed about the role of ferritin in gestational DM, and patients with impaired glucose tolerance, as cases with some degree of insulin resistance and in the pre-diabetic stage.

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