Original Article

Serum ferritin has correlation with HbA1c in type 2 diabetic patients

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Abstract

Background: Serum C-reactive protein (CRP) and ferritin are two acute phase reactants. CRP may be related to metabolic syndrome and ferritin which in turn could cause resistance to insulin and dysfunction of β cells of pancreases. The aim of the study was the evaluation of the relationship of these two acute phase reactants with some indices of diabetic control.

Materials and Methods: In a quasi-experimental study, 67 patients with type 2 diabetes, serum CRP, ferritin, Fasting Blood Sugar (FBS), post prandial BS, Hemoglobin A1c (HbA1c), triglyceride, Low Density Lipoprotein Cholesterol (LDL) and High Density Lipoprotein cholesterol (HDL) were checked before and 3 months after the control of hyperglycemia and hyperlipidemia.

Results: The mean age of the patients was 56.5 ± 9.7 (30 to 82) years. There was no significant difference between CRP before and after study; however, serum ferritin significantly decreased after study with control of hyperglycemia. FBS, 2 hours post-prandial blood sugar (2hppBS), HbA1c and triglyceride of patients decreased significantly after control of hyperglycemia and hyperlipidemia ($P < 0.05$); however, HDL and LDL cholesterol didn't change ($P > 0.05$).

Conclusion: Based on our results, serum ferritin decreased after decline of patients' blood sugar, so might be we used it as one of the diabetes control indices for diabetic patients.

Key Words: C-reactive protein, diabetes control indices, ferritin

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INTRODUCTION

Type 2 diabetes mellitus (DM2) is an important health problem worldwide affecting about 8 percent of population.[1] The prevalence of disease continued to rise over the recent decades.[2-6] The probable role of inflammatory factors and cytokines in producing DM was described by Pickup JC in 1998.[7] Similar results also were found by other studies which showed that acute phase reactants may be useful for predicting DM;[8-11] however, these findings were not found in some other studies.[12]

Acute phase reactants are proteins that respond to acute stress such as infection, trauma, surgery and tissue necrosis. Some of these agents are alpha-acid glycoprotein, haptoglobin, fibrinogen, C-reactive

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protein (CRP) and ferritin.[13-15] CRP is produced by liver cells and could activate complement system and T and B lymphocytes. Erythrocyte Sediment Rate (ESR), as an acute phase reactant, is less important than CRP for evaluation of inflammation.[9,16] Ferritin is a complex globular protein that stores iron as soluble and non-toxic component. In oxidative stress, Fe^{2+} enters to cells and then changes to Fe^{3+}, linked to ferritin and then protect cells from oxidative stress.[17] Increasing concentration of iron and ferritin in cells could cause resistance to insulin and dysfunction of β cells of pancreases. Hyperinsulinemia due to resistance to insulin may be responsible for increasing serum ferritin. It has been suggested that disturbance of iron metabolism could cause insulin resistance, hyperinsulinemia, dyslipidemia, HTN and central obesity.[18,19]

Since serum CRP and ferritin are two important positive acute phase reactants and increased serum level of them might be related to metabolic syndrome and insulin resistance, we have planned this study to evaluate the association between serum "CRP and ferritin" with some indices of diabetic control.

MATERIALS AND METHODS

This quasi-experimental study was performed on 67 known cases of DM2, based on ADA[20] in Emam Ali Clinic of Shahrekord, Iran. Inclusion criteria were age greater than 18 years and glomerular filtration rate (GFR) >60 mL/min based on Cockcroft-Gault formula (140-age × body weight/72 × serum creatinine). Exclusion criteria were consumption of steroid or immunosuppressive drugs and presence of infectious or autoimmune disease based on history and physical exam. Demographic information including age, gender, body weight, length, body mass indexes (BMI), duration of diabetes, blood pressure, and also laboratory findings including fasting blood sugar (FBS), 2 hours post prandial BS (2hppBS), ferritin, CRP, blood urea nitrogen (BUN), serum creatinine (Cr), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), triglyceride, HbA1C were recorded in patients' files. FBS, 2hppBS, serum BUN and Cr was checked by BioTechnica Instruments (BT 3000). Serum CRP as a quantitative factor was measured with immunoturbidimetric method by BT 3000. Serum ferritin was checked with electrochemiluminescence method, by ELEXIS (made by Italia). The patients were visited monthly by nephrologist or endocrinologist for control of blood glucose, lipid profile and blood pressure based on WHO guidelines. Patients' blood glucose was controlled by insulin or oral hypoglycemic agents. All laboratory tests were checked at beginning of study and 3 months later in the same laboratory. Recommendations for lifestyle modifications such as regular exercise and diet were done for all patients. This study was approved by ethical committee of Shahrekord University of Medical Science.

The relationships were evaluated with Spearman's rho and *t*-test using SPSS software (version of 17). The results were expressed as mean ± standard deviation (SD). In order to compare variables before and after study procedure, paired *t*-test were used. *P* value less than 0.05 were considered statistically significant.

RESULTS

Forty five (67.2%) patients were women. At the beginning of the study, mean age of the patients was 56.5 ± 9.7 (30 to 82) years, mean BMI was 28.5 ± 4 (22 to 42), mean glomerular filtration rate (GFR) was 77.9 ± 12.9 (99 to 36) mL/min, and mean duration of diabetes was 6.3 ± 4.1 (1 to 15) years. Despite HDL and LDL cholesterol, which didn't change during the study, the factors of FBS, 2hppBS, HbA1C and triglyceride decreased significantly during the study ($P < 0.05$).

Mean serum CRP, before and after the study were 1.43 ± 0.09 mg/L and 1.42 ± 0.08 mg/L, respectively (normal range: 1 to 3 mg/L). There was a significant negative correlation between serum ferritin and duration of diabetes ($r = 0.259$; $P = 0.034$). There was a weak positive correlation between CRP and HbA1c at beginning of study ($r = 0.251$; $P = 0.042$) [Table 1]. In one patient, serum CRP was 115 and 111, respectively, before and after study; therefore, this patient was excluded from analysis.

Mean serum ferritin, before and after the control of hyperglycemia were 115 ± 109.4 ng/mL and 91.4 ± 61.9 ng/mL, respectively (normal range: Males: 23 to 336 ng/mL and Females: 11 to 306 ng/mL). There was no significant difference between CRP before and after the study; however, serum ferritin significantly decreased after 3 months follow-up, which means that

Table 1: Summary of variables of the patients during the study

Inflammation indices	Before study		After study		*P* value
	Min-max	Mean±SD*	Min-max	Mean±SD	
FBS (mg/dl)	87-294	155.6±48.6	86-285	129.4±33.9	<0.001
2hppBS (mg/dl)	124-457	238.3±73.1	123-356	206.3±48.4	<0.001
HbA1C (%)	4-11	7±1.2	4-8	6.3±0.8	<0.001
TG (mg/dl)	63-800	196.9±125.3	70-449	175.6±91.8	0.03
LDL (mg/dl)	4-197	99.5±28.9	40-197	97.3±32.4	0.477
HDL (mg/dl)	30-105	47.7±11.5	30-70	47.3±8.4	0.747
CRP$ (mg/L)	1.25-1.67	1.43±0.09	1.25-1.55	1.42±0.08	0.192
Ferritin (ng/mL)	5.7-610.6	115±109.4	5.7-327	91.4±61.9	0.004

*SD: Standard deviation, FBS: Fasting blood sugar, 2hppBS: 2 hours post-prandial blood sugar, HbA1C: Hemoglobin A1C, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, $CRP: C-Reactive protein

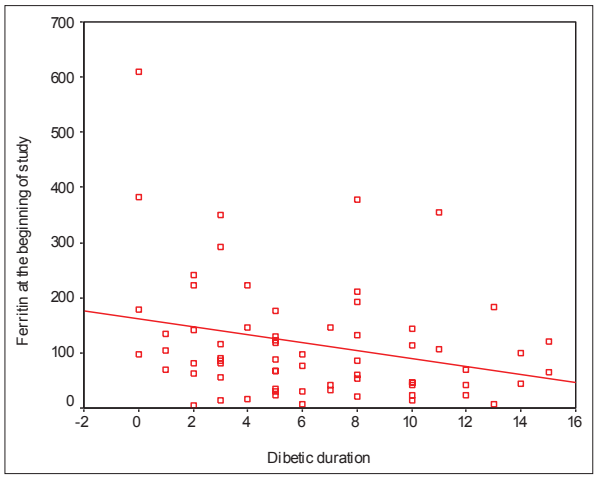

Figure 1: Scatter plot of ferritin based on diabetic duration at the beginning of study

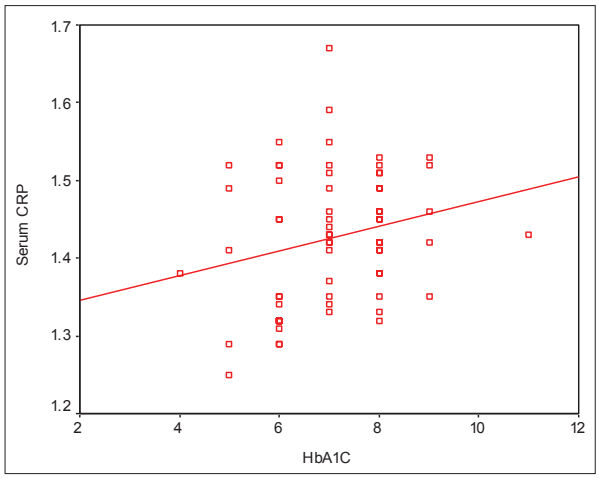

Figure 2: Scatter plot of Serum CRP based on HbA1C at the beginning of study

serum ferritin would decrease with reducing serum FBS and post-prandial BS [Figures 1 and 2].

DISCUSSION

This study was conducted to evaluate the relationship between two acute phase reactants (CRP and ferritin) with diabetic control indices (FBS, 2hppBS, HbA1c). Our study showed that in diabetic patients, despite the improvement of diabetic control indices, the amount of serum CRP was not changed; however, serum ferritin level had a relationship with hyperglycemia and its level decreased with lowering of serum blood glucose. There are different and sometimes controversial results in the other studies. In Ebrahimi's study, in 80 cases and 73 controls among participant of Tehran glucose lipid cohort study, whom followed for 3.6 years, serum CRP was correlated with systolic and diastolic blood pressure, total cholesterol and triglyceride and FBS, but not with HDL cholesterol and 2hppBS. The authors concluded that CRP may have a role in production of diabetes and can use as a predictor of DM in the future.[21] In another study, Festa evaluated 1407 cases who were at high risk of developing DM for 5 years and observed that DM was developed in 144 cases, who had greater serum level of CRP, fibrinogen and plasminogen activator inhibitor-1 compared to another patients.[9] In 9486 adult population, Ford checked serum insulin, hemoglobin A1C (HbA1c), fasting blood sugar (FBS), ferritin, and found a significant correlation between serum ferritin with HbA1c, FBS and serum insulin. He concluded that elevated serum ferritin is a risk factor of DM.[22] Similar results were obtained in our study, so after improvement of diabetes indexes, ferritin was decreased. Wrede in a study on 2000 German population showed that serum ferritin is higher in patients with BMI >25 kg/m^2, cholesterol >200 mg/dl, systolic blood pressure >160 mmHg and in women with diabetes. He found a positive correlation between serum ferritin and presence of insulin resistance syndrome in a representative population.[23] In Ashoorapour's study, there was a correlation between serum ferritin and FBS, HbA1C, serum insulin.[19] Thorand B in MONICA study showed that men with high levels of CRP had a 2.7 times higher risk of developing diabetes compared with men in the lower CRP. He concluded that low-grade systemic inflammation is correlated with an increased risk of type 2 diabetes mellitus in middle-aged men; however, after adjustment for BMI, smoking and systolic blood pressure (SBP), the observed association was substantially reduced and became not significant.[8]

Our study had some limitations such as difficulty of regular follow-up of the patients during the study, relative small sample size, necessity of performance of exams only in a single laboratory and non-cooperation of some patients, which may cause them to be excluded from study.

CONCLUSION

Based on our results, serum ferritin decreased after decline of patients' blood sugar which might be used it as one of the diabetes control indices for diabetic patients.

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