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CLINICAL INVESTIGATIONS

The Level of Ferritin in Diabetic and Nondiabetic Patients with Acute Myocardial Infarction

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Abstract: An elevated serum ferritin level is proposed as a risk factor for coronary heart disease. The role of diabetes mellitus on serum ferritin levels in myocardial infarction has recently been investigated. The purpose of this study was to assess the effects of diabetes mellitus on serum ferritin levels in patients with acute myocardial infarction (AMI).

In this study, we studied patients (104 nondiabetic, 26 diabetic patients) with acute myocardial infarction (AMI). AMI was diagnosed according to typical clinical history, ECG changes and cardiac enzyme elevations. Blood samples for ferritin, iron and total iron binding capacity (TIBC) and haemogram tests were obtained in the morning within the first 3 consecutive days and were measured by immunoradiometric assay (IRMA), ferrene assay and ferrozine assay respectively. Whole blood (K_3 EDTA as anticoagulant) was analyzed using Beckman Coulter Hmx hematology. The comparison of groups and subgroups was done using one-way varians analysis (ANOVA) and Tukey's Multiple Comparison Test respectively, while the unpaired t test and the Mann Whitney U test were used for the analysis of the 2 groups and the qualificational data were analyzed using the chi square test .

Serum ferritin levels were significantly increased in the diabetic group. The results were evaluated with a 95% safety margin ($P < 0.05$).

In the presence of diabetes mellitus, serum ferritin levels may be elevated, which may increase the risk of coronary heart disease.

Key Words: Ferritin, Diabetes Mellitus, Myocardial Infarction

Introduction

In patients who have had an episode of unstable coronary artery disease, levels of inflammation markers such as acute-phase proteins, C-reactive protein, and fibrinogen tend to be higher, which is the result of an increase in the risk of cardiovascular disease. Fibrinogen plays a key role in both coagulation cascade and platelet aggregation, which is a determinant of plasma viscosity (1). Free radical species are important agents in both myocardial ischemic and reperfusion injuries. Superoxide is capable of releasing iron from ferritin, and the released iron can cause hydroxyl formation from H_2O_2 (2).

Most of the ferritin is found in the liver cells, spleen and bone marrow. It is also found in the heart, pancreas and kidney. Human serum contains a small but significant quantity of ferritin. Serum ferritin levels are affected by age and sex. In normal individuals, ferritin levels are slightly higher at birth and decrease during childhood until puberty. After puberty, body iron storage in males increases progressively with a proportional rise in serum ferritin, whereas serum ferritin levels are lower and more stable in females the during reproductive period. Ferritin levels only increase after the menopause. Literally, may the difference in hemorheological properties in female blood is caused by the increased concentration of younger red blood cells(RBCs) and the reduced population of older RBCs. Higher viscosity, increased RBC aggregation and decreased RBC deformability are observed in male compared with female blood. The Oxygen Delivery Index (a ratio of hematocrit levels to blood viscosity) is significantly lower in the male population. There is also a higher risk of cardiovascular disease due to decreased oxygen delivery, increased RBC aggregation and

decreased RBC deformability (3). The normal basal loss of iron from the body is about 1 mg daily in a 70 kg man and 0.8 mg in a 55 kg woman.

In myocardial infarction, a gradual increase in serum ferritin levels can be detected. Furthermore, a significant increase in ferritin content can be found in peripheral blood monocytes. May peripheral blood monocytes activated by steroids during stress could be the cause of increased serum ferritin levels following AMI (4). There is a hypothesis that iron depletion improves vascular dysfunction in type 2 diabetic patients with high ferritin concentrations (5).

The relationship between inflammation and insulin resistance has long been accepted . Insulin resistance is also associated with atheromatous risk factors, such as central obesity, hyperinsulinemia, hyperglycemia and hypertriglyceridemia. These are also associated with a cluster of thrombotic risk factors, notably increased levels of PAI-1, factor VII, factor XII and fibrinogen. Smoking, increased body mass and inflammatory responses may influence the level of serum fibrinogen. Fibrinogen levels are increased in both type II diabetes and metabolic syndrome (6). In addition higher iron storage is associated with an increased risk of type 2 diabetes in healthy women, independent of known diabetes risk factors (7). Moreover, increased Hb and ferritin are associated with gestational diabetes mellitus (8).

Inflammatory processes play a role in the initiation of unstable coronary artery disease because they destabilize the atherosclerotic plaque and enhance the formation of thrombus (9). Several factors may influence the levels of C-reactive protein and fibrinogen (10, 11).

Materials and Methods

One hundred and four nondiabetic (88 male, 16 female) and 26 diabetic patients (19 male, 7 female) with acute myocardial infarction (AMI) were examined in this cross-sectional pilot study. All patients had a typical history, ECG changes and cardiac enzyme rises relevant to AMI. All diabetic patients had a type 2 diabetes mellitus history and had taken antidiabetic agents. According to ADA-2003, the criteria for the diagnosis of diabetes mellitus are:

*Symptoms of diabetes plus casual plasma glucose concentration ≥ 200 mg/dl or

*Fasting plasma glucose ≥ 126 mg/dl or

*2-h plasma glucose ≥ 200 mg/dl during an OGTT

Patients were not statistically different in terms of age. Exclusion criteria from the study were a history of anemia and/or taking iron preparations on admission. All patients were admitted to the coronary intensive care unit within the first 12 h from the onset of the pain. AMI complications (hypotension, first and second degree block and complete AV block, arrythmia and heart failure) were increased in all patients. All patients received parenteral nitrates, heparin infusion, aspirin (300 mg/day), and parenteral and oral beta blockers except for those patients who had contraindications for these medications. Thrombolytic therapy was administered to patients with medical indications within the first 24 h (13). Blood samples for ferritin, iro and total iron binding capacity (TIBC) and haemogram tests were obtained in the morning within the first 3 days and were measured by immunoradiometric assay (IRMA), ferrene assay and ferrozine assay, respectively. Whole blood (K_3 EDTA as anticoagulant) was analyzed using Beckman Coulter Hmx hematology analyzer.

The Graph Pad Prisma V.3 packet program was used for statistical analysis. The comparisons of groups and subgroups were done using ANOVA and Tukey's Multiple Comparison Test, respectively. The unpaired t test, and the Mann Whitney U test were used for the analysis of both groups, and qualificational data were analyzed using the chi square . The results were evaluated with a 95% safety margin ($p < 0.05$ level).

Results

According to the demographic data, there was no statistically significant difference between the diabetic and nondiabetic groups ($P > 0.05$, Table 1). According to the available data, neither antidiabetic therapy (OAD or insulin) nor diabetic age have any effect on iron, TIBC or ferritin levels ($P > 0.05$ Table 2).

In terms of hemogram parameters, iron and TIBC, no significant difference was found between the diabetic and the nondiabetic groups whereas ferritin levels were higher in the diabetic group ($P < 0.05$. Table 3).

Although there was no statistically significant difference between the 2 groups in terms of AMI localization, the incidence of AMI complications was higher in the diabetic group ($P < 0.01$ Table 4).

Table 1. Demographic data.

		Nondiabetic group (n: 104)	Diabetic group (n: 26)	
Age		57.62 ± 12.08	59 ± 9.46	> 0.05
Cigarettes	Negative	60 (57.7%)	10 (38.5%)	X^2: 3.09
	Positive	44 (42.3%)	16 (61.5%)	P > 0.05
Hypertension	Negative	55 (52.9%)	14 (53.8%)	X^2: 0.08
	Positive	49 (47.1%)	12 (46.2%)	P > 0.05

AMI: Acute myocardial infarction

Table 2. Antidiabetic therapies, diabetic age and iron status.

	OAD (n:18)	Insülin (n: 8)	t	P
Age	58.72 ± 8.29	59.63 ± 12.32	-0.22	>0.05
WBC	15894.44 ± 20240.10	9612.50 ± 2628.11	0.87	>0.05
Hb (g/dl)	14.15 ± 0.77	12.60 ± 1.72	3.22	<0.01
HCT (%)	41.04 ± 3.84	38.51 ± 5.38	1.37	>0.05
MCV (fl)	88.68 ± 6.69	88.65 ± 8.39	0.01	>0.05
PLT	183833.33 ± 28520.89	200250 ± 60652.99	-0.95	>0.05
Iron (µ/dl)	64.72 ± 32.90	56.13 ± 35.62	0.60	>0.05
TIBC (µ/dl)	348.39 ± 66.62	327 ± 42.67	0.83	>0.05
Ferritin (ng/ml)	152.6	104.55	0.89	>0.05

Diabetic age	r	P
WBC	-0.25	>0.05
Hb (g/dl)	-0.11	>0.05
HCT (%)	-0.05	>0.05
MCV (fl)	0.19	>0.05
PLT	-0.04	>0.05
Iron (µ/dl)	-0.10	>0.05
TIBC (µ/dl)	-0.13	>0.05
Ferritin (ng/ml)	0.06	>0.05

TIBC: Total iron binding capacity, OAD: oral antidiabetic agents

Table 3. Comparison of the diabetic and nondiabetic AMI groups.

	Nondiabetic group (n: 104)	Diabetic group (n: 26)	t	P
Age	57.62 ± 12.08	59 ± 9.46	-0.54	>0.05
WBC	13000 ± 15831.22	13961.54 ± 17007.25	-0.27	>0.05
Hb (g/dl)	13.26 ± 1.89	13.67 ± 1.33	-1.05	>0.05
HCT (%)	39.61 ± 7.37	40.26 ± 4.42	-0.43	>0.05
MCV (fl)	89.84 ± 7.09	88.67 ± 7.08	0.75	>0.05
PLT	187951.92 ± 65515.64	188884.62 ± 40532.78	-0.07	>0.05
Iron (µ/dl)	64.92 ± 27..31	62.08 ± 33.28	0.45	>0.05
TIBC (µ/dl)	343.83 ± 77.40	341.81 ± 60.24	0.12	>0.05
Ferritin (ng/ml)	85.67	135.84	-1.98	< 0.05

TIBC: Total iron binding capacity

Table 4. AMI localizations in the diabetic and nondiabetic AMI groups.

		Nondiabetic group (n: 104)	Diabetic group (n: 26)	
AMI localization	Anterior	44 (44%)	14 (53.8%)	
	Inferior	40 (40%)	6 (23.1%)	
	NONQ	11 (11%)	6 (23.1%)	X^2: 5.58
AMI complications	Negative	7 (17.9%)	8 (61.5%)	X^2: 9.02
	Positive	32 (82.1%)	5 (38.5%)	P < 0.01

AMI: Acute myocardial infarction

Table 5. Thrombolytic therapy in the nondiabetic group.

Nondiabetic group	SKZ (n: 35)	TPA (n: 6)	MW	P
Age	56.49 ± 10.68	41.17 ± 11.53	34.5	<0.01
WBC	13111.43 ± 17533.34	12433.33 ± 10108.54	98	>0.05
Hb (g/dl)	13.18 ± 1.51	13.77 ± 2.38	86.5	>0.05
HCT (%)	40.93 ± 9.68	41.20 ± 6.88	89	>0.05
MCV (fl)	90.17 ± 6.90	87.02 ± 12.93	101.5	>0.05
PLT	193200 ± 66379.83	225333.33 ± 87257.47	90	>0.05
Iron (µ/dl)	60.86 ± 25.11	64.50 ± 23.02	95.5	>0.05
TIBC (µ/dl)	338.63 ± 70.07	346.33 ± 114.65	104.5	>0.05
Ferritin (ng/ml)	110.2	91.39	85.5	>0.05

SKZ; Streptokinase, TPA: Tissue plasminogen activator

Nondiabetic group		SKZ	TPA	
Gender	Male	30 (85.7%)	4 (66.7%)	X^2: 1.31
	Female	5 (14.3%)	2 (33.3%)	P > 0.05
AMI localization	Anterior	13 (38.2%)	5 (83.3%)	
	İnferior	19 (55.9%)	1 (16.7%)	X^2: 14.22
	NONQ	2 (5.9%)		P > 0.05
AMI complication	Negative	4 (23.5%)		X^2: 11.70
	Positive	13 (76.5%)	6 (100%)	P > 0.05

SKZ: Streptokinase, TPA: Tissue plasminogen activator

Although nondiabetic patients receiving SKZ therapy had a higher mean age than those receiving t-PA therapy (p < 0.01 Table 5), in terms of hemogram parameters, iron, TIBC, ferritin, AMI localization and AMI complication no statistically significant difference determined. In addition, in the diabetic patients the mean ages of both groups were not statistically different and the hemogram parameters, iron, TIBC, ferritin, AMI localization and AMI complications were not statistically different r (P > 0.05, Tables 5-7).

Age, hemogram parameters, iron, TIBC and ferritin levels did not affect AMI localization in the nondiabetic group (P > 0.05, Table 8). The mean age of the inferiorly localized patients and that of patients with NON-Q localization were higher than the mean age of the patients with anterior localization (P < 0.05).

In terms of TIBC, among patients with anterior, inferior and NON-Q localization there was no statistically significant difference, whereas TIBC levels in patients with NON-Q AMI were higher than the TIBC levels of

Table 6. Thrombolytic therapy in the diabetic group.

Diabetic group	SKZ (n: 4)	TPA (n: 4)	MW	P
Age	59.75 ± 11.09	47.25 ± 4.65	2.5	>0.05
WBC	33350 ± 41837.66	9900 ± 920.14	1	>0.05
Hb (g/dl)	13.88 ± 0.31	13.95 ± 0.73	6.5	>0.05
HCT(%)	41.75 ± 2.42	41.45 ± 4.04	8	>0.05
MCV (fl)	83.83 ± 6.74	87.85 ± 4.02	4	>0.05
PLT	200250 ± 57314.19	211.750 ± 81846..91	7	>0.05
Iron (µ/dl)	65 ± 27.94	62..50 ± 29..95	8	>0.05
TIBC (µ/dl)	341.75 ± 33.71	327.25 ± 33.69	7	>0.05
Ferritin (ng/ml)	189.19	94.49	4	>0.05

SKZ; Streptokinase, TPA: Tissue plasminogen activator

Diabetic group		SKZ	TPA	
Gender	Male	3 (75%)	3 (75%)	X^2: 0.01
	Female	1 (25%)	1 (25%)	P >0.05
AMI localization	Anterior	2 (50%)	4 (100%)	X^2: 2.66
	Inferior	2 (50%)		P > 0.05
AMI complication	Negative	3 (75%)	4 (100%)	X^2: 1.14
	Positive	1 (25%)		P >0.05

Table 7. Comparison of iron status between thrombolytic therapy positive and negative patients in diabetic and nondiabetic group.

		Thrombolytic therapy negative (n:63)	Thrombolytic therapy negative (n: 41)	t	P
Nondiabetic group	Iron (µ/dl)	67.22 ± 28.91	61.39 ± 24.58	1.07	>0.05
	TIBC (µ/dl)	346.48 ± 78.60	339.76 ± 76.31	0.43	>0.05
	Ferritin (ng/ml)	74.03	136.8	-1.63	>0.05
		Trombolytic therapy negative (n:18)	Trombolytic therapy negative (n:8)		
Diabetic group	Iron (µ/dl)	61.33 ± 36.47	63.75 ± 26.85	-0.17	>0.05
	TIBC (µ/dl)	345.06 ± 69.82	334.50 ± 32.15	0.41	>0.05
	Ferritin (ng/ml)	136.8	133.7	0.05	>0.05

patients with inferior AMI (P < 0.05). In the diabetic group no significant difference was found between the anterior and inferior AMI groups in terms of ferritin levels. Ferritin levels in the patients anterior and inferior AMI groups were significantly higher than the ferritin levels of the NON-Q AMI patients (P< 0.01, Tables 9, 10).

In the nondiabetic group hemoglobin (P< 0.0001) hematocrit (P < 0.05) and ferritin (P < 0.001) levels were significantly higher in females, whereas sex did not affect the hemoglobin, hematocrit and ferritin levels in the diabetic group (Table 11). In addition, sex had no effect on iron, ferritin or TIBC in either groups (P> 0.05, Table 12). Although no significant effect of hypertension

Table 8. Ferritin and AMI localizations in the nondiabetic AMI group.

	Anterior (n: 46)	Inferior (n: 42)	NONQ (n: 16)	F	P
Age	57.84 ± 11.52	56.15 ± 12.94	60.55 ± 10.94	0.71	>0.05
WBC	14256.82 ± 18381.49	10720 ± 5165.68	20063.64 ± 30315.81	1.22	>0.05
Hb (g/dl)	13.25 ± 1.88	13.29 ± 1.90	12.21 ± 2.05	2.00	>0.05
HCT (%)	38.88 ± 5.39	40.84 ± 9.77	36.67 ± 5.61	1.07	>0.05
MCV (fl)	89.47 ± 7.82	89.94 ± 7.39	89.70 ± 5.03	0.21	>0.05
PLT	189022.73 ± 61598.28	187750 ± 68055.69	186727.27 ± 66059.20	0.12	>0.05
Iron (µ/dl)	62.20 ± 25.13	68.13 ± 31.53	55.82 ± 17.81	1.60	>0.05
TIBC (µ/dl)	345.20 ± 80.18	342.83 ± 72.45	358.36 ± 42.55	0.15	>0.05
Ferritin (ng/ml)	100.62	84.63	57.11	0.88	>0.05

FE: iron, TIBC: Total iron binding capacity, anterior myocardial infarction, inferior myocardial infarction, NONQ: non-Q myocardial infarction

Table 9. Ferritin and AMI localizations in the diabetic AMI group.

	Anterior (n: 14)	Inferior (n: 6)	NONQ (n: 6)	F	P
Age	54.79 ± 10.24	63.50 ± 6.38	64.33 ± 5.09	3.669	<0.05
WBC	11642.86 ± 3690.47	23450 ± 35571.38	9883.33 ± 1565.14	1.262	>0.05
Hb (g/dl)	13.84 ± 0.78	13.20 ± 1.47	13.75 ± 2.18	0.483	>0.05
HCT (%)	40.86 ± 3.82	37.45 ± 5.14	41.67 ± 4.50	1.748	>0.05
MCV (fl)	89.12 ± 5.56	85.93 ± 9.88	90.37 ± 7.74	0.629	>0.05
PLT	199928.57 ± 51718.86	178833.33 ± 16916.46	173166.67 ± 14648.09	1.171	>0.05
Iron (µ/dl)	56.14 ± 23.01	50.50 ± 21.39	87..50 ± 51.66	2.643	>0.05
TIBC (µ/dl)	334.07 ± 48.25	308.50 ± 64.48	393.17 ± 57.20	3.979	<0.05
Ferritin (ng/ml)	182..34	197.08	47.10	6.341	<0.01

TIBC: Total iron binding capacity, anterior myocardial infarction, inferior myocardial infarction, NONQ: non-Q myocardial infarction

Table 10. Comparison of age ,TIBC, ferritin levels in the diabetic group.

	Age	TIBC (µ/dl)	Ferritin (ng/ml)
Anterior/Inferior	P < 0.05	P > 0.05	P > 0.05
Anterior/NONQ	P < 0.05	P > 0.05	P < 0.01
Inferior/NONQ	P > 0.05	P < 0.05	P < 0.01

or smoking on iron, TIBC or ferritin levels was observed in the diabetic group (P> 0.05), Iron levels were higher (P < 0.05) in hypertensive and smoking patients in the nondiabetic group (Table 13).

Discussion

Hughes K et al. evaluated cardiovascular risk factors in type 2 and non-diabetics among Asians in Singapore. This study showed that females with type 2 diabetes mellitus (DM) had higher mean serum fibrinogen levels compared with nondiabetics, which could explain the greater cardiovascular effect of DM in females than in males. Mean levels of serum ferritin were higher in the type 2 DM group than in the control group (14). They also found that smoking was unrelated to serum ferritin levels. In our study, we found higher Hb, Hct and ferritin levels in males compared with females within the nondiabetic AMI group (P < 0.001). In the diabetic AMI

Table 11. Body iron status in male and female patients in two groups.

Nondiabetic	Male (n: 88)	Female (n: 16)	t	P
Age	57.49 ± 11.86	58.31 ± 13.64	-0.25	>0.05
WBC	12088.64 ± 13397.82	18012.50 ± 25459.61	-1.38	>0.05
HGB (g/dl)	13..57 ± 1.74	11.58 ± 1.83	4.17	<0.0001
HCT (%)	40..38 ± 7..56	35.41 ± 4.38	2.54	<0.05
MCV (fl)	91 ± 5.87	83.05 ± 9.70	0.44	>0.05
PLT	184943.18 ± 62989..21	204500 ± 78206.56	-1.10	>0.05
Iron (µ/dl)	64.85 ± 28..35	65.31 ± 21.42	-0.06	>0.05
TIBC (µ/dl)	340.76 ± 80.24	360.69 ± 58.58	-0.95	>0.05
Ferritin (ng/ml)	100..2	36..55	3.40	<0.001
Diabetic	Male (n: 19)	Female (n: 7)	t	P
Age	57.16 ± 9.78	64 ± 6.76	-1.70	>0.05
WBC	10784.21 ± 3324.70	22585.71 ± 32454.45	-1.62	>0.05
Hb (g/dl)	13.84 ± 1.19	13.23 ± 1.68	1.04	>0.05
HCT (%)	40.46 ± 4.27	39.71 ± 5.11	0.38	>0.05
MCV (fl)	89.83 ± 6.11	85.53 ± 9.02	1.40	>0.05
PLT	190894.74 ± 44286.81	183428.57 ± 30231.65	0.41	>0.05
Iron (µ/dl)	61.95 ± 33.27	62.43 ± 35.97	-0.03	>0.05
TIBC (µ/dl)	338.11 ± 60.62	351.86 ± 62.75	-0.51	>0.05
Ferritin (ng/ml)	160.28	86.69	1.43	>0.05

Table 12. Comparison of iron status between males and females in the diabetic and nondiabetic AMI groups.

		Nondiabetic group (n: 88)	Diabetic group (n: 19)	t	P
Male	Iron (µ/dl)	64.85 ± 28.35	61..95 ± 33..27	0.39	>0.05
	TIBC (µ/dl)	340.76 ± 80.24	338.11 ± 60.62	0.14	>0.05
	Ferritin (ng/ml)	100.2	160..28	-1.77	>0.05
		Nondiabetic group (n: 16)	Diabetic group (n: 7)		
Female	Iron (µ/dl)	65.31 ± 21.42	62.43 ± 35..97	0.24	>0.05
	TIBC (µ/dl)	360.69 ± 58.58	351.86 ± 62.75	0.33	>0.05
	Ferritin (ng/ml)	36..55	86.69	-1.65	>0.05

group we found no statistically significant difference between males and females. When we compared the 2 groups in terms of body iron status and gender, we again found no statistically significant differences between diabetic and nondiabetic males and females. This result is in agreement with those in the literature. There were no statistically significant differences in terms of serum iron or TIBC between the 2 groups. When we compared the 2 groups, we found that the serum ferritin level was significantly increased in the diabetic MI group ($P< 0.05$). We also evaluated smoking and hypertension as having no effect on serum ferritin levels, again in agreement with the literature.

Oba et al. showed that the mean serum ferritin, glycosylated ferritin and non-glycosylated ferritin levels in serum were significantly higher in older patients (age >60) with retinopathy compared with those in healthy controls. Our results suggest that diabetic

Table 13. Comparison of iron status in smokers versus nonsmokers and hypertensive versus normotensive patients in diabetic and nondiabetic myocardial infarction groups.

		Nonsmoker (n: 60)	Smoker (n: 44)	t	P
Nondiabetic group	Iron (μ/dl)	59.22 ± 25.19	72.3 ± 28.63	-2.41	<0.05
	TIBC (μ/dl)	333.7 4 ± 83.68	357.59 ± 66.38	-1.56	>0.05
	Ferritin (ng/ml)	101.74	67.77	1.80	>0.05
		Nonsmoker (n: 10)	Smoker (n: 16)		
Diabetic group	Iron (μ/dl)	68.90 ± 41.77	57.81 ± 27.37	0.82	>0.05
	TIBC (μ/dl)	316.70 ± 58.84	357.5 ± 57.35	-1.74	>0.05
	Ferritin (ng/ml)	188.71	110.61	1.35	>0.05
		HT (-) (n: 55)	HT (+) (n: 49)		
Nondiabetic group	Iron (μ/dl)	62.65 ± 25.62	67.47 ± 29.14	-2.41	<0.05
	TIBC (μ/dl)	338.29 ± 79.14	350.04 ± 75.73	-1.56	>0.05
	Ferritin (ng/ml)	77.48	95.90	1.80	>0.05
		HT (-) (n: 14)	HT (+) (n: 12)		
Diabetic group	Iron (μ/dl)	70.36 ± 42.29	52.42 ± 14.64	0.82	>0.05
	TIBC (μ/dl)	346.64 ± 65.63	336.17 ± 55.61	-1.74	>0.05
	Ferritin (ng/ml)	85.75	232.33	1.35	>0.05

microangiopathy is associated with abnormal increased ferritin levels in serum. They also determined that none of these values differ in patients with or without macroangiopathy or in healthy controls (15). Canturk et al. evaluated the association between serum ferritin concentrations and diabetes mellitus complications in 329 patients and 269 healthy controls. They found a correlation between ferritin levels and diabetic retinopathy (16). However, in our study serum ferritin levels were significantly increased in the diabetic AMI group ($P< 0.05$). This result suggests that patients with diabetic macroangiopathic complications like AMI, had higher serum ferritin levels in our series. We did not compare serum ferritin levels in diabetic microvascular complications because we did not evaluate other complications of diabetes mellitus.

Epidemiological evidence concerning the role of iron, a lipid peroxidation catalyst, in coronary heart disease is inconsistent. A study from Eastern Finland, performed by Toumainen et al. involved 99 men with an AMI history and 98 controls during 6.4 years of follow up, this showed an association between increased body iron stores and increased risk of AMI (17). In addition, Halle et al. demonstrated that increased serum ferritin concentrations between 200 and 500 mg/l are a strong risk factor for acute myocardial infarction in Finnish men, although they could not account for this association. However, the findings are thought to show a correlation between serum ferritin and insulin resistance syndrome factors in the Finnish population. They assumed an association between ferritin and an atherogenic LDL sub fraction profile, a result that could n explain the observed

relationship between ferritin and atherosclerosis. They found that men with moderately higher ferritin levels had a significantly worse coronary risk profile than men with lower levels (18).

In the literature mean serum ferritin levels were higher in men and postmenopausal women who had a higher risk of atherosclerosis than did the corresponding controls (19). In addition thrombolytic therapy may have an effect on serum ferritin levels in patients with AMI. Cottin et al. determined the importance of the temporal relationship between lipid peroxidation and iron status after thrombolytic therapy in 17 men with myocardial infarction. The peak iron level was observed at 9.4 ± 7.3 h after thrombolytic therapy, and this returned to the pre-reperfusion levels at 48 h (2). In our study, there was no difference in ferritin levels between TPa and SKZ within the diabetic and nondiabetic groups. There was also no statistically significant difference between diabetic and nondiabetic MI groups who received or did not receive thrombolytic therapy. In our study serum ferritin levels were highest in inferior MI, anterior MI and non-Q MI among diabetic patients, in that order yet we found no differences in terms of MI localization and serum ferritin levels compared with nondiabetic patients. Another study, on type I diabetic men, by Carenini et al. showed that hyperglycemia does affect the range of enzymatic glycosylation of serum ferritin (20). Our patients were all type 2 diabetics so we were not able to compare the 2 diabetic types in terms of iron status.

There are some epidemiologic studies, that do not support the hypothesis of a relationship between iron and heart disease risk. For example, in an NHANES study (21) that included 1604 patients without CHD, no statistically significant associations between serum ferritin and coronary heart disease were found. In another prospective study, by Ascherio et al. there were no significant associations found between body iron stores and the risk of coronary heart disease. In that prospective study, 38244 healthy men (blood donors) were examined over 4 years of follow up (22). In the Rotterdam study it was shown that are other risk factors like diabetes, smoking, hypercholesterolemia or serum ferritin may adversely affect ischemic heart disease risk in older patients (23). We could not find any relationship between body iron status and age. Antidiabetic agents (insulin and oral antidiabetics) have no effect on ferritin levels. We could not find any significant differences between smokers and nonsmokers in either group. Interestingly serum iron levels showed a statistically significant increase in smokers and hypertensive patients within the nondiabetic MI group ($P < 0.05$).

Armaganijan et al. showed that the serum levels of ferritin and other organic iron indicators (transferrin saturation, TIBC, hemoglobin and hematocrit) were neither risk factors nor risk markers for coronary atherosclerosis. Moreover, they demonstrated that serum iron levels were higher in the group without atherosclerosis (24).

Conclusion

Men with type 2 diabetes have increased serum ferritin levels and this condition may adversely affect the risk of coronary heart disease in this population.

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