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Association between serum ferritin, cardiorespiratory fitness and risk of type 2 diabetes: Aerobics Center longitudinal study

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Abstract: Recent studies suggest that an elevated serum ferritin concentration is considered an independent factor associated with increased risk of type 2 diabetes, and cardiorespiratory fitness (CRF) is inversely associated with diabetes.
The cross-sectional study investigates 6,230 participants' data from the Aerobics Center Longitudinal Study, The Cooper Institute (Dallas, Texas). The authors explored whether CRF level is associated inversely with lower serum ferritin concentration and is associated with a lower prevalence of type 2 diabetes.
Participants with high ferritin levels and high triglyceride were 1.89 and 1.57 times, respectively, more likely to have diabetes. Overweight or obese individuals were 1.35 to 1.40 times more likely to have diabetes. Participants with a family history of type 2 diabetes were 3.96 times more likely to have diabetes.
Lower serum ferritin concentration was associated with lower risk of diabetes in those participating in cardiorespiratory fitness. It suggests that physicians may use patients' ferritin concentrations as a marker for predicting their risk for new-onset diabetes, and patients should be encouraged to participate in cardiorespiratory fitness or physical activities.

Keywords: *physical activity, ferritin,, cardiorespirarory fitness, type 2 diabetes*

1. INTRODUCTION

Ferritin is an iron-phosphorus-protein complex that is an index of body iron stores. Iron is essential for oxygen transportation to tissues and major functions in cellular oxidation mechanisms (Newman Dorland, 1994) . Elevated serum iron leads to increased serum ferritin concentration (Jehn et al., 2007; Yamanishi et al., 2007). Ferritin level serves as a biomarker for evaluating body iron contents. Tissue and organ damage occurs when iron concentrations are elevated (Ikeda et al., 2006) because increased iron accumulation or serum ferritin concentration may be a cause for the impaired insulin effect, impaired hepatic insulin extraction, and may affect insulin synthesis and secretion in the pancreas (Fernandez-Real et al., 2002; Niederau et al., 1984) .

Recently in some studies in European countries, ferritin concentration has been found as an independent factor that predicts the development of type 2 diabetes (Acton et al., 2006; Canturk, Cetinarslan, Tarkun, & Canturk, 2003; Forouhi et al., 2007) and a risk factor associated with higher prevalence of type 2 diabetes (Ikeda et al., 2006; Jehn et al., 2007) , when controlling for physical activity and other risk factors. Fourouhi and colleagues found that serum ferritin might be an important marker to predict new-onset type 2 diabetes (Forouhi et al., 2007). Individuals with high ferritin levels were 7.4 times more likely to have type 2 diabetes compared to those in the lowest quartile of ferritin levels (Ikeda et al., 2006) .

Similarly, in a study conducted in Finland by Salonen et al. (1998), males with high body iron stores were 2.4 times more likely to have diabetes as compared to those with lower body iron stores. Serum ferritin concentration, therefore, has been associated with type 2 diabetes (Lecube et al., 2004).

Serum ferritin concentration has been positively associated with body mass index (BMI), alcoholic intake, triglyceride levels, and diastolic and systolic pressure (Galan et al., 2006; Milman & Kirchhoff, 1999) . Particularly in those with type 2 diabetes, serum ferritin concentration has been significantly associated with plasma oxidized LDL, but not with LDL-cholesterol (Ikeda et al., 2006) . Meanwhile, other researchers have reported a significant association between ferritin concentration and cholesterol (Galan et al., 2006; Hedley G. Peach, Nicole E. Barnett, 2002) .

Recent studies reported that physical activities play an important role in reducing serum ferritin concentration (Furqan, Nafees, Jilani, & Hijazi Muhammed, ; Lakka, Nyyssonen, & Salonen, 1994; Liu et al., 2003) . An increase in physical activity decreased serum ferritin concentration (Furqan et al.,) , and a decrease in serum ferritin concentration was shown to depend on duration and frequency of physical activity (Lakka et al., 1994) . Naimark et al. (1996) found a similar pattern for performance and ferritin concentration. The mean serum ferritin decreased significantly after 24 weeks in those who walked 5 days per week, but not in those who walked 3 days per week (Naimark et al., 1996). Furqan at al. (2002) reported moderate physical activity to be more important in lowering serum ferritin than vigorous activity. Bartfay et al. (1995) demonstrated regular exercise could decrease serum ferritin concentrations. Lakka, Nyyssonen, and Salonen (1994) reported mean ferritin concentration to be 16.8% lower in individuals with the highest quartile of physical activity (>2.6 hours per week) as compared to those with the lowest duration of activity (<0.4 hours per week), and to be 19.9% lower in individuals with the highest category of physical activity frequency (>3 sessions per week) as compared to those with the lowest activity frequency (<1 session per week).

Many researchers have found an association between physical activity and diabetes (CDC, 1999; Church et al., 2004; Church, LaMonte, Barlow, & Blair, 2005; Wei et al., 1999; Wei, Gibbons, Kampert, Nichaman, & Blair, 2000) , serum ferritin and diabetes (Acton et al., 2006; Forouhi et al., 2007; Jehn et al., 2007; Jiang et al., 2004; Lecube et al., 2004; Oba et al., 1997; Salonen, Tuomainen, Nyyssonen, Lakka, & Punnonen, 1998) , and physical activity and serum ferritin (Bartfay et al., 1995; Furqan et al., ; Lakka et al., 1994; Naimark et al., 1996). However, the relationships among different levels of cardiorespiratory fitness and serum ferritin on type 2 diabetes have not been investigated. Therefore, in this study, I investigated the association between cardiorespiratory fitness and serum ferritin concentration on type 2 diabetes.

2. METHODS

The ACLS is an ongoing epidemiologic study being conducted by the Cooper Institute since 1970. In this study, we analyzed 6,230 participants enrolled in the Aerobics Center Longitudinal Study (ACLS) between 1995 and 2001, who had completed a comprehensive medical examination, a medical survey questionnaire, and serum ferritin evaluation at the baseline. The study protocol was reviewed and approved by the Institutional Review Boards (IRB) of the University of North Texas Health Science Center at Fort Worth and the Cooper Institute in Dallas.

Variables used in this study include serum ferritin concentrations, comprehensive medical and physical examinations conducted after participants had fasted at least for 12 hours, anthropometric measurements, electrocardiograms, blood chemistry analyses, blood pressure assessments, maximal exercise treadmill tests, self-reports of health habits, personal and family medical histories, and participants' demographic characteristics.

Self-reported diabetes was defined as the participant using insulin, being diagnosed by a physician, or having fasting plasma glucose equal to or higher than 126 mg/dl (≥ 7.0 mmol/l) at baseline. Overweight was defined as having a body mass index (BMI) of 25.0 kg/m^2 to 29.9 kg/m^2; obese having a BMI being equal to or greater than 30.0 kg/m^2; and normal weight as having a BMI from 18.5 kg/m^2 to 24.9 kg/m^2. Alcohol consumption was classified as light (less than 5 drinks per week) and moderate (greater or equal to 5 drinks per week). Smoking status was classified as never smoked, former smoker, or current smoker.

Cardiorespiratory fitness (CRF) was measured using a maximal treadmill exercise test. It was quantified as the duration (minutes) of a maximal graded treadmill exercise using a modified Balke protocol set as 3.3 mph (5.311 km/hr), 0% incline for first minute, 2 % for the second minute, plus a 1% incline for each additional minute up to a 25 % incline, then increasing 0.2 mph (0.3219 km/hr) for each additional minute as participants walked until they achieved exhaustion (Balke & Ware, 1959). CRF was classified into quintiles of age-specific distributions of maximal exercise duration and was categorized from the lowest to highest quintile, level I to level V respectively, as established by Blair et al., (Blair, S. N., Kampert, J. B., Kohl, H. W.,3rd, Barlow, C. E., Macera, C. A., Paffenbarger, R. S.,Jr, et al., 1996) . These cutpoints were established on the entire ACLS cohort, and the proportion of participants in the present study differs from the expected 20 % in each quintile, because of the selection criteria used for these analyses. Serum parameters, including serum ferritin, cholesterol, HDL, glucose, fibrinogen, and hematocrit, were classified into normal and high or low based on Mosby's Diagnostic and Laboratory Test Reference (3rd ed.) as established by Pagana and Pagana (1997).

Logistic regression was used to calculate odds ratios (OR) for having diabetes. Both crude OR(s) and adjusted OR(s) for confounders stratified by CRF quintile levels were used to explore the associations between risk factors and type 2 diabetes based on BMI levels and blood glucose levels. Crude OR for each diabetes risk factor was measured using logistic regression. Chi-square tests, Spearman's rank correlation coefficients, and Kruskal-Wallis tests were used for the statistical analyses. The statistical significance level was set at $\alpha = 0.05$. SAS version 9.1.3 for Windows (SAS Institute, 2006) was used to analyze all data.

3. RESULTS

Table 1 shows the characteristics of 1,995 females and 4,235 males in the study with mean (± SD) age of 47 (± 9) years and age ranging from 20 to 88 years. The participants were predominantly white (95%). Among the participants in the study, the proportions of participants being overweight and obese were 46.0 % and 24.6 %, respectively. Approximately 12 % of the subjects consumed 5 or more drinks per week, 13 % were current smokers, and 17.2 % were former smokers. More than 5 % of participants had a high serum ferritin concentration (serum ferritin concentration ≥300 ng/ml in males and ≥150 ng/ml in females). About 15 % of participants had high cholesterol (≥240 mg/dL). Eighteen percent of participants had low HDL (<40 mg/dL). Approximately 3 % of participants had high blood glucose (>126 mg/dL). About 6.7 % of participants had high fibrinogen concentration (>400 mg/dL) with a mean of 304.04 ± 59.20 mg/dL. More than 99 % of participants showed normal hematocrit levels with the mean of 43 ± 3.5 %. More than 25 % were in the highest CRF quintile level and only 10.24 % were in the lowest CRF quintile level. Only 6.36 % of the subjects reported having diabetes and 3.66 % of the subjects reported a family history of diabetes. There was a significantly positive association of diabetes with family history of diabetes ($p < 0.001$).

Table 2 shows the results of the association between risk factors and type 2 diabetes after adjustment for age, sex, and ethnicity. Individuals with a high ferritin concentration were 1.89 times more likely to have type 2 diabetes (OR: 1.89; 95% CI: 1.31, 2.73) compared to those with normal ferritin. Overall, CRF levels were inversely associated with type 2 diabetes ($p < 0.0001$) and diabetes was strongly associated with CRF levels, especially for those in the highest quintile level who reduced their risk of getting type 2 diabetes by 55 % as compared to the lowest quintile level. Similarly, other CRF quintile levels showed inverse associations with reducing the risk of getting type 2 diabetes by 14 % (OR: 0.86; 95% CI:0.60, 1.23), 38 % (OR: 0.62; 95% CI: 0.42, 0.91), and 29 % (OR: 0.71; 95% CI: 0.51, 1.01) comparing with fitness levels II, III, and IV to the lowest fitness (level I), respectively.

A family history of diabetes was a significant risk factor for type 2 diabetes. Compared to those without a family history of diabetes, individuals with a family history were 3.96 times more likely to have type 2 diabetes (OR: 3.96; 95% CI: 2.81, 5.58). The risk of getting type 2 diabetes was reduced by 26 % among those having high or normal serum HDL concentrations compared to those with low HDL levels (OR: 0.74; 95% CI: 0.67, 0.96). A high triglyceride level was a strong risk factor for type 2 diabetes. Individuals with high triglyceride levels were 1.57 times more likely to have diabetes compared to those with normal triglyceride levels (OR: 1.57; 95% CI: 1.20, 2.05). Cholesterol, hematocrit, and high blood pressure generated no significances between high and normal levels (OR: 0.88; 95% CI: 0.65, 1.19; OR: 2.94; 95% CI: 0.85, 10.23; and OR: 1.13; 95% CI: 0.89, 1.42), respectively.

In this study, CRF appeared to be a protective factor and serum ferritin concentration was a risk factor for type 2 diabetes. These results were similar to many previous studies.[19-23] Logistic regression analysis was used to estimate the odds ratios for prevalence of type 2 diabetes based on ferritin levels or CRF quintile levels, with and without controlling for some or all possible confounders for risk of type 2 diabetes. Three models were used. Model I calculated crude odds ratios only. In Model II, odd ratios of prevalence of diabetes were calculated after adjusting CRF levels and ferritin levels. In Model III, odds ratios of prevalence of diabetes were estimated after adjusting for numerous possible confounders, including age, ethnicity, sex, fitness level, BMI, smoking, drinking, cholesterol level, triglyceride level, fibrinogen level, and blood pressure. For ferritin level, participants who had a high ferritin level were 1.94 times (OR: 1.94; 95% CI: 1.35, 2.77), 1.80 times (OR: 1.80; 95% CI:1.25, 2.57), and 1.48 times (OR: 1.48; 95% CI: 1.02, 2.26) more likely to have diabetes compared to normal ferritin levels in adjusted Model I, Model II, and Model III, respectively.

CRF was significantly inversely associated with diabetes in all three models. In Model I, all CRF levels seemed to be associated with diabetes. The prevalence of type 2 diabetes were 19% and 55% lower for the CRF quintile level II and V, respectively, as compared to the CRF quintile level I, the lowest level ($p_{\text{trend}} < 0.0001$). This pattern was the same in Model II, after adjusting for CRF and ferritin levels ($p_{\text{trend}} < 0.0001$). In Model III, only the highest CRF level (level V) was associated with diabetes and the prevalence of type 2 diabetes was 46% lower when compared to the lowest CRF quintile level ($p_{\text{trend}} = 0.0041$) . The other CRF quintile levels showed inverse associations with the prevalence of type 2 diabetes at some levels, but none were statistically significant.

The median serum ferritin concentrations were measured in quintiles for CRF levels across BMI levels and stratified by diabetes and non-diabetes and given in Table 5. Among participants without diabetes, the median range for serum ferritin concentrations in the lowest and highest CRF levels were 76.0 ng/ml and 47.5 ng/ml respectively for normal weight participants and 131.5 ng/ml and 96.0 ng/ml respectively for obese participants. Among participants with diabetes, the median ferritin concentration was 148 ng/ml for the lowest CRF level group compared with 104.0 ng/ml for the highest CRF level group. Correlations between each CRF level across BMI status were determined with Spearman's correlations and showed significant differences in those with and without diabetes. The median ferritin levels significantly decreased with increased CRF quintile levels and correlated directly with increasing BMI levels. Among non-diabetic individuals, the median serum ferritin decreased by 37.5%, 20.6%, and 27.0 % among normal weight, overweight, and obese individuals, respectively, when participants in the highest CRF quintile level were compared to those in the lowest CRF quintile level.

Among participants with diabetes, ferritin levels were associated with CRF quintile levels across BMI status as shown by the Spearman's correlation coefficients in Table 5. Particularly, the median ferritin concentrations in obese diabetic participants at the highest fitness levels decreased 29.7 %, compared to those at the lowest fitness levels. The Kruskal-Wallis tests showed the median ferritin concentrations to be statistically significantly different among the five levels of CRF when stratified by diabetes status, i.e., non-diabetes ($p < .0001$), and diabetes (p =0.02).

4. DISCUSSION AND CONCLUSIONS

An inverse association between serum ferritin concentration and CRF was found in this study, in which ferritin concentration was significantly correlated with CRF or physical exercise (Furqan et al., ; Malczewska, Stupnicki, Blach, & Turek-Lepa, 2004; Wilkinson, Martin, Adams, & Liebman, 2002) . Participants having high ferritin concentrations were 48% more likely to have type 2 diabetes when compared to those with normal ferritin levels. Similarly, recent studies have focused on elevated serum ferritin concentrations that contributed to increased risk of diabetes (Acton et al., 2006; Canturk et al., 2003; Forouhi et al., 2007; Ikeda et al., 2006; Jehn et al., 2007; Jiang et al., 2004; Lecube et al., 2004) . Serum ferritin concentration can be an independent predictor for development of type 2 diabetes (Forouhi et al., 2007). Wilkinson et al. (2002) found that mean (± SD) serum ferritin decreased significantly from 55.9 (± 9.7) to 42.2 (± 8.0) ng/ml after a 6-week high-intensive cycle training program. In another longitudinal study on the effect of a running-based training program on serum ferritin and other serum parameters, Kaiser and Van Wersch (1989) found a significant inverse association between running and serum ferritin. Similarly, in this study, I found serum ferritin concentrations among normal weight, overweight, and obese non-diabetic participants in the highest quintile CRF level were reduced by 37.5%, 20.6%, and 27.0%, respectively, as compared to similar participants at the lowest CRF level. For obese diabetic participants in the highest CRF quintile level, serum ferritin concentrations were reduced by 29.7% as compared to similar participants in the lowest CRF level. Elevated body iron stores have been suspected to be a risk factor for type 2 diabetes (Ikeda et al., 2006) , although Elis et al.(2004) found that iron or ferritin concentrations did not play a major role in new-onset of diabetes or diabetic retinopathy.

Researchers studied the effects of running and swimming on ferritin, haptoglobin, and red cell indexes and found that serum ferritin and hemoglobin were lower in runners even though the runners had an adequate dietary iron intake compared with the baseline (Pizza, Flynn, Boone, Rodriguez-Zayas, & Andres, 1997) . Elevated iron load or ferritin concentration significantly increased the risk of type 2 diabetes in the offspring of type 2 diabetic persons with unaffected glucose tolerance, and ferritin concentration was related to insulin resistance (Psyrogiannis, Kyriazopoulou, Symeonidis, Leotsinidis, & Vagenakis, 2003) . Similarly, in my study, individuals having a family history of diabetes were 3.96 times more likely to have diabetes.

Low CRF and low physical inactivity have been found to be risk factors for development of type 2 diabetes because a low level of fitness or sedentary lifestyle were risk factors for impaired fasting glucose (Wei et al., 2000) . Impaired fasting glucose and high BMI, age, blood pressure, triglyceride levels, and family history of diabetes were directly related to risk for type 2 diabetes

(Wei et al., 1999). Church et al. (2004) found an inverse association between fitness and mortality in a cohort of men with diabetes. Many researchers found positive correlations between serum ferritin and impaired fasting glucose, so the reduction of serum ferritin level improved glucose tolerance and reduced the incidence of type 2 diabetes (Oba et al., 1997).

The mean serum ferritin was significantly higher in those with diabetic retinopathy than in healthy controls, and Oba et al. (1997) found diabetic microangiopathy associated with elevated serum ferritin concentration. Diabetes is a major risk for cardiovascular disease and ferritin concentration was found to be an independent risk factor for cardiovascular disease. In addition to reducing the incidence of cardiovascular disease by a reduction in the incidence of diabetes, decreasing ferritin concentration reduced the influence of risk factors for cardiovascular disease, especially acute myocardial infarction (Bartfay et al., 1995; Forouhi et al., 2007; Lakka et al., 1994; Salonen et al., 1992; Tuomainen, Punnonen, Nyyssonen, & Salonen, 1998) . According to the findings from my study and from other studies, a lower serum ferritin concentration is associated with a lower prevalence of type 2 diabetes and an increased CRF level is associated with a decreasing serum ferritin concentration. A strong positive association between serum ferritin and blood glucose and a family history of diabetes play important roles in the development of diabetes in an individual. Therefore, physicians may want to consider measuring patient ferritin concentrations as a predictor of a risk for new-onset diabetes, to control the incidence of diabetes, to prevent diabetic complications, and to encourage patients to participate in physical activity.

The major limitation of this study was it was a cross-sectional design that did not allow the evaluation of causal relationships between type 2 diabetes and a participant's risk factors as well what role of CRF played. Furthermore, a relatively small number of participants who had an evaluation of serum ferritin concentration across cardiorespiratory fitness quintile levels had type 2 diabetes (n= 395). Therefore, associations between CRF levels and diabetes were not statistically significant as shown in Table 4, although CRF at all quintile levels was found as a protective factor from type 2 diabetes. Because of the cross-sectional study, data were used for the analysis selected from observations at baseline could not estimate incidence rates of type 2 diabetes stratified by physical activity levels. In future research, more studies should be conducted to explore how serum ferritin concentrations impact the incidence of type 2 diabetes and how CRF or physical activity levels influence the reduction of mortality and morbidity rates of diabetes.

The risk of type 2 diabetes was directly associated with serum ferritin levels and was inversely associated with cardiorespiratory fitness (CRF) levels. Although no statistically significant interaction between cardiorespiratory fitness levels and serum ferritin concentration on type 2 diabetes was found by testing, the median serum ferritin concentrations among the five levels of CRF levels stratified by BMI categories and diabetic status were significantly different and were inversely associated with CRF levels. Therefore, increasing CRF levels or physical activity can reduce serum ferritin concentration and decrease risk of type 2 diabetes. An individual with a family history of diabetes has four times higher risk for the development of diabetes as compared to those without family diabetic history, so physicians might consider measuring patients' ferritin concentrations to predict a risk of new-onset diabetes, control the incidence of diabetes, and encourage patients to participate in physical activity.

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Male (n=4,235)	68.0
Age (yr)	47 ± 9
Race (white)	94.9
Race (other)	5.1
BMI	
Overweight	46.0
Obese	24.6
Drinking (≥ 5 drinks/wk)	11.7
Smoking	13.4
Ferritin	
Mean ± SD ng/ml	114.2 ± 98.1
High [>300 (male); >150 (female)]	5.3
Cholesterol	
Mean ± SD mg/dL	201.9 ± 37.5
High (>240 mg/dL)	15.0
HDL	
Mean ± SD mg/dL	54.0± 16.3
Low (<40 mg/dL)	17.8
Glucose	
Mean ± SD mg/dL	98.7 ± 16.9
High (>126 mg/dL)	2.8
Fibrinogen	
Mean ± SD mg/dL	304.1 ± 59.2
High (>400 mg/dL)	6.7
Hematocrit	
Mean ± SD %	43.0 ± 3.5
High [>52% (Male); >47% (Female)]	0.3
CRF quintile level §	
I	10.2
II	17.8
III	18.0
IV	28.0
V	26.0
Family history of diabetes	3.7
Type 2 diabetes	6.4

Data are percentages unless indicated as mean ± SD; CRF- Cardiorespiratory Fitness
§ CRF quintile level [I- Lowest; V- Highest];SD- Standard deviation, BMI- Body Mass Index
HDL- High-density lipoprotein

Table 1

Demographic Characteristics of Study Participants from the Aerobics Center Longitudinal Study, 1995-2001

Table 2 Association of Risk Factors for Type 2 Diabetes (Adjusted for Age, Sex, and Ethnicity) among Aerobics Center Longitudinal Study Participants, 1995-2001

Risk Factor	Diabetes	
	OR	95% CI
Ferritin (High vs. Normal)	1.89	1.31- 2.73
Fitness (II vs. I (Lowest))	0.86	0.60- 1.23
Fitness (III vs. I)	0.62	0.42- 0.91
Fitness (IV vs. I)	0.71	0.51- 1.01
Fitness (V (Highest) vs. I)	0.45	0.31- 0.66
HDL (High vs. Low)	0.74	0.67- 0.96
BMI (Overweight vs. Normal)	1.36	1.02- 1.82
BMI (Obese vs. Normal)	1.40	1.01- 1.94
Family History of Diabetes (Yes vs. No)	3.96	2.81- 5.58
Cholesterol (High vs. Normal)	0.88	0.65-1.19
Triglyceride (High vs. Normal)	1.57	1.20- 2.05
Hematocrit (High vs. Normal)	2.94	0.85- 10.23
High Blood Pressure	1.13	0.89- 1.42

OR- Odds Ratio;HDL- High-Density Lipoprotein;BMI- Body Mass Index;CI- Confidence Interval

Table 3 Odds Ratios of Serum Ferritin Levels and Cardiorespiratory Fitness Levels with Type 2 Diabetes, Aerobics Center Longitudinal Study, 1995 - 2001

Variable		Odds Ratios of Type 2 Diabetes		
		Crude (Model I)	Adjusted* (Model II)	Adjusted** (Model III)
Ferritin Level				
High vs. Normal		1.94 (1.35, 2.77)	1.80 (1.25, 2.57)	1.48 (1.02, 2.26)
CRF Quintile Level §				
	II vs. I	0.81 (0.57, 1.15)	0.81 (0.57, 1.15)	0.96 (0.65, 1.43)
	III vs. I	0.66 (0.46, 0.94)	0.67 (0.46, 0.96)	0.73 (0.46, 1.11)
	IV vs. I	0.71 (0.51, 0.99)	0.73 (0.53, 1.02)	0.89 (0.59, 1.34)
	V vs. I	0.45 (0.32, 0.65)	0.47 (0.33, 0.68)	0.54 (0.34, 0.86)
	P_{trend}	<0.0001	<0.0001	0.004

* Adjusted for Ferritin level or Fitness level
** Adjusted for all variables (Age Group, Ethnic, Sex, BMI, smoking, drinking, glucose, cholesterol, triglyceride, fibrinogen, high blood pressure, family history of diabetes, and [ferritin level or fitness level])
§ Age specific fitness quintile [I- Lowest; V-highest]

Table 4 Median Serum Ferritin among Participants Stratified by Diabetes and BMI Status, Aerobics Center Longitudinal Status, 1995-2001

	Non-Diabetes BMI (Kg/m^2)					Diabetes BMI (Kg/m^2)				
	Normal	Overweight	Obese		p-value	Normal	Overweight	Obese		p-value
CRF Level §										
I	76	124	131.5		0.0203	--	64.	148		0.0052
II	56	108	128		<0.0001	67	122	133.5		0.0337
III	61	112	140.5		<0.0001	64	91	137		0.0343
IV	52	97	102		<0.0001	47	99	149		<0.0001
V	47.5	98.5	96		<0.0001	64.5	115	104		0.0024

-- No participant with low CRF (cardiorespiratory fitness) and normal BMI (body mass index)
§ Age specific fitness quintile [I- Lowest; V-highest]
- Data are medians of ferritin concentration, unless otherwise indicated
- Kruskal-Wallis test shows that median ferritin are statistically significant difference among the 5 levels of fitness (χ^2 with 4 degrees of freedom = 287..99 ($p < .0001$) and 11.98 ($p= 0.0175$) among non-diabetic participants and diabetic participants, respectively)