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Association between Body Iron Status and Leukocyte Telomere Length, a Biomarker of Biological Aging, in a Nationally Representative Sample of U.S. Adults

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Abstract

Background: Excess iron levels can induce oxidative stress and therefore, they might affect telomere attrition. However, little is known about the impact of body iron status on telomere length.

Objective: To examine the association between serum ferritin concentrations, an indicator of body iron status, and leukocyte telomere length in U.S. adults.

Design: Nationwide, population-based, cross-sectional study.

Participants/Setting: We used data from the National Health and Nutrition Examination Survey (NHANES) 1999–2002. We included 7,336 adults aged 20 years or older who had available data on serum ferritin levels and telomere length.

Exposures: High ferritin levels were defined as a serum ferritin level >200 ng/mL in women and >300 ng/mL in men. Low ferritin levels were defined as a serum ferritin level <30 ng/mL.

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Author contributions:

WB has full access to all of the data in this study and assumes responsibility for study supervision. WB and BL contributed to the conception and design of the study. BL performed the statistical analyses and drafted the manuscript. All authors contributed to the acquisition, analysis, or interpretation of the data, and critically revised the manuscript for important intellectual content.

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Competing interests:

All the authors declared no conflict of interest.

Main outcome measures: Leukocyte telomere length was assayed using the quantitative polymerase chain reaction method.

Statistical analyses: Linear regression with survey weights was performed to estimate the association between serum ferritin levels and telomere length.

Results: The prevalence of adults with high and low serum ferritin levels was 10.9% and 17.6%, respectively. High ferritin levels, compared to normal ferritin levels, were inversely associated with telomere length. After adjustment for demographic, socioeconomic and lifestyle factors, BMI, C-reactive protein, and leukocyte cell type composition, the β coefficient for log-transformed telomere length was -0.020 (SE 0.009 , $P=0.047$). The association was stronger in adults aged 65 years or older (β coefficient -0.081 , SE 0.017 , $P<0.001$) than in adults 20–44 years old (β coefficient -0.023 , SE 0.019 , $P=0.24$) or adults 45–64 years old (β coefficient 0.024 , SE 0.015 , $P=0.10$) (P for interaction 0.003). Low ferritin levels, compared with normal ferritin levels, were not significantly associated with telomere length.

Conclusions: In a U.S. nationally representative population, high body iron status was associated with shorter telomeres, especially in adults aged 65 years or older.

Keywords

Ferritin; iron; telomere length; aging; adults

BACKGROUND

Telomeres are repetitive nucleotide sequences located at the ends of chromosomes, which maintain genomic stability and integrity by preventing nucleolytic degradation and irregular fusions and recombination.¹ During aging, telomeres gradually shorten with each somatic cell division. Therefore, telomere length is considered a biomarker of biological cellular aging.^{2–5} Telomere shortening is associated with biomarkers of aging-related biological processes, such as oxidative stress and inflammation.⁶ Longitudinal studies in animal models suggest that telomere length in early life can predict lifespan.⁷ In humans, shorter leukocyte telomere length has been associated with increased risk of age-related chronic diseases, such as type 2 diabetes,⁸ cardiovascular disease,⁹ and Alzheimer's disease,^{10, 11} as well as mortality from all causes and cardiovascular disease.¹² Telomere length variability and attrition rate are determined not only by genetic background, but also by environmental and dietary factors.^{13–20}

Iron is an essential micronutrient for humans. It is an important compound of hemoglobin and also plays vital roles in metabolism and immune and endocrine function because it is a cofactor for various enzymes and a key player in oxygen transport, electron transfer, and cell growth and differentiation.²¹ Iron deficiency is prevalent worldwide and associated with a wide range of symptoms in the body.²² However, it is worth noting that iron is also a redox-active transitional metal with pro-oxidant properties. Excessive amounts of iron are potentially hazardous, leading to over-production of reactive oxygen species and oxidative stress.²³ Previous epidemiologic studies have shown that elevated iron status is associated with higher risk of type 2 diabetes, cardiovascular disease, and mortality.^{23–25} In addition, high ferritin levels were found to be associated with shortened telomeres, a biomarker of

biological aging and age-related chronic diseases, among patients with overt iron overload due to diseases.^{26, 27} However, the association between body iron status and telomere length in the general population remains unknown.

To address this question, we used nationally representative data from the general U.S. population to examine the association between body iron status, reflected by serum ferritin concentration, and leukocyte telomere length.

MATERIALS AND METHODS

Study population

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the civilian, non-institutionalized US population. It is conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). NHANES uses a complex, multistage, probability sampling design to ensure population representativeness. The ongoing survey combines interviews and physical examinations of about 5,000 individuals per year. Data from NHANES are released in 2-year cycles and available online for public access. NHANES has been approved by the NCHS Ethics Review Board. Written informed consent was obtained from all participants.

In the present study, we used data from NHANES 1999–2000 and 2001–2002, because telomere length was measured only in these two cycles. In 1999–2000, 69.4% of adults selected for the survey participated in the examination. In 2001–2002, the response rate was 72.7%. We included all participants aged 20 years or older with available data on both serum ferritin and leukocyte telomere length. Pregnant women were excluded because of the high possibility they take iron supplements. The process for the inclusion and exclusion of participants is shown in Figure 1.

Serum ferritin assay

Ferritin was measured using an immunoradiometric assay (QuantImmune Ferritin IRMA kit, Bio-Rad Laboratories). In this assay, the highly purified ¹²⁵I-labeled antibody to ferritin was the tracer, and the ferritin antibodies were immobilized on polyacrylamide beads as the solid phase. Serum samples or ferritin standards were mixed with the combined tracer/solid-phase antibody reagent, and the mixture was incubated at room temperature for 30 min. During incubation, both the immobilized and the ¹²⁵I labeled antibodies bound to the ferritin antigen in the serum or standards. After incubation, the beads were diluted with saline, centrifuged, and decanted. The level of ¹²⁵I-labeled ferritin found in the pellets was measured by using a gamma counter.

There is currently no consensus on the cutoff points of serum ferritin levels to determine iron status.²⁸ In this analysis, serum ferritin levels were classified consistent with previous literature.^{29, 30} Normal ferritin levels were defined as a serum ferritin level equal to or higher than 30 ng/mL and equal to or lower than 200 ng/mL in women or 300 ng/mL in men. High ferritin levels were defined as a serum ferritin level higher than 200 ng/mL in women or higher than 300 ng/mL in men. Low ferritin levels were defined as a serum ferritin level lower than 30 ng/mL.^{28,31}

Telomere length assay

Using standardized procedures, DNA was extracted from whole blood samples and stored at -80°C before the assay. Leukocyte telomere length was assayed using the quantitative polymerase chain reaction method to measure telomere length relative to standard reference DNA (T/S ratio), as previously described.^{32, 33} Each sample was assayed three times on three different days. The samples were assayed in duplicate wells, resulting in six measurements per sample. The mean of the T/S ratio values was calculated without potential outliers. The leukocyte telomere length assay lab was blind to the sample characteristics. The interassay coefficient of variability for telomere length was 6.5%. The CDC conducted a quality control review before linking the telomere data to the NHANES 1999–2002 public use data files.

Questionnaire and examination data

Individual-level information on age, gender, race/ethnicity, family income, education, smoking status, and physical activity was collected using questionnaires administered by trained interviewers. Race/ethnicity was categorized into Hispanic (including Mexican and non-Mexican Hispanic), non-Hispanic white, non-Hispanic black, and others. Family income-to-poverty ratio was categorized as 1.30 or lower, 1.31–3.50, and greater than 3.50.³⁴ Self-reported education status was grouped as lower than high school, high school, and college or higher (including some college or associates degree, college graduate, or higher). In accordance with NCHS classifications, individuals who smoked less than 100 cigarettes in their lifetime were defined as never smokers; those who had smoked more than 100 cigarettes, but did not smoke at the time of survey, were considered former smokers; and those who had smoked 100 cigarettes in their lifetime and smoked cigarettes at the time of survey were current smokers.³⁵ Dietary information was collected by 24-h dietary recall interview using the US Department of Agriculture Automated Multiple-Pass Method.³⁶ Total energy intake was calculated by the National center for Health Statistics based on the Food and Nutrient Database for Dietary Surveys. Alcohol intake was categorized as non-drinker (0 g/day), moderate drinker (0.1–27.9 g/day for men, 0.1–13.9 g/d for women), or heavy drinker (≥ 28 g/day for men, ≥ 14 g/day for women). Physical activity was categorized as < 150 minutes/week, 150–299 minutes/week, and ≥ 300 minutes/week of moderate intensity activities.³⁷ Trained health technicians assessed weight and height according to the NHANES Anthropometry Procedures Manual. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. White blood cell counts were performed using the Beckman Coulter MAXM instrument for each cell type including the following: white blood cells (SI), lymphocytes (%), monocytes (%), neutrophils (%), eosinophils (%), and basophils (%).³⁸

Statistical analysis

We followed the NHANES Analytic Guidelines provided by the National Center for Health Statistics.³⁹ In brief, we accounted for the sample weights to obtain proper variance estimation in the data, using the stratified multistage probability design. Taylor series linearization was used for variance estimation. Leukocyte telomere length was natural logarithm-transformed prior to analysis because of skewed distributions and was fitted as a

dependent variable. Multivariable linear regression was used to estimate the association between serum ferritin concentration and leukocyte telomere length. In Model 1, we adjusted for age (20–44, 45–64, ≥65 years), gender (men and women), and race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other). We additionally adjusted for education (lower than high school, high school, college or higher), family income to poverty ratio (<1.30, 1.31–3.50, >3.50), smoking status (never, current, and ever), alcohol intake (none, moderate, and heavy), physical activity (<150, 150–299, ≥300), total energy intake (quartile), BMI (<25.0, 25.0–29.9, and ≥30), and white blood cell count (quartile) in Model 2. A previous study has shown significant variability of telomere length across subpopulations of leukocytes,³⁸ therefore we included leukocyte cell type composition (quartile) in Model 2 as well. In Model 3, we additionally adjusted for the inflammatory marker C-reactive protein (quartile), because ferritin could be elevated under inflammatory conditions.³¹ To evaluate effect modification, we conducted stratified analyses according to age (20–44, 45–64, and ≥65 years), gender (men, women), and race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other racial/ethnic groups). P values for heterogeneity were derived from the multiplicative interaction term coefficients (exposure variable × effect modifier variable) added to the main effects multivariable model.

All statistical analyses were conducted using survey modules of SAS software version 9.4 (SAS Institute, Cary, NC). Two-sided P-values < 0.05 were considered statistically significant.

RESULTS

This study consisted of 7,336 adults (average age: 50.7±18.5 years old; women: 46.3%). The geometric mean of relative leukocyte telomere length was 1.02 (Standard errors [SE], 0.01). The weighted prevalence of adults with normal, low, and high ferritin levels were 71.4%, 17.6%, and 10.9%, respectively. Compared to adults with normal ferritin levels, adults with high ferritin levels were more likely to be people aged 65 years or older, men, non-Hispanic blacks, current or ever smokers, heavy drinkers, and those with lower education status, lower physical activity level, and higher BMI (Table 1). Compared to those with normal ferritin levels, adults with low ferritin levels were more likely to be people younger than 65 years old, women, non-Whites, non-smokers, non-drinkers, and those with lower family income and lower BMI (Table 1). The telomere length among various population groups could be seen in Table 2.

Compared with normal ferritin levels, high ferritin levels were significantly associated with shorter telomere length (Table 3). The β coefficient between high ferritin levels, relative to normal ferritin levels, and telomere length was -0.02 (SE, 0.009; $P = 0.047$), after adjustment for demographic, socioeconomic and lifestyle factors, BMI, C-reactive protein, and leukocyte cell type composition. There was no significant association between low ferritin levels, as compared with normal ferritin levels, and telomere length. The multivariable-adjusted β coefficient between low ferritin levels, relative to normal ferritin levels, and telomere length was 0.009 (SE, 0.007; $P = 0.21$).

Stratified analyses revealed associations between high ferritin levels and telomere length were more pronounced in adults aged 65 years or older (P for interaction, 0.0007; Table 4). The multivariable-adjusted β coefficient between high ferritin levels and telomere length was -0.081 (SE, 0.017; $P < 0.0001$) for adults aged 65 years or older, 0.024 (SE, 0.015; $P = 0.10$) for adults 45–64 years old, and -0.023 (SE, 0.019; $P = 0.24$) for adults 20–44 years old. The association between high serum ferritin levels and telomere length looks stronger in women and non-Hispanic Whites (Table 4), although the effect modifications were not significant (gender: P for interaction, 0.12; race/ethnicity: P for interaction, 0.93). There were no significant interaction effects of age, gender, race/ethnicity between low serum ferritin levels and telomere length (data not shown).

DISCUSSION

In this study, we found a significant association between high serum ferritin levels and shorter leukocyte telomere length even after adjustment for known confounders. The association was stronger in adults aged 65 years or older compared with young adults.

Our results are consistent with previous studies among patients with extremely high ferritin concentrations due to heredity or diseases. Among patients with hereditary hemochromatosis, a genetic condition causing iron overload by HFE gene mutations, elevated serum ferritin concentration was associated with shortened telomeres.²⁶ Similarly, an inverse association between ferritin levels and leukocyte telomere length was reported in hemodialysis patients.²⁷ In addition, our results were also in accord with recent studies using transferrin saturation as an indicator of body iron status.^{40, 41} Similar to our findings, those studies showed that high body iron status, indicated by elevated transferrin saturation, was associated with shorter telomere length.^{40, 41}

The association between high body iron status and shorter telomere length is biologically plausible, although the detailed molecular mechanisms are unclear.⁴² Iron can be a powerful pro-oxidant and catalyst, promoting the formation of hydroxyl radicals.²¹ Excessive iron storage is involved in the imbalance between compounds favoring the formation of reactive oxygen species and antioxidants leading to oxidative stress, which could contribute to the acceleration of telomere attrition.^{6, 42} In mice, chronic oxidative stress was found to cause telomere shortening in several tissues including testis, fat, tail, and skin.⁴³ An *in vitro* study demonstrated that high-intensity stresses could reduce telomere length directly by inducing telomeric double-strand breaks at high frequency.^{44, 45} Therefore, it is probable that high body iron status could induce the loss of telomeric sequences through oxidative stress.⁴² In addition, we found in the present study that the association between serum ferritin levels and telomere length was stronger in people aged 65 years or older. Older people have decreased endogenous antioxidant function,^{46, 47} which may make them more sensitive or vulnerable to oxidative stress resulting from iron overload. More research is needed to clarify the underlying mechanisms.

The present study has important clinical and public health implications. Differences in telomere length emerge prior to the manifestation of chronic diseases in later life.⁷ Our study suggests that people with high ferritin levels might unknowingly be subject to accelerated

telomere shortening, which is a biomarker of biological aging and age-related chronic diseases. This is in line with previous studies that reported the association between high ferritin levels and chronic diseases (diabetes, cardiovascular disease, etc) and mortality.^{48, 49} However, much less attention has been paid on excessive iron status compared to iron deficiency. Only 4.97% of individuals with iron overload were informed of their iron overload status.⁴⁰ Taken together, findings from the present study and previous studies underscore the importance of identifying and managing excessive iron status, especially among a population in which iron is relatively replete.

This study has several strengths. The multi-ethnic/racial, national representative data from NHANES allows us to generalize our findings to a broader population. NHANES measured biomarkers of iron status and leukocyte telomere length in a large sample, providing high statistical power to detect the associations between them. In addition, we adjusted for a variety of potential confounders by taking advantage of the abundant data from NHANES. In particular, we adjusted for leukocyte cell type composition in view of the significant variability of telomere length in each type of leukocyte.³⁸ We acknowledge there are several limitations in this study. First, our results might be subject to reverse causation due to the nature of cross-sectional studies. Second, diseases, such as cancer or CVD, are associated with telomere length.^{5, 25} However, in our sensitivity analyses, after excluding individuals with cancer and CVD (data not shown), there were no appreciable changes in the results. Third, we don't know if iron overload in some participants was caused by hemochromatosis because of the data limitation. Since ferritin level in a large percentage of general population was lower than 1,000 ng/mL,⁵⁰ we conducted a sensitivity analysis by excluding adults with ferritin level higher than 1,000 ng/mL. The association between high ferritin levels and telomere length was robust (data not shown). Fourth, we cannot rule out the possibility of residual confounding, although a variety potential confounders have been considered.

Conclusions

In a multi-ethnic/racial, nationally representative population, we found that high serum ferritin levels were significantly associated with shorter telomeres, especially in people aged 65 years or older.

Acknowledgments

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Research Snapshot**Research Question:**

Was body iron status associated with telomere length?

Key Findings:

In a U.S. nationally representative population, high serum ferritin concentrations, an indicator of body iron status, were significantly associated with shorter telomeres, especially in adults aged 65 years or older.

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Figure 1.
The flow chart of participant inclusion and exclusion.

Table 1

Characteristics of population in various ferritin status from NHANES 1999–2002 (N = 7,336)

Variable	Normal ferritin level	Low ferritin level	P*	High ferritin level	P [†]
No. of participants (%)	5180 (71.4%)	1244 (17.6%)		912 (10.9%)	
Age, % (SE)					
20–44 years	49.1 (1.1)	65.0 (1.8)		32.5 (2.5)	
45–64 years	33.4 (1.1)	24.5 (1.6)	<0.001	42.0 (2.4)	<0.001
65 years	17.5 (0.7)	10.5 (1.1)		25.5 (1.8)	
Gender, % (SE)					
Men	56.4 (0.6)	11.0 (1.2)	<0.001	67.6 (1.8)	<0.001
Women	43.6 (0.6)	89.0 (1.2)		32.4 (1.8)	
Race/ethnicity, % (SE)					
non-Hispanic White	74.3 (1.8)	71.6 (2.3)		70.3 (2.7)	
non-Hispanic Black	8.2 (1.0)	10.2 (1.3)	0.003	13.6 (1.8)	0.001
Mexican American	6.6 (0.8)	8.6 (1.0)		5.7 (1.2)	
Other	10.9 (1.8)	9.5 (2.0)		10.4 (2.4)	
Education, % (SE)					
Less than high school	21.1 (1.0)	19.1 (1.6)		26.3 (1.5)	
High school	25.3 (1.1)	25.8 (1.7)	0.40	32.2 (2.3)	<0.001
College or higher	53.6 (1.5)	55.1 (2.9)		41.5 (2.6)	
Smoker, % (SE)					
Never smoker	48.8 (1.4)	59.1 (1.8)		42.7 (2.1)	
Current smoker	25.6 (1.2)	20.5 (1.7)	<0.001	24.8 (1.4)	0.003
Ever smoker	25.7 (0.9)	20.4 (1.5)		32.5 (1.9)	
Family income to poverty ratio, % (SE)					
1.30	18.9 (1.4)	23.4 (2.3)		20.7 (1.6)	
1.30–3.50	32.8 (1.2)	31.8 (1.3)	0.04	32.9 (1.8)	0.20
>3.5	40.8 (1.9)	38.2 (2.6)		37.0 (2.0)	
Missing	7.6 (0.8)	6.6 (1.2)		9.4 (1.7)	
Physical activity, min/week, % (SE)					
< 150	41.6 (1.3)	41.1 (2.6)		49.9 (2.0)	
150–299	15.4 (0.8)	16.9 (1.8)	0.70	12.1 (1.6)	<0.001
300	43.1 (1.4)	42.0 (2.5)		38.0 (2.2)	
Alcohol, g/d, mean (SE)					
Non-drinker	66.6 (1.5)	75.0 (1.9)		64.4 (2.3)	
Moderate drinker	14.9 (0.9)	11.9 (1.3)	<0.001	14.5 (1.2)	0.44
Heavy drinker	15.1 (0.8)	9.1 (1.1)		17.7 (1.7)	
Missing	3.4 (0.4)	4.0 (0.6)		3.4 (0.8)	
BMI, % (SE)					
<25.0	33.3 (1.0)	41.9 (1.9)		24.0 (2.2)	
25–29.9	35.4 (1.0)	27.4 (1.7)	0.001	36.7 (2.3)	<0.001
30.0	29.0 (1.0)	27.8 (2.1)		35.6 (2.7)	

Variable	Normal ferritin level	Low ferritin level	p*	High ferritin level	p [†]
Missing	2.2 (0.2)	2.9 (0.7)		3.6 (0.6)	
Total energy intake, Kcal/d, mean (SE)	2273.0 (19.5)	1972.4 (23.7)	<0.001	2253.1 (53.2)	0.74
C-reactive protein, mg/mL, geometric mean (SE)	0.19 (0.01)	0.16 (0.01)	0.005	0.26 (0.01)	0.007
Relative telomere length, mean (SE)	1.05 (0.01)	1.10 (0.02)	<0.001	1.00 (0.02)	<0.001
Ferritin concentrations, ng/mL, geometric mean (SE)	94.0 (0.8)	13.7 (0.4)	<0.001	393.0 (6.3)	<0.001

SE: Standard errors

Values were weighted mean (SE) for continuous variables and weighted percentages (SE) for categorical variables except number of participants.

* indicates P value for the comparison between low vs. normal ferritin levels.

[†] indicates P value for the comparison between high vs. normal ferritin levels.

Normal ferritin levels were defined as a serum ferritin level higher than 30 ng/mL and lower than 200 ng/mL in women or 300 ng/mL in men. High serum ferritin levels were defined as a serum ferritin level > 200 ng/mL in women and > 300 ng/mL in men. Low serum ferritin levels were defined as a serum ferritin level < 30 ng/mL.

Table 2Telomere length among various population groups from NHANES 1999–2002 (N = 7,336)[#]

Variable	Telomere length	P
Overall	1.02 ± 0.015	
Age, % (SE)		
20–44 years	1.14 ± 0.016	
45–64 years	1.01 ± 0.018	<0.001
65 years	0.89 ± 0.016	
Gender, % (SE) *		
Men	1.05 ± 0.015	0.003
Women	1.06 ± 0.017	
Race/ethnicity, % (SE) *		
non-Hispanic White	1.04 ± 0.016	0.04
non-Hispanic Black	1.10 ± 0.019	
Mexican American	1.05 ± 0.018	
Other	1.10 ± 0.030	
Education, % (SE) *		
Less than high school	1.01 ± 0.016	0.002
High school	1.05 ± 0.018	
College or higher	1.07 ± 0.014	
Alcohol, g/d, mean (SE) *		
Non-drinker	1.04 ± 0.016	0.30
Moderate drinker	1.06 ± 0.020	
Heavy drinker	1.09 ± 0.015	
Missing	1.11 ± 0.036	
Physical activity, min/week, % (SE) *		
< 150	1.03 ± 0.016	0.006
150–299	1.05 ± 0.016	
300	1.08 ± 0.015	
Smoker, % (SE) *		
Never smoker	1.07 ± 0.016	0.048
Current smoker	1.07 ± 0.018	
Ever smoker	1.01 ± 0.015	
Family income to poverty ratio, % (SE) *		
1.30	1.07 ± 0.020	0.34
1.30–3.50	1.04 ± 0.016	
>3.5	1.06 ± 0.016	
Missing	1.07 ± 0.034	
Ferritin concentrations, ng/mL *		

Variable	Telomere length	P
low ferritin	1.10 ± 0.017	0.001
normal ferritin	1.05 ± 0.015	
high ferritin	1.00 ± 0.018	
BMI,%(SE) *		
<25.0	1.09 ± 0.017	0.07
25–29.9	1.04 ± 0.016	
30.0	1.03 ± 0.015	
Missing	1.01 ± 0.032	

Values were weighted

* Age-adjusted to the 2000 US Census population using the age groups 20–44 years, 45–64 years, and 65 years or older

Table 3.

Associations between serum ferritin levels and telomere length (n=7,336)

Model	Normal ferritin level	Low ferritin level		High ferritin level	
		β coefficient (SE)	P	β coefficient (SE)	P
No. of participants	5180	1244		912	
Model 1	0(ref)	0.016 (0.007)	0.03	-0.027 (0.010)	0.01
Model 2	0(ref)	0.012 (0.007)	0.10	-0.022 (0.010)	0.03
Model 3	0(ref)	0.009 (0.007)	0.21	-0.020 (0.009)	0.047

SE: Standard errors

Model 1: adjusted for age, gender, and race /ethnicity.

Model 2: adjusted for model 1 + education, family income, smoking status, alcohol intake, physical activity, total energy intake, BMI, white blood cell count, lymphocyte percentage, monocyte percentage, segmented neutrophils, eosinophils percentage, and basophils percentage.

Model 3: model 2 + C-reactive protein.

Normal ferritin levels were defined as serum ferritin levels higher than 30 ng/mL and lower than 200 ng/mL in women or 300 ng/mL in men. High serum ferritin levels were defined as serum ferritin levels > 200 ng/mL in women and > 300 ng/mL in men. Low serum ferritin levels were defined as serum ferritin levels < 30 ng/mL.

Table 4.

Stratified analyses for the associations between serum ferritin levels and telomere length

Variable	N	Normal ferritin level	Low ferritin level		High ferritin level	
			β coefficient (SE)	P	β coefficient (SE)	P
Age, years						
20–44	3072	0(ref)	0.015 (0.012)	0.24	−0.023 (0.019)	0.24
45–64	2272	0(ref)	0.023 (0.015)	0.15	0.024 (0.015)	0.10
>65	1992	0(ref)	0.002 (0.023)	0.95	−0.081 (0.017)	<0.001
Gender						
Men	3752	0(ref)	0.012 (0.021)	0.58	−0.002 (0.013)	0.91
Women	3584	0(ref)	0.010 (0.009)	0.29	−0.057 (0.017)	0.003
Race/ ethnicity						
non-Hispanic White	3737	0(ref)	0.013 (0.010)	0.21	−0.027 (0.011)	0.03
non-Hispanic Black	1272	0(ref)	0.007 (0.017)	0.68	−0.018 (0.015)	0.23
Mexican American	1742	0(ref)	0.002 (0.010)	0.88	−0.016 (0.020)	0.43
Other	585	0(ref)	−0.005 (0.033)	0.88	0.022 (0.033)	0.50

SE: standard errors

Adjusted for age, gender, race /ethnicity, education, family income, smoking status, alcohol intake, physical activity, total energy intake, BMI, white blood cell count, lymphocyte percentage, monocyte percentage, segmented neutrophils, eosinophils percentage, basophils percentage, and C-reactive protein, except the stratified variables.

Normal ferritin levels were defined as serum ferritin levels higher than 30 ng/mL and lower than 200 ng/mL in women or 300 ng/mL in men. High serum ferritin levels were defined as serum ferritin levels > 200 ng/mL in women and > 300 ng/mL in men. Low serum ferritin levels were defined as serum ferritin levels < 30 ng/mL.