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The relationship between whole blood iron and fasting blood glucose in community-dwelling elderly people: a cross-sectional study

Shu-Zi-Qi Chen[1], Rou-Jun Pan[1], Meng-Yan Sun[1], Lian-Ping He[1*] and Cui-Ping Li[1*]

Abstract

Iron overload increases fasting blood glucose level in mice, leading to insulin insensitivity. However, no such relationship has been shown in the population. The relationship between whole blood iron levels and fasting blood glucose levels remained unclear. This study aimed to determine whether whole blood iron levels were associated with fasting blood glucose levels in community-dwelling older adults. This cross-sectional study was based on a community population and analyzed the distribution of whole blood iron and fasting blood glucose in a community population. A sample of 1560 community residents had their fasting blood glucose, gender, and age measured during the study. Covariates were assessed using correlation analysis, partial correlation analysis, and Student's t-test. To further investigate the impact of confounding factors in this study, we compared variations in whole blood iron levels between genders. Pearson correlation analysis showed no correlation between whole blood iron and fasting blood glucose. After adjusting for age and gender, no correlation was found between whole blood iron and fasting blood glucose as well. However, Pearson correlation analysis showed a correlation between whole blood iron and age($P<0.05$, $r=-0.181$). whole blood iron concentrations gradually decreased with age. At the same time, mean whole blood iron concentrations were lower 420 mg/l among women and men in the community. And the mean levels of whole blood iron were higher in men(504.08 mg/l ± 45.98 mg/l) than in women(453.80 mg/l ± 38.13 mg/l). Our study indicated no association between whole blood iron. Age was a covariate, but fasting blood glucose was not, and fasting blood glucose was independently associated with whole blood iron concentrations, suggesting that older women in this community need adequate iron supplementation.

Keywords Whole blood iron, Fasting blood glucose, Elderly, Community care, Correlation analysis

*Correspondence:
Lian-Ping He
lianpinghe@tzc.edu.cn
Cui-Ping Li
lcpyxy@tzc.edu.cn
[1]School of Medicine, Taizhou University, No.1139, Shifu Avenue, Jiaojiang 318000, Zhejiang, China

Introduction

As of 2021, 521 million people worldwide have diabetes, with an age-standardized prevalence rate of 6.1%, of which 96.0% have type 2 diabetes [1]. An estimated 485 million people aged 20–79 years have diabetes [1]. The regions with the highest age-standardized rates are North Africa and the Middle East, with a national age-standardized rate of 9.3%, and Oceania, with 12.3% [2]. Monitoring glycated hemoglobin(HbAlc) and fasting blood glucose(FBG) is crucial for diabetes management [3]. The International Diabetes Federation estimated that by 2021, approximately 319 million adults(6.2% of the global adult population) had impaired fasting glucose(IFG). By 2045, this number is expected to increase to 441 million, accounting for 6.9% of the world's adult population. FBG is suitable for assessing blood glucose levels in the entire population [4]. Therefore, in our study, we used FBG as a variable to investigate whether FBG is associated with iron in a specific population.

Iron is an important trace element in the human body and plays a vital role in various functions such as oxygen transport, DNA repair [5], reactive oxygen species(ROS) generation and other functions, especially in the hematopoietic process [6]. Whole blood iron is bound to transferrin and is required for many biochemical processes such as electron transport reactions, genetic regulation, oxygen binding and transport, cell growth and differentiation, and immune system function [7]. Studies showed a link between iron and glucose metabolism: Elevated serum ferritin levels increase the risk of type 2 diabetes [8]. The hypothesis was put forward that iron may play a key role in type 2 diabetes. This hypothesis is based on previous research. For example, serum soluble transferrin receptor is inversely associated with the risk of type 2 diabetes [9]. Furthermore, ferroptosis can lead to metabolic disorders and insulin deficiency [10]. According to the transferrin receptor and ferroptosis hypothesis, the accumulation of whole blood iron can lead to ferroptosis, and the occurrence of ferroptosis can lead to impaired blood glucose metabolism. Therefore, we hypothesized that there was a relationship between whole blood iron and FBG levels. These findings maybe will provide more clues about the cause of type 2 diabetes.

Recently, iron has been implicated in the pathogenesis of common cardiovascular diseases in the elderly, including type 2 diabetes mellitus and atherosclerosis [11]. In the United States, approximately 10% of women and 11% of men aged 65 and older have anemia; however, the prevalence doubles in adults 85 and older [12]. Increased iron stores in older adults may be associated with the development of age-related diseases due to increased oxidative stress [13]. Therefore, our study targeted the elderly population aged 60 years and above.

Our study investigated whether whole blood iron status affects FBG through correlation.

Subjects and methods

Study subjects

This study was observational. Elderly persons who underwent consecutive health examinations in 2021 were retrospectively recruited. Therefore, 1,561 residents aged 60 years and older were involved. They were considered eligible if they met all of these criteria: (1) Local community housing; (2) Testing information was complete. (3) Participants with missing data on whole blood iron and FBG were excluded. Informed consent was obtained from the participants.

Measurement of whole blood iron and FBG

The measurement of whole blood iron and FBG have been completed from 9 June 2021 to 29 June 2021. Physical examinations were conducted according to certain standards. After fasting for more than 8 h, blood sugar and insulin concentrations reach a balanced or stable state [14]. FBG was measured by the glucose oxidase method. Whole blood iron was measured by ferrous benzoxazines directly colorimetric in Jinyu Inspection Company. Normal FBG should be lower than 6.1 mmol/l. Higher than 6.1 mmol/l means FBG impaired [15]. The reference range for whole blood iron is 420.00 to 660.80 mg/l [16].

Statistical analysis

Data were expressed as means(standard deviation). All data correspond approximately to a normal distribution. To estimate the association between whole blood iron and FBG, we used correlation analysis and partial correlation analysis with adjusting: (1) considering only matching factors, (2) adjusting for the two confounders' age and gender. Differences in categorical variables between groups were tested using the Student's t-test.

All statistical tests were two-sided. $P<0.01$ were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics 26.0. The study protocol and details were not pre-registered anywhere.

Results

General demographic characteristics of participants

The main characteristics of the study population at the time of sampling are shown in Table 1, including gender distribution, age range, whole blood iron content, and FBG. The mean level of age was 70.45±6.83 years old, of which 755 were males(48.36%) and 806 were females(51.63%). After descriptive iron analysis, frequency analysis was performed to determine the 95% confidence interval for population iron levels to be

Table 1 General demographic characteristics

Items	Categories	*N*	Mean	SD
Gender	female	806	-	-
	male	755	-	-
Projects(mmol/l)	Whole blood iron	-	478.11	49.03
	FBG	-	5.99	1.64
Age(years)	-	-	70.45	6.83

Table 2 Statistical tables of changes in the correlation between whole blood iron and FBG before and after age control in groups of males and females

	Whole blood iron(mg/l)			
	*r**	*P*	*r***	*P*
FBG in females(mmol/l)	0.06	0.11	0.06	0.10
FBG in males(mmol/l)	0.03	0.44	0.02	0.50

Note: Correlation is significant at the 0.05 level(2-tailed) *. Before adjusting for age; **. After adjusting for age

478.11±49.03 mg/l. Normal FBG should be lower than 6.1 mmol/l. Higher than 6.1 mmol/l means blood sugar is too high. The reference range for whole blood iron is 420.00 to 660.80 mg/l.

Relationship between whole blood iron and FBG assessed by pearson correlation analysis

Analyzed the correlation between whole blood iron levels and FBG in this population. As the result showed, there was no correlation between whole blood iron levels and FBG($P>0.005$, r=-0.027).

We then performed a correlation analysis and found that there was a certain correlation between whole blood iron levels and age. As can be seen from the result, age is negatively correlated with whole blood iron levels($P<0.05$, r=-0.181), suggesting that this factor may affect the correlation analysis between whole blood iron levels and FBG.

Partial correlation analysis between whole blood iron and FBG

Table 2 showed the results considering the confounders of age and gender. This table illustrated the correlation between whole blood iron and FBG in males and females in this population. There was no significant correlation between whole blood iron and FBG among males and females in this community($P>0.05$).

In contrast, the above result shows the correlation between age and whole blood iron. Therefore, to better investigate the phenomenon of whole blood iron falling below the reference range in certain community populations, we examined the association of whole blood iron with age and gender.

Table 3 T′-test of independence in different gender groups in whole blood iron

Study groups	Whole blood iron (mg/l)				
	N	Mean	SD	t	*P*
Females	806	453.80	38.13	23.57	< 0.001
Males	755	504.08	45.98		

Note: Correlation is significant at the 0.01 level(2-tailed)

Analysis of the student's t-test between whole blood iron and gender

To examine whether there was a statistical significance in whole blood iron between the genders, we used the Student's t-test(Table 3). Table 3 showed that there were differences in whole blood iron between elderly males and females in this community, and the difference was statistically significant(t=23.75, $P<0.001$). Therefore, age and whole blood iron should be tested separately in males and females.

Age and gender factors related to whole blood iron in groups

All of males and females that over 60 years old were grouped by age and divided into 7 groups useing a group distance of 4.99. Figure 1 showed that the whole blood iron of men aged 60 to 70 years old in the community decreaseed with age, while the whole blood iron of people 85–93 years old increaseed. Obviously, the whole blood iron levels of women in this group was generally lower than those of men, and the whole blood iron levels of females in 85–93 years old decreased rapidly.

Discussion

In this cross-sectional study, no statistically significant association was found between whole blood iron concentrations and FBG. The results were inconsistent with the predictions because whole blood iron may be affected by other factors such as inflammation, infection, medication use, diet, and chronic disease. However, the true link between iron in the body and FBG remains to be examined. A more accurate way to measure iron in the body is to measure tissue iron through a liver biopsy or bone marrow aspirate [17]. Perhaps in the future we can use liver biopsies and bone marrow aspiration to study whether there is a link between iron and FBG.

However, age was inversely related to whole blood iron levels, with significant gender differences. In particular, the whole blood iron levels in men over 60 years old showed a downward trend within the reference range, while the decrease was more obvious in women of the same age group. This supports existing literature indicating that older women are more likely to be iron deficient than men, with a global prevalence of 15–18% [18].

For the female population, we found that there was a study that showed the dysregulation of serum iron and

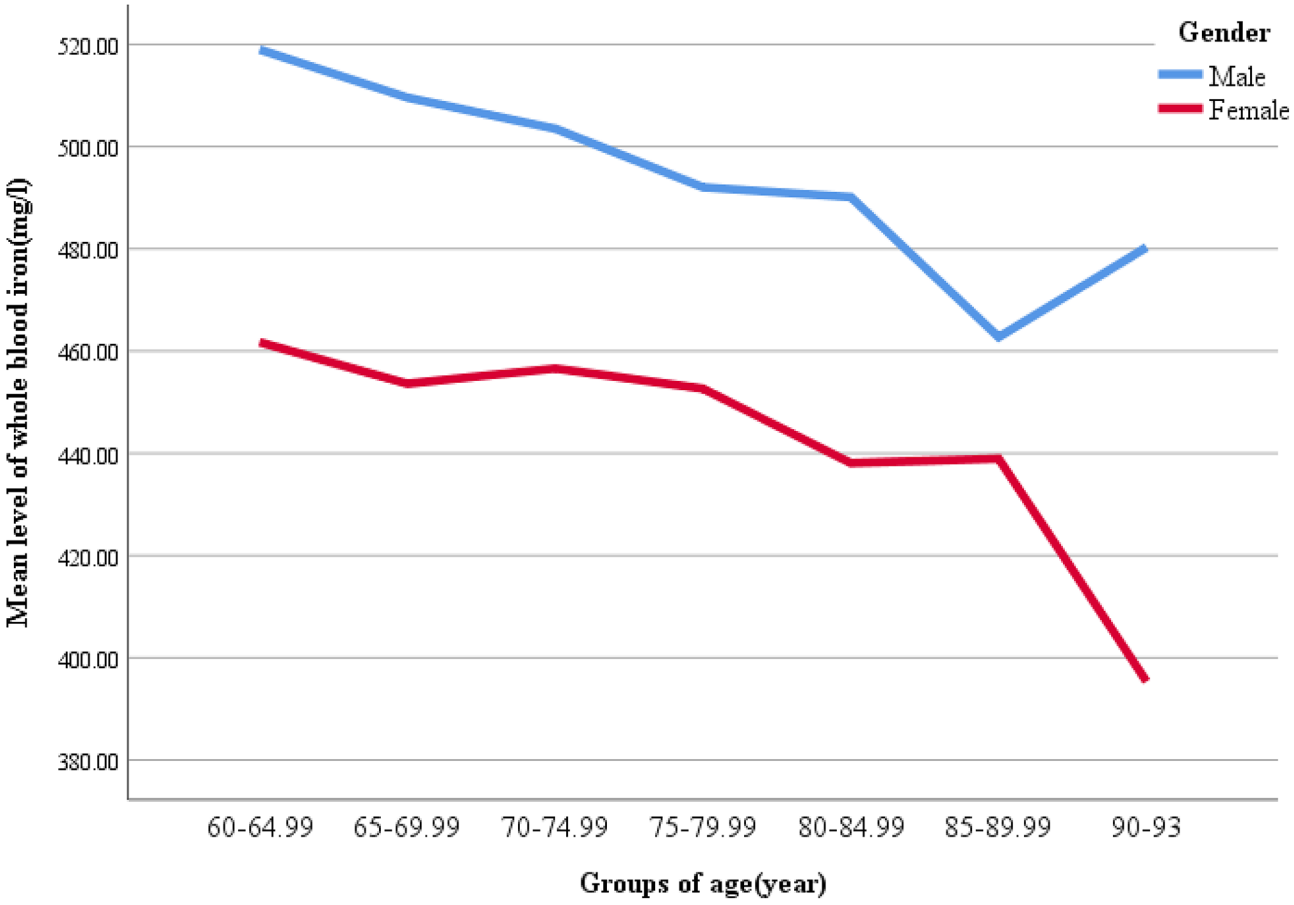

Fig. 1 The effect of age on whole blood iron content in male and female over 60 years of age. Note: Number of Persons in each group: 60-64.99: female:180; male:156, 65-69.99: female:270; male:192, 70-74.99: female:192; male:178, 75-79.99: female:92; male:111, 80-84.99: female:60; male:66, 85-89.99: female:27; male:26, 90–93: female:8; male:3

hepcidin concentrations in obesity and inflammation [19]. At the same time, relevant studies have shown that healthy obese women is associated with elevated serum hepcidin, inflammation, dyslipidemia, and depressed serum iron concentrations [20]. Whether there is a similar association between obesity and whole blood iron deserves investigation. In the future, we need to assess obesity in older women in this population and consider it as a contributing factor after controlling for obesity.

The slight elevation of whole blood iron in men aged 85–93 years old deserves our attention. Excessive iron accumulation can also lead to deposition in extrahepatic organs such as the spleen, endocrine glands, and heart [21]. Iron overload is caused by an excess of iron in the blood, which triggers ferroptosis(a form of cell death). This occurs when intracellular levels of lipid reactive oxygen species(L-ROS) levels exceed the antioxidant capacity of glutathione-dependent peroxidase(GPX4), disrupting cellular redox balance and leading to iron-induced cell death [22]. Therefore, elderly men over 85 years old in this area may need to have their heart and liver function tested at the same time. This is to prevent iron overload due to increased iron levels in whole blood, which can lead to damage to the heart, endocrine glands and liver.

Although reduced whole blood iron levels may indicate the presence of anemia, measurement of serum ferritin is the most accurate method of diagnosing iron deficiency anemia and its relationship to chronic anemia [23]. Serum ferritin levels can be determined in future studies. This was used to help verify that whole blood iron levels decrease with age, causing anemia. This may play a role in the early prevention of anemia in the elderly.

Previous studies have shown that age-dependent and sex-specific changes in tissue iron in different strains of mice. Studies show that there are significant gender differences between BALB/c and DBA/2J strains [24]. Age was considered a potential confounder that could affect the study results. Whole blood iron concentrations may vary among different age groups. To reduce the effects of gender on the relationship between whole blood iron and FBG, participants in this study were stratified by gender.

Field surveys in the Chinese communities provided valuable physical examination and highly reliable whole

blood iron data. The use of whole blood iron levels as an independent marker of short-term iron deficiency anemia risk may be useful in high-risk populations, as these groups were the primary targets of prevention strategies. Whether the association between lower whole blood iron levels and age is causal or a marker of age-related chronic disease burden associated with aging remains controversial. Findings from this region have significant implications for healthcare practice in this community.

However, the study had limitations. This study exclusively focused only on the older population in one community, which may limit the generalizability of the results. The sample size was considered insufficient given the multi-factorial nature of whole blood iron levels and the individual differences in iron levels in older adults. The impact of dietary habits on iron levels has not been thoroughly studied, so rigorous prospective studies are needed to validate the observed associations.

Conclusions

Contrary to expectations, our findings showed that whole blood iron levels were not associated with FBG in community-dwelling older adults. However, the variability of whole blood iron levels in women was greater than in men, was inversely proportional to age, and generally showed a downward trend. These results have important clinical and nursing implications, particularly in the context of micronutrient supplementation in the elderly. In the future community nursing practice, it is necessary to monitor changes in iron levels in individuals aged 60 years and above and provide educational interventions to promote timely iron supplementation, prevent iron overload, and improve the overall well-being of this population.

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Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by L. P. H., S. Z. Q. C., R. J. P., C.P.L. and M. Y. S.. The first draft of the manuscript was written by S. Z. Q. C., R. J. P. and M. Y. S..All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

Informed consent
All participants have been informed and given consent.

Conflict of interest
The authors declare that they have no competing interests.

Consent to publication
The authors affirm that human research participants provided informed consent for publication of the images in Fig. 1.

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