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Association between serum ferritin level and lipid profile among diabetic patients

A retrospective cohort study

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Abstract

High serum ferritin (SF) levels have been linked to obesity, metabolic syndrome, atherosclerosis, diabetes, dyslipidemia, and cancer. This study aimed to investigate the association between SF and dyslipidemia in adults diagnosed with diabetes mellitus. This cross-sectional study retrospectively analyzed the electronic medical records of eligible patients from 3 primary locations in Saudi Arabia namely – Abha, Khamis Mushyt, and Jeddah – from 2010 to 2020. The study included adult patients aged 18 years or older who were diagnosed with diabetes mellitus and identified with an HbA1c level of ≥6.5. This study involved 3674 participants, with males accounting for 26.6% of the total. The mean age of the studied population was 48.0 ± 18.4 years. The median [interquartile range] of SF among males was higher than females, however, this difference was not statistically significant (60.0 [23.4–125.8] vs 55.4 [24.0–113.4], $P = 0.204$). On the other hand, age and region were significantly associated with SF ($P = .032$ and 0.035). SF had a significant positive correlation with cholesterol ($r = 0.081$, $P < .001$), low-density lipoprotein cholesterol ($r = .087$, $P < .001$), and triglycerides ($r = 0.068$, $P < .001$) and negative correlation with high-density lipoprotein cholesterol ($r = –0.13$, $P < .001$). Multivariate analysis revealed that age, sex, residence, and HbA1c were significantly affecting the lipid profile. Clinicians should consider including SF testing as part of the comprehensive evaluation of patients with diabetes and dyslipidemia.

Abbreviations: BUN = blood urea nitrogen, CVDs = cerebrovascular diseases, DM = diabetes mellitus, ESR = erythrocyte sedimentation rate, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SF = serum ferritin, TC = total cholesterol.

Keywords: cardiovascular risk, cholesterol, diabetes mellitus, HDL cholesterol, hyperlipemia, iron levels, LDL cholesterol, serum ferritin, sex differences, triglycerides

1. Introduction

Dyslipidemia is a metabolic disorder characterized by elevated levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), as well as reduced levels of high-density lipoprotein cholesterol (HDL-C).[1] Dyslipidemia is the leading cause of morbidity and mortality worldwide, as they have the potential to impair endothelial function.[2] Although dyslipidemia may not exhibit symptoms at its onset, it can play an important role in cardiovascular diseases such as coronary heart disease and stroke.[2] Increased levels of TC, LDL-C, and TC/HDL-C ratio, along with reduced levels of HDL-C, are strong indicators of coronary heart disease.[3] Furthermore, dyslipidemia was found to be associated with various disorders, such as obesity, hypertension, and type 2 diabetes.[4–6] Zheng et al[7] found that high levels of LDL-C caused 1.47 and 1.41 times more deaths and disability-adjusted life-years globally in 2019 compared to 1990. The rates were higher in males and increased with age, with Eastern Europe having the highest rates. High-income North America, however, experienced a decrease in risk. Moreover, the authors found a positive correlation between the age-standardized rate and the sociodemographic index.

It is important to identify patients who require treatment for dyslipidemia, as the condition typically presents them with no

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Patient consent was not required as this study was based on retrospectively available data.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The ethical approval for this study was granted by the Research Ethics Board of the University of King Khalid (ECM#2021-4405).

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symptoms. All adults above the age of 21, as well as those with additional risk factors, such as a family history of early cerebrovascular diseases (CVDs) and severe dyslipidemia, should undergo a fasting lipid test every 4 to 6 years to screen for dyslipidemia.[8] This test measures levels of TC, triglycerides, HDL-C, LDL-C (calculated using the Friedewald equation or done directly when triglyceride level is below 400 mg/dL), and non-HDL-C.[9,10] The 2018 guidelines from the American Association of Clinical Endocrinologists and American College of Endocrinology suggest that individuals with atherosclerotic CVDs should be placed in the extreme risk category, and their target LDL-C level should be set at 55 mg/dL or lower. In addition, patients with diabetes, stage 3 or 4 chronic kidney disease, heterozygous familial hypercholesterolemia (heFH), or a history of premature atherosclerotic CVDs (men under 55 years, women under 65 years) are also considered to be at high risk.[10]

Saudi Arabia ranks second in the Middle East and seventh worldwide in terms of the prevalence of diabetes mellitus.[11] In Saudi Arabia, research was conducted among individuals aged 30 to 70 years. Out of the 16,917 survey respondents, 4,004 individuals (23.7% of the population) had been diagnosed with diabetes.[12] However, Saudis have a higher prevalence rate of diabetes ranging from 26.0 to 61.8%.[13,14] It is essential to screen for diabetes and its complications including dyslipidemia. The International Diabetes Federation emphasizes lifestyle modifications like increased physical activity and adopting a healthy diet as effective measures to prevent or delay the onset of DM and associated dyslipidemia.[15]

Iron is an essential mineral for human health. However, too much iron can be harmful to the cells and cause disease by promoting oxidative stress and pathogenic catalytic processes.[16] When body consume iron-rich foods, it is absorbed through the small intestine and transported to the tissues that need it through transferrin. Any excess iron is stored as ferritin, which is a clinical biomarker for assessing iron status and controlling iron homeostasis.[17,18] Ferritin is an acute-phase protein that increases when there is tissue injury or inflammation.[19] Elevated iron levels could affect cholesterol levels and worsen cardiovascular disease or increase its risk by increasing pro-inflammatory cytokines, lipid oxidative stress, and other processes.[20] High serum ferritin (SF) levels have been linked to obesity, metabolic syndrome, atherosclerosis, diabetes, dyslipidemia, and cancer.[21,22] Additionally, dietary iron intake affects ferritin levels, and some research suggests that a higher total dietary iron level may be associated with an increased risk of CVDs and cancer mortality.[23]

Li et al[24] examined the link between SF levels and dyslipidemia in American adults. They found that dyslipidemia was highest in the fourth quartile of SF in both males and females. The risk of high TC and high LDL-C increased progressively in both genders, but the risk was higher in females. The study also found a significant association between total daily iron intake and dyslipidemia, and with high-triglycerides dyslipidemia in females.

It is crucial to understand the association between ferritin levels and lipid profile in identifying individuals who are at risk of dyslipidemia and related metabolic disorders. By discovering this association, clinicians can evaluate the cardiovascular risk profile of diabetic patients more effectively and implement targeted interventions to reduce the risk of metabolic syndrome and CVDs. This study aimed to investigate the association between SF levels and dyslipidemia in diabetic patients. Therefore, the primary objective of this investigation was to examine the relationship between SF levels and lipid profile among patients with diabetes, given their increased susceptibility to metabolic syndrome and CVDs. Additionally, we explored differences in ferritin levels among male and female diabetic patients.

2. Materials and methods

2.1. Study design

This cross-sectional study included electronic medical records of all eligible patients from 2010 to 2020. The data were collected from 3 main locations in Saudi Arabia namely Abha, Khamis Mushyt, and Jeddah. We included adult patients aged 18 years or above with DM as indicated by HbA1c ≥ 6.5. We excluded pregnant females, those patients using antihyperlipemia drugs, and those with high C-reactive protein. The SF and blood lipid values which we utilized in this study were derived from the existing datasets.

2.2. Sample size calculation

Using G*power software, we determined the minimum required sample size to be 3321 based on the following assumptions: a power of 95%, an alpha error of 0.05, the null hypothesis set at 0, and the alternative hypothesis at 0.06. (correlation between SF and lipid profile).

2.3. Studied outcomes

The dependent variable was the lipid profile including cholesterol, triglycerides, LDL, and HDL. The predictors were SF, age, sex, blood pressure, and complete blood picture profile.

2.4. Data collection

From the records, we collected the following data: systolic and diastolic blood pressure; complete blood count (platelet count, total leukocytic count, basophils, eosinophils, lymphocytes, monocytes, neutrophils, hemoglobin, red blood cell count (RBCs), reticulocyte distribution width, mean corpuscle hemoglobin, mean corpuscle hemoglobin concentration, mean corpuscle volume) lipid profile (cholesterol, triglycerides, cholesterol/HDL, HDL-C, LDL/HDL, LDL-C), HbA1c %, erythrocyte sedimentation rate (ESR), C-reactive protein, blood urea nitrogen (BUN), blood urea, SF, and serum iron.

2.5. Study confounders

The potential confounders in this study encompass age, sex, blood pressure, components of the complete blood count, HbA1c %, markers of inflammation (ESR), renal function markers BUN, and serum iron levels. These factors may influence both SF levels and lipid profiles, thereby potentially confounding the association between SF and lipid profile among diabetic patients.

2.6. Statistical analysis

We used R version 4.2 for doing statistical analysis. Categorical variables were summarized using frequencies and percentages, while quantitative variables were described using mean and standard deviation. In cases where the data were skewed, median and interquartile range were utilized instead. Spearman correlation was used to test the correlation between nonnormally distributed data, while Pearson correlation was utilized for normally distributed data. The Kruskal-Wallis test and the Mann–Whitney *U* test, nonparametric statistical tests, were used to analyze differences between groups when the assumptions of parametric tests were violated. Wilks' Lambda, a multivariate statistical test, was used to assess the significance of the overall relationship between age, gender, residence, SF (predictors), and the dependent variables (LDL-C, HDL-C, cholesterol, and triglycerides). Levene's Test of Equality of Error Variances was used to see if the variances of the residuals (or errors) were roughly equal across groups.

2.7. Ethical approval

This study was conducted under the approval of the ethical committee of King Khalid University (ECM#2021-4405), adhered to stringent ethical standards in accordance with the Declaration of Helsinki. Data analysis was carried out with a commitment to anonymity, where all personal identifiers were carefully removed, and participants' confidentiality was strictly maintained.

3. Results

Table 1 presents a comprehensive overview of data collected from a sample of 3674 individuals, categorized by region, gender, and age. Most of the population hailed from Jeddah, comprising 2810 individuals (76.5%), followed by Khamis Mushyt with 544 individuals (14.8%), and Abha with 320 individuals (8.7%). Males constituted 26.6% of the sample, totaling 977 individuals. The mean age of the studied population was 48.2 ± 18.4 years. Table 1 presents various laboratory test findings.

Table 2 shows that the median [interquartile range] level of SF level was higher among females compared to males 60.0 [23.4–125.8] versus 55.4 [24.0–113.4], however, this difference was not statistically significant $P = .204$. On the other hand, age and region were significantly associated with SF ($P = .032$ and 0.035). Interestingly increasing in HbA1c level was significantly associated with SF.

Table 3 presents the correlation coefficients (r) and their corresponding P values, indicating the correlations between SF and various other variables. SF showed a weak positive correlation with cholesterol ($r = 0.081$, $P < .001$), LDL-C ($r = 0.087$, $P < .001$), triglycerides ($r = 0.068$, $P < .001$), ESR ($r = 0.065$, $P < .001$), and BUN ($r = 0.103$, $P < .001$). There was an intermediate positive correlation between SF and serum iron ($r = –0.316$, $P < .001$). However, SF showed a statistically negative correlation with HDL-C ($r = –0.126$, $P < .001$), platelets ($r = –0.190$, $P < .001$), and transferrin ($r = –0.426$, $P < .001$).

Figure 1 illustrates a significant positive correlation between SF and triglycerides, LDL-C, and TC, alongside a negative correlation with HDL-C, observed across both male and female participants.

Among males, SF showed a statistically significant association with triglycerides ($r = 0.05$), LDL-C ($r = 0.09$). On the other hand, SF and HDL-C showed negative correlation ($r = –0.11$) (Fig. 1A). Among females, SF and cholesterol showed a positive correlation ($r = 0.09$). SF and LDL-C had positive correlation ($r = 0.09$). Furthermore, SF and triglycerides were positively correlated ($r = 0.05$). On the other hand, SF and HDL-C had a negative correlation ($r = –0.11$) (Fig. 1B).

The Wilks' Lambda test of the overall model is significant ($P < .0001$), indicating that the overall model is statistically significant. Age, sex, residence, and HbA1c significantly affected the lipid profile (Table 4).

4. Discussion

4.1. The study main findings

In this study, our objective was to assess the association between SF and dyslipidemia among patients with diabetes in Saudi Arabia. SF levels were higher among men compared to women; however, no statistically significant difference was observed across genders. We found a significant positive correlation between all components of the lipid profile (cholesterol, LDL, and triglycerides), with the SF level. Conversely, HDL exhibited a significant negative correlation with SF. Additionally, except for cholesterol level among males, there was a significant association between ferritin and different components of the lipid profile across genders. In multivariate analysis, ferritin emerged as a significant predictor of cholesterol, LDL, HDL, and triglycerides.

Table 1

Sociodemographic characteristics of patients with diabetes mellitus (N = 3674).

Variables	Level	Mean ± SD	Median [q1–q3]
Region	Jeddah	2810 (76.5%)	
	Khamis Mushyt	544 (14.8%)	
	Abha	320 (8.7%)	
Gender	Female	2697 (73.4%)	
	Male	977 (26.6%)	
Age (years)		48.2 ± 18.4	49.0 [35.0–62.0]
Blood pressure	Systolic (mm Hg)	136.0 ± 20.1	132.0 [121.0–149.0]
	Diastolic (mm Hg)	78.6 ± 10.3	80.0 [71.0–85.0]
CBC	Platelet count ($\times 10^3/\mu L$)	288.2 ± 81.1	279.0 [234.0–331.0]
	Total leucocytic count ($\times 10^3/\mu L$)	7.2 ± 2.3	6.9 [5.6–8.5]
	RBCs ($\times 10^6/\mu L$)	4.7 ± 0.5	4.7 [4.4–5.1]
	Hematocrit (%)	38.4 ± 4.2	38.6 [35.9–41.2]
	Hemoglobin (g/dL)	12.8 ± 1.6	12.8 [11.8–13.9]
	MCH (pg)	27.1 ± 2.9	27.6 [25.7–29.0]
	MCHC (g/dL)	33.2 ± 1.6	33.3 [32.2–34.3]
	MCV (fL)	81.5 ± 7.1	82.5 [78.2–86.0]
	RDW (%)	14.5 ± 2.0	14.0 [13.2–15.1]
Lipid profile	Cholesterol (mg/dL)	193.0 ± 46.0	190.0 [160.0–220.0]
	LDL-C (mg/dL)	121.2 ± 41.7	117.0 [91.0–147.0]
	Triglycerides (mg/dL)	153.9 ± 84.7	136.0 [101.0–184.0]
	HDL-C (mg/dL)	49.1 ± 13.2	47.0 [40.0–57.0]
Iron profile	Serum iron (µg/dL)	70.4 ± 30.1	68.0 [49.2–88.0]
	Serum ferritin (ng/mL)	88.9 ± 56.4	116.0 [24.0–108.5]
	Transferrin (mg/dL)	270.9 ± 83.7	265.5 [231.5–301.2]
	Blood urea nitrogen (mg/dL)	48.2 ± 8.7	49.0 [35.0–48.2]
HbA1c		8.8 ± 1.6	8.4 [7.6–9.7]

CBC = Complete blood count, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, q1 = first quartile, q3 = third quartile, RDW = red cell distribution width.

Table 2

association between serum ferritin and different factors including diabetes control.

Variable	Level	N	Median	q1	q3	*P*
Region	Abha	320	59.5	24.4	140.7	.035*
	Khamis	544	64.5	25.7	125.0	
	Jeddah	2810	54.1	23.8	112.9	
Sex	Female	2697	60.0	23.4	125.8	.204†
	Male	977	55.4	24.0	113.4	
Age (years)	18–	532	53.2	20.5	23.2	.032*
	30–	797	49.7	21.1	102.8	
	40–	555	56.6	23.9	124.0	
	50–	658	54.3	24.5	117.5	
	60–	108	58.9	20.6	128.4	
	70–	61	46.7	163.4	97.6	
	Above 70 years	407	63.8	27.7	132.0	
HbA1c	<7	168	48.5	19.6	101.6	.001*
	7–	2697	53.8	23.3	110.3	
	≥10	809	68.1	29.5	142.2	

HbA1c = hemoglobin A1c, q1 = first quartile, q3 = third quartile.

* Kruskal-Wallis test.

† Mann–Whitney *U* test.

Table 3

Correlation between serum ferritin and different laboratory parameters.

		Age	SBP	DBP	Platelets	RBCs	WBC	Cholesterol	LDL chol	TG	HDL chol	Transferrin	Hb A1c	BUN	S. iron	ESR
Ferritin	r	0.019	0.031	0.029	−.190	.040	−0.014	.081	.087	.068	−.126	−.426	.089	.103	.316	.065
	P	.246	.084	.110	.0001	.015	.387	.0001	.0001	.0001	.0001	.0001	.0001	.0001	.0001	.518

BUN = blood urea nitrogen, DSP = diastolic blood pressure, ESR = erythrocyte sedimentation rate, RBCs = red blood cells, SBP = systolic blood pressure, TG = triglycerides.

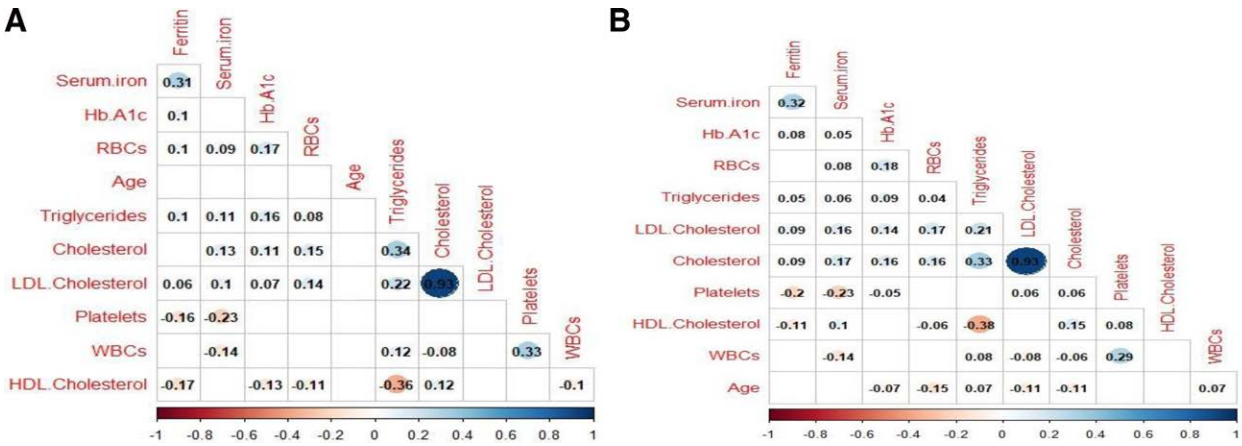

Figure 1. The correlation between ferritin and different lipid profile components among males (A) and females (B).

4.2. Interpretation of the study findings

4.2.1. Age and sex. SF is widely recognized as a marker of iron reserves in the body and serves as an acute-phase protein, influenced by dietary iron intake.[25] Previous studies have consistently shown that elevated SF is associated with an increased risk of cardiovascular disease.[26,27] Moreover, heightened ferritin levels have been associated with dyslipidemia,[28] elevated blood glucose, fasting insulin levels,[29] and have been identified as a predictor for the development of type 2 diabetes.[30,31] In this study, we found that age was significantly associated with SF. In the same vein, the findings of Cankurtaran et al[32] study suggest that ferritin levels may increase with aging. This is a component of the ongoing asymptomatic chronic systemic inflammatory state known as inflammaging. In our study, despite observing higher SF levels among females, we did not identify a statistically significant association between SF levels and gender. This finding contrasts with the results of a study conducted by Han et al[33] which reported a significant difference in SF levels between male and female diabetic patients. Specifically, the study by Han et al found that SF levels were tripled in male diabetic patients compared to females. This discrepancy in findings may stem from variations in study populations, sample sizes, or other factors influencing SF levels in different contexts. It is essential to consider these factors when interpreting and comparing results across studies.

4.2.2. Diabetes control and ferritin level. We found a significant association between HbA1c, a proxy of diabetes control, and SF. Higher HbA1c levels were significantly associated with higher ferritin levels. This association could imply potential links

Table 4

Multivariate analysis of factors associated with lipid profile parameters.

Source	Dependent variable	F	*P*
Corrected model	Cholesterol	15.678	.0001
	LDL cholesterol	13.329	.0001
	Triglycerides	9.395	.0001
	HDL cholesterol	29.511	.0001
Intercept	Cholesterol	1180.668	.0001
	LDL cholesterol	524.484	.0001
	Triglycerides	93.099	.0001
	HDL cholesterol	1333.595	.0001
Age (years)	Cholesterol	13.667	.0001
	LDL cholesterol	16.944	.0001
	Triglycerides	11.686	.001
	HDL cholesterol	1.752	.186
Sex	Cholesterol	1.206	.272
	LDL cholesterol	0.119	.730
	Triglycerides	1.16	.281
	HDL cholesterol	0.587	.444
HbA1c	Cholesterol	63.471	.0001
	LDL cholesterol	47.136	.0001
	Triglycerides	45.415	.0001
	HDL cholesterol	2.323	.128
Ferritin	Cholesterol	17.957	.0001
	LDL cholesterol	22.604	.0001
	Triglycerides	11.633	.001
	HDL cholesterol	54.564	.0001
Region	Cholesterol	2.252	.105
	LDL cholesterol	0.868	.420
	Triglycerides	0.373	.688
	HDL cholesterol	66.007	.000
Sex × region	Cholesterol	1.116	.328
	LDL cholesterol	0.42	.657
	Triglycerides	0.246	.782
	HDL cholesterol	0.262	.770

HDL = high-density lipoprotein, LDL = low-density lipoprotein.

between glycemic control and iron metabolism, which could be explored further in the context of diabetes management and its complications. Indeed, several studies have suggested a potential association between elevated body iron stores and serum insulin levels[34] as well as glucose levels.[29] These findings imply a possible role of iron metabolism in glucose homeostasis and insulin regulation, which could have implications for conditions such as diabetes and metabolic syndrome.

4.2.3. Dyslipidemia. Dyslipidemia is estimated to account for over one-third of deaths resulting from ischemic heart disease or ischemic stroke in both developed and developing countries.[35] Consequently, we investigated the potential of SF as a preventive indicator for dyslipidemia. Our findings suggest that higher SF levels were more likely to be associated with dyslipidemia in diabetic Saudi adults. The correlation coefficient ranged from 0.068 to 0.128. Higher correlation was reported by Srivastav et al.[36] Similarly, Li et al[37] (0.39 for cholesterol, 0.46 for triglycerides, 0.60 for LDL-C, and –0.60 for HDL) explored the independent relationship between SF levels and dyslipidemia. They used data from the China Health and Nutrition Survey (2009 CHNS). They concluded that the SF level was significantly associated with lipid parameters, regardless of glucose metabolism disorders and components of metabolic syndromes. Likewise Li et al[24] examined the association between SF level and dyslipidemia in American adults. Data from the National Health and Nutrition Examination Surveys before the pandemic (NHANES) were used to analyze the correlation between lipid and SF concentrations. The study found that dyslipidemia was highest in the fourth quartile of SF in both males and females. The risk of high triglycerides was 2.16 times higher in women. SF concentrations were significantly associated with dyslipidemia, and daily dietary iron intake, and it was associated with high-triglycerides dyslipidemia in females. Al Akl et al[35] explored the association between SF levels and energy metabolism abnormalities in Qatari adults. Findings show that the odds ratio of dyslipidemia increase progressively and significantly across SF quartiles, up to twofold in Q4 for women and men. Elevated SF levels were suggested as a potential risk biomarker for dyslipidemia and metabolic syndrome in adult Qatari men and women, and diabetes and insulin resistance in women only. Collectively, these studies imply a potential correlation between elevated SF levels and the prevalence of dyslipidemia in diverse populations. However, more research is warranted to elucidate the underlying mechanisms and clinical implications of this association more comprehensively.

4.3. Implications of this study

Our findings provide insights into the relationship between SF levels and a variety of factors. While gender differences in SF levels were observed, their statistical insignificance suggests that gender may not be a significant factor in SF concentration determination. Significant associations between SF levels and age, as well as region, highlight potential demographic influences on SF concentrations, emphasizing the importance of tailored approaches to understanding and managing dyslipidemia. Besides that, the significant correlation between elevated HbA1c levels and increased SF levels suggests a possible link between glycemic control and iron metabolism, which is especially important in diabetic patients. Furthermore, SF showed several correlations with lipid profile components, indicating a potential role in lipid metabolism and inflammation. Finally, the significant findings of the multivariate analysis highlight the combined impact of age, residence, and HbA1c on the lipid profile, emphasizing the multifactorial nature of dyslipidemia. These insights lay the groundwork for future research to fully understand the underlying mechanisms and clinical implications.

4.4. Strengths and limitations

To the best of our knowledge, this is one of the first few studies to evaluate the association between SF and dyslipidemia among patients with diabetes. Second, the study utilized electronic medical records spanning a decade (2010–2020) from multiple healthcare locations. However, the study had many limitations. First, the quality of retrospective electronic medical records can vary, and data may contain errors or missing values. Second, excluding pregnant women and diabetic patients on antihyperlipemia drugs can limit the generalizability of the findings to this specific population. Third, retrospective studies are susceptible to confounders and causal relationships cannot be established. Finally, we did not include factors like duration of the diseases, medication used, and comorbidities.

5. Conclusions

While females had higher SF levels than males, the difference was not statistically significant. Notably, age and region were found to be significant predictors of SF level, indicating demographic influences on iron metabolism dynamics among participants. Furthermore, the study found a significant link between elevated HbA1c levels and increased SF concentration, emphasizing the interplay between glycemic control and iron metabolism in diabetes patients. In terms of lipid profile correlations, SF had a weak positive association with cholesterol, LDL-C, and triglyceride levels. Although it showed a statistically significant negative correlation with HDL-C. The multivariate analysis confirmed this association. Clinicians should consider including SF testing as part of the comprehensive evaluation of patients

with diabetes and dyslipidemia. Furthermore, more research is needed to understand the underlying mechanisms and clinical implications of these associations to guide more targeted interventions and treatment strategies for this patient population.

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