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Effects of Smoking on Serum Ferritin levels in Adult Population Living in Sulaymaniyah, Iraq: A Retrospective Cross-sectional Study

Jihad M. Hadi[1,2,*], Shanya B. Shawkat[2], Hwda Gh. Rauf[3], Soma A. Hama Karim[2], Ayman M. Mustafa[2], Soz N. Muhammad[2], Mhamad S. Abdullah[2]

[1]Nursing Department, College of Nursing, University of Human Development, Sulaymaniyah, Kurdistan Region, Iraq.
[2]Department of Medical Laboratory of Science, College of Health Sciences, University of Human Development, Kurdistan Regional, Iraq.
[3]Kurdistan Technical Institute, Sulaymaniyah, Kurdistan Region, Iraq.
*Correspondence to: Jihad M Hadi (Email: jihad.chemist@gmail.com)
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Abstract
Objectives: The current study aims to examines the effect of smoking on serum ferritin levels of adult populations in Sulaymaniyah.
Methods: The study was conducted on 80 smokers and 20 non-smokers, totally 100 persons. Their ages ranged from 18 to 65 years.
Results: This study showed that the majority of smokers had elevated ferritin levels. A *p*-value of less than 0.05 indicated a significant difference in ferritin levels between smokers and non-smokers groups. The average ferritin level among smoker group was 227.40 mg/L, while the average ferritin level among non-smokers group was 118.3 mg/L. Regarding the associated between age groups and average ferritin levels, the average ferritin level is highest in the age groups between 51–61 years old. In addition, obesity may play a role in raising ferritin levels, people with obese conditions (BMI > 30) have the highest average ferritin levels than others.
Conclusion: This study provides evidence that smoking negatively affect serum ferritin levels, since increases in mean ferritin levels are very striking in smoking and obese group.
Keywords: Smokers, serum ferritin, BMI, Obese, Iraq

Introduction

Worldwide, smokers numbering a billion are responsible for consuming almost all of the six trillion cigarettes produced annually, with the consumption figure being 5.8 trillion. Despite the decline in smoking rates in wealthy countries, there is a growing trend of young people in developing countries embracing smoking, which has led to an increase in global cigarette consumption. While the negative effects of smoking on human health are well-established, the effects of tobacco use on the environment are not widely understood. These impacts include the growth of tobacco on land and water, the use of harmful chemicals on tobacco farms, deforestation, and carbon emissions caused by the production and transportation of tobacco, as well as the creation of non-biodegradable litter and toxic waste. Furthermore, cigarette butts' inappropriate disposal has been linked to a variety of disastrous home and wildland fires.[1]

Tobacco usage is the world's greatest cause of preventable death, causing close to six million deaths annually. In the US, tobacco usage is directly responsible for 20% of all deaths. These fatalities are a result of smoking's numerous harmful health impacts, including heart disease, cancer, lung disease, and problems with reproduction.[2]

More than 7,000 different substances can be found in cigarette smoke, at least 69 of which are carcinogenic, and many of which are hazardous to human health. The majority of tobacco's ingredients are produced when burning tobacco and paper; however, some are added during production (such as ammonia), and some are found naturally in tobacco, such as nicotine (e.g., acrolein). Benzene, 1,3-butadiene, formaldehyde, and tobacco-specific nitrosamines (nicotine-derived nitrosamine ketone or NNK, and N-Nitrosonornicotine or NNN) are among the carcinogenic substances found in cigarettes.[2]

Many volatile and semi-volatile chemical species are released when a cigarette burns or smoulders. Both the gaseous and particle phase are capable of distributing these species. The mainstream contains fresh cigarette-burning particles (CBPs) at a concentration of 10^{10} particles/cm^3. Moisture during cigarette smouldering can modify the gas-to-particle partitioning and change the chemical makeup of the emission. The 4,800 identified chemicals in cigarette smoke represent a complex chemical makeup in a highly dynamic aerosol system. The volatile and semi-volatile species are reactive, which makes it difficult to characterize the emission during cigarette smoking. For many years, researchers have also looked at how to characterize the chemical combination in both the gas and particle phase.[3]

Iron has a vital role in cells since it contributes to the formation of heme-iron-sulfur clusters within the mitochondria. These clusters are significant components of numerous proteins and enzymes that participate in essential biological functions such as respiration, metabolic reactions, host defence, and the replication and repair of nucleic acids. Iron is necessary for the synthesis of haemoglobin. Iron is necessary for life, but it also has the potential to be hazardous due to its catalytic role in oxidative stress. A crucial transport function in cell metabolism is played by the intracellular iron found in ferritin. The principal intracellular cytosolic storage protein for iron is ferritin, which releases excess iron during an iron overload and stores it during an iron deficit. The ferritin superfamily encompasses diverse iron species, while the process of oxidative phosphorylation initiates the synthesis of encapsulated iron oxide, Fe_2O_3, which sequesters ferrous iron within its core.[4] Serum ferritin (SF) is the predominant intracellular protein that securely stores iron in a soluble form. This protein is ubiquitously present in both prokaryotic and eukaryotic organisms. The aforementioned protein complex is globular in shape and comprises of 24 subunits. Its primary function is to serve as a reservoir for iron. It protects against both iron overload and deficiency in humans. It

protects against both iron overload and deficiency in humans. According to certain researcher, SF is present in large quantities in tumor cell, and raising SF levels can aid in the identification of malignant tumors.[5]

There are various factors that affect the levels of ferritin in individuals, but lifestyle choices such as diet and exercise have been linked to these levels. It is believed that factors that impair the supply of oxygen increase the synthesis and release of ferritin. However, research on the correlation between smoking and increased levels of circulating ferritin is limited. An earlier study found that older smokers had higher levels of plasma ferritin than non-smokers.

In a large cohort of over 15,000 Korean participants, higher serum ferritin levels were associated with reduced lung function attributable to cigarette smoking. Ghio et al. also discovered that smokers with and without chronic obstructive pulmonary disease (COPD) had higher levels of circulating iron, ferritin, and transferrin saturation compared to those who never smoked. The reasons for this increase remain unknown. Tobacco use, especially in the lungs, appears to raise the concentration of iron in the body. Oxidative stress and inflammation have been identified as causes of altered iron metabolism. Freely floating iron can cause toxic effects, so ferritin synthesis is induced to store iron safely.[6]

Cigarette smoking has been associated with alterations in iron balance, not only in the lungs but also in other parts of the body. Specifically, there have been reports of increased iron levels in alveolar macrophages and bronchoalveolar lavage fluid.[7] Iron plays a crucial role in several metabolic processes that are essential for life on Earth, including humans. These processes include oxygen transport, DNA synthesis, and electron transport.[8] Iron helps haemoglobin and myoglobin transport oxygen, while cytochrome C, which is primarily made up of iron, is necessary for electron transmission within the mitochondria. Smokers have higher levels of serum iron, calcium, phosphate, sodium, and potassium, which are positively associated with time and daily cigarette consumption, although total binding capacity is significantly reduced.[9]

The study aims to provide insights into the impact of smoking on ferritin levels and identify potential health risks associated with smoking-related changes in ferritin levels. By comparing the ferritin levels between smokers and non-smokers, the study intends to contribute to a better understanding of the health consequences of smoking and the importance of maintaining optimal ferritin levels.

Materials and Methods

Materials

The materials we used for the testing included needles, a tourniquet, a test tube, an alcohol pad, cotton, a cold box, and gloves. The samples were collected from the University of Human Development and Sulaymaniyah located in the center of the city. During the testing procedure, a variety of equipment and instruments were used, including a sample rack, a centrifuge, gel tubes, and the Mini Vidas enzymatic method.

Data Collection

The data was collected between December 2022 and January 2023 to evaluate serum ferritin levels in 100 individuals, including 80 smokers and 20 non-smokers. At the beginning of the study, we obtained permission from the participants to collect their samples. We also asked them about their daily cigarette consumption and the duration of their smoking habits. The samples were withdrawn from the cubital vein using gel tubes (yellow tubes) with clot activators. The serum was then separated from the cells by centrifugation for 10 minutes and stored at a low temperature.

Laboratory Testing Determination on Serum Ferritin

First of all, 80 serum sample were collected from smoker people, and 20 serum sample were collected from non-smoker people, which smoker aged between (18–65) and healthy non-smoker people aged between (18–45), in the Mini Vidas device the normal range of male was between (30–350) mg/ml and for female was between (20–250) mg/ml.

Results

In this study, 100 patients were documented. Generally, some disease such as heart disease, diabetes mellitus, hypertension, kidney and liver disease are found in some patients tested for ferritin.

The 100 participants were divided into two groups: the smoker group (80 patients), which accounted for approximately 80% of the total, and the non-smoker group (20 patients), which made up approximately 20%. Figure 1 shows that the average serum ferritin level was higher in the smoker group (227.40) than in the non-smoker group (118.3). In terms of gender, 83 were male and 17 were female (Table 1).

The age range of participants was between 18 and above 62 years, with the majority (40%) being between 18 and 28 years old, and the mean age being 36.4 years. The highest average serum ferritin level was observed among participants aged between 51–61 years (373.84), while the lowest average ferritin level was recorded among those aged between 18–28 years (Table 1).

All participants' body mass index (BMI) was calculated, and the average serum ferritin level was found to be higher among the obese group (BMI > 30) compared to other groups (257.4). The lowest level of ferritin was recorded among underweight groups (BMI below 18) (Figure 2).

As per the findings presented in Table 2, the *t*-test, Two-Sample Assuming Unequal Variances, indicated a noteworthy distinction in the ferritin level between individuals who smoke and those who do not, with a *P*-value below 0.05. The null

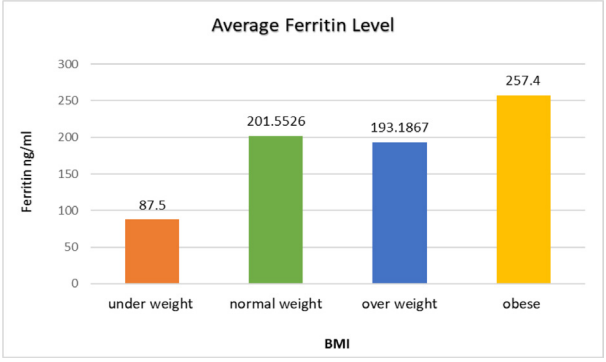

Fig. 1 **The variation of ferritin levels along with statements for the whole 100 patients.**

Table1. **Demographic characteristics of smokers and non-smokers, including serum ferritin level, gender, age level, and BMI**

Statement	Patients no.	% ($n = 100$)	Average ferritin levels
Smoking status			
Smoker	80	80%	227.40
Non-smoker	20	20%	118.3
Age level			
18–28	40	40%	144.40
29–39	22	22%	198.78
40–50	19	19%	191.28
51–61	15	15%	373.84
Over 62	4	4%	291.7
Body Mass Index (BMI)			
Underweight (< 18)	1	1%	87.5
Normal weight (18–24.99)	38	38%	201.55
Overweight (25–29.99)	45	45%	193.18
Obese (> 30)	16	16%	257.4
Normal			
Smoker	61	76%	154.19
Non-smoker	19	95%	123.70
Increased			
Smoker	18	18%	487.26
Non-smoker	0	-	-
Decreased			
Smoker	1	1%	15.6
Non-smoker	1	1%	15.6
Gender			
Male	83	83%	202.53
Female	17	17%	220.47

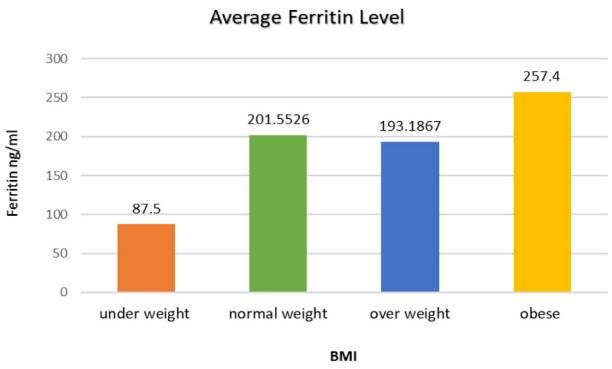

Fig. 2 **The level of ferritin in the patients according to the BMI.**

hypothesis (H0) was rejected and the alternative hypothesis (H1) was accepted based on the *t* stat of 4.56 being greater than the two-tailed value of 1.98.

Table 2. ***t*-Test: Two-sample assuming unequal variances for smokers and non-smokers**

Serum ferritin	Smoker	Non-smoker
Mean	227.40	118.3
Variance	28981.25	4191.68
Observations	80	20
Difference	0	
df	82	
t-stat	4.56	
$P(T <= t)$ one-tail	8.77×10^{-6}	
t critical one-tail	1.66	
$P(T <= t)$ two-tail	1.75×10^{-5}	
t critical two-tail	1.98	

Table 3. ***t*-Test: Two-sample assuming equal variances (relationship between smoking rate versus serum ferritin)**

	Smoking rate	Serum ferritin
Mean	25.31	227.40
Variance	258.77	28981.25
Observations	80	80
Pooled variance	14620.01	
Difference	0	
Df	158	
t stat	–10.57	
$P(T <= t)$ one-tail	2.18×10^{-20}	
t critical one-tail	1.65	
$P(T <= t)$ two-tail	4.35×10^{-20}	
t critical two-tail	1.97	

Table 3 demonstrates the *t*-Test: Two Sample Assuming Equal Variances, which was conducted to determine the relationship between smoking rate and serum ferritin level. The null hypothesis (H0) was rejected, and the alternative hypothesis (H1) was accepted, as the *t* stat of –10.57 was much smaller in magnitude than the absolute value of the two-tailed value of the *t*-distribution with the appropriate degrees of freedom, and the *P*-value was less than 0.05.

Figure 3 shows that among all 100 participants, 73% did not have any comorbid disease, while diabetes mellitus and hypertension were equally distributed among 7% of participants. Kidney disease accounted for approximately 6% of the total, while liver and heart disease were found in 3% of participants equally.

Discussion

Iron plays a crucial role in various essential functions of our body. It is required for the production of red blood cells and for energy production in muscle and heart cells. However, iron can be toxic when it generates free radicals that can harm tissues and cells. To prevent this, the body has special proteins

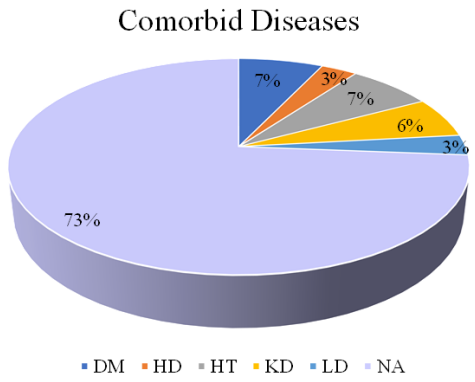

Fig. 3 **Percentage of comorbid diseases of all 100 patients.**

like ferritin that store and deliver iron securely to where it is needed.[10] Moreover, ferritin also contributes to the immune response and increases during diseases such as chronic inflammation, infection, and cancer.[11]

Several studies have shown that increased serum ferritin levels are associated with inflammatory diseases, chronic kidney disease, autoimmune diseases, acute infections, cancer,[11] chronic anemia,[12] type 2 diabetes,[13] metabolic syndrome,[14] atherosclerosis,[15] patients with fatty liver disease,[15] hemophagocytic syndrome,[10] Still's Disease,[11] and coronavirus infectious.[16]

Our study found a strong association between increased serum ferritin levels and smoking among smokers compared to non-smokers. This is because smoking contains free radicals that lead to oxidative stress, which, in turn, increases the level of serum ferritin among smokers.[17] Smoking remains a major hazard for premature mortality, and the tobacco epidemic is a significant threat to public health, causing over 8 million fatalities annually, including 1.2 million due to exposure to secondhand smoke. Nicotine, an addictive substance found in tobacco, increases the risk of numerous debilitating medical conditions, such as over 20 types or subtypes of cancer, cardiovascular and respiratory diseases, and many others.[18]

A study in Korea investigated the correlation between smoking and serum ferritin levels in the adult population, revealing that rising serum ferritin levels were strongly linked to smoking and lung function.[7] This finding is supported by various other studies. However, this study has limitations, such as a small number of smokers enrolled and some smokers having a disease that affects the serum ferritin level. In addition, other iron-related indicators, such as serum iron, transferring, or CBC tests, were not included in the study. The samples were only collected from healthy individuals who were not hospitalized, except for the elderly who had some illnesses. Further prospective research is necessary to verify and clarify these findings.

Conclusion

In conclusion serum ferritin is a crucial clinical biomarker that can be used to assess iron status. Our study provides evidence that smoking has a deleterious impact on serum ferritin levels, as seen by the significantly increased mean ferritin levels in the smoking and obese groups. Furthermore, our findings suggest that the number of cigarettes smoked may directly affect serum ferritin levels, with higher cigarette consumption resulting in higher serum ferritin levels and negative health consequences. These results emphasize the importance of smoking cessation interventions to improve overall health and prevent iron-related disorders.

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Institutional Review Board Statement

The current retrospective cross-sectional work was approved by the ethics committee of the University of Human Development and informed consent was waived.

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Conflicts of Interest

The authors declare no conflicts of interest.

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