Egyptian Journal of Medical Research
Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Serum ferritin and changes in pulmonary functions in Egyptian smokers

Shaban Mohammed Ramadan [1], Neveen Ahmed Youssef [2], Basma Abutaleb Mostafa [1*], Noha Mahmoud Fahmi [1]

[1] *Chest diseases department, Faculty of Medicine, Beni-Suef University, Beni-Suef 62511, Egypt*

[2] *clinical and chemical pathology department, Faculty of Medicine, Beni-Suef University, Beni-Suef 62511, Egypt*

Article Info

Corresponding Author:
Basma Abutaleb Mostafa
bassmaabutaleb@gmail.com

Keywords
Serum ferritin, pulmonary functions, Egyptian smokers.

Abstract

Background: Ferritin is a crucial regulator of iron homeostasis and can contribute to oxidative tissue damage. Elevated ferritin levels may indicate inflammatory processes. Tobaccocan affect ferritin concentrations, potentially causing airway inflammation. High ferritin levels in smokers may be linked to emphysema and lung cancer. **Objectives:** This study aimed to investigate the possible relationship between serum ferritin and changes in pulmonary function in Egyptian cigarette smokers. **Methods**: This Cross-sectional prospective study was conducted in Beni-Suef university hospital, department of chest diseases from September 2022 to March 2023. **Results:** The study found significant positive correlations between ferritin levels, age, smoking years, daily cigarette consumption, height, BMI, Hb, and TLC.

Conclusion: we identified significant positive correlations between Ferritin levels and Age, Smoking years, number of cigarettes per day, Smoking Index, BMI, Hb and TLC. In contrast, there were significant negative correlations between Ferritin and FEV_1, FVC, FEV_1/FVC ratio, FEF_{25-75}, and SO_2. Weight and Hct did not exhibit any significant correlations with Ferritin.

1. Introduction:

Ferritin, an essential component, controls the body's iron homeostasis. A number of studies have shown that ferritin, despite its ubiquitous role in regulating in vivo iron metabolism, generates free radicals, which may cause oxidative tissue damage [1]. An elevated ferritin level might be a reliable indicator of inflammation, as it is thought to reflect both short-term and long-term inflammatory processes. Cigarette smoking may affect the levels of alveolar and systemic ferritin because tobacco contains a significant amount of iron (440–1150 µg/g). Elevated ferritin levels in lung tissue may facilitate airway inflammation [2]. According to research by Nelson and colleagues [3], who used the broncho-alveolar lavage test, smokers' extracellular ferritin concentrations were higher than nonsmokers'. This suggests a possible association between elevated ferritin levels and lung cancer and emphysema.

There has been little investigation into ferritin's impact on lung function; nevertheless, it is still unknown how ferritin affects pulmonary function in those who do not smoke. Epidemiologic studies evaluating ferritin's effect on lung function found conflicting results [4].

2. Patient and methods:

2.1. Patients:

This cross sectional study was conducted at the Beni-Suef University Hospital Department of Chest Diseases. The study ran from September 2022 to March 2023. We calculated the sample size using G Power Version 3.1.9.2, and the study should include at least 34 patients. We approached the administrative authorization and the Beni-Suef University Ethical Committee for ethical approval. All participants were required to sign an

informed consent form. We assured the participants that we would securely store and keep their information anonymous. We also communicated the research's goals and methods to them. Ethical Committee Approval number was (FMBSUREC/11092022/Mostafa).

2.2. Criteria of inclusion and exclusion:

Inclusion criteria: Adult male smokers more than 18years old

Exclusion criteria: Smokers <18years old**.** Subjects with clinical conditions that may affect serum ferritin level as follow: Active malignancy**,** Active tuberculosis or pneumonia**,** Hepatitis B or C**,** Hyperthyrodism**,** Rheumatoid arthiritis**,** Bleeding tendancy

2.3. Methods

The study was conducted on 40 adult male Egyptian smokers who were admitted to chest department in Beni-Suef university hospital for different causes. History was taken in the form of name, age , smoking history, Anthropometric variables such as height and weight were measured by a trained medical personnel, Body mass index (BMI) was calculated as kg/m^2, and was categorized into four groups (underweight <18.5 Kg/m^2, healthy weight 18.5-24.9 Kg/m^2, overweight 25-29.9 Kg/m^2 and Obese >30Kg/m2) [5].

2.3.1. All patients included in the study were subjected to

1. Laboratory investigations: CBC, serum ferritin leveL

   Ferritin level was meaured by using cobas e 411(rack system) Device SN 56k9-30 by electrochemiluminescence Which combines electrochemical reactions and luminescence, converting electrical energy to light.
2. Pulse oximetry
3. Pulmonary function test

Spirometry was done by Spirolab spirometer MIR via del Maggiolino125 00155 Roma-Italy

The patient stood straight during the whole evaluation. We connect the spirometry equipment to a plastic mouthpiece and fasten a clamp to the patient's nose. The next step is to have him tightly clamp his lips over the mouthpiece as he takes a large breath in and then quickly and forcefully lets it out [6].

2.3.2. Obstructive lung disease (OLD) is concluded when:

1. decreased FEV_1
2. Normal FVC
3. The ratio of forced expiratory volume in 1 second (FEV_1) divided by forced vital capacity (FVC) of <70%based on

the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria

2.3.3. Degree of FEV_1 impairment (obstruction) defined as (**Pellegrino R et al.,2005).**

- mild: FEV_1 ≥80% predicted
- moderate: 50% ≤ FEV_1 <80% predicted
- severe: 30% ≤ FEV_1 <50% predicted
- very severe: FEV_1 <30% predicted.

2.3.4. Restrictive lung disease (RLD) is defined as:

1. FVC<80% predicted
2. FEV_1 decreased
3. FEV_1 /FVC ratio normal

2.4. Ferritin level measurement:

We collected blood samples from participants who had fasted for 12 hours the previous night. We used a Plan vacutainer to collect three milliliters of blood and let it coagulate. We then used centrifugation for 10 minutes at 3000 rpm to separate the serum. Koorts AM et al. [8] observed that ferritin levels in men typically vary from 30 to 300 ug/mL.

2.5. Statistical analysis:

data were encoded into the Windows - based SPSS statistical program, version 22. and analyzed. We used percentages and frequencies to characterize the qualitative characteristics. In order to characterize the quantitative variables, the mean and standard deviation (mean ± SD) were used. For this purpose, we compared qualitative variables using the chi-square (x^2) test. student T test for numerical data, and Person's correlation coefficient for correlations .

3.Results:

Table (1): Demographic information in the studied group

	(N=40) Mean±SD	(N=40)**Range**
Age (years)	54.72± 15.69	24-76
Wight (kg)	74.15±11.59	55-96
Hight(Cm)	168.15±6.9	155-196
BMI(Kg/m^2)	25.92±3.55	20_33

Table (2): smoking history in the studied group

	(N=40) Mean±SD	**Range**
Smoking years	25.82±13.13	4-50
Smoking index	635±436.31	60-1800
N-of cig/day	24.02±11.29	(6-60)

Table (3): forced expiratory volume in 1 second and forced vital capacity in all subjects (mean±SD)

	Studied group (N=40)
FEV_1% predicted	50.02±24.99
F VC % predicted	61.75±20
FEV_1/F VC Ratio	64.95±18.2

Table (4): Impairment of forced expiratory volume in 1 second in the studied group

	Studied group (N=40)
Impairment	
Mild	7(17.5%)
Moderate	8(20%)
Sever	15(37.5%)
Very sever	10(25%)

Table (5): Laboratory data in the studied group

	Studied group (N=40)Mean±SD
Ferritin(ng/ml)	298.92±61.81
Hb (g/ dl)	12.92±1.40
Hct (%)	38.2±5.09
Tlc(cmm)	8.27±2.97
SO_2(%)	92.32±1.81

Table (6): Correlation between ferritin and different parameters

	Ferritin	
	Pearson Correlation	P. Value
Age	0.705	<0.0001*
Smoking years	0.685	<0.0001*
Number of Cigarettes per day	0.479	0.0018*
Smoking Index	0.664	<0.0001*
Weight	0.262	0.1023
Height	0.359	0.0228*
BMI	0.621	<0.0001*
FEV_1	-0.350	0.027*
F VC	-0.402	0.0102*
FEV1/FVC ratio	-0.386	0.008*
Hb	0.699	<0.0001*
Hct	-0.199	0.2182
TLC	0.729	<0.0001*
SO_2(%)	-0.816	<0.0001*

4. Discussion:

One of the most important proteins in the body for storing iron is ferritin [9]. Ferritin protects lipids, DNA, and proteins from iron's potentially damaging effects while facilitating iron's accessibility for critical cellular processes [10].

When ferritin levels fluctuate in a clinical context, it usually means that iron balance or metabolism is off [11]. A number of other disorders, including inflammatory, neurological, and cancerous ones, are now known to include ferritin [12].

The exact function of serum ferritin in the inflammatory cycle, whether as a reflection of inflammation, a cause of inflammation, or both, is still up for debate [14].

Regular tobacco use significantly increases the amount of iron that enters the lungs. The range of iron concentrations in tobacco smoke is between 440 and 1,150 µg/g.The daily iron consumption of an individual smoking 20 cigarettes is around 5.2-13.8 µg, as stated by Cloonan et al. [14].

A study by Malenica et al. [15] found that smoking cigarettes increases blood Hb levels. This might have a preventative impact on anemia. Still, as pointed out by Sankar and Villa [16], smoking may harm hematopoiesis and cause polycythemia, which affects the likelihood of anemia and its identification.

Pregnant women who smoke are more likely to experience anemia, and this habit exacerbates iron deficiency and diseases like sickle cell anemia [17]. Serum ceruloplasmin levels are lower in smokers than in nonsmokers, according to research by Cohen et al. [18]. This suggests that reactive Fe2+ may be more of a problem for smokers.

The major goal of this study was to look for any link between cigarette smoking and changes in blood ferritin levels. The study was conducted at the Beni-Suef University Hospital Department of Chest Diseases. This experiment had a total of forty individuals. In summary, our study yielded the following findings: With a correlation value of -0.35 and a P-value of 0.027, our current analysis has shown significant negative correlation between ferritin and FEV_1.

Lee J. et al., [19] demonstrated a strong association between a decrease in FEV_1% and hyperferritinemia. There was also negative relationship between serum ferritin levels and FEV_1, as shown by Gothwal SK et al. [20]. in

contrast to our results Shibata Y et al. [21], noted that serum ferritin levels may have a positive correlation with FEV_1. Ghio AJ et al. [22] also found a positive correlation between the forced expiratory volume at 1 second and serum ferritin.

We noted a negative correlations between ferritin and FVC (r = -0.402, P-value = 0.0102) in our study.

Our results are in line with those of Lee J. et al. [19], who found that hyperferritinemia is strongly associated with a decrease in FVC%. Furthermore, Kim SY et al.'s [23] found a negative correlation between serum ferritin levels and females' FVC. In addition, Gothwal SK et al. [20] discovered a significant negative relationship between serum ferritin concentration and FVC. While Brigham EP et al. [24] found no correlation between elevated ferritin levels and improved lung function. however, Shibata Y et al. [21] noted a positive correlation. Similarly, Ghio AJ et al. [22] evaluated the greatest value for FVC in mL and found a positive correlation between blood ferritin levels and FVC.

Our research revealed negative correlation between the ferritin level and FEV_1/FVC ratio (r = -0.386, p = 0.008). Ghio AJ et al. [22] also found that that serum ferritin had the most negative correlation with FEV_1/FVC. According to the FEV_1/FVC ratios, blood ferritin levels varied significantly among smokers with airway obstruction. Three categories were used to classify these ratios: >75%, 60% to 74%, and <60%. When the FEV_1/FFVC ratio was lowest, suggesting the most severe airway obstruction, serum ferritin levels were the highest. Furthermore, Kim et al. [23] found a negative correlation between serum ferritin levels and the FEV_1/FVC ratio, especially in females.

Furthermore, Gothwal SK et al. [20] demonstrated a strong negative correlation between serum ferritin levels and FEV_1/FVC ratio. These finding, which confirms a positive association between serum ferritin and airway constriction, is consistent with other studies that found an inverse relationship between serum ferritin level and the FEV_1/FVC ratio.

Our results are in line with those of the research by Lee et al. [4], which looked at a large representative sample of people and looked at how cigarette smoking correlated with lung function and serum ferritin levels. Their findings revealed that 18.61% of people were current smokers, and 21.73% smoked

more than the usual number of pack years. Anyone who has smoked, whether now or in the past, is more likely to have airway obstruction, and the risk rises in proportion to cigarette consumption.

Our results are in agreement with those of Lee et al. [19], who also found a ferritin level of 368.7 ng/mL (329.0-434.2) and a median level of 199.3 (141.5-275.5) ng/mL. Inal et al.'s [25] study also found that tobacco users had certain blood chemistry levels, such as a WBC count of 7.36±1.85 uL, a PLT of 246.62±70.17 uL, a Hb of 15.11±1.42 g/dL, a Htc of 44.76±5.45%, and a ferritin level of 82.06±65.64 ng/mL.

Ferritin levels positively correlate with a number of variables, according to our research. Age (r=0.705, P-value=0.0001), years of smoking (r=0.685, P-value=0.0001), number of cigarettes smoked per day (r=0.479, P-value=0.0018), smoking index (r=0.664, P-value=0.0001), body mass index (r=0.621, P-value=0.0001), hemoglobin (r=0.699, P-value=0.0001), and total lipoprotein (r=0.729, P-value=0.0001) are all variables that contribute to this complex.

Our results are in line with those of Ghio et al. [22], who also found that serum ferritin levels increase with aging. Smokers with airway obstruction had higher serum ferritin levels were higher in smokers who had airway obstruction. low-grade chronic inflammatory disorder, may be responsible for the increase in ferritin levels that occurs with age [26]. There is a correlation between aging and the existence of chronic, low-level inflammation [27]. Kim et al. [23] discovered a robust positive correlation between ferritin levels in serum and age, BMI in women, and number of pack-years (pack-years) in females. Researchers found a positive correlation between serum ferritin and CRP levels and BMI. The existence of inflammatory diseases associated with increased adipose tissue might explain this. The long-term buildup of cigarette smoke particles, which disturb systemic iron homeostasis, may explain the observed higher correlation between smoking years and ferritin levels. Cigarette smoke particles particularly affect the lung's iron homeostasis. Ryan et al. [28] found that individuals with a high TLC, a biomarker of inflammation, had significantly higher ferritin levels.

there is no evidence that ferritin affects lung function in previous studies [29]. Ghio et al. [22] found something similar

to what we did that oxidative stress, produced by the disruption of iron balance that smoking causes, can set off pathways that lead to COPD.

Our results are in agreement with those of Lee et al. [4], who found that men averaged 56.5 years old (43% of the total) and women 56.9 years old (57% of the total). In the 13.4% incidence of airway obstruction, there was a significant gender gap, and present or former smokers were more likely to have this condition. In terms of serum ferritin levels, the groups with airway obstruction, restrictive patterns, and normal lung function had the highest and lowest median values, respectively. In all three spirometric subgroups (normal, restrictive, and obstructive), higher median ferritin levels were associated with smoking status and quantity. There was an inverse relationship between cigarette smoking and serum ferritin levels.

5. Conclusion:

We identified significant positive correlations between Ferritin levels and Age, Smoking years, Number of Cigarettes per day, Smoking Index, BMI, Hb and TLC. In contrast, there were significant negative correlations between Ferritin and FEV_1, FVC, FEV_1/FVC ratio, and SO_2.

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