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Original article

Study of lung function test in association with laboratory findings of serum iron in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: The current cross-sectional study analyses patients' plasma iron measurements and spirometry to determine the relationship between serum iron, percent transferrin saturation, serum ferritin, total iron-binding capacity (TIBC), and forced expiratory flow (FEF 25–75%), forced expiratory volume 1(FEV1)/Forced vital capacity (FVC), FVC, and FEV1.

Methods: Spirometry measurements were assessed by comparing reference values based on age, height, sex, and race. Descriptive analysis of data included percentages, means, and standard deviations. Multivariate analyses were done using the Pearson correlation test and the multiple linear regression method.

Results: According to the findings, the average age of those who participated in the study was 59.63 ± 10.32 years old. Serum iron concentrations were shown to be extremely significant and positively correlated with the percent anticipated values of FVC, FEV1/FVC FEV1, and FEF (25–75%). The total iron-binding capacity was extremely significant and linked strongly with the percent expected values of FVC, FEV1, FEF (25–75%), and FEV1/FVC. The percent transferrin saturation was extremely significant and linked positively with the percent anticipated values of FVC, FEV1, FEF (25–75%), and FEV1/FVC.

Conclusion: Plasma iron levels were independently linked with both FEV1 and FEF (25–75%) percent predicted in the current investigation. Consequently, the blood iron concentration in COPD patients can be utilized as a biomarker for assessing disease severity because it is relatively simple and inexpensive.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a respiratory tract illness that results in decreased airflow attributable to inflammation and remodeling of the pulmonary alveoli.[1,2] COPD destroys lung parenchyma, which leads to the development of emphysema; it causes abolition of the pulmonary alveoli with increased air spaces.[3] The standard gold test for assessment of COPD is spirometry or Pulmonary function tests (PFTS). To get a COPD diagnosis, based on investigating FVC and FEV1. The FVC is the greatest quantity of air that may be forcedly expelled after complete inspiration. The FEV1 is the maximum amount that can be exhaled forcibly during the first second of your exhalation. A patient is diagnosed with COPD if their FEV1/FVC ratio is less than 0.7.

For any particular case, when we measure the severity of disease normal value of FEV1 is anticipated based on parameters like age, sex,

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and height which is called FEV1% predicted. COPD in response to consequent hypoxemia leads to secondary polycythemia with elevated erythropoietin. In COPD patients, anemia is relatively common and is related to increased mortality.[4] Despite many factors contributing to anemia, it is mainly caused by COPD because of its inflammatory nature, which increases cytokine production, thus causing iron-deficiency anemia.[5] The iron status of COPD patients reflects the equilibrium of erythropoietin stimulated by hypoxia and depressed by inflammation. The current cross-sectional study analyses patients' serum iron values and spirometry to determine the relationship between percent saturation of transferrin, serum iron, serum ferritin, TIBC, FVC, and forced expiratory flow (FEF 25–75%), FEV1/FVC, and FEV1.

2. Methods

After the ethics committee approved, the cross-sectional research was done in the Department of Medicine at J.L.N. Medical College & Hospitals, Ajmer. The study was conducted from January 2019 to August 2020 on 100 randomly selected COPD patients>18 years of age regardless of gender. Data was collected through a preformed and pretested proforma from each patient with written consent. Study participants underwent detailed history, clinical examination, hematological investigations, and chest X-ray. Haematological investigations included Haemoglobin (gm/dl), Serum iron (μg/dL), Serum potassium (mEq/L), Total iron-binding capacity (μg/dL), Serum creatinine (mg/dl), Serum sodium (mEq/L), Serum ferritin (ng/ml), % transferrin saturation which is obtained by the following formula – Serum iron x 100 ÷ TIBC. Spirometry determines FVC, FEV1, FEV1/FVC, and FEF 25–75%. Spirometry measurements were assessed by comparing reference values based on age, height, sex, and race. The coding of data was done and entered into a Microsoft Excel spreadsheet. An appropriate statistical test was applied using IBM SPSS version 20. Descriptive analysis of data included percentages, means, and standard deviations. Multivariate analyses were done using the Pearson correlation test and the multiple linear regression method. P-value less than 0.05 at 95% CI is deemed statistically significant.

3. Results

The blood hemoglobin level was not significantly correlated with the % predicted value of FVC or FEV1 or FEF (25–75%) and FEV1/FVC. The serum iron concentration and the total iron-binding capacity were highly significant and positively correlated with the % predicted value of FVC, FEV1andFEF (25–75%), and FEV1/FVC (Table 1). The % transferrin saturation was highly significant and positively correlated with the % predicted value of FEV 1, FVC and FEF (25–75%) and FEV1/FVC. The serum ferritin concentration was significantly and negatively correlated with the % predicted value of FVC, FEV 1 and FEF (25–75%) and FEV1/FVC (Table 2).

Multiple linear regression analysis only identified a link between FEV1 and serum iron and total iron-binding capacity (percent predicted). However, the proportion of FEV1 and FVC was positively associated with the serum iron. In addition, the % predicted value of FEF (25–75%) was significant and positively associated with the serum iron concentration (Table 3).

Table 1
Baseline characteristics of study population.

Characteristics	Minimum	Maximum	Mean ± S.D.
Age (Year)	35	83	59.63 ± 10.31
Height (cm)	146	182	164.85 ± 8.69
Weight (kg)	42	100	61.47 ± 13.36
BMI (kg/m2)	15.24	34.24	22.53 ± 4.03
Hemoglobin (gm/dL)	9	17.6	14.38 ± 1.60
Serum iron (μg/dL)	15.4	186	88.52 ± 51.56
Total iron binding capacity(μg/dL)	171	477	338.94 ± 63.35
%Transferrin saturation	6.02	45.81	24.03 ± 11.28
Ferritin (ng/mL)	44	479	183.98 ± 112.55
FVC(L)	0.6	3.44	1.93 ± 0.66
FVC(% Predicted)	21	106	63.63 ± 18.50
FEV 1 (L)	0.34	2.3	1.03 ± 0.47
FEV1(% Predicted)	17	90	46.41 ± 18.84
FEV1/FVC (%)	33.33	69.9	52.54 ± 11.15
FEF (25–75) (L/S)	0.19	3.04	0.66 ± 0.56
FEF(25–75%)%Predicted	6	73	21.92 ± 13.59

4. Discussion

The mean age of the studied participants was found to be 59.63 ± 10.32 years, similar to the study done by Jayachandran (2009)[6], where the mean age was 51.32 years, but study participants were from the 40–60 years of age group. In the present study, the maximum number of participants (37.00%) were from 60 to 70years, followed by the age group 50–60 years (29.00%). In anthropological studies, it was found that the mean height of the patients was 164.85 ± 8.69 cm. The mean body wt. was found to be 61.47 ± 13.36 kg with a mean BMI of 22.53 ± 4.03. Comparatively higher body weight and BMI (74.10 kg and 28.2 kg/m^2 respectively) were reported by Soler et al. (2004)[7], and comparatively lower body weight and BMI (55.10 kg and 21.40 kg/m^2 respectively) were reported by Jayachandran (2009).[6]

The blood examination found that the average value of hemoglobin was 14.38 ± 1.60 gm/dl and the average serum iron concentration was 88.52 ± 51.56 μg/dl. In contrast, the mean value of total iron-binding capacity was 338.94 ± 63.36 μg/dl. The mean % transferrin saturation was found to be 24.03 ± 11.28%. The mean value of serum ferritin was found to be 183.98 ± 112.55 ng/ml. According to the results of a research conducted by Kim et al. (2018),[8] the average hemoglobin, serum iron, serum ferritin, percent transferrin saturation, and TIBC were 14.50 ± 1.42 gm/dl, 83.58 ng/ml, 39.38%, and 302 μg/dl, respectively, in the participants.

Spirometry is a useful screening tool to detect the airflow restrictions in the very early course of COPD. In the spirometry, it was found that the mean value of FVC was found to be 1.93 ± 0.66 L, while the mean value of the predicted percentage of FVC was 63.63 ± 18.50%. In this line, the severity of COPD was measured by FEV1. The mean value of FEV1 was 1.03 ± 0.48 L, and the mean predicted percentage of FEV 1 was 46.41 ± 18.84%. Lakshmi (2013)[9] reported mean FEV1 to be 2.6 ± 0.6, which is higher than the findings of this study. Soler et al. reported the mean predicted percentage of FEV1 to be 44.60% and 65.60%, respectively. The proportion of FEV1 and FVC was found to be 52.54 ± 11.15%.

FEF 25–75% is the major predictor of small airway obstruction. In the present study, the average value of FEF (25–75%) was 0.66 ± 0.56

Table 2
Correlations between FVC(% Predicted), FEV1(% Predicted), FEV1/FVC, FEF (25–75%) % Predicted and Serum Iron parameters.

Serum Iron Parameters		FVC (% Predicted)	FEV1 (% Predicted)	FEV1/FVC (% Predicted)	FEF (25–75%) (% Predicted)
Hemoglobin (gm/dL)	r	−0.07	−0.100	−0.063	−0.15
	Pvalue	0.47	0.32	0.53	0.11
Serum iron (μgm/dL)	r	0.76	0.95	0.55	0.64
	P value	<0.001	<0.001	<0.001	<0.001
TIBC (μg/dL)	r	0.71	0.82	0.44	0.52
	P value	<0.001	<0.001	<0.001	<0.001
% Transferrin saturation	r	0.58	0.71	0.39	0.44
	P value	<0.001	<0.001	<0.001	<0.001
Ferritin(ng/mL)	r	−0.72	−0.82	−0.46	−0.57
	P value	<0.001	<0.001	<0.001	<0.001

r = Pearson correlation coefficient.

Table 3
Multiple linear regression analysis of hemoglobin and serum iron parameters with lung function test (% predicted).

Lung function test (% predicted)	Serum iron parameters	β	Std. Error	P value	R^2 (adjusted R^2)
FEV1	Hemoglobin (gm/dL)	0.279	0.236	0.239	0.96 (0.92)
	Serum iron (μgm/dL)	0.318	0.025	<0.001 (S)	
	TIBC (μg/dL)	0.034	0.015	0.02 (S)	
	% Transferrin saturation	−0.003	0.060	0.960	
	Ferritin(ng/mL)	−0.003	0.009	0.755	
FVC	Hemoglobin (gm/dL)	0.819	0.738	0.270	0.79 (0.62)
	Serum iron (μgm/dL)	0.106	0.096	0.271	
	TIBC (μg/dL)	0.061	0.033	0.067	
	% Transferrin saturation	0.259	0.442	0.559	
	Ferritin(ng/mL)	−0.035	0.022	0.120	
FEV1/FVC	Hemoglobin (gm/dL)	0.021	0.412	0.959	0.56 (0.31)
	Serum iron (μgm/dL)	0.096	0.044	0.03 (S)	
	TIBC (μg/dL)	−0.004	0.026	0.873	
	% Transferrin saturation	−0.029	0.105	0.786	
	Ferritin(ng/mL)	−0.012	0.015	0.423	
FEF (25–75%)	Hemoglobin (gm/dL)	−0.714	0.674	0.292	0.65 (0.43)
	Serum iron (μgm/dL)	0.218	0.087	0.01 (S)	
	TIBC (μg/dL)	−0.003	0.030	0.911	
	%Transferrin saturation	−0.471	0.404	0.246	
	Ferritin(ng/mL)	−0.025	0.020	0.229	

β – Regression coefficient, R^2 = Explanatory power of variables on FEV_1 (% predicted),S=Significant.

L/S, and the average value of FEF (25–75%) % predicted was 21.92 ± 13.59% in the studied population, while in a study done by Kim et al., reported FVC, FEV1, FVC (predicted %), FEV1 (predicted %) and FEV1/FVC to be 3.59 ± 0.90 L, 2.28 L,90.98 ± 13.46, 79.28 and0.66, respectively.

In present study, the serum iron concentration was found to be highly significant and positively correlated with % predicted value of FVC ($r = 0.76$, p value < 0.001), FEV1($r = 0.95$, p value < 0.001) FEF (25–75%) ($r = 0.64$, p value < 0.001) and FEV1/FVC ($r = 0.55$, p value < 0.001). The total iron binding capacity was highly significant and positively correlated with % predicted value of FVC ($r = 0.71$, p value < 0.001), FEV1($r = 0.82$, p value < 0.001), FEF (25–75%) ($r = 0.52$, p value < 0.001) along with FEV1/FVC ($r = 0.44$, p value < 0.001). The % transferrin saturation was highly significant and positively correlated with %predicted value of FVC ($r = 0.58$, p value < 0.001), FEV1($r = 0.71$, p value < 0.001) and FEF (25–75%) ($r = 0.44$, p value < 0.001) along with FEV1/FVC ($r = 0.39$, p value < 0.001). Kim et al. (2018)[8] reported FEV1 to be significantly associated with hemoglobin ($\gamma = 0.37$, $p < 0.001$), serum iron ($\gamma = 0.20$, $p < 0.001$), transferring saturation ($\gamma = 0.19$, $p < 0.001$) and with serum ferritin ($\gamma = 0.22$, $p < 0.001$). The serum ferritin concentration was highly significant and negatively correlated with % predicted value of FVC ($r = -0.72$, p value < 0.001), FEV1($r = -0.82$, p value < 0.001), FEF (25–75%) ($r = -0.57$, p value < 0.001) and FEV1/FVC ($r = -0.46$, p value < 0.001). Statistically significant results were also observed in a research by Lee et al. (2020)[10] was, showing that those with lower FEV1% and FVC percent levels had significantly increased levels of ferritin in comparison to those with normal ferritin levels.

However, there was no significant change in the FEV1/FVC ratio across groups ($p = 0.797$). Schneckenpointner et al. (2014)[11] observed that while low blood iron levels are linked with COPD's worse pulmonary performance and disease severity, they are also directly related to an increased risk of death in individuals with chronic respiratory failure. Hirayama (2010)[12] found that reducing iron consumption increased COPD severity and dropped the projected FEV1%.

Kim et al. discovered that despite elevated ferritin levels, increased production of acute-phase proteins such as ferritin and hepcidin and a blockade of iron mobilization from endothelial iron stores resulted in a deficiency of iron in individuals with COPD.

Serum iron was positively linked with FEV1 (percent predicted) in multiple linear regression analysis (=0.318, p 0.001). There was a good correlation between FEV1 and TIBC (percent predicted) ($\beta = 0.034$, $p = 0.02$). The proportion of FEV1and FVC was positively associated with serum iron ($\beta = 0.096$, $p = 0.03$). The serum iron content was substantially positively linked with the percent anticipated value of FEF (25–75%) (=0.218, $p = 0.01$). It was also shown in research by Kim et al. (2018)[8] that serum iron and transferrin saturation were independently linked with the FEV1.

5. Conclusion

According to the current investigation findings, serum iron levels were shown to be independently linked with FEV1% predicted and FEF (25–75%) percent predicted. COPD severity may therefore be assessed by measuring the quantity of iron in the patient's serum since it is reasonably easy and affordable to do so.

Authors' contributions

Conceptualization: [Sunil Kumar Gothwal]; Formal analysis and investigation: [Vikram Palsaniya, Harish Chandra Barjatiya]; Writing – original draft preparation: [Ruchita Banseria], [Piyush Sharma], [Pramod Goyal], [Vasudeva Murthy Challakere Ramaswamy], [Yogendra Singh]; Writing – review and editing: [Gaurav Gupta]; Funding acquisition: [N/A]; Resources: [N/A]; Supervision: [Ruchita Banseria].

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Consent to participate

All the authors mutually agree to participate in this work.

Consent for publication

All the authors mutually agree to submit the manuscript for publication.

Declaration of competing interest

On behalf of all listed authors, the corresponding author declares that there is not any sort of financial and non-financial conflict of interest in the subject materials mentioned in this manuscript.

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