



**ORIGINAL RESEARCH PAPER**

**Physiology**

**GENDER-DIFFERENCES IN THE LUNG FUNCTION AND CIRCULATING LEUKOCYTES IN COPD PATIENTS ATTENDING A TERTIARY CARE HOSPITAL IN MANIPUR, INDIA**

**KEY WORDS:** COPD, Leukocytes, Spirometer

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**ABSTRACT**

**Background-** Chronic obstructive pulmonary disease (COPD) is one of the most prevalent health conditions, and a major cause of morbidity and mortality around the globe. Once thought of primarily as a disease of men, COPD is now known to be increasingly prevalent among women. However, little is known about gender-related differences in the lung function and circulating levels of leukocyte in COPD. **Objective-** To study the possible gender-related differences in the lung function and leukocyte levels in the blood of COPD patients. **Methods-** It is a cross-sectional study enrolling 40 COPD patients (22 males and 18 females). 12 out of 18 female patients already attained menopause. Lung function was studied by computerized spirometer (Helios 401/701) and blood leukocyte counts (absolute neutrophil count, absolute eosinophil count, absolute basophil count, absolute lymphocyte count and absolute monocyte count) were determined by using suitable diluting fluids. **Results-** A higher FVC, FEV1, FEV1/FVC, PEFR and FEF25-75 in male as compared to female COPD patients are seen but not statistically significant (P>0.05). The mean neutrophil concentration is found to be higher in female patients whereas eosinophil, lymphocyte and monocyte counts are found to be higher in male patients but these findings are again statistically not significant (P>0.05). **Conclusion-** There seems to be a propensity for the female gender to suffer from COPD and have severe form of the disease when compared to male patients. A gender-related difference in systemic inflammation in patients with COPD in terms of circulating leukocyte levels can also be seen.

**1. INTRODUCTION:**

Chronic obstructive pulmonary disease (COPD) is becoming an increasing clinical problem in women. The number of females dying from COPD in the US has outnumbered that in males since the year 2000. (1) In 2006, for the first time, more female (1291) than male (1274) patients died in Sweden from COPD, according to official death statistics. (2) Apart from tobacco smoke, indoor air pollution, especially from biomass fuel may play an important role in COPD development in women. (3)

The occurrence of systemic inflammation in COPD patients with severe disease has been reported in several studies, and COPD is now regarded as a disease with systemic complications, including an increase in circulating markers of inflammation. (4)

Findings of leukocytosis dominated by neutrophils and elevated levels of C-reactive protein (CRP) are frequently reported in studies on COPD patients. (5-7)

In this study, we examined whether there is a gender-related difference in lung function and circulating markers of systemic inflammation in patients with COPD by comparing the concentrations of circulating leukocytes in female and male COPD patients.

**2. MATERIALS AND METHODS:**

**Study design**

This is a cross-sectional study carried out in the Department of Physiology Churachandpur Medical College and Department of Physiology JNIMS, Imphal in collaboration with Department of Respiratory Medicine, JNIMS Imphal Manipur, India. After obtaining approval from the institutional ethics committee and written informed consent of both, a total of 40 COPD patients of both sexes between the ages of 18 to 65

years who attended Respiratory Medicine OPD and ward admitted patients were enrolled in the study.

**Exclusion criteria**

Patients with diseases like asthma, worm infestations, atopic skin disease and other allergic diseases, cardiac problems, renal failure, diabetes mellitus, hypertension, pulmonary fibrosis, neuromuscular diseases, and ascites were excluded.

**Data collection procedure**

A) Spirometric studies were conducted by means of a Computerized Spirometer- Helios 401/701 of the Recorders and Medicare system, Chandigarh. The study variables recorded by spirometry include Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1), FEV1/FVC, Peak Expiratory Flow Rate (PEFR), Forced Expiratory Flow (FEF<sub>25-75%</sub>).

B) Assessment of blood leukocyte counts was done by using 1ml of blood collected by venipuncture from the subjects. The count was made under a compound microscope in an Improved Neubauer's chamber using Turk's fluid and Leishman's stain. After finding out Total Leukocyte Count(TLC) and Differential Leukocyte Counts(DLC), Absolute Leukocyte Counts was determined by using the formula-

$$\text{Absolute leukocyte count} = \text{DLC}/100 \times \text{TLC}$$

**Statistical analysis**

Appropriate statistical analysis like Students't-test (Independent sample) was made wherever necessary, using standard software (Microsoft Excel 2010 and SPSS version 16.0). Data are presented in the form of Mean ± Standard Deviation (SD) and Mean ± Standard Error Mean (SEM). Level of statistical significance was set at p < 0.05, two-tailed.

**3. RESULTS:**

The present study is based on the primary data of 40 COPD (22 male and 18 female) patients who attended the Respiratory Medicine OPD and ward admitted patients.

**Table 1: Socio-demographic profile of the COPD patients**

PARAMETERS	MALE	FEMALE
No. of patients, n (%)	22(55)	18(45)
Age (mean) in years	50.27±7.41	57±12.37
Residence, n (%)	Urban= 18(81.82) Rural= 4(18.18)	Urban= 10(55.56) Rural= 8(44.44)
Smoking status, n (%)	Smoker= 6(27.27) Non-smoker= 4(18.18) Ex-smoker= 12(54.55)	Smoker= 2(11.12) Non-smoker= 10(55.55) Ex-smoker= 6(33.33)

**Table 2: Profile of menstrual history in female COPD patients**

PHASE	NO. OF PATIENTS, N (%)
Menstrual phase	0
Proliferative phase	1(16.67)
Secretory phase	5(83.33)

Total no. of female patients= 18  
 No. of patients who attained menopause= 12(66.67%)  
 No. of patients who has not attained menopause= 6(33.33%)

Table 2 shows that maximum of female COPD patients (66.67%) have attained menopause whereas only 33.33% of female patients are still having menstrual cycle. Out of these patients, 16.67% are in the proliferative phase and 83.33% are in the secretory phase.

**Table 3: Mean±SD of flow parameters in male and female COPD patients**

PARAMETERS	MALE	FEMALE	p-value
FVC(L)	1.33±0.73	1.12±0.67	0.498
FEV1 (L/sec)	1.15±0.73	0.86±0.76	0.377
FEV1/FVC (%)	85.09±14.04	69.42±24.08	0.077
PEFR(L/sec)	3.26±2.34	1.83±2.02	0.231
FEF25-75 (L)	2.02±1.59	1.20±1.56	0.350

Table 3 shows the comparison of mean±SD of FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, PEFR and FEF<sub>25-75</sub> between male and female COPD patients. All the flow parameters are higher in male patients as compared to female patients but not statistically significant.

**Table 4: Mean±SEM of absolute leukocyte counts in male and female COPD patients**

PARAMETERS	MALE	FEMALE	p-value
ANC	6412.57±842.47	8817±168.43	0.217
AEC	341.63±84.93	185.36±50.86	0.130
ABC	0	0	
ALC	2257.62±181.55	1687±211.58	0.054
AMC	375.98±97.79	339±81.78	0.775

(ANC= absolute neutrophil count, AEC= absolute eosinophil count, ABC= absolute basophil count, ALC= absolute lymphocyte count, AMC= absolute monocyte count)

Table 4 shows the mean±SEM of various absolute leukocyte counts in male and female COPD patients.

Absolute neutrophil count is higher in female patients whereas absolute eosinophil, lymphocyte and monocyte counts are higher in male patients which are statistically not significant. Absolute basophil count is nil in both the group of patients.

**4. DISCUSSION:**

The present study was done to explore possible gender-related differences in the lung function and leukocyte levels

in the blood of COPD patients. The study was based on the primary data collected from 40 COPD patients (22 male and 18 female).

A higher FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, PEFR and FEF<sub>25-75</sub> in males as compared to females are seen in Table 3. There seems to be a propensity for the female gender to suffer from OAD. There are studies showing that female patients have more severe form of the disease when compared to male patients.<sup>(8)</sup> Possible explanation for this may be the differences in lung geometry between the sexes, because females, on average, would be expected to have smaller airways and smaller lung volumes than males.<sup>(9)</sup> Hormonal differences<sup>(10)</sup> and a higher susceptibility of females to the deleterious effects of smoking than males<sup>(11)</sup> are other factors to be considered. As majority of the female patients attained menopause in this study, they are expected to experience several changes affecting their lung function as menopause is associated with poorer lung function and more respiratory symptoms.<sup>(12)</sup>

Male smokers seem to have a more generalized inflammatory reaction with elevation of CRP, fibrinogen, white-blood cells count and plasma viscosity; whereas women only have elevation of white-blood cells and fibrinogen. That is, the association of systemic inflammation induced by smoking is stronger in men than women. This may explain the higher leukocyte counts except neutrophil count in male patients in this study. Interestingly, ex-smokers seem to have an ongoing inflammation despite having ceased to smoke as they have higher levels of inflammatory markers than never-smokers.<sup>(13,14)</sup>

Our study shows a higher mean neutrophil concentration in female than in male patients with COPD (Table 4) which is consistent with the findings of Larsson S et al<sup>(15)</sup>. They found higher concentrations of the neutrophil-mobilizing cytokines IL-6 and IL-8 in the malnourished female COPD patients. Possible explanation of increased neutrophil count in female patients in our study may be the menopausal effect. Menopause is associated with rapid onset of the metabolic syndrome with more central body fat. Khera et al<sup>(16)</sup> recently reported that the quantity and distribution of body fat influences CRP to a greater extent in women than men, as women with increasing abdominal fat mass had a larger increase in CRP. This may explained the endocrine function of the adipose tissue, producing hormones and cytokines, affecting CRP levels and contributing to the systemic inflammation. As 83.33% of female patients with menstrual cycle are in the secretory phase, this can also add to the explanation of high neutrophil count in female patients as 17-β estradiol promotes granulopoiesis during the secretory phase.

**5. CONCLUSION:**

There are studies which show that gender-related differences exist in the lung function and the inflammatory markers in COPD. Our study also shows, to some extent, a gender differences in the lung function and leukocyte counts in COPD patients. Male patients have higher flow parameters than female patients.

Absolute neutrophil count is higher in female patients whereas absolute eosinophil, lymphocyte and monocyte counts are found to be higher in male patients. Possible explanations for these findings include differences in lung geometry between the sexes, hormonal differences, environmental and socio-cultural differences with a higher susceptibility of females to the deleterious effects of smoking than males.

In our study, majority of female patients attained menopause which could have contributed to the decrease in the lung function and increased neutrophil count. However, while interpreting the results, history of smoking status, presence of

respiratory infections, and use of bronchodilators & inhaled corticosteroids for treatment should be considered as these factors can influence the results.

Further studies of the pathophysiologic mechanisms by which gender differences exist in the lung function and blood leukocyte counts along with other systemic inflammatory markers involving more number of patients seems indicated.

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