PEFR and FEF ₂₅₋₇₅ in Rheumatoid Arthritic Female and their Relationships with Duration of the Disease

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Background: Rheumatoid Arthritis (RA) is a chronic, progressive multisystemic inflammatory disorder of unknown etiology affecting approximately 1% of the population. Pulmonary involvement is a frequent extraarticular manifestation in rheumatoid arthritis. Objective: To observe PEFR, FEF 25-75 in female patients of RA in order to find out their relationships with duration of the disease. Methods: This cross-sectional study was carried out in the Department of Physiology, BSMMU, Dhaka, between January and December 2009 on 90 RA female patients of 30-50 years age (Group B). For comparison, 30 age and BMI matched apparently healthy subjects (Group A) were also studied. According to the duration of disease, RA patients were subdivided into B₁ (newly diagnosed), B₂ (3-5 years) and B₃ (6-10 years). They were selected from the Out Patient Department of Physical Medicine of Bangabandhu Sheikh Mujib Medical University, Dhaka. PEFR, FEF₂₅₋₇₅ of all the subjects were measured by a digital MicroDL spirometer. Results were expressed as percentage of predicted value. For statistical analysis One-Way ANOVA, Unpaired Student's 't' test and Pearson's correlation coefficient test were performed. **Results:** The mean percentage of predicted values of these lung function parameters in the healthy female subjects and newly diagnosed (B₁) RA patients were within normal ranges. The mean percentage of predicted values of both the spirometric variables were significantly lower in B₃ compared to those in B_2 (PEFR p<0.001, FEF₂₅₋₇₅ p<0.001), B_1 (PEFR p<0.05, FEF₂₅₋₇₅ p<0.02) and A (PEFR p<0.05, FEF₂₅₋₇₅ $_{75}$ p<0.01). Again the same parameters were significantly lower in B₂ in comparison to those of B₁ $(PEFR p < 0.001, FEF_{25-75} p < 0.05)$ and $A(PEFR p < 0.001, FEF_{25-75} p < 0.05)$. In addition both the ventilatory variables had significant (p<0.001) negative correlation with durations of disease. Conclusion: This study reveals that pulmonary functions may be lower in patients with RA and their lung function is inversely related to the duration of disease.

Key Words: PEFR; FEF₂₅₋₇₅, Rheumatoid Arthritis

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Introduction

heumatoid Arthritis (RA) is the most common inflammatory disorder mediated through the immune system^{1,3} Symptoms of Rheumatoid Arthritis include pain, swelling, stiffness and nodules of joint.⁴ Women are 2 to 3 times more affected than men. Onset may be at any age, most frequently occur between 35 to 50 year.⁵

The etiology of Rheumatoid Arthritis is still unknown, but there is evidence for genetic predisposition to the disease. The presence of HLA-DR4 is significantly common among white sufferers of Rheumatoid Arthritis⁶. A good number of investigators reported association of abnormal pulmonary function tests in RA patients ⁷⁻¹¹.

ESR values were significantly higher in the presence of lung involvement than in the absence of lung involvement. Pulmonary involvement is an important marker for the systemic involvement of Rheumatoid Arthritis. Some investigators

suggested that immune mediated processes in Rheumatoid Arthritis are responsible for he inflammatory processes in the lung ¹². Inflammatory processes on air sacs or alveoli and their supporting structures make them fibrosed resulting in impaired lung function^{4, 13}.

The incidence of rheumatoid lung disease in women was 33.3% who had no evidence of other pulmonary disease ¹⁰. Symptoms of rheumatoid lung disease are shortness of breath, cough, chest pain, fever etc ⁴.

Some investigators reported small airway involvement may appear as the commonest form of pulmonary involvement of rheumatoid lung disease though Interstitial Lung Disease is the most common form of pulmonary abnormality¹². Pulmonary manifestations of RA are characterized by pleural effusion, nodular lung disease, diffuse interstitial fibrosis, pulmonary vasculitis, alveolar hemorrhage, obstructive pulmonary disease, and infections¹⁴. Again some researchers reported that lung functions tests had relationship with duration of disease ^{15, 16}.

Rheumatoid Arthritis is a chronic form of disabling disease with 1% prevalence in Bangladesh. Usually the patients are treated by the physician with an aim to relieve the symptoms, ignoring the fate of organic complications. Therefore, pulmonary involvements in RA may remain undiagnosed which can be easily detected by simple pulmonary functions tests. Therefore, pulmonary functions tests in these patients are crucial for early detection of associated pulmonary involvement in RA patients.

Many researchers have investigated pulmonary functions in these group of patients in other countries ^{9-11,17-18}. To the best of our knowledge no such study has been under taken to explore the pulmonary function status in RA patients in Bangladesh. Therefore the present study was conducted to observe some aspects of lung function status in RA patients and also to

evaluate their relationships with duration of the disease.

Methods

This cross-sectional study was carried out in the Department of Physiology, BSMMU, Dhaka, between January and December 2009 on 90 female diagnosed patients of Rheumatoid Arthritis, according to American Rheumatism Association 1987 revised criteria aged 30-50 years (Group B) ¹⁹. For comparison 30 age and BMI matched apparently healthy female subjects were also studied (Group A). Based on duration of disease, study group was further divided into Group B₁ (newly diagnosed), Group B₂ (2-5 years duration) and Group B₃ (6-10 years duration). All the RA patients were selected from the Out Patient Department (OPD) of Physical Medicine, BSMMU. Subjects with history of any form of tobacco consumption, asthma, COPD, pulmonary fibrosis, pneumonia, hypertension (>140/90 mm of Hg), diabetes mellitus (Serum glucose 2hr after breakfast>11mmol/L), any heart disease, chronic renal failure (Serum creatinine>1.5mg/dl), severe anemia (Hb<11mg/dl) were excluded from the study. After selection all the subjects were thoroughly informed about the aim, objectives and benefits of this study to encourage their voluntary participation. Informed written consent was taken from each of them. A detail personal, family and medical history were taken and thorough physical examinations of each subject were done. All the information were recorded in a prefixed questionnaire. Then the subjects were taken to the Respiratory Laboratory for Pulmonary Function Test. The detailed procedure of spirometric examination was explained to the subject and the values of PEFR and FEF₂₅₋₇₅ were obtained according to the manufacturer's instruction by a Digital Micro DL Spirometer manufactured by Clement Clarke International Ltd. ²⁰ Data were analyzed by One-way ANOVA, Independent sample 't' test and Pearson's Correlation Coefficient test.

Results

Table I presents the results of PEFR, FEF $_{25-75}$. The mean percentage of predicted values of all these parameters were significantly lower in B $_2$ (PEFR, p<0.001; FEF $_{25-75}$ p<0.05, B $_3$ (PEFR, p<0.05; FEF $_{25-75}$, p<0.01) and B $_1$ (FEF $_{25-75}$, p<0.05) in comparison to those of group A. Though the value of PEFR was lower in B $_1$ compared to that of A but the difference was statistically non significant. Again, these values were significantly lower in B $_2$ (PEFR, p<0.001; FEF $_{25-75}$, p<0.05)

and B_3 (PEFR, p<0.01; FEF₂₅₋₇₅ p<0.05) than those of B_1 . In addition, these values were also significantly lower in B_3 (PEFR, p<0.001; FEF₂₅₋₇₅, p<0.001) than those of B_2 .

Correlations of the study variables with the duration of the disease in RA patients are shown in Figure 1 and 2. Here PEFR (B_1 r=-0.92, B_2 r=-0.97, B_3 r=-0.99) and FEF₂₅₋₇₅ (B_1 r=-0.92, B_2 r=-0.98, B_3 r=-0.93) showed significant (p<0.001) negative correlation with the duration of disease in all the study groups.

Table I: Percentage of predicted values of PEFR and FEF₂₅₋₇₅ in different groups (n=120)

Groups	PEFR	FEF ₂₅₋₇₅
	(% of predicted value)	(% of predicted value)
A(n=30)	100.6± 12.75	93.33±14.62
$B_1(n=30)$	82.33 ±7.85	69.3 ± 25.29
$B_2(n=30)$	57.03 ± 20.61	51.2 ± 19.33
$B_3(n=30)$	36.1 ± 18.80	43.13 ±7.89

Statistical analysis:

Groups	P value		
A vs B ₁ vs B ₂ vs B ₃ ^a	0.000***	0.000***	
A vs B ₁ ^b	0.483 ns	0.029	
A vs B ₂ ^b	0.000***	*0.039*	
A vs B ₃ b	0.026*	0.01**	
$B_1 vs B_2^b$	0.000***	0.021 *	
$B_2 vs B_3^b$	0.001**	0.001**	
$B_1 \text{ vs } B_3^{b}$	0.005**	0.022*	

Data were expressed as mean \pm SD. .

a = one way ANOVA, b = independent sample t - test.

Group A: Apparently healthy subjects (control group)

Group B: Rheumatoid Arthritis (study group)

B₁ : Newly diagnosed patients.

B₂: Patients with 3-5 yrs.

 B_3 : Patients with 6-10 yrs.

**** = (p<0.001)

**=(P<0.01)

* = (P < 0.05)

 $ns = non \ significant \ (\ p > 0.05)$

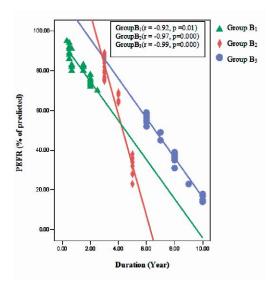


Figure 1: Correlation of percentage predicted value of PEFR with duration of Rheumatoid Arthritis in study groups (n=90)

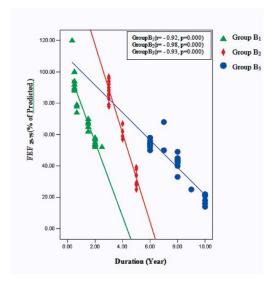


Figure 2: Correlation of percentage predicted value of FEF₂₅₋₇₅ with duration of Rheumatoid Arthritis in study groups (n=90)

Discussion

The present study was undertaken to observe some aspects of spirometric variables of pulmonary functions in female patients with Rheumatoid Arthritis. In this study, values of PEFR and FEF₂₅₋₇₅ of healthy subjects were within normal limit and were almost similar to those reported by different investigators of other countries ^{11, 17, 21} as well as in our country ^{22, 23}.

In the current study, all the study parameters in patients of RA with different durations were significantly lower than those of healthy subjects but these values are almost similar in newly diagnosed patient and healthy subjects. Several investigators from different countries ^{9,11,12,24} observed almost similar findings. Again, these parameters were significantly lower in patients with 3-5 years duration compared to that of newly diagnosed and also in 6-10 years duration than those in 3-5 years duration patients. Similar findings were also reported by some investigators ^{19, 25}.

Significant negative correlations of PEFR and FEF₂₅₋₇₅ with the duration of disease in all patients of Rheumatoid Arthritis in the present study are similar to those observed by other investigators^{16, 17}.

Various mechanisms have been proposed for these observed changes in lung function in Rheumatoid Arthritis. Some investigators suggested that the inflammatory process might spread from other organs to the lung interstitial tissue causing lung inflammation and dysfunction¹⁰. Continuous systemic inflammatory process brings modification of structural and functional features of bronchi and bronchioles¹⁵. Again mucosal edema secondary to pre-existing airways inflammation may lead to bronchial narrowing and may cause airways obstruction²¹. Immune complex deposits in the alveolar wall of patients may also cause progressive idiopathic interstitial fibrosis²⁶.

Decreased percentage of predicted values of PEFR, FEf₂₅₋₇₅ in patients of Rheumatoid Arthritis in comparison to healthy subjects is most likely due to pulmonary fibrosis and bronchial narrowing as a result of chronic inflammation in lung tissue. Again decreased lung compliance in RA patients may be due to costochondral joint disease or respiratory muscle weakness.

Reduced values of both the lung function parameters in the present study indicate early stage of small airway obstruction in the RA patients of the present series which is most likely due to the interstitial fibrosis and airway inflammation as a consequence of the chronic inflammatory processes involved in rheumatoid arthritis. Moreover, in this study, the significant negative correlations of the study variables with different duration of Rheumatoid Arthritis and the significant lowering of these parameters in patients with longer duration of RA also indicate that duration of inflammation influences the degree of deterioration of lung function.

Conclusion

This study reveals that pulmonary functions may be lower in patients of Rheumatoid Arthritis and the lung function is inversely related to the duration of disease.

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