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Lung Function Status and Associated Factors Among Rheumatoid Arthritis Patients, Southwest Ethiopia: A Comparative Cross-Sectional Study

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Abstract

Background: *Rheumatoid arthritis (RA) is a chronic progressive autoimmune multi-systemic inflammatory disease. Pulmonary involvement and complications remain an important cause of morbidity and mortality among RA patients. Spirometry is a simple, less expensive, and first-line tool in the screening of pulmonary function disorders.*

Objective: *The study aimed to assess the lung function status and associated factors among RA patients, Southwest Ethiopia, 2023.*

Methods: *An institution-based comparative cross-sectional study was conducted among 248 participants at JMC and MKH in Southwest Ethiopia ,2023. A face-to-face interview, utilizing a semi-structured questionnaire, was employed, and the DAS28-ESR was assessed for each RA participant. spirometry parameters, including FVC (L), FEV1 (L), FEF 25-75% of the FVC (L/s), and PEFR (L/s), were measured using a digital spirometer (SP10) and interpreted according to American Thoracic Society guidelines. Collected data were analyzed using SPSS version 26. Finally, descriptive statistics, independent t-tests, and binary and multiple logistic regression analyses were performed, with statistical significance set at a 5% level.*

Results: *The present study indicated that the means of the spirometry parameters among RA patients were significantly*

lower when compared to their age, sex, area of residence ,and weight-matched healthy adult study participants (FVC(L) (m = 3.00 ± 0.38) vs. (m=3.60 ± 0.35), (FEV1(L) ((m = 2.31± 0.34) vs. (m=2.81 ± 0.38, (PEFR(L/s) (m = 5.77 ± 0.84) vs. (m=6.63 ± 0.81, and (FEF25-75 % (L/s) patients (m = 2.41 ± 0.37) vs. (m=2.82 ± 0.34). Generally, 53 (42.8%) and 7 (5.7%) of the RA and healthy adult respondents had at least one pulmonary function abnormality, respectively. Physical inactivity [AOR=5.5, 95% CI=1.4-21.8], biomass exposure [AOR=4.4, 95% CI=1.3-14.8], Moderate-high disease activity [AOR=4.2, 95% CI=1.71-12.4], and WC > 80 cm and > 90 cm for males and females, respectively [AOR=3.6, 95% CI=1.06-11.94] were all independent predictors of pulmonary function abnormality in RA patients.

Conclusions: *Compared to the healthy adults, patients with RA exhibited significantly lower spirometry results, indicating a higher prevalence of pulmonary function abnormalities. Physical inactivity, exposure to biomass, moderate-high disease activity, and increased waist circumference, specifically greater than 80 cm for females and 90 cm for males were independent predictors of impaired pulmonary function in RA patients.*

Keywords: Rheumatoid arthritis, Rheumatoid interstitial lung diseases, Spirometry

Abbreviations

ACPA- Anti -Citrullinated Peptide Autoantibody
BMI- Body Mass Index
DALY- Disability-Adjusted Life Years
EAM- Extra- Articular Manifestation
DAS28-ESR- Disease activity score 28-erythrocyte sedimentation rate
EULAR- European League Against Rheumatism
FEV1- Forced Expiratory Volume in 1st second
FEF25-75%- Forced Expiratory Flow in the middle portion of the FVC
FVC- Forced Vital Capacity
HRCT- High-Resolution Computed Tomography
LLN- Lower Limit of Normal
PEFR- Peak Expiratory Flow Rate
RA- Rheumatoid Arthritis
RF- Rheumatoid factor
RA-ILD- Rheumatoid Interstitial Lung Disease

1. Introduction

Rheumatoid arthritis (RA) is a chronic progressive autoimmune multi-systemic inflammatory disease that is mainly characterized by severe pain, swelling, and symmetric polyarthritis. Damage to joints due to inflammatory conditions often results in articular cartilage and bone erosion, which ultimately leads to physical disabilities. Although joint disease is the most common manifestation of RA, there are also cardiac, pulmonary, renal, hematological, ocular, endocrine, integumentary, and gastrointestinal tract diseases [1,2].

The prevalence and incidence of RA are nearly three times higher in females than in males, frequently occurring in those between 25 and 55 years of age and peaking at about the age of 70. The most striking aspect of RA lung involvement is that virtually all components of the lung structure are potential targets of injury, including the pleura, vasculature, airways, and parenchyma [3,4].

Host genetic predisposition, smoking, mucosal microbiome disturbance, infections, and premature senescence of cells plays a significant role in the development of rheumatoid-associated lung diseases. The interaction of genes and environmental factors is highly incriminated in self-protein citrullination and the production of autoantibodies against citrullinated peptides in the lungs [5,6].

The cellular inflammatory response triggers a secondary fibroproliferative mechanism that may progress autonomously, independent of the initial causative factors, ultimately resulting in pulmonary fibrosis. As the inflammatory process extends to neighboring regions of the interstitium and vasculature, the condition transitions into a chronic phase, culminating in interstitial fibrosis. This progression leads to the formation of irreversible scar tissue, which severely disrupts ventilatory function and impairs gas exchange [7,8].

Progressive lung injury, chronic colonization, and secondary persistent inflammation may contribute to the frequent development of airway obstruction during the disease course. Bronchi and bronchioles are one of the main targets of autoimmunity in RA patients. Bronchiolar inflammation may secondarily induce mucosal edema and airway resistance, which eventually lead to the development of small and large airway obstruction [9,10].

Spirometry is a relatively simple, less expensive, and first-line tool in screening pulmonary function disorders by measuring volume and volume against time [11]. While international studies have extensively documented lung involvement in RA, a significant gap exists in local, context- specific evidence concerning the prevalence, types of pulmonary impairments, and their underlying determinants within the Ethiopian population. Furthermore, the variability in findings across different regions and the influence of various determinant factors remain underexplored. This necessitates targeted research to provide crucial information for developing relevant clinical guidelines and intervention strategies tailored to this setting.

1.1. Objective

The study aimed to assess the pulmonary function status and associated factors among RA patients, Southwest Ethiopia, 2023.

2. Methods

2.1. Study Design and Setting

An institutional-based prospective comparative cross-sectional study was conducted from September 1 to December 30, 2023, at Jimma Medical Center (JMC) and Mattu Karl Hospital (MKH), both located in the Oromia Regional State in southwestern Ethiopia. These hospitals are referral and teaching institutions that provide healthcare services to approximately 25 million people in the southwestern region of Ethiopia. The study focused on RA patients receiving care at the chronic disease clinics of JMC and MKH. These patients are typically scheduled for follow-up appointments at intervals of one to four months to receive ongoing medical services.

2.2. Source Population

2.2.1. Case Group

All adult RA patients on a follow-up at JMC and MKH

2.2.2. Comparative Group

All healthy adults who are patients' attendants, either from outpatient or inpatient departments.

2.3. Study Population

2.3.1. Case Group: All selected patients who were diagnosed with RA and have none of the exclusion criteria.

2.3.2. Comparative Group: All selected healthy adults free of exclusion criteria matched for age, sex, area of residence, and weight with the case group were selected from the same environment.

2.4. Eligibility Criteria

2.4.1. Inclusion Criteria for Cases

All adult RA patients with no exclusion criteria.

2.4.2. Inclusion Criteria for the Comparative Group

All healthy adults came as patient attendants with no exclusion criteria.

2.5. Exclusion Criteria for Cases

All patients with cardiorespiratory diseases, pregnancy, history of any abdominal or thoracic surgery in the last 3 months, cigarette smokers, cleaners, and wood and cobblestone workers.

Exclusion criteria for the comparative group Participants with a documented history of RA and current signs and symptoms of RA checked by the 2010 revised American College of Rheumatology and European League against rheumatism (ACR/EULAR criteria), cardiorespiratory diseases, pregnant, history of any abdominal or thoracic surgery of last three months, cigarette smokers, cleaners, wood, and cobblestone workers.

2.6. Sample Size Determination and Sampling Technique

2.6.1. Sample Size Determination

The double proportion formula for the difference in means and continuous exposure was employed for sample size calculation. Research done in the semi-urban part of India in 2015 calculated the means and the standard deviation for FVC, FEV1, FEV1/FVC, and PEFR for both the cases and the comparative group [17]. With the assumption of Z/2, 95% (1.96), and Z, 80% (0.84), the sample size was calculated for all parameters. Finally, the largest number which could represent the rest of the parameters was calculated using FEV1/FVC (%) for cases 82.31± 14.93 and the comparative group 95.43±1.98 to be 124. Since an equal ratio of cases and controls were used, the final sample size was nx2 = 2x124 = 248.

2.7. Sampling Technique

Patients were proportionally selected from both centers and a consecutive sampling technique was employed for every RA patient that was available at the time of data collection and those eligible for the test were selected. Age, sex, area of residence, and weight matched individuals that came with patients as attendants either from inpatient or outpatient departments and were selected as a comparative group purposively.

2.8. Data Collection Procedures

Medical records of the patients were thoroughly reviewed to identify health conditions that may prevent the worker from safely performing maximal efforts in spirometry according to the third national health nutrition and Examination Survey, respiratory health, and spirometry procedure manual recommendation [18]. Then, a face-to-face interview was conducted using a semi-structured questionnaire to assess information about the patient's socio-demographic factors and behavioral factors.

2.9. Anthropometric Measurements

Height was measured as the subject stood straight against the erect measuring stadiometer and their head, shoulder, buttocks, and heels touched the scale, and the subject's vision faced forward horizontally. Height was measured without shoes to the nearest 1 cm, and weight was also measured with light clothing to the nearest 0.1 kg. Finally, the body mass index (kg/m2) was calculated by dividing weight (kg) by height (m2). Waist circumference was measured using a non-stretchable measuring tape as all the participants stood upright in a comfortable position with both feet together on a horizontal surface. Then WC was measured at the midpoint between the costal margin and iliac crests at the end of expiration.

2.10. The Disease Activity Score 28 - Erythrocyte Sedimentation Rate (DAS28-ESR)

DAS28-ESR assessment involves the evaluation of 28 specific joints for tenderness and swelling, a blood test measuring erythrocyte sedimentation rate (ESR), and the patient's self-perception of overall health. The 28 joints examined include the shoulders, elbows, wrists, metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, and knees [13].

2.11. Erythrocyte Sedimentation Rate (ESR) Measurement

The ESR was determined using the Westergren method. This procedure involves adding 2 ml of venous blood to a tube containing 0.5 mL of sodium citrate. The blood mixture is then

drawn into a Westergren-Katz tube up to the 200 mm mark. The tube is subsequently placed in a strictly vertical position in a rack for 1 hour at room temperature. After 1 hour, the distance from the lowest point of the surface meniscus to the upper limit of the red cell sediment is measured. The result, expressed in millimeters per hour (mm/hour), represents the distance of fall of erythrocytes [14].

2.12. Patient's Global Assessment of Health

A Visual Analog Scale (VAS) was utilized to assess the patient's overall well-being. This scale features anchors at each end worst imaginable health state and best imaginable health state, which guide the patient in indicating their perceived health status. Patients are instructed to mark a point on the line that best represents their current global health status. The position of this mark quantifies their self-assessment of overall health [15]. Finally, DAS28-ESR score was calculated using the following formula, which integrates the tender joint count, swollen joint count, ESR, and the patient's global assessment of health: DAS28(ESR)=0.56∗TJC28 +0.28∗SJC28+0.70∗ln(ESR)+0.014∗GH Where: TJC28 = Tender Joint Count (out of 28 joints) SJC28 = Swollen Joint Count (out of 28 joints) ESR = Erythrocyte Sedimentation Rate (mm/hour) GH = Patient's Global Assessment of Health (0-100 mm VAS) [16].

2.13. Spirometry

Participants were assigned unique coded identifiers that do not reveal their group status (RA or healthy adults). The personnel conducting spirometry were unaware of the participants' clinical diagnosis and inclusion group, with the data recorded under these coded identifiers. The spirometry was performed using a digital spirometer (model SP10 Ltd., China), and study participants were made to sit with their chin slightly elevated after they were introduced to the instrument, procedures, and demonstration thoroughly. Study participants' data, including sex, age, height, and weight, were fed into the spirometer. Study participants sat comfortably on chairs with their legs uncrossed. Tight clothing, such as a tie, vest, or belt, which might restrict maximal breathing efforts, was loosened [17].

After wearing a nose clip and having their lips sealed against the mouthpiece to prevent air leakage, the subjects were instructed to take slow and deep inspirations and then to blow out forcefully and rapidly through the mouthpiece of the spirometer as long as they could. Three readings were undertaken by giving three to five minutes of rest in between. The study participants underwent three consistent spirometry tests that met reproducibility criteria, and the two highest values for FVC and FEV1 were taken from acceptable forced expiratory maneuvers with minimal variability (the two largest FVC and FEV1 values should agree within 150 ml). FVC(L), FEV1(L), FEV1/FVC (%), PEFR (L/S), and FEF25-75% (L/S) test readings were used as the final reading. But the procedure was abandoned and rescheduled if a participant was unable to produce an acceptable and repeatable measurement after eight attempts [18,19].

2.14. Study Variables

2.14.1. Dependent variable

Lung function status

2.14.2. Independent variables

Age, sex, area of residence, occupation, educational status, biomass exposure, alcohol consumption behavior, physical activity, disease activity, RF status, treatment category, height (m), weight (kg), waist circumference (cm), and BMI (kg/m2) are all measurements.

2.15. Data Processing and Analysis

After checking for completeness and consistency, the data were entered into Epi-data version 4.4.2 and exported to SPSS version 26 for analysis. The exported data were explored to check for outliers, missing values, and assumptions. Descriptive statistics were utilized to summarize the sociodemographic characteristics of the study participants. An independent sample t-test was used to determine whether the difference between the means of the lung function parameters was statistically significant between patients with RA and non-RA individuals. Cross-tabulations and binary variable analyses were performed to select variables for multivariable analysis.

Variables with a p-value of 0.25 in the bivariable analysis were taken as candidates for multivariable analysis. Finally, a multivariable logistic regression analysis using backward selection was performed. Variables with a p-value of 0.05 were considered statistically significant predictors of pulmonary function abnormalities. The odds ratio with its 95% CI was used to show the degree of association and estimation between the independent and outcome variables, and the results were presented in the form of text, tables, and figures.

2.16. Data Quality Management

The spirometer used was an electronic SP10 that had been pre-calibrated, and the calibration was verified according to the National Institute for Occupational Safety and Health guidelines for calibration limits (±3.5%) of the true value and met these standards. The weight scale was calibrated daily with a known kilogram material. A pre-test was done on 12 (5%) of the study subjects at Agaro Hospital before the actual data collection to ensure the clarity, understandability, consistency, accuracy, and content of the questionnaire, and modifications were made accordingly.

3. Results

3.1. Socio-Demographic Characteristics

A total of 248 study participants, including 124 RA patients and an equal number of non-RA comparative group individuals, were interviewed and underwent spirometry, achieving a 100% response rate. The majority of the study participants with rheumatoid arthritis, 93 (75%), were females, exhibiting the same sex distribution as non-rheumatoid arthritis participants.

The mean age of RA patients and non-rheumatoid arthritis participants was 44.71 ± 8.40 years and 44.32 ± 8.46 years, respec-

tively, with a minimum age of 24 and a maximum of 64 years. Furthermore, most of the RA patients, 47 (37.9%), fell into the 40-49 years age category. More than half, 77 (62.1%), of rheumatoid arthritis patients were found to be urban residents. Regarding the occupation of rheumatoid arthritis patients, daily laborers, merchants, farmers, and government employees accounted for 16 (12.9%), 42 (33.9%), 21 (16.9%), and 34 (27.4%), respectively. As for the educational level of the patients with RA, 27 (21.8%) could not read and write, 22 (17.7%) had a diploma, and 10 (8.1%) had an education level of above diploma (Table 1).

Variables		**RA Patients, (n = 124)**		**Healthy Adults, (n = 124)**	
		Frequency	Percent	Frequency	Percent
Sex	Male	31	25	31	25
	Female	93	75	93	75
Age category	<30	4	3.2	6	4.8
	30-39	29	23.4	27	21.8
	40-49	47	37.9	49	39.5
	50-59	27	21.8	22	17.7
	>60	17	13.7	20	16.2
Age in years		44.71±8.40		44.32±8.46	
Place of residence	Urban	77	62.1	86	69.4
	Rural	47	37.9	38	30.6
Occupational status	Gov't employees	34	27.4	19	15.4
	Merchants	42	33.9	27	21.8
	Farmers	21	16.9	22	17.7
	Daily laborer	16	12.9	18	14.5
	Others*	11	8.9	38	30.6
Educational level	Don't read and write	27	21.8	39	31.5
	Primary	35	28.2	22	17.7
	Secondary	30	24.2	32	25.8
	Diploma	22	17.7	19	15.3
	First-degree & above	10	8.1	12	9.7
* *Private, NGO, Housewife.*					

Table 1: Frequency Distribution of Sociodemographic Characteristics of The Study Participants at JMC and MKH, Southwest Ethiopia, 2023.

3.2. Anthropometric Parameters of the Respondents

The mean height of respondents with RA and healthy adults was 1.64 m±0.07 and 1.65 m±0.06, respectively. Patients with RA and healthy adults had mean weights of 63.42 kg±6.15 and 63.36 kg±4.98, respectively. The mean BMI for patients with RA and healthy adults was 23.56 kg/m^2 ±2.64 and 23.36 kg/m^2±1.96, respectively (Table 2).

	RA Patients, (n=124)				**Healthy Adults, (n=124)**		
Anthropometric Parameters	**Category**	**No**	**%**	**Mean ± SD**	**No**	**%**	**Mean ± SD**
BMI (kg/m^2)	Low risk	97	78.3	23.56± 2.64	103	83.1	23.36± 1.96
	Increased risk	27	21.7		21	16.9	
WC (cm)	Low risk	63	50.8	86.05± 9.12	54	43.5	86.70± 7.16
	Increased risk	61	49.2		70	56.5	
Height(m)	1.64 ± 0.07			1.65 ± 0.06			
Weight(kg)	63.42 ±6.15			63.36± 4.98			
Abbreviation: SD± Standard Deviation							

Table 2: Anthropometric Parameters of The Respondents at JMC and MKH, Southwest Ethiopia, 2023.

3.3. Clinical Characteristics Parameters of Ra Patients

The study exhibited several notable clinical characteristics. The majority of patients had a prolonged duration of RA illness, with 60 (48.4%) having an illness duration exceeding five years. Rheumatoid factor was positive in 74 (59.7%) patients and negative in 50 (40.1%). Regarding pharmacological management, 74 (59.7%) patients were receiving Disease-Modifying Antirheumatic Drugs (DMARDs), followed by 27 (21.8%) on corticosteroids, and 23 (18.5%) on Nonsteroidal Anti-inflammatory Drugs (NSAIDs). Disease activity, as assessed by the DAS28-ESR, indicated that the majority of patients, 57 (46%), had mild disease activity. Moderate disease activity was observed in 39 (31.4%) patients, while 17 (13.7%) patients had achieved remission. Furthermore, the erythrocyte sedimentation rate (ESR) was moderately elevated in 54 (43.6%) patients.

Parameters	Category	No	%
Disease duration	<1year	11	8.9
	1-5years	53	42.7
	>5years	60	48.4
ESR (mm/Hr)	<20	36	29
	20-40	34	27.4
	40-70	54	43.6
Treatment category	NSAIDs	23	18.5
	Steroids	27	21.8
	DMARDs	74	59.7
DAS28-ESR	Remission	17	13.7
	Mild disease activity	57	46.0
	Moderate disease activity	39	31.4
	High disease activity	11	8.9
Rheumatoid factor	Positive	74	59.7
	Negative	50	40.1

Table 3: Clinical characteristics of the RA respondents at JMC and MKH, Southwest Ethiopia ,2023.

3.4. Comparison of Means of The Spirometry Among Ra Patients and Healthy Adults

After applying the independent samples t-test, there was no statistically significant difference in mean age, sex, area of residence and weight of rheumatoid patients and the non-RA comparative group (P>0.05).

Therefore, the possible variation in the indices of Spirometry due to age, sex, area of residence and weight would not be a factor for this study outcome. Then, independent samples t-test was performed to compare means of FVC (L), FEV1(L), FEV1/FVC%, PEFR(L/s), and FEF25-75%(L/s) among RA patients and healthy adults. Assumptions of the independent samples t-test like normality based on the mean of pulmonary function tests parameters and homogeneity of variance were performed and met based on findings of Shapiro-Wilk and Levene's tests at the p-value >0.05.

The present study showed that there was a significantly reduced mean of FVC(L)among rheumatoid arthritis patients (3.00 ± 0.38) compared to healthy adults (3.60 ± 0.35, p<0.001). The study also indicated that the mean of FEV1(L) was significantly reduced among rheumatoid arthritis patients (2.31± 0.34) when compared to healthy adults (2.81 ± 0.38, p<0.001). Also, this study indicated that the mean of PEFR(L/s) was significantly reduced among RA patients (5.77 ± 0.84) when compared to healthy adults (6.63 ± 0.81, p<0.001) and significantly reduced the mean score of FEF25-75% (L/s) among RA patients (2.41 ± 0.37) compared to healthy adults (2.82 ± 0.34 was seen, p<0.001) (Table 3).

Spirometry Parameters	Study Participants	Mean	sd	t-test	ci
FVC(L)	RA patients	3.00	0.38	-10.12	(-0.72, - 0.48) **
	Healthy adults	3.60	0.35		
FEV_1(L)	RA patients	2.31	0.34	-8.53	(-0.61, -0.38) **
	Healthy adults	2.81	0.38		
FEV_1/FVC%	RA patients	77.31	6.87	-1.04	(-3.6,1.2)
	Healthy adults	78.5	7.85		
PEFR(l/s)	RA patients	5.77	0.84	-7.11	(-1.11, -0.60) **
	Healthy adults	6.63	0.81		
$FEF_{25-75\%}$ (l/s)	RA patients	2.41	0.37	-6.50	(-0.52, -0.30) **
	Healthy adults	2.82	0.34		

Note: *The mean difference is highly significant at **p < 0.001.*
Abbreviations: *L/s = liter per second; CI = Confidence interval; SD ± Standard Deviation.*

Table 4: Comparison of the Means of Spirometry Among RA Patients and Healthy Adults at JMC and MKH, Southwest Ethiopia, 2023.

3.5. Prevalence of Pulmonary Function Abnormalities

Generally, 53 (42.8%) and 7(5.7 %) of RA and Non-RA respondents had at least one type of pulmonary function abnormality respectively (Figure 1).

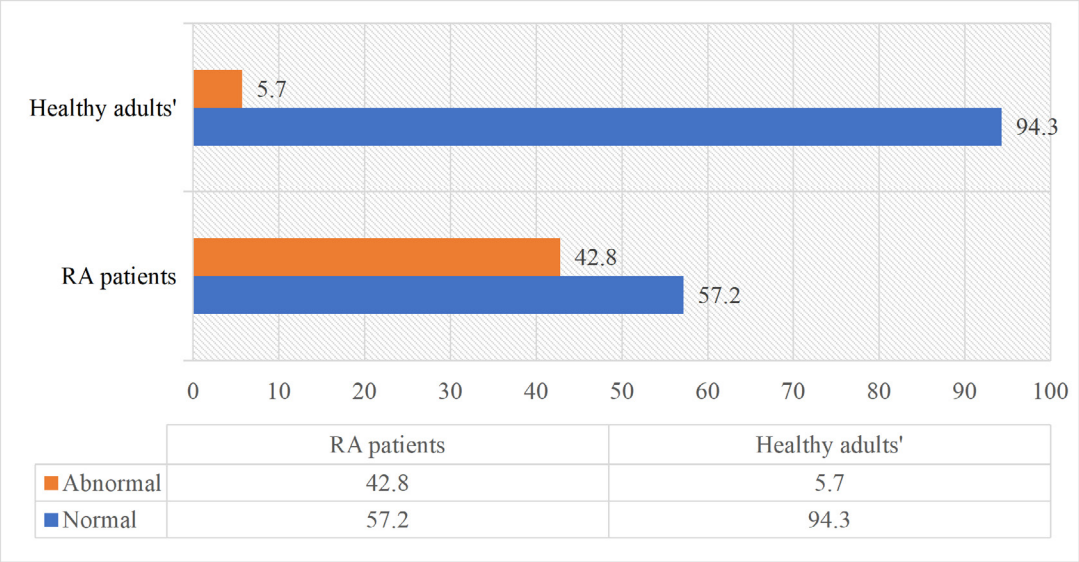

Figure 1: Pulmonary function status of RA patients and healthy adults at JMC and MKH, Southwest Ethiopia, 2023 (N = 248).

3.6. Types of Pulmonary Function Abnormalities

The prevalence of restrictive lung disorder was 27 (21.8%) and 2 (1.6%) among RA and non-RA study participants, respectively, while obstructive lung disorder accounted for 23(18.6%) and 5 (4.0%) among RA and non-RA study participants, respectively. Only 3 (2.4%) of RA patients had mixed types of ventilatory defects (Figure 2).

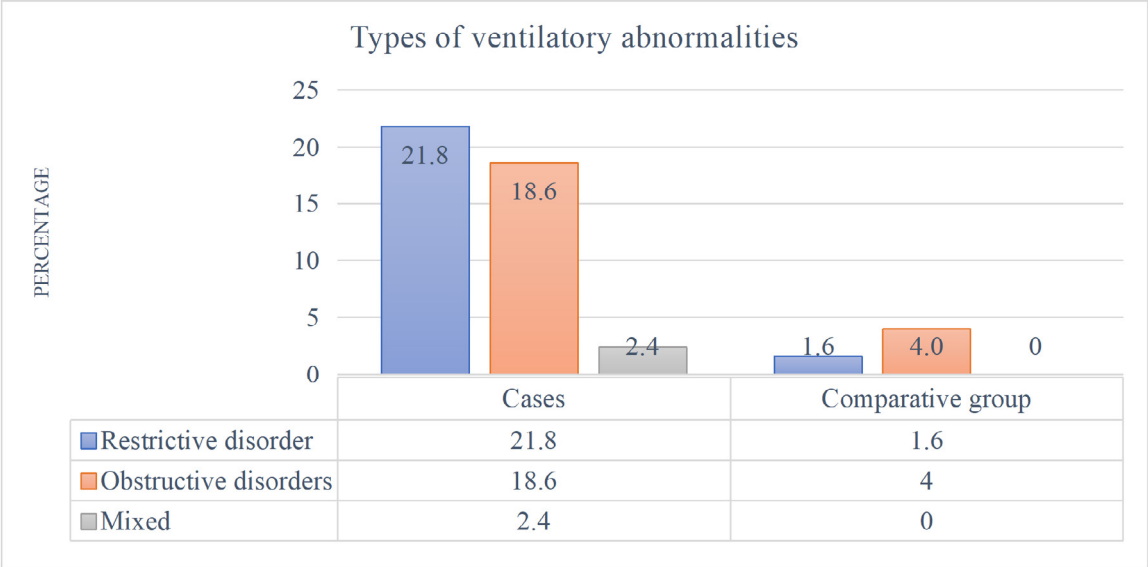

Figure 2: Magnitude and Types of Ventilatory Disorders Among RA Patients and Healthy Adults at JMC and MKH, Southwest Ethiopia, 2023 (N = 248).

3.7. Factors Associated with Pulmonary Function Abnormalities

3.7.1. Binary and Multivariable Analysis for Cases

For bivariate analysis, variables like sociodemographic factors, behavioral factors, clinical characteristics parameters and body composition measurements were included. From these variables, sex, disease activity treatment category, RF status occupation, biomass exposure, WC category, physical activity category, and alcohol consumption behavior were associated with pulmonary function abnormalities at a P-value of less than 0.25. The findings of multivariable logistic regression indicated that physical inactivity, biomass exposure, increased risk of waist circumference and moderate to high disease activity were independently associated with pulmonary function abnormality (Table 4).

Variable	Category	Pulmonary function status		COR (95% CI)	AOR (95% CI)
		Normal (%)	Abnormal (%)		
Sex	Female	52(41.9)	41(33.2)	1.3[.78-6.46]	3.6[.84-15.7]
	Male	19(15.3)	12(9.6)	1	1
Occupation	Farmer	14(11.3)	7(5.6)	.91[.24-6.4]	.62[.08-5.10]
	Daily labor	8(6.5)	8(6.5)	1.8[.55-10.8]	5.3[.52-53.4]
	Merchant	22(17.7)	20(16.1)	1.7[.21-4.70]	.94[.11-8.10]
	Others	5(4.1)	6(4.8)	2.2[.52-17.2]	1.6[.07-16]
	Gov't	22(17.7)	12(9.7)	1	1
Alcohol consumption behavior	Low risk	66(53.2)	45(36.3)	1	1
	Increased risk	5(4.0)	8(6.5)	2.4[.54-11.0]	1.7[.14-20.1]
Biomass exposure	No	44(35.5)	18(14.5)	1	1
	Yes	27(21.8)	35(28.2)	3.2[1.24-8.2] *	4.4[1.3-14.8] *
Physical activity	Inactive	34(27.5)	37(29.8)	2.5[.98-6.51]	5.5[1.4-21.8] *
	Active	37(29.8)	16(12.9)	1	1
WC category	Low risk	41(33.1)	22(17.7)	1	1
	Increased risk	35(28.2)	26(21.0)	1.4[.80-5.10]	3.6[1.06-11.9] *
Medication category	DMARDs	42(33.9)	32(25.8)	1.3[.79-8.23]	2.4[.85-7.1]
	NSAIDs	12(9.7)	11(8.9)	1.6[.85-7.86]	1.7[0.98-6.9]
	Steroids	17(13.7)	10(8.1)	1	1
DAS28-ESR	Remission-Mild	47(37.8)	27(21.8)	1	1

	Moderate-High	24(19.4)	26(21.0)	1.9(1.64-7.66)	4.2(1.71-12.4) *
Rheumatoid factor	Positive	34	40	3.35[.02-2.73]	.08[.04-1.71]
	Negative	37	13	1	1
** p<0.05 Significant.* *COR =Crude odds ratio, AOR =Adjusted odd ratio*					

Table 5: Binary and Multivariable analysis of factors associated with pulmonary function abnormalities among RA patients at JMC and MKH, Southwest Ethiopia, 2023.

4. Discussion

The results of this study show that the number of RA female patients exceeds that of male patients, with a ratio reaching as high as 3.1:1. This is consistent with worldwide reports that demonstrate the prevalence of RA disease in the female gender. This disparity is largely explained by the difference in the capability of immune system reactivity and factors related to a decline in ovarian function and sex hormone bioavailability, all contributing to RA development [2,3].

Fifty-three (42.8%) of the RA respondents had at least one type of pulmonary function abnormality. This finding is comparable with studies conducted in Spain (45%), Iraq (37.5%), semi-urban parts of eastern India (43.4%) and Kenya (38.5%) [12,20-22].But, it is lower than the study done in Egypt (63.9%) [23].On the other hand, the present finding was higher than the studies conducted in the USA (28%), Brazil (30.1%), and India Bengal (33.3%) [24-26]. These differences may be attributed to variations in socioeconomic factors, healthcare systems, disease definitions, the presence of other comorbidities, study design, selection criteria, sample size, and the presence or absence of other risk factors.

Of total pulmonary function abnormalities, restrictive ventilatory defect 27 (21.8%) was seen to be higher in RA respondents. This finding is in line with the study conducted in Iraq in 2017, Iran in 2016, India in 2015, and Egypt in 2011 [12,23,27,28]. But, the present finding is not supported by the research done in the USA in 2010, Kenya in 2010, and France Lille in which obstructive defect was higher [22,24,29]. These differences may be attributed to the difference in presence of other co-morbidities, the presence or absence of other risk factors, environmental or geographical area, and genetic variations.

Regarding pulmonary function parameters, the present study showed that means of FVC, FEV1, FEF25-75%, and PEFR were significantly reduced among rheumatoid arthritis patients than healthy adults. This finding was in line with the study conducted in the UK, Iraq, and India [12,27,30]. This reduction of FVC and FEV1 may be attributed to the shifting of an immune response against citrullinated peptides taking place at the joints to the lungs and possibly cause an immune response to trigger airways inflammation resulting in increased airways resistance and differentiation of fibroblasts in the lungs into myofibroblasts ultimately resulting in lung fibrosis [31].

The reduction of FEF25-75% and PEFR is perhaps due to the injury to the lung mucosa, airways, and interstitium by ACPA and RF as they form immune complexes and activate cells by binding to the Fc portion of receptors resulting in widespread inflammation to small and large airways [1,32,33]. Besides, prolonged physical restriction caused by RA may lead to the decrement of respiratory muscle strength and respiratory effort in the long run due to cardiopulmonary deconditioning and ultimately contribute to the reduction of PEFR at most [34,35].

The present study revealed that waist circumference greater than 80cm for females and greater than 90cm for males was associated with pulmonary function abnormality. The study participants who had increased risk WC category were 3.6 times more likely to develop pulmonary function abnormality than those with low-risk WC. This finding was supported by the study conducted in Daegu Korea and the United Kingdom in which pulmonary function changes in those with increased waist circumference individuals compared with the normal individuals [36,37]. The mechanical properties of the lungs and chest wall are altered significantly among centrally obese subjects, largely due to fat deposits in the mediastinum and the abdominal cavities. These alterations might reduce the compliance of the lungs, reduced inspiratory capacity, and fall of a diaphragm which will finally derange the respiratory function of individuals [38].

Biomass smoke exposure was identified as a predictor of pulmonary function abnormalities in the present study. Rheumatoid arthritis patients who were exposed to biomass smoke were 4.4 times more likely to develop pulmonary function abnormalities than those who were not exposed. This may be due to different and a significant number of toxic compounds emitted from biomass that are inhaled into the respiratory system, subsequently triggering the development of a pulmonary and systemic inflammatory state by increasing the genotoxic effect of oxidative stress [39].

Physical inactivity was also identified as an independent predictor of pulmonary function dysfunction. Rheumatoid arthritis patients who were physically inactive had a 5.5 times greater chance of developing pulmonary function abnormalities than their physically active counterparts. This finding aligns with a study conducted in India which showed that physically inactive respondents had abnormal pulmonary function compared to physically active groups [40]. Physical activity plays a key role in cardiopulmonary health, with its benefits dependent on intensity and duration. It can partially improve lung function by strengthening the respiratory

muscles, and an increased duration of activity further helps prevent other risk factors that impair lung function [35].

Moderate to high RA disease activity has been identified as an independent predictor of pulmonary function dysfunction. Patients with moderate to high RA disease activity demonstrated a 4.2-fold increased likelihood of developing pulmonary function abnormalities compared to those with no to mild disease activity. This association can be primarily attributed to direct inflammatory damage on lung tissues. In active RA, immune cells infiltrate the lung parenchyma, leading to the thickening and scarring of alveoli and surrounding tissues. This process results in reduced lung compliance and elasticity, thereby impairing proper lung expansion and contraction [41].

Secondly, the management of high RA disease activity often necessitates the use of immunosuppressive medications. While crucial for controlling systemic inflammation, these treatments can compromise the immune system, increasing patient susceptibility to respiratory infections. Such infections can further exacerbate lung tissue damage and impair pulmonary function [42]. Furthermore, the joint pain and reduced mobility characteristic of moderate to high RA activity can inadvertently limit a patient's physical activity. This reduction in exertion may mask early respiratory symptoms, such as dyspnea, as patients might subconsciously avoid activities that trigger breathlessness rather than recognizing a decline in lung function. Consequently, this can lead to a delay in the diagnosis and timely treatment of lung involvement in RA patients [43].

6. Conclusion

In this study, a significant number of the RA patients had at least one pulmonary function abnormality. The mean values of FVC (L), FEV1 (L), FEF25-75% (L/s), and PEFR (L/s) were significantly lower among RA patients compared to the relatively healthy non-RA comparative group. Physical inactivity, WC > 80 cm and > 90 cm for males and females respectively, moderate to high disease activity, and exposure to biomass smoke were all independent predictors of pulmonary function abnormality.

Study Limitations

The use of a cross-sectional study design limits the ability to establish a causal relationship between the examined factors and pulmonary function abnormalities. Additionally, the reliance on self-reported exposure data introduces the potential for recall or reporting bias.

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Authors' contribution

All authors made a significant contribution to the work reported. They have participated in either conception, acquisition of data, analysis, and interpretation; took part in drafting, and critically reviewing the articles, or gave final approval of the version to be published; have agreed on the journal to which the manuscript has been submitted; and agreed to be accountable for all aspects of the work.

Availability of data and materials

No datasets were generated or analyzed during the current study.

Competing interests

The authors declare they have no competing interests.

Consent for publication

Not applicable

Ethics declarations

Ethical clearance was obtained from the ethical review board of Jimma University, Institute of Health with Ref. No: IHR 53/2023.

References

1. Shaw, M., Collins, B. F., Ho, L. A., & Raghu, G. (2015). Rheumatoid arthritis-associated lung disease. *European Respiratory Review, 24*(135), 1.
2. Jameson, J. L. (2018). Harrison's Principles of Internal Medicine. *McGraw-Hill Education.* 2527-2528.
3. Alpízar-Rodríguez, D., Pluchino, N., Canny, G., Gabay, C., & Finckh, A. (2017). The role of female hormonal factors in the development of rheumatoid arthritis. *Rheumatology, 56*(8), 1254-1263.
4. Yunt, Z. X., & Solomon, J. J. (2015). Lung disease in rheumatoid arthritis. *Rheumatic diseases clinics of North America, 41*(2), 225.
5. Sokolove, J., Johnson, D. S., Lahey, L. J., Wagner, C. A., Cheng, D., Thiele, G. M., ... & Robinson, W. H. (2014). Rheumatoid factor as a potentiator of anti–citrullinated protein antibody–mediated inflammation in rheumatoid arthritis. *Arthritis & rheumatology, 66*(4), 813-821.
6. Guo, Q., Wang, Y., Xu, D., Nossent, J., Pavlos, N. J., & Xu, J. (2018). Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. *Bone research, 6*(1), 15.
7. Paulin, F., Doyle, T. J., Fletcher, E. A., Ascherman, D. P., & Rosas, I. O. (2015). Rheumatoid arthritis-associated interstitial lung disease and idiopathic pulmonary fibrosis: shared mechanistic and phenotypic traits suggest overlapping disease mechanisms. *Revista de investigacion clinica, 67*(5), 280-286.
8. Bendstrup, E., Møller, J., Kronborg-White, S., Prior, T. S., & Hyldgaard, C. (2019). Interstitial lung disease in rheumatoid arthritis remains a challenge for clinicians. *Journal of clinical medicine, 8*(12), 2038.
9. Mori, S., Koga, Y., & Sugimoto, M. (2011). Small airway obstruction in patients with rheumatoid arthritis. *Modern rheumatology, 21*(2), 164-173.
10. Ma, Y., Tong, H., Zhang, X., Wang, M., Yang, J., Wu, M., ... & Pan, F. (2019). Chronic obstructive pulmonary disease in rheumatoid arthritis: a systematic review and meta-analysis.

Respiratory research, 20(1), 144.
11. Graham, B. L., Steenbruggen, I., Miller, M. R., Barjaktarevic, I. Z., Cooper, B. G., Hall, G. L., ... & Thompson, B. R. (2019). Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement. *American journal of respiratory and critical care medicine, 200*(8), e70-e88.
12. Chattopadhyay, K., Chaudhuri, A., Hussain, S. A., & Biswas, A. (2015). A comparative study of functional pulmonary involvement in patients with rheumatoid arthritis in a semi-urban population of Eastern India. *Saudi Journal of Sports Medicine, 15*(1), 26-30.
13. Van Riel, P. L., & Renskers, L. (2016). The Disease Activity Score (DAS) and the Disease Activity Score using 28 joint counts (DAS28) in the management of rheumatoid arthritis. *Clin Exp Rheumatol, 34*(5 Suppl 101), S40-S44.
14. Kratz, A., Plebani, M., Peng, M., Lee, Y. K., McCafferty, R., Machin, S. J., & International Council for Standardization in Haematology (ICSH). (2017). ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate. *International journal of laboratory hematology, 39*(5), 448-457.
15. Åström, M., Thet Lwin, Z. M., Teni, F. S., Burström, K., & Berg, J. (2023). Use of the visual analogue scale for health state valuation: a scoping review. *Quality of Life Research, 32*(10), 2719-2729.
16. Wells, G., Becker, J. C., Teng, J., Dougados, M., Schiff, M., Smolen, J., ... & Van Riel, P. L. C. M. (2009). Validation of the 28-joint Disease Activity Score (DAS28) and European League Against Rheumatism response criteria based on C-reactive protein against disease progression in patients with rheumatoid arthritis, and comparison with the DAS28 based on erythrocyte sedimentation rate. *Annals of the rheumatic diseases, 68*(6), 954-960.
17. Pellegrino, R., Viegi, G., Brusasco, V., Crapo, R. O., Burgos, F., Casaburi, R. E. A., ... & Wanger, J. (2005). Interpretative strategies for lung function tests. *European respiratory journal, 26*(5), 948-968.
18. Centers for Disease control and prevention. (2011). Respiratory Health Spirometry Procedures Manual. Centers for Disease Control and Prevention.
19. Occupational Safety and Health Administration, Labor, U.S. Department of Labour. Spirometry Testing in Occupational Health Programs: Best Practices for Healthcare Professionals. Osha. 2013;1–62.
20. Robles-Perez, A., Luburich, P., Rodriguez-Sanchon, B., Dorca, J., Nolla, J. M., Molina-Molina, M., & Narvaez-Garcia, J. (2016). Preclinical lung disease in early rheumatoid arthritis. *Chronic respiratory disease, 13*(1), 75-81.
21. Al-Assadi, T., Al-Shemery, A., & Salman, S. (2009). Correlation of lung function with disease activity rheumatoid arthritis. *Oman Medical Journal, 24*(2), 84.
22. Biomdo, I. C. (2013). Assessment of pulmonary function in Rheumatoid arthritis patients attendin-g Rheumatology clinics in nairobi (Doctoral dissertation, University of Nairobi).
23. Youssef, A. A., Machaly, S. A., El-Dosoky, M. E., & El-Maghraby, N. M. (2012). Respiratory symptoms in rheumatoid arthritis: relation to pulmonary abnormalities detected by high-resolution CT and pulmonary functional testing. *Rheumatology international, 32*(7), 1985-1995.
24. Pappas, D. A., Giles, J. T., Connors, G., Lechtzin, N., Bathon, J. M., & Danoff, S. K. (2010). Respiratory symptoms and disease characteristics as predictors of pulmonary function abnormalities in patients with rheumatoid arthritis: an observational cohort study. *Arthritis research & therapy, 12*(3), R104.
25. Kawassaki, A. M., Pereira, D. A. S., Kay, F. U., Laurindo, I. M. M., Carvalho, C. R. R., & Kairalla, R. A. (2015). Pulmonary involvement in rheumatoid arthritis: evaluation by radiography and spirometry. *Jornal Brasileiro de Pneumologia, 41*, 331-342.
26. Gantait, K., Jamirul, I., Barman, H., & Santra, T. (2019). Pulmonary function test with DAS28 score and duration of Rheumatoid arthritis: A comparative analysis. *Res Gate, 18*(1), 54-62.
27. Kadhum, H. J., Hamza, A.N Al, Bader, A. (2017). Pulmonary function test in arthritis patients. *MJBU. 35*(2):1–8.
28. Zayeni, H., Haji-Abbasi, A., Foumani, S. A. A., Tohidi, M., Masooleh, I. S., Parsa, B. G., ... & Maafi, A. A. (2016). Pulmonary involvement in rheumatoid arthritis: A cross-sectional study in Iran. *Lung India, 33*(1), 49-52.
29. Cortet, B., Perez, T., Roux, N., Flipo, R. M., Duquesnoy, B., Delcambre, B., & Rémy-Jardin, M. (1997). Pulmonary function tests and high resolution computed tomography of the lungs in patients with rheumatoid arthritis. *Annals of the rheumatic diseases, 56*(10), 596-600.
30. Hassan, W. U., Keaney, N. P., Holland, C. D., & Kelly, C. A. (1994). Bronchial reactivity and airflow obstruction in rheumatoid arthritis. *Annals of the rheumatic diseases, 53*(8), 511-514.
31. Paulin, F., Babini, A., Mamani, M., Mercado, J., & Caro, F. (2017). Practical approach to the evaluation and management of rheumatoid arthritis-interstitial lung disease based on its proven and hypothetical mechanisms. *Revista de investigacion clinica, 69*(5), 235-242.
32. Wilsher, M., Voight, L., Milne, D., Teh, M., Good, N., Kolbe, J., ... & Dalbeth, N. (2012). Prevalence of airway and parenchymal abnormalities in newly diagnosed rheumatoid arthritis. *Respiratory medicine, 106*(10), 1441-1446.
33. Clavel, C., Nogueira, L., Laurent, L., Iobagiu, C., Vincent, C., Sebbag, M., & Serre, G. (2008). Induction of macrophage secretion of tumor necrosis factor α through Fcγ receptor IIa engagement by rheumatoid arthritis–specific autoantibodies to citrullinated proteins complexed with fibrinogen. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 58*(3), 678-688.
34. Çimen, Ö. B., Deviren, S. D., & Yorgancıoğlu, Z. R. (2001). Pulmonary function tests, aerobic capacity, respiratory muscle strength and endurance of patients with rheumatoid arthritis. *Clinical rheumatology, 20*(3), 168-173.
35. Burton, D. A., Stokes, K., & Hall, G. M. (2004). Physiological effects of exercise. Continuing Education in Anaesthesia,

Critical Care & Pain, 4(6), 185-188.
36. Park, J. E., Chung, J. H., Lee, K. H., & Shin, K. C. (2012). The effect of body composition on pulmonary function. *Tuberculosis and respiratory diseases, 72*(5), 433.
37. Wehrmeister, F. C., Menezes, A. M. B., Muniz, L. C., Martínez-Mesa, J., Domingues, M. R., & Horta, B. L. (2012). Waist circumference and pulmonary function: a systematic review and meta-analysis. *Systematic reviews, 1*(1), 55.
38. Peters, U., Dixon, A. E. (2019). Obesity and Lung Compliance. *Rev Respir Med. 12*(9):755–67.
39. Silva, R., Oyarzún, M., & Olloquequi, J. (2015). Pathogenic mechanisms in chronic obstructive pulmonary disease due to biomass smoke exposure. *Archivos de Bronconeumología (English Edition), 51*(6), 285-292.
40. Vedala, S., Paul, N., Mane, A. B. (2013). Differences in Pulmonary Function Test among the Athletic and Sedentary Population. *Natl J Physiol, 3*(2):118-23.
41. Ito, Y., Ichikawa, Y., Murashima, S., Sakuma, H., & Nakajima, A. (2024). Rheumatoid arthritis disease activity significantly impacts on the severity of interstitial lung disease. *Arthritis Research & Therapy, 26*(1), 95.
42. Radu, A. F., & Bungau, S. G. (2021). Management of Rheumatoid Arthritis: An Overview. *Cells 2021, 10,* 2857.
43. Hernández-Hernández, M. V., & Díaz-González, F. (2017). Role of physical activity in the management and assessment of rheumatoid arthritis patients. *Reumatología Clínica (English Edition), 13*(4), 214-220.