PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT EXTRA ARTICULAR MANIFESTATIONS

DISSERTATION SUBMITTED TO THE TAMILNADU

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Registration Number: 201711362

DEPARTMENT OF GENERAL MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

MAY-2020

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled "**PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT EXTRA ARTICULAR MANIFESTATIONS"** submitted by **Dr.S.PADMA PRIYA** , to the Tamilnadu Dr. M.G.R Medical University, Chennai, in partial fulfillment of the requirement for the award of M.D. Degree Branch – I (General Medicine) is a bonafide research work carried out by her under direct supervision & guidance.

Professor & Head of the Department,
Department of General Medicine
Tirunelveli Medical College,
Tirunelveli.

Unit Chief,
Department of General Medicine
Tirunelveli Medical College,
Tirunelveli.

CERTIFICATE BY THE DEAN

I hereby certify that this dissertation entitled "**PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT EXTRAARTICULAR MANIFESTATIONS"** is a record of work done by **Dr. S.PADMA PRIYA** , in the Department of General Medicine, Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2016- 2019. This work has not formed the basis for previous award of any degree.

Date :
Place : TIRUNELVELI

The DEAN

Tirunelveli Medical College,

Tirunelveli - 627011.

DECLARATION

I solemnly declare that the dissertation entitled **"PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT EXTRAARTICULAR MANIFESTATIONS"** Tirunelveli Medical College Hospital, Tirunelveli Under the guidance and supervision of Prof.Dr.L.Rajagopala marthandam M.D, the dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

Place: Tirunelveli
Date:

Dr.S.PADMA PRIYA
Registration No.: 201711362
Postgraduate Student,
M.D General Medicine,
Department of General Medicine,
Tirunelveli Medical College
Tirunelveli.

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TIRUNELVELI MEDICAL COLLEGE

INSTITUTIONAL RESEARCH ETHICS COMMITTEE
TIRUNELVELI, STATE OF TAMILNADU, SOUTH INDIA PIN 627011
91-462-2572733-EXT; 91-462-2572944; 91-462-2579785; 91-462-2572611-16
online@tvmc.ac.in, tirec@tvmc.ac.in; www.tvmc.ac.in

CERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO:1214/GM/2017

PROTOCOL TITLE: PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS WITHOUT EXTRA ARTICULAR MANIFESTATIONS.
PRINCIPAL INVESTIGATOR: Dr.S.PADMA PRIYA, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE STUDENT
DEPARTMENT & INSTITUTION: GENERAL MEDICINE - TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear Dr.S.PADMA PRIYA., MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 15.12.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
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6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
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   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

Dr.K.Shantarama, MD
Registrar, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

Dr.J.SureshDurai, MD
Member Secretary, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

CERTIFICATE – II

This is to certify that this dissertation work entitled **" PULMONARY FUNCTION TEST IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT EXTRAARTICULAR MANIFESTATIONS"** of the candidate **Dr.S.PADMA PRIYA** with registration Number **201711362** for the award of **M.D.** Degree in the branch of **GENERAL MEDICINE (I).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **9 percentage** of plagiarism in the dissertation.

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Sources included in the report:

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Instances where selected sources appear:

CONTENT

LIST OF ABBREVIATIONS

ACR : American college of Rheumatology

Anti-CCP : Anti-cyclic citrullinated protein

COPD : Chronic Obstructive Pulmonary Disease

DAS : Disease activity score

DAS 28 : Disease activity score 28 joints

DMARDS : Disease modifying anti-rheumatic drugs

DLCO : Diffusion Capacity of Carbon Monoxide

ESR : Erythrocyte Sedimentation Rate

FEF 25-75 : Forced Expiratory Flow at 25% to 75% of vital capacity

FEV1 : Forced Expiratory Volume in one Second

FVC : Forced Vital Capacity

FEV1/FVC : Ratio that shows Restriction and Obstruction of the airways

FRC : Functional Residual Capacity

GOLD : Global Initiative on Obstructive Lung Disease

HRCT : High Resolution Computed Tomography of the Chest

ILD : Interstitial Lung Disease

IP : Interstitial Pneumonia

MTX : Methotrexate

NSAID : Non steroidal anti-inflammatory drugs

NSIP : Non specific interstitial pneumonia

OP : Organising pneumonia

PFTS : Pulmonary Function Tests

RV : Residual Volume

RA : Rheumatoid arthritis

RF : Rheumatoid factor

TLC : Total Lung Capacity

TNF : Tumor Necrosis Factor

UIP : Usual interstitial pneumonia

INTRODUCTION

Rheumatoid arthritis is one of the commonest auto immune disorders affecting females commonly and smoking males. Rheumatoid arthritis is more prevalent in Asian population .HLA DR4 is the Major Histo Compatibility involved. The triggering factors are smoking, infections by Porphyromonas gingivalis and Mycoplasma pneumonia.

In RA, acute synovitis occurs early followed by chronic synovitis and finally erosive arthritis which is irreversible. The mechanism is mediated by release of all proteolytic enzymes causing fibrous deposition and finally leading to ankylosis or a fixed deformity. One of the important extraarticular manifestation is involvement of pulmonary system. The pulmonary manifestations observed are pleuritis, transudative pleural effusion and interstitial lung disease (particularly smokers). Hence a PULMONARY FUNCTION TEST is done among the affected individuals.

The detailed analysis of this test helps us in understanding the incidence of pulmonary manifestations of rheumatoid arthritis, its effect on respiratory volumes and aids us in further management.

AIMS AND OBJECTIVES

- To know the incidence of pulmonary manifestations of Rheumatoid arthritis
- To assess further improvement in treating our patients

REVIEW OF LITERATURE

Rheumatoid arthritis (RA) is the most commonly encountered connective tissue disease. Rheumatoid arthritis is a chronic inflammatory and systemic disease. It is manifested by a persistent symmetric polyarthritis involving the small joints of the hands ,wrist, and feet.[1]. The prevalence of Rheumatoid arthritis is 0.5% to 1% is worldwide . The primary site involved is the synovium of diarthrodial joints. The female to male ratio of RA is 2.5:1 and is most frequently seen in the 25-55 year age group. The etiology is unknown , but an environmental exposure inciting an autoimmune response in a genetically predisposed individuals has been established.

ETIOLOGY

Genetic factors

Genetic factors account for 60% of an individual's susceptibility to rheumatoid arthritis as studied in Twin studies[2] .Alleles confering higher risk of RA are located in Major histocompatibility complex. HLA DRB1 gene Bestows a high risk of disease along with regional variations. Shared epitope is found on HLA DRB1 alleles *0401, *0404 and *0101 in European ancestry and *0405 in Asian ancestors. Genome wide association studies have found multiple other non- MHC gene loci. Epigenetic factors also play a role.[3]

Environmental factors

Factors implicated in the development of RA includes

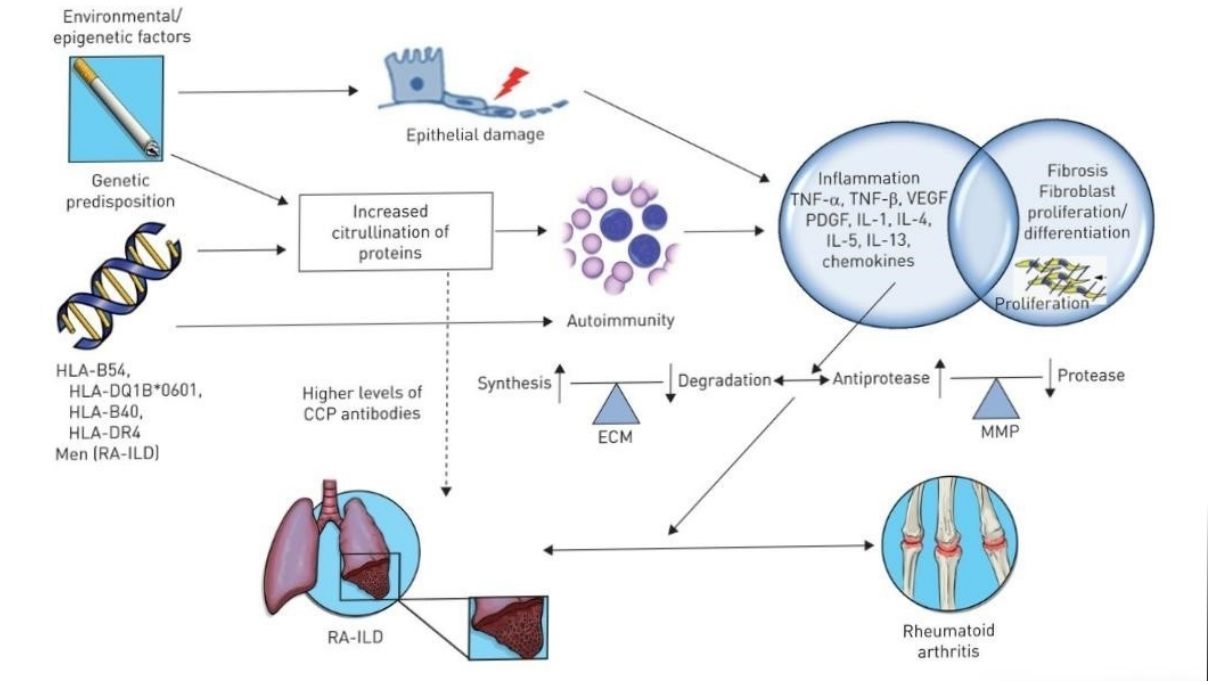
- Smoking
- Porphyromonas gingivalis in patients with chronic periodonitis
- Aggregatibacter actinomycetemcomitans by inducing hypercitrullination [2]
- Diet including coffee intake
- Viruses (EBV,Parvovirus,Mycoplasma)
- Alcohol intake and statins may decrease RA risk.

Host factors

- Hormonal and reproductive factors
- Nulliparity
- Timing of pregnancy
- Lack of breastfeeding
- Oral contraceptives

Pathogenesis

Complex interplay of genetic , environmental, and immunologic factors



causes dysregulation of the immune system and a breakdown in self tolerance. [4]

Clinical presentation

Onset of systemic and articular involvement is slow and insiduous. Patients present with fatigability and arthritic symptoms of pain , swelling , warmth, morning stiffness with number of joints increasing over weeks to months. 10% may have acute presentation with explosive onset of polyarthritis with profound fatigue , fever and weight loss.

Joint involvement in RA

Metacarpophalangeal 90 to 95%

Proximal interphalangeal 75 to 90%

Wrist 75 to 80%

Knee 60 to 80%

Shoulder 50 to 70%

Metatarsophalangeal 50 to 60 %

Ankle 50 to 60 %

Cervical spine 40 to 50%

Elbow 40 to 50%

Hip 20 to 40%

EXTRA ARTICULAR MANIFESTATIONS IN Rheumatoid arthritis [5]

General	**Ocular**	**Hematologic**
Fever Lymphadenopathy Weight loss Fatigue	Episcleritis Keratitis Choroid and retinal nodules	Felty syndrome Large granular lymphocyte syndrome Lymphoma
Dermatologic Palmar erythema Subcutaneous nodules Small vessel vasculitis	**Cardiac** Pericarditis Myocarditis Coronary vasculitis Nodules	**Others** Sjogrens synsrome Amyloidosis Osteoporosis Atherosclerosis

Pulmonary Pleuritis Nodules Interstitial pulmonary fibrosis Cryptogenic organizing pneumonia Constrictive bronchiolitis	**Neuromuscular** Entrapment neuropathy Peripheral neuropathy Mononeuritis multiplex	

Poor prognosis in RA

- Generalized polyarthritis involving both small and large joints
- Rheumatoid factor and ACCP Positive
- Poor functional status at baseline
- Extra articular manifestations
- Persistently elevated ESR and CRP
- Radiographic erosions within 2 years of disease onset
- ANA positivity
- Manual labour contributing to joint damage

Laboratory diagnosis of RA

- Complete blood test - normocytic normochromic anemia caused by anemia of chronic infection and relative thrombocytosis
- Leucocyte count usually normal

- Serum Albumin may be decreased due to inflammation mediated supression of hepatic synthesis
- Slight elevation of total protein
- Urinalysis normal
- ESR elevated (inflammation mediated and due to hypergammaglobulinemia)
- CRP elevated – for monitoring of disease activity
- Rheumatoid factor – autoantibodies directed against antigenic determinant on Fc portion of IgG (High titres are also seen in cryoglobulinemia, systemic lupus erythematosus, Sjogrens syndrome

)
- Anti cyclic citrullinated protein antibodies – 95% specific .These are directed against filaggrin,vimentin, fibrinogen, collagen II , alpha enolase by posttranslational modification of aminoacids.
- Antinuclear antibodies- 30% of patients show ANA positivity.
- Complements C3 & C4 – normal
- Synovial fluid analysis shows inflammatory pattern

Radiographic studies

- Radiographs of the hands ,wrists,and feet

- Earliest change noted is periarticular osteopenia
- Other changes are juxtaarticular bony erosions and symmetrical joint space narrowing can occur

CLASSIFICATION CRITERIA EULAR 2010

A .Joint involvement

1 large joint. 0

2 to 10 large joints. 1

1 to 3 small joints. 2 +/- involvement of large joints

4 to 10 small joints. 3

>10 joint

(at least 1 small joint) 5

B.Serology

Negative RF and negative 0

ACPA

Low positive RF/ACCP 2

High positive RF / ACCP 3

C. Acute phase reactants (CRP and ESR)

Normal. 0

Abnormal. 1

D. Duration of symptoms

<6 weeks. 0

>6 weeks. 1

Add score of categories A to D . A score of more than or equal to 6/10 is needed for classification of a patient having definite RA.

Seronegative rheumatoid arthritis :

Approximately 20–25% of patients who meet criteria for RA are negative for both IgM-RF and anti-CCP [6]. Few"seronegative" RA patients have a positive ANA or antibodies against mutated citrullinated vimentin or carbamylated proteins. Compared to seropositive RA, genetic factors contribute somewhat less to the risk of developing seronegative RA. The shared epitope alleles at the HLA-DRβ1 locus are not significant. A nonHLA gene variant of the ankyrin repeat domain-55 (ANKRD55)locus on chromosome 5 has shown a genetic association with seronegative RA. This gene is highly expressed in CD4+ T cells. The initial polyarticular presentation of seronegative RA can be similar toclassical presentation of seropositive RA. Joint damage can be severe. Seronegative RA patients have a better prognosis, fewer extraarticular manifestations , and better survival. Seronegative RA patients are treated similar

to seropositive RA patients but are less likely to respond to abatacept or rituximab treatment.

Differential Diagnosis

- **Common**

  Seronegative spondyloarthropathy

  Calcium pyrophosphate deposition disease

  Systemic lupus erythematosus

  Systemic sclerosis

  Sjogren's syndrome

  Polymyositis

  Mixed connective tissue disease

  Osteoarthritis

  Polyarticular gout

  Fibromyalgia

  EBV

  HIV

  Rubella

  Hepatitis C

Uncommon

Hypothyroidism

Rheumatic fever

Hemochromatosis

Sarcoidosis

Lyme disease

Amyloid arthropathy

Paraneoplastic syndrome

Behcet's disease

TREATMENT OF RHEUMATOID ARTHRITIS

1.DMARDs

DMARD	Dose	Side effects	Precautions/monitoring
Methotrexate	10–25 mg/ week oral or sc	Nausea, stomatitis, alopecia, pneumonitis, myelosuppression, ↑ LAEs	Viral hepatitis B and C screening; do not use if GFR < 50 cc/min. Teratogenic CBC, Cr, LAEs q8–12 weeks
Leflunomide	20 mg qd	Nausea, diarrhea, rash, alopecia, ↑ LAEs	Viral hepatitis B and C; teratogenic CBC, Cr, LAEs q8–12 weeks
Hydroxychloroquine	5 mg/kg/day (max 400 mg qd)	Nausea, rash, skin hyperpigmentation, retinopathy	Ophthalmologic exam at baseline, at year 5, then yearly if low risk
Sulfasalazine	1000–1500 mg BID	Nausea, abdominal bloating, rash, ↓ WBCs, ↑ LAEs	CBC, LAEs q12 weeks
Azathioprine	1–2 mg/kg/ day	Nausea, rash, alopecia, myelosuppression, ↑ LAEs	TPMT screen, CBC, LAEs q12 weeks

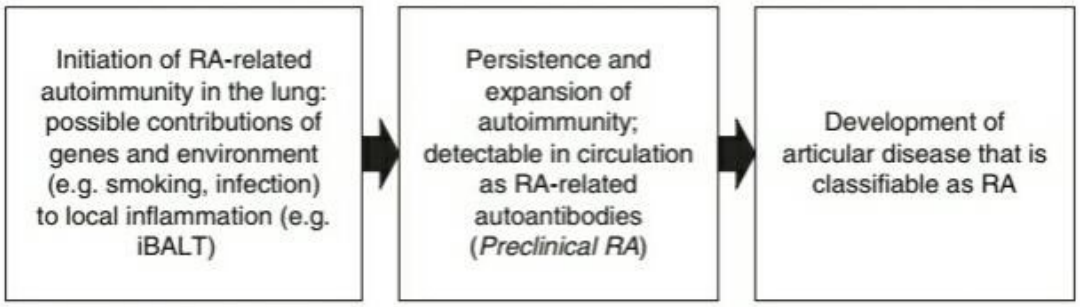
2.BIOLOGIC TREATMENT

Biologic	Dose	MOA	Precautions/monitoring
TNF inhibitors		Inhibit TNF	Bacterial, TB, fungal, viral infections, lymphoma, cytopenias, heart failure, demyelinating disorders, hepatotoxicity, DILE, psoriasis, sarcoidosis. CBC, LAEs periodically
– Etanercept	50 mg sc qwk		
– Adalimumab	40 mg sc qowk		
– Infliximab	3–5 mg/kg IV q4–8wks		
– Golimumab	50 mg sc q4wks;		
	2 mg/kg IV q8wks		
– Certolizumab	200 mg sc qowk		
Tofacitinib	5 mg BID; 11 mg qd	JAK inhibitor	Infections esp zoster, ↓Hct, ↓WBCs, ↑LAEs, ↑ lipids, ↑creatinine. CBC, Cr, LAEs, lipids q12wks
Abatacept	125 mg sc qwk; monthly IV: 500 mg (<60 kg) 750 mg (<100 kg) 1000 mg (>100 kg)	Inhibits B7-1/B7-2 binding to CD28 which inhibits T cell costimulation	Infections
Tocilizumab	162 mg sc qowk; 4–8 mg/kg IV q4wks	Binds IL-6 receptor; inhibits IL-6 binding to receptor	Infections, neutropenia, ↑ LAEs, ↑lipids, GI perforations. CBC, LAEs q1-2 mos, Lipids q 6 mos
Rituximab	1000 mg IV twice 2 weeks apart	B cell depletion; anti-CD20	Infusion reaction, infections, PML, neutropenia, hypogammaglobulinemia, hepatitis B reactivation. CBC periodically

THE LUNG – SITE OF INITIATION OF RA

Lungs play pivotal role in initiation of RA as evidenced by immune and autoimmune responses triggered by inducible bronchus associated lymphatic tissue [6]

Environmental exposures increased the risk of RA [3].



PLEUROPULMONARY MANIFESTATIONS OF

RHEUMATOID ARTHRITIS

- Pleural disease
- Pleuritis
- Pleural effusion
- Pneumothorax
- Bronchopleural fistula
- Empyema

- Rheumatoid nodules
- Necrobiotic nodules
- Caplan's syndrome
- Rheumatoid nodules
- Interstitial lung disease
- Airway involvement
- Airway obstruction
- Upper airway disease
- Bronchiectasis
- Bronchiolitis obliterans with organizing pneumonia
- Bronchiolitis obliterans
- Pulmonary vascular disease
- Vasculitis
- Primary or secondary pulmonary hypertension
- Drug-related lung disease

Miscellaneous

- Infection
- Fibrobullous disease
- Amyloidosis

Pulmonary involvement is the most common extraarticular manifestations of Rheumatoid arthritis and is seen in about 60 to 80 % of RA patients. It is a leading cause of death in patients with RA and is the second most common cause of death in RA. Pulmonary complications are directly responsible for 10 to 20% of all mortality [7].

Lung diseases directly related to RA is more common than pulmonary infections and drug toxicity . The lung is involved in rheumatoid disease because of the abundant vasculature and connective tissue which is involved in collagen vascular diseases. RA can affect the lung parenchyma, airways, and the pleura, with variable amounts of pathological inflammation and fibrosis.

The diagnostic modality will have an impact on the type of lesions detected [10]. Both restrictive and obstructive lung disease produce clinically important effects in patients with RA. However, their diagnosis is often delayed as the early signs and symptoms may be insiduous, non-specific and masked by reduced physical activity due to articular disease. Respiratory complaints are not much reported and are often unrecognized in RA patients with lung disease. This is because the individuals with RA are generally less physically active due to joint pain and chronic fatigue and thus are less likely to experience symptoms such as dyspnea on exertion. In addition the nature of the symptoms of lung involvement overlap with symptoms of cardiac disease, another common co morbidity in RA.

INTERSTITIAL LUNG DISEASE

Interstitial lung disease is a common manifestation of rheumatoid lung disease and remains asymptomatic in most people, the prevalence of is range upto 44%. Patient with early rheumatoid disease who were screened with investigations including pulmonary function tests , Chest radiography, bronchoalveolar lavage had abnormalities that was suggestive of ILD. Of those who had undergone investigations, 15% were clinically apparent and about 45% were asymptomatic.

The prevalence of ILD in rheumatoid patients is variable and depends on modality of investigation used for evaluation.Chest radiography diagnoses only 1 to 5% of the rheumatoid lung.[8] In most cases it may be normal even when the patient is symptomatic. High resolution CT is a highly sensitive modality and has 20 to 44% sensitivity but its availability is limited and is expensive.

Spirometry detects 30 to 40 % abnormality in restrictive pattern and it is a relatively cheaper modality. Articular manifestations of RA is followed by development of ILD by years.Once fibrosis develops the patient become symptomatic. The median age of presentation is 50 to 60 years of age. Radiographic changes and abnormalities in pulmonary function tests may

precede symptoms by years. Clinically manifested ILD is associated with significant mortality.

PATHOPHYSIOLOGY

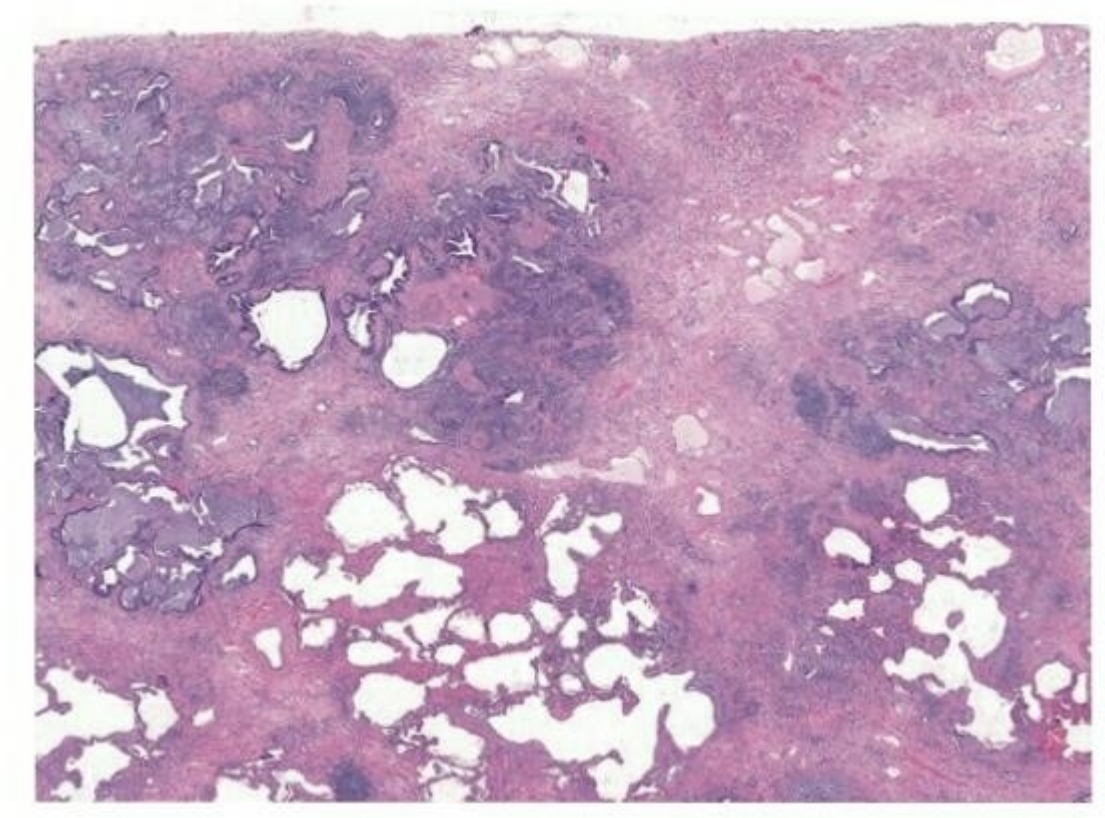
Environmental and genetic factors have been implicated in the development of lung disease in RA.RA ILD is more common in males than in females which is in contrast to other connective tissue disorders.Late onset disease, high titres of rheumatoid factor, smokers are more prone to develop ILD.

The development of lung fibrosis in RA is a cellular inflammatory process which initiates a secondary fibroproliferative process , which may become progressive. An injury to the epithelial surface causes inflammation in air spaces and walls of alveoli .Once the disease becomes chronic , inflammation spreads to adjacent portions if the interstitium and vasculature and causes interstitial fibrosis. Ventilatory function and gas exchange is impaired with development of irreversible scarring.

Various types of interstitial pneumonia are seen with associated airway disease. These disorders not only affect the interstitium but also the adjacent airspaces, peripheral airways and the vessels.

Usual interstitial pneumonia is the most common histopathological pattern followed by nonspecific interstitial pneumonia and organizing pneumonia.[12]

Usual interstitial pneumonia



Serum biomarkers in RA ILD

- Surfactant protein A Surfactant protein D
- KL 6

  These markers reflect disruption of blood alveolar barrier and disease activity of ILD

HRCT Criteria for UIP

- Subpleural , basal predominance
- Reticular abnormality
- Honeycomb with or without traction bronchiectasis
- Absence of features of inconsistent UIP

Features inconsistent with UIP pattern

- Upper or mid lung predominance
- Peribronchovascular predominance
- Extensive ground glass abnormalities
- Profuse micronodules
- Discrete cysts
- Air trapping
- Consolidation in bronchopulmonary segment

Risk factors for acute exacerbation of RA ILD

- Older age at diagnosis
- UIP pattern on HRCT
- Methotrexate usage

Clinical factors with development of RA ILD

- Presence of high titres of RF
- Smoking

- Male
- Older age
- Longer duration of disease
- Higher articular disease activity

Risk factors for mortality in RA ILD

- Male
- Smoking
- Older age
- HRCT Pattern
- Fibrosis on HPE
- Low % predicted forced vital capacity

DIAGNOSIS

- Clinical
- Pulmonary function tests
- HRCT
- Lung biopsy in rare cases

Pulmonary function tests showed decreased lung volumes and DLCO even in asymptomatic. Reduced DLCO was found to be the most sensitive marker for interstitial pneumonia. Progressive dyspnea as assessed by standard questionnaire

remains a strong predictor of survival. Serial changes in pulmonary physiology with decrease in Forced vital capacity is used for follow up of disease progression .

TREATMENT

Glucocorticoid therapy is the treatment of choice in RA ILD. More aggressive treatment is needed in patients with inflammation in HRCT, lymphocytes on bronchoalveolar lavage, and non UIP pattern on biopsy. Initial doses of oral prednisolone are typically recommended at 0.5 to 0.75mg /kg/ day and then gradually tapered.

Cyclophosphamide an alkylating agent shows immunosuppressive effects on lymphocytes and neutrophils. Oral regimen is 1 to 2 mg /kg/m2 and Intravenous pulse regimen is 500 to 1000mg /m2 every 2 to 4 weeks .

Azathioprine administered in doses 2 to 3 mg /kg /day with initial dose of 50mg /day .

Mycophenol mofetil reduces the proliferation of T cells and B cells by inhibiting the purine synthesis pathway and thus have antifibrotic effect.The dose is 500 to 2000mg /day orally.

Rituximab , a chimeric monoclonal antibody against CD20 expressed on B cells and eliminates B cells from body.

Non pharmacological treatment

- Cessation of smoking
- Oxygen therapy
- Pulmonary rehabilitation
- Vaccination for pneumococcus and influenza are recommended in patients receiving immunosuppressive therapy
- Lung transplantation considered for patients with end stage RA ILD.

PLEURAL DISEASE

The most common manifestation of RA in the lung is pleural disease with or without pleural effusion. They are commonly detected in X ray films obtained for other causes. Pleural biopsy reveals nonspecific inflammation . Unresolved rheumatoid effusion result in marked pleural thickening, a trapped lung with progressive restriction of lung volume .

Pleural effusion is more commonly seen in men with long-standing joint disease and subcutaneous nodules. Most rheumatoid pleural effusions are small, unilateral, and asymptomatic . The pleural fluid is exudative by biochemical

parameters with a low glucose level (usually <30 mg/dL) and a high rheumatoid factor titer . For persistently symptomatic pleural effusions, treatment with corticosteroids (Prednisone 10–20 mg per day), other immunosuppressive therapies and nonsteroidal anti-inflammatory agents has been found to be effective .Pleurodesis is rarely needed in patients with rheumatoid pleural effusion .

Rarely , the rheumatoid pleural effusion shows features of pseudochylothorax (also known as chyliform, pseudochylous, or cholesterol pleural effusion) and appears turbid or milky white with a high cholesterol level (typically >200 mg/dL) . This is associated with a chronic pleural effusion and a thickened pleura. Sterile empyema-like pleural effusion due to rupture of necrobiotic nodules can be seen occasionally. Pleural biopsy, when performed, reveals thickened pleura, replacement of normal mesothelial cells by epithelioid cells, and the presence of nodules . Severe forms of pleural disease that occur rarely include include spontaneous pneumothorax, empyema, fibrothorax, and bronchopleural fistula .

Management of these complications involves surgical maneuver as well.

PULMONARY AIRWAY DISEASE

Rheumatoid arthritis causes both upper and lower airway disease .Major manifestations of large airways involvement are the Cricoarytenoid arthritis and Bronchiectasis. Major manifestations of small airway disease include Bronchiolitis, Follicular bronchiolitis, obliterative bronchiolitis .

UPPER AIRWAY DISEASE

Upper airway obstruction resulting from cricoarytenoiditis can be life-threatening [21]. Cricoarytenoiditis results from synovitis of the cricoarytenoid (CA) joint and correlates with duration and severity of the disease. The CA joints are diarthrotic joints made of two triangular cartilages resting on the signet of the cricoid cartilage. The two movements of it include rotatory movement on the anteroposterior direction and gliding movement in a mediolateral direction. These joints work closely with vocal cords; they rotate with the vocal cords as they abduct and adduct to the pitch and tone of the voice. Patients with cricoarytenoiditis present with dysphagia, odynophagia, laryngeal tenderness, hoarseness, progressive dyspnea, and stridor. Dyspnea and stridor are usually occur at later stage of the disease and may lead to hypoxia and cardiovascular collapse .

The prevalence of this complication in RA is 15–65% . Cricoarytenoiditis is diagnosed with clinical, laryngoscopy, and radiologic studies. [19, 20, 25]. In late stages, difficulties in abduction of the vocal cords and reduced glottic rims are seen in laryngocopy. The combined use of direct laryngoscopy with indirect laryngoscopy increases the diagnosis upto 70% . When cricoarytenoiditis is bilateral and severe it shows a fixed airflow obstruction, flattening in the inspiratory and expiratory limbs of the flow-volume loop on pulmonary function testing . HRCT is also be useful with a diagnostic yield of upto 66% [ ].Treatment of cricoarytenoiditis requires surgical intervention with mobilization of the cricoarytenoid joints.

BRONCHIOLITIS

These are seen in patient with positive rheumatoid factor and active joint disease. Bronchiolar disease seen in patients with RA differs with individuals . The most serious form of bronchiolar disease in this population is constrictive bronchiolitis (also called obliterative bronchiolitis or bronchiolitis obliterans). Rarely , constrictive bronchiolitis can progress to worsening of airflow obstruction and eventually respiratory failure [7]. Symptoms include persistent exertional dyspnea and cough. Auscultation reveals no crackles or wheezes . Pulmonary function testing shows airflow obstruction with air trapping and hyperinflation. Airflow obstruction is irreversible with no or minimal response to

inhaled bronchodilator. Diffusing capacity measurement, is normal or only mildly reduced. A mosaic pattern with patchy regions of air trapping which becomes more pronounced on expiratory views is detected by HRCT chest.

Follicular bronchiolitis is characterised by presence of abundant lymphoid tissue , in the walls of the bronchioles and to some extent in larger bronchi and shows the lymphoid hyperplasia in response to an extrinsic immune stimulus or altered systemic immune response. Symptoms include dyspnea and non productive cough.PFT reveal airflow obstruction with reduced ratio of forced Expiratory volume in one second to Forced Vital

Capacity due to air trapping , small nodular opacities in centrilobular distribution , patchy areas of low attenuation and peribronchial thickening seen in HRCT , and DLCO is usually normal.

Reduced lung compliance is due to inflammatory changes of interstitial tissues. Restrictions of lung volume is due to pleurisy, reduction in thoracic rigidity and to rheumatoid myopathy.

BRONCHIECTASIS

Use of HRCT as an evaluative tool has demonstrated that bronchiectasis is a common finding in RA, though clinically evident bronchiectasis is not usual . Radiographic findings of bronchiectasis or bronchiectasis have been reported in

as many as 30% of patients with RA undergoing HRCT. Patients with RA may have an increased susceptibility to airway infection; recurrent respiratory tract infections might thus lead to the development of bronchiectasis.

Because patients with RA also seem to have an increased incidence of obstructive airway disease, they may be predisposed to airway inflammation and subsequent structural abnormalities. Furthermore, a genetic predisposition for the development of bronchiectasis may exist. For example, a study by Hillar by et al demonstrated that certain HLA loci showed phenotypic association with bronchiectasis in patients with RA.[20] **PULMONARY VASCULAR DISEASE**

Systemic vasculitis associated with RA usually presents with skin ulcers, mononeuritis multiplex, and digital ischemia. Primary pulmonary vasculitis is rarely seen in RA. It can result in alveolar haemorrhage. Pulmonary hypertension is seen in advanced ILD .

RHEUMATOID NODULES

Necrobiotic nodules are a common finding in RA. Subcutaneous nodules occur in 20% of patients seropositive for rheumatoid factor but are rarely seen in patients with seronegative RA. These may regress

spontaneously or in response to therapy directed at joint or systemic disease. Pathologically, rheumatoid nodules are composed of a central area of fibrinoid necrosis surrounded by palisading mononuclear cells with an outer zone of chronic inflammatory cells and granulation tissue[9] .The pathogenesis of these lesions is linked to small vessel vasculitis as evidenced histologically by the area of central necrosis.

Necrobiotic pulmonary nodules are known to be the only specific pleuropulmonary manifestation of rheumatoid arthritis. The reported prevalence of these lesions varies depending on whether they are identified by plain chest radiograph, CT of the chest, or by lung biopsy. Nodular disease was the second most commonly observed radiographic abnormality after bronchiectasis.

The radiographic and pathologic patterns of rheumatoid pulmonary nodules demonstrate that nodular disease is seen most frequently in a peripheral or subpleural distribution or associated with interlobular septa . Nodules are usually asymptomatic. Their anatomical proximity to the pleural surface is a reason for some of the complications of nodules including pleural effusion, pneumothorax, pyopneumothorax, and bronchopleural fistula.Cavitation of parenchymal nodules may also result in hemoptysis and pulmonary infections. Of the pulmonary manifestations , nodules are associated with the most favorable

prognosis. It should be noted that nodules, in the subcutaneous tissue and in the lung, may precede
clinical arthritis.

The presence of RA does not eliminate the possibility that a nodular pulmonary parenchymal density may be of other causes including malignancy, infection, or other inflammatory disease. Thus, the evaluation of a pulmonary nodule in a patient with RA may involve the usual diagnostic pathway of any patient with pulmonary nodules. Unless the lesion is known to have been radiographically stable over at least a 2-year period of time, appropriate evaluation whether by serial radiographic observation, contrast enhanced CT scanning, positron emission tomography scanning, biopsy, or resection should be made.[10]

CAPLAN S SYNDROME

Caplan ‘s syndrome is characterised to have multiple lung nodules seen in patient with both RA and pneumoconiosis that is related to coal, silica, asbestos, or inorganic dust particles.Necrobiotic nodules are also seen.[11] .In few instances nodules occur rapidly in crops resembling tuberculoma.Even with multiple nodules the patient can be still asymtomatic, usually accompanied by peripheral eosinophilia and an elevated erythrocyte sedimentation rate.Chest

radiograph usually shows bilateral interstitial infiltrates. Broncho Alveolar Lavage fluid may show a marked eosinophilia.

DRUG INDUCED DISEASE

The development of respiratory complications of treatment is thus particularly problematic in patients with such coexistent lung disease, and there have been many reports of respiratory complications of both nonbiologic disease-modifying antirheumatic drugs (nbDMARDs) and biologic DMARD (bDMARD) therapy. Clinicians are frequently encountered with decisions about balancing risk and benefit of treatments in patients with RAILD who have active articular disease. Serious respiratory adverse events

(SRAEs) in the patient with RA on treatment for their joint disease may be due to induction of 'pneumonitis' or idiosyncratic adverse drug reactions (ADRs), acceleration of pre-existing ILD or increased predisposition to infection in a susceptible host. Several non biologicalDMARDs and biologicalDMARDs have been implicated in the development of ILD. Conversely, treatment of the underlying disease process may be beneficial in halting the progression of the lung disease.

Methotrexate (MTX) has been described as the anchor drug in RA treatment, as it is often used first line at diagnosis, in combination with other

Non biological DMARDs and concomitantly with biologics, following failure of traditional nonbDMARDs for controlling articular disease. It inhibits folic acid and purine metabolism along with T-cell activation. MTX-induced pulmonary injury was initially reported in children with Leukaemia. Methotrexate pneumonitis is seen in about 63% of cases with RA (dose range 2.5–15 mg/week), 23% occurred during intensification/consolidation treatment for leukaemia (dose range 20–80 mg/week), and 8% were in patients treated for other malignancies (dose range 15–1400 mg/week) . The mortality rates have been reported up to 17%. Hypersensitivity pneumonitis is reported to be a rare in RA patients. In a systematic literature review of 3463 patients with RA on MTX, 84 patients (2%) had some type of lung toxicity, but only 15 patients were found to be definitive cases of pneumonitis attributable. [15]

The clinical presentation of acute MTX pneumonitis is generally nonspecific, with symptoms (fever, rigors, malaise, nonproductive cough, dyspnoea, chest pain) that can be progressive over several days. Criteria proposed by Searles and McKendry is generally accepted for defining MTX pneumonitis and can sometimes help in differentiating the disease from RAILD and respiratory infections, although it is possible to fulfil the criteria with conditions other than pneumonitis, for example, infection or a progression of pre-existing

RA-ILD Searles and McKendry criteria have since been adapted by Kremer et al. [16] categorising them into major and minor. All rely on a combination of clinical features, radiological, histology and exclusion of infection.

Studies have explored other factors that might differentiate these clinically similar respiratory diseases. Histological findings in MTX pneumonitis such as cellular interstitial infiltrates, diffuse alveolar damage, tissue eosinophils and granuloma formation are nonspecific and have all been seen in RA lung disease . Highresolution computer tomography (HRCT) studies in MTX pneumonitis typically show ground-glass changes, centrilobular nodules +/− diffuse parenchymal opacification [13]. Bronchoalveolar lavage (BAL) cell profiles in MTX pneumonitis show a lymphocyte alveolitis with a preferential increase in CD4+ cells compared to normal RA controls , though comparisons have not been made between BAL Various criteria for diagnosis of methotrexate-associated pneumonitis

Searles and McKendry criteria

Clinical

1. Clinical course consistent with hypersensitivity

Radiology

2. Resolving infiltrates on chest radiograph after discontinuing methotrexate

Exclusion of infection

3. Exclude infection or other pulmonary disease

Histology

4. Pathology consistent with drug-induced injury (i.e. hypersensitivity pneumonitis or toxic drug reaction

Probable: 3 or 4 criteria

Possible: 2 criteria

Unlikely: 1 criterion

Clinical

1. Acute onset dyspnoea

2. Fever >38.0 °C

3. Tachypnoea ≥28/min and dry cough

4. Radiological evidence of pulmonary interstitial or alveolar infiltrates

Laboratory

5. White blood cell count ≤15.0 × 10 to power 9 with or without eosinophilia

6. PO2 <7.5 kPa on air Exclusion of infection

7. Negative blood or sputum cultures (mandatory)Pulmonary function tests
8. Restrictive defect and decreased diffusion capacity on pulmonary functiontests Histology
9. Consistent with bronchiolitis or interstitial pneumonitis with giant cellsand without evidence of infection Definite ≥6 criteria, Probable: 5 of 9 criteria present ,Possible: 4 of 9 criteria present

Current guidelines on the use of MTX recommend that all patients should have a baseline chest radiograph with or without PFTs. There appears to be little evidence to support this; however, PFTs may be useful in patients with RA deemed to be at high risk of ILD or known to have RA-
ILD to assess for progression

LEFLUNAMIDE

Leflunomide is an isoxazole derivative, which inhibits de novo pyrimidine synthesis, resulting in several downstream anti-inflammatory effects such as suppression of TNF-induced cellular responses and inhibition of matrix metalloproteinases and osteoclasts. Leflunomide-induced pneumonitis is rare but well reported.Interstitial pneumonia as an adverse reaction of leflunomide is rare. Several risk factors of leflunomide-induced pneumonitis have been reported in small numbers of patients in case series and retrospective studies including

preexisting lung disease , a prescribed loading dose, smoking, low body weight and increased C-reactive protein, hypoalbuminaemia, hypoxia and lymphopaenia . Treatment includes cessation of the drug, treatment with glucocorticoids with some benefit reported with activated charcoal and cholestyramine as washout treatments. Whilst conclusions of use in RA-ILD are limited from studies due to channelling bias, leflunomide should be avoided in patients with previous MTX pneumonitis and should be used with caution in patients with preexisting ILD.

Sulphasalazine

Sulphasalazine is a 5-aminosalicyclic acid (5-ASA) derivative metabolised to sulphapyridine, which is the active moiety in RA. Pulmonary hypersensitivity reactions such as eosinophilic pneumonias [37, 38], fibrosing alveolitis and bronchiolitis obliterans have been well described, with over 50 case reports in the literature . Drug reaction with eosinophilia and systemic symptoms (DRESS) is also reported . Typical presentation of sulphasalazineinduced lung disease reported is with new-onset dyspnoea and infiltrates on chest radiograph (with or without peripheral eosinophilia with eosinophilic pneumonitis). Cough and fever are the most common symptoms with sputum production, whilst allergy history, rash, chest pain and weight loss were inconsistent findings . Glucocorticoids

Infection – Dose and duration of treatment related to infection risk – Co-prescription of

bDMARDs may increase risk NSAIDs Eosinophilic pneumonia – Idiosyncratic reactions, sometimes reported in patients on high doses nbDMARDs Methotrexate – Pneumonitis .There is possible increase in infections including reports of opportunistic infections (e.g. Pneumocystis jirovecii, cytomegalovirus, varicellazoster virus, Nocardia, mycobacteria or other fungi) .Pulmonary lymphoproliferative disease – Co-prescription of bDMARDs may increase risk of chest/opportunistic infections Leflunomide – Pneumonitis (especially Japanese/Korean patients) – Progression of pulmonary nodules +/− pneumothorax .Co-prescription of bDMARDs may increase risk of chest/opportunistic infections Sulphasalazine – Pneumonitis – Eosinophilic pneumonias most commonly reported – Reported sometimes with DRESS Hydroxychloroquine is rarely assosiated with pneumonitis – Reported sometimes with DRESS bDMARDs TNFis are the infection such as Streptococcus pneumoniae, Haemophilus influenzae and opportunistic infections (Mycobacterium tuberculosis, mycobacteria other than M. tuberculosis, Mycoplasma, Legionella, Pneumocystis jirovecii) –

Pneumonitis – Congestive heart failure

– Non-infectious granulomatous disease, e.g. sarcoidosis – Pulmonary vasculitis (rare) New lung nodules (rare) .Co-prescription of glucocorticoids (in patients with high disease activity) further increases infection risk (continued)

INFECTIONS

Respiratory tract infection is an important source of morbidity in patients with RA. The exact prevalence of pulmonary infection in this population is reported variably. The presence of bronchiectasis, airway abnormalities, and parenchymal lung disease may increase the likelihood of infections and the morbidity with which these infections are associated.

Patients with severe interstitial lung disease, for instance, tolerate a lower respiratory tract infection less well than if the parenchymal lung disease were not present. Furthermore, patients with RA are often treated with immunosuppressive drugs which may increase morbidity and contribute to mortality.The distinction between lower respiratory tract infection and acute pulmonary disease associated with RA, particularly BOOP, bronchiolitis obliterans, and rapidly progressive interstitial lung disease, can be difficult. A thorough evaluation of the patient with RA and fever with pulmonary infiltrates requires evaluation for the aforementioned causes.

AMYLOIDOSIS

Secondary amyloidosis can occur as a complication of RA. Perivascular and alveolar amyloid and parenchymal nodular lesions are seen . Amyloid deposits may be limited to the lung with the absence in other sites.[18]

PULMONARY FUNCTION TESTS

INDICATIONS

- Spirometry

  Evaluate dyspnea

  Smokers over age 45 to detect COPD

  Check recovery from exacerbation of asthma, COPD.

  Chronic cough or chest tightness

- Spirometry with bronchodilator

  Suspect asthma or COPD

  Determine response to specific bronchodilator therapy

Differential diagnosis of abnormal spirometry Diffusing capacity for carbon monoxide (DLco or transfer factor) Obstruction: asthma versus COPD

Restriction: interstitial versus chest wall Infiltrates on chest X-ray Suspect pulmonary vascular disease

Evaluate dyspnea

- Lung volumes

  Low FVC on spirometry: restriction versus hyperinflation or mixed

Dyspnoea on exertion, disability evaluation

- Oximetry with exercise or sleep

Check adequacy of supplemental oxygen Screen for abnormal breathing during sleep

- Methacholine challenge

  Suspect asthma but normal spirometry

- Respiratory pressures

  Muscle weakness, diaphragm paralysis, myasthenia, ALS, polio follow up

- Flow volume loop (FIVC) Inspiratory stridor

Technique of performing spirometry

Spirometry requires a maximum coordinated effort.

1.Ask the patient to take a deep breath as possible

2.Ask the patient to blow out the air into the spirometer

3.Ask the patient to exhale for several more seconds

Acceptable effort Includes

Adequate inspiration before starting test

No hesitation at start of test

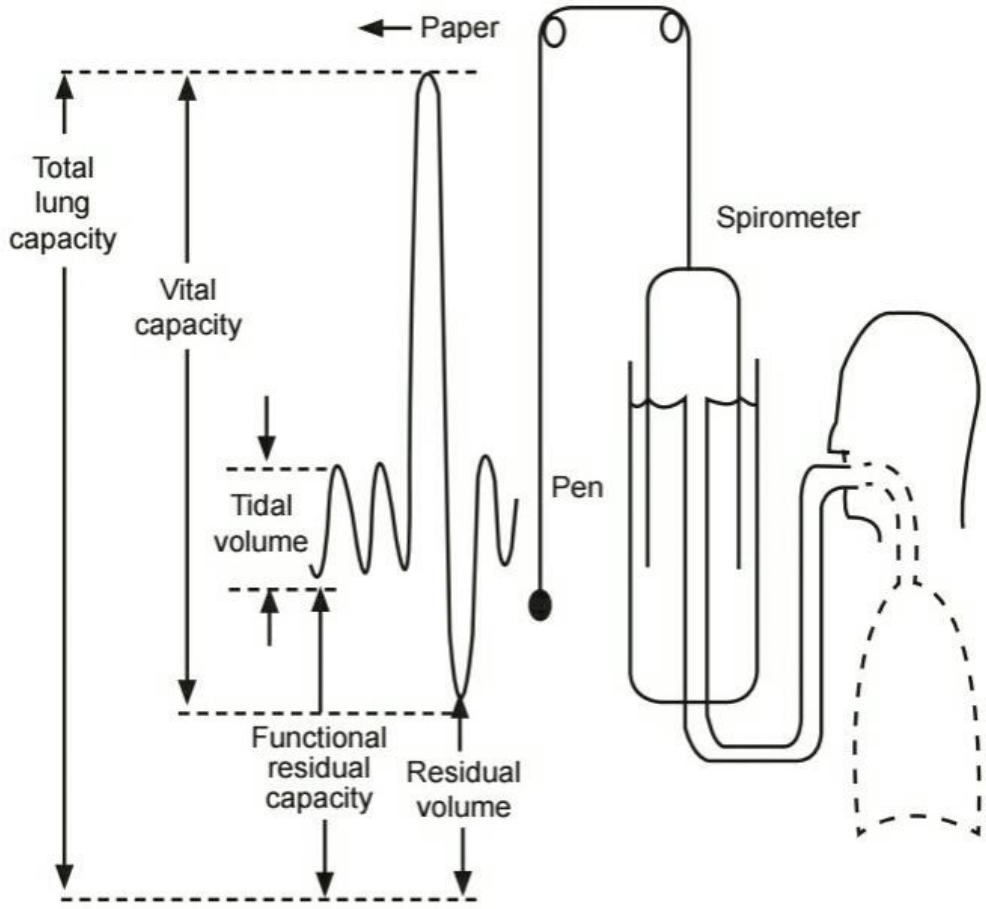
Absence of cough in early part of expiration

Full exhalation for a minimum of six seconds

No premature termination of test

Unacceptable FVC Manoeuvres

- Hesitating start
- Poor peak flow effort
- Excessive coughing
- Premature termination



COMMON TEST VALUES IN FVC TESTS

- Forced vital capacity(FVC) – The total amount of air that one can forcibly blow out after full inspiration . It is measured in litres
- Fores expiratory volume in one second (FEV1) – the amount of air that one can forcibly blow out in one second. It is measured in litres. One of the primary indicator of pulmonary functions.
- FEV1/FVC – the ratio of FEV1 to FVC. In healthy adults 75 to 80 %

- Forced expiratory time (FET)- This measures the length of the expiration in seconds
- Peak expiratory flow rate (PEFR)- the maximum speed of air moving out of lungs at the beginning of expiration. Measured in litres per second.
- Tidal volume – During normal breathing, a specific volume of air is drawn into and then expired out of the lungs.
- Slow vital capacity – total amount of air that can be exhaled slowly after full inspiration.

n of the effort.Peak Expiratory Flow Rate

Height	PEFR (L/min)
120	215
130	260
140	300
150	350
160	400
170	450
180	500

Flow Volume Curve

It is a graphic illustration of a patients spirometric efforts. Flow is plotted against volume to show a continuous loop from inspiration to expiration. A normal flow volume loop has a rapid peak expiratory flow rate and a negative inspiratory portion.

Abnormal pattern in peak

- Blunt peak – shows inadequate effort and the test is to be repeated
- Notch – in initial part notch indicates a cough or hesitant start
- Delayed peak – defective start and the test should be repeated
- Flat peak – indicates intrathoracic obstruction.

Abnormal pattern in slope

- Steep curve - Is seen in restrictive lung diseases
- Rat tail appearance – Is seen in severe airway obstruction in which the airflow starts with a sharp peak , but the flow rapidly declines due to airway collapse .
- Notches on slope – Undulating descending slope is seen with cough .
- Abrupt termination of the slope- This happens when the patients stops expiration before complete inhalation

Pattern of Obstruction in Major Airways

Characteristics that help in identification of lesions by FV loop

- If the lesion reduces the flow equally during inspiration and expiration it is said to be fixed e.g. fixed , narrowed paralysed vocal cords and if reduces differently during inspiration and expiration it is called variable .e.g. compressible trachea malignancy
- Location of the lesion – extrathoracic or intrathoracic

Volume Time Curve

It gives the amount of air expired from the lungs as a function to time. The normal volume time curve has a rapid up slope and becomes a plateau soon after exhalation.

Abnormal patterns

- Steep ascent – Restrictive defects .Here the duration of expiration is reduced
- Shallow ascent – Shallowness is due to low flow rate and here the expiration is prolonged.

  The Three Main Types of Ventilatory Dysfunctions Observed on Spirometry In obstructive lung disorders, the FEV1 is usually decreased, FVC is usually normal and the ratio FEV1/FVC is

  decreased.

In restrictive lung conditions, the FEV1 and FVC are both decreased, leaving anormal FEV1/FVC. In mixed function disorders, all the three parameters FVC, FEV1 and FEV1/FVC are reduced.

How to Classify the Severity of Lung Abnormality?

A. Normal: The test is interpreted as normal, if both VC and the FEV1/VC ratio are in the normal range.

B. Obstructive abnormality: When FEV1 /VC ratio is below the normal range. The severity of the abnormality may be graded based on % predicted FEV1 as follows:

a) Mild : ≥70

b) Moderate : 50-69

c) Severe : 35-49

d) Very severe : <35

C. Restrictive abnormality: This is most reliably interpreted on the basis of TLC. If TLC is not available one may interpret a reduction in VC without a reduction in FEV1 /VC ratio as restrictive abnormality.

The severity of restriction may be graded as follows:

a) Mild : % pred. VC < LLN* but ≥70

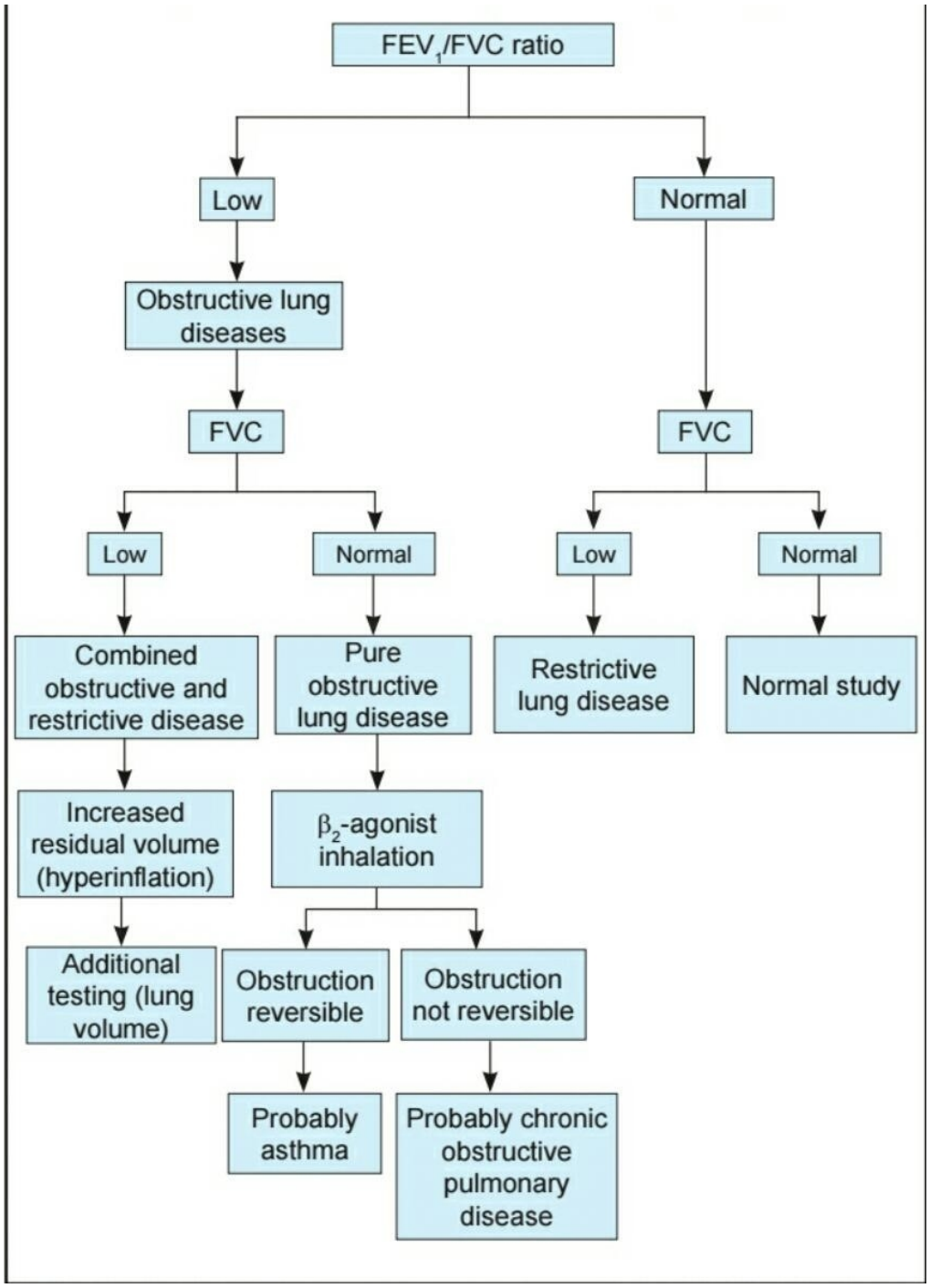
b) Moderate : % pred. VC 50-69

c) Severe : % pred. VC 35-49

d) Very severe : % pred. VC <35

* LLN: Lower limit of normal for patient's age, height and sex.

INTERPRETATION OF SPIROMETRY REPORT


FEV1/FVC ratio
Low
Normal
Obstructive lung diseases
FVC
FVC
Low
Normal
Low
Normal
Combined obstructive and restrictive disease
Pure obstructive lung disease
Restrictive lung disease
Normal study
Increased residual volume (hyperinflation)
β2-agonist inhalation
Additional testing (lung volume)
Obstruction reversible
Obstruction not reversible
Probably asthma
Probably chronic obstructive pulmonary disease

MATERIALS AND METHODS

Sample size : 100

Type of Study : Prospective Cross sectional Study **Study**

design and sampling :

All the patients of Rheumatoid Arthritis with inclusion and exclusion criteria.

Inclusion criteria :

Known Rheumatoid Arthritis patient who have been clinically examined and investigated and fulfilling the American College of Rheumatology Criteria for Rheumatoid Arthritis 2010 **Exclusion criteria :**

1. Pregnant females
2. Skeletal deformities
3. Associated pulmonary disorders
4. Chest trauma
5. Neoplasms

6.Patients not willing to participate in the study

Methodology :

This prospective cross sectional study is carried out in RHEUMATOID ARTHRITIS patients (clinically and serologically confirmed) with respect to inclusion and exclusion criteria, who attend the Rheumatology outpatient clinic or in General Medicine ward of Tirunelveli Medical College and Hospital between April 2018 and April 2019

Written informed consent was obtained from the patients selected for the study . They have been elaborated history and subjected to clininal examination . Investigations including Complete blood count , Renal function test , Liver function test , serum uric acid and RA factor were done

. Then the patient subjected to perform Pulmonary function testing in the Thoracic Department Tirunelveli medical College.

The values including FEV1 ,FVC , FEV/ FVC , PEF were obtained.

Clinical Disease Severity Index Score was calculated from for all the selected patients in the study which denotes the disease severity and activity in the patient. From the formula,

Clinical Disease Activity Index = SJC (28)+ TJC(28)+PGA+ EGA

Where

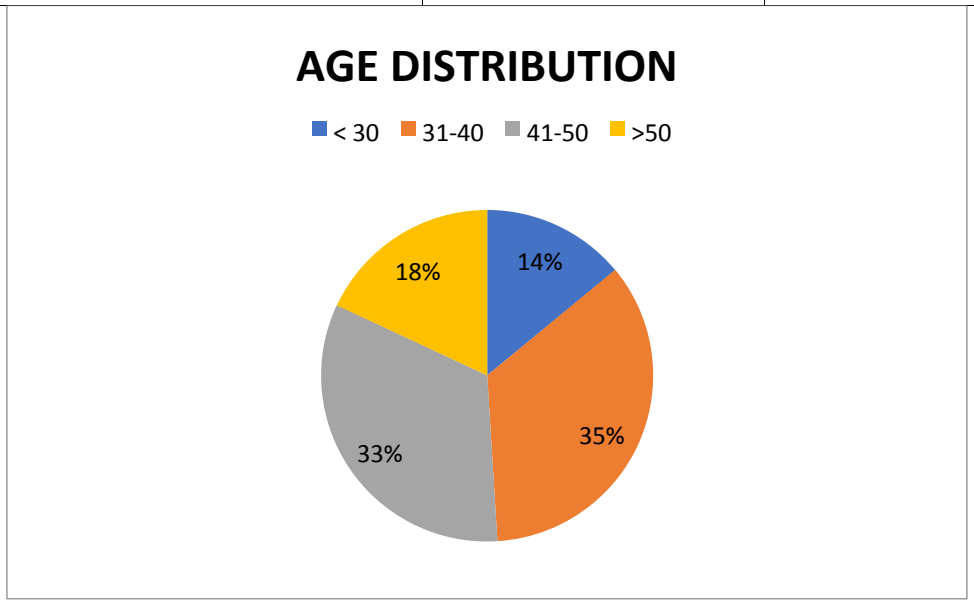
- SJC denotes swollen joint count (28)
- TJC denotes tender joint count (28)
- PGA denotes Patient Global disease activity scale 1 - 10
- EGA denotes Evaluators' Global disease activity scale ranging from 1 – 10.

Interpretation was made by studying the pulmonary function abnormalities and pattern of pulmonary involvement in Rheumatoid Arthritis patients and their correlation with disease activity and risk factors were studied.

RESULTS

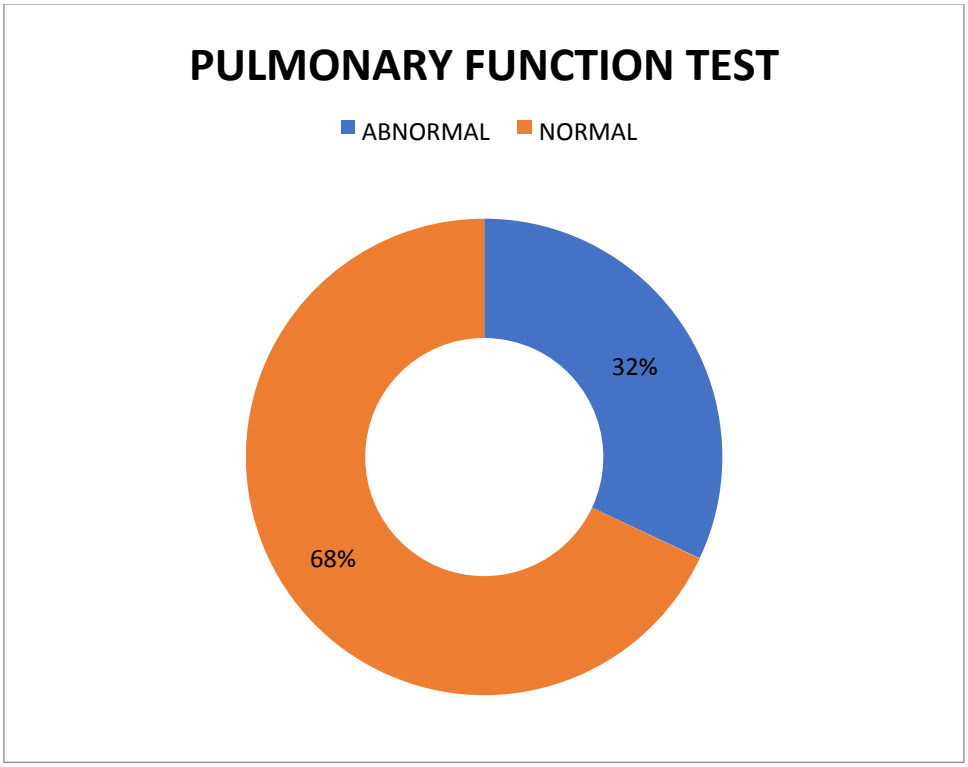
Table 1 AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 30	14	14%
31-40	35	35%
41-50	33	33%
>50	18	18%



31 to 35 years of age is the most common age group affected in Rheumatoid arthritis.

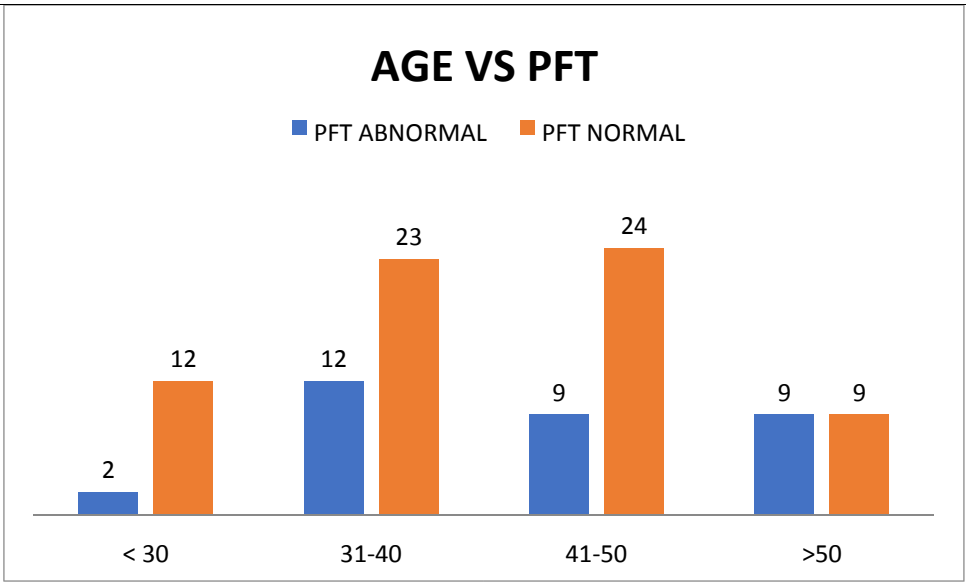
PULMONARY FUNCTION TEST



Pulmonary function testing revealed abnormality in 32% of the subjects studied.

Table2 Distribution of abnormal PFT with respect to age

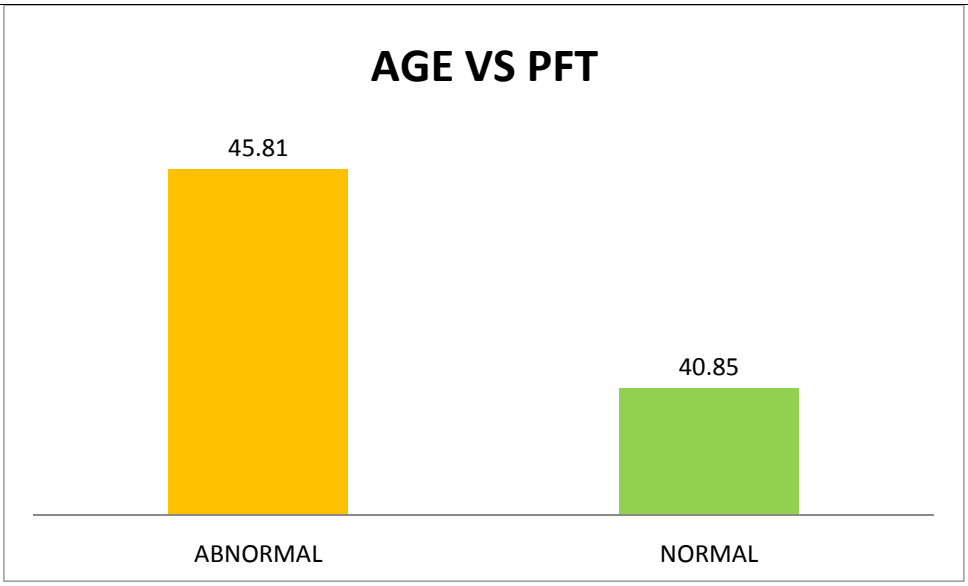
AGE IN YEARS	PFT	
	ABNORMAL	NORMAL
< 30	2	12
31-40	12	23
41-50	9	24
>50	9	9
P VALUE - 0.033		
KRUSKAL WALLIS TEST		
NON SIGNIFICANT		



The prevalence of pulmonary abnormality increases with increased age.

Table 3 AGE VS PFT in Rheumatoid arthritis

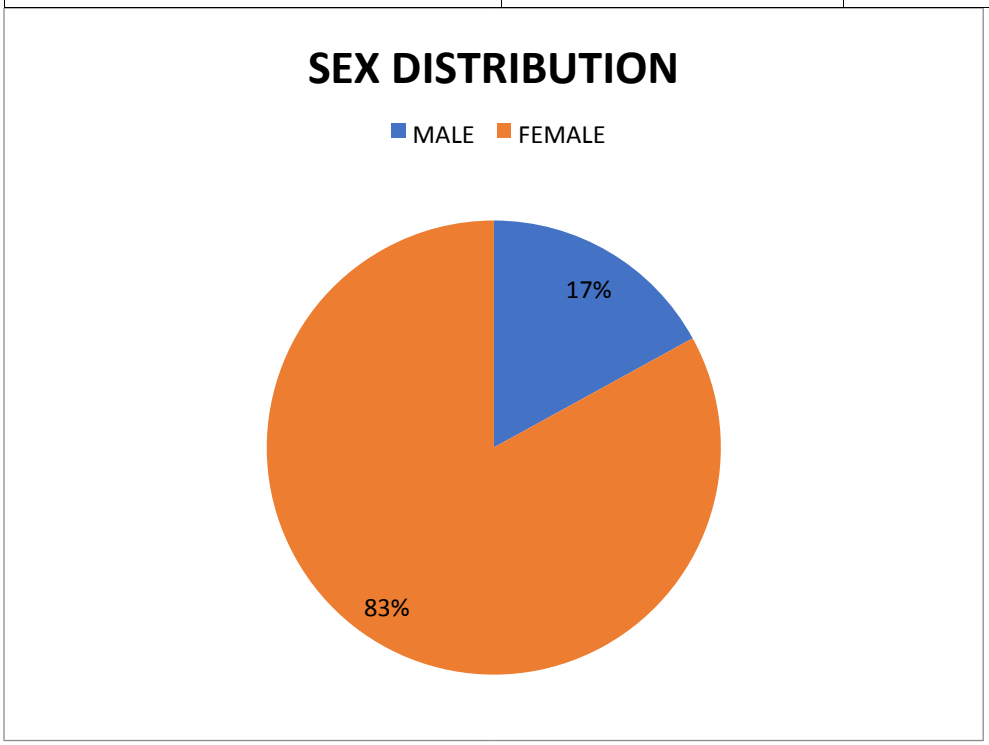
PFT	AGE IN Y RS	
	MEAN	SD
ABNORMAL	45.81	10.9
NORMAL	40.85	10.4
P VALUE - 0.033		
UNPAIRED TEST		
SIGNIFICANT		



The mean age of abnormal PFT is 45.81 years. This is found to be significant by Unpaired test method.

Table 5.SEX DISTRIBUTION of patients with Rheumatoid arthritis

SEX	NO OF PATIENTS	PERCENTAGE
MALE	17	17%
FEMALE	83	83%



Our study population has 83% females and 17% males.

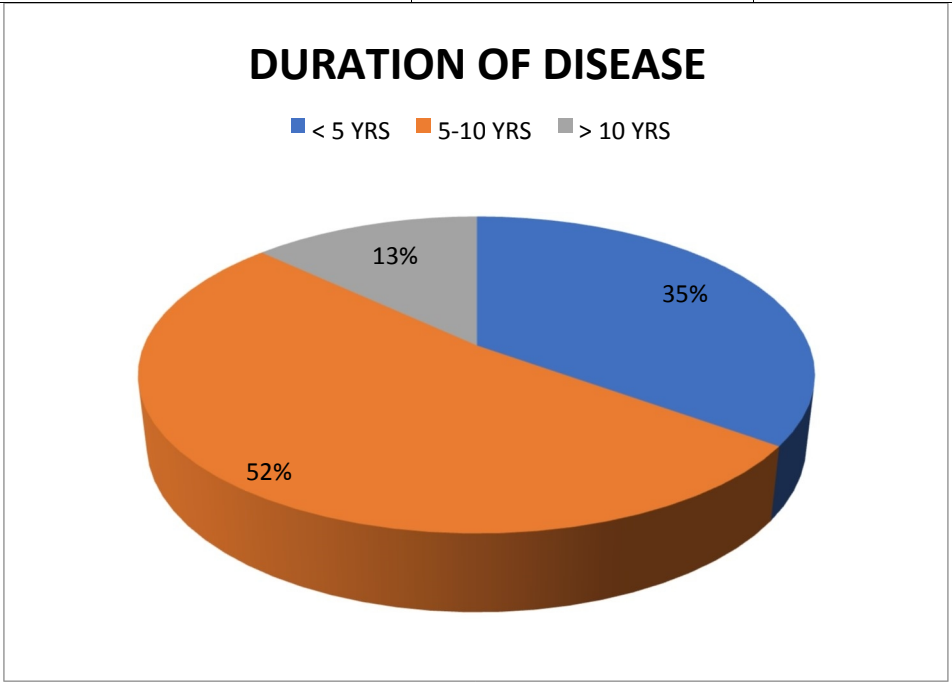
Table 5 Prevalence of abnormal PFT with respect to gender

SEX	PFT	
	ABNORMAL	NORMAL
MALE	6	11
FEMALE	26	57
P VALUE - 0.749		
MANN WHITNEY U TEST		
NON SIGNIFICANT		

Among 83 % of female population studied 26% had abnormal PFT. The p value by Mann Whitney U test is 0.746 and is not significant.

Table 6 Distribution of patients with Rheumatoid arthritis in relation to duration of the disease

DURATION OF DISEASE	NO OF PATIENTS	PERCENTAGE
< 5 YRS	35	35%
5-10 YRS	52	52%
> 10 YRS	13	13%



52% of the study population had 5 to 10 years of Rheumatoid arthritis **Table 7**

DISTRIBUTION OF ABNORMAL PFT IN RELATION TO

DURATION OF DISEASE

DURATION OF DISEASE	P T	
	ABNORMAL	NORMAL
< 5 YRS	7	28
5-10 YRS	20	32
> 10 YRS	5	8
P VALUE - 0.163		
KRUSKAL WALLIS TEST		
NON SIGNIFICANT		

20% of abnormal PFT is seen with 5 to 10 years of duration of illness.The p value by Kruskal Wallis test is 0.163 and is not significant.

Table 8

DURATION OF TREATMENT

DURATION OF TREATMENT	NO OF PATIENTS	PERCENTAGE
< 5 YRS	45	45%
5-10 YRS	48	48%
> 10 YRS	7	7%

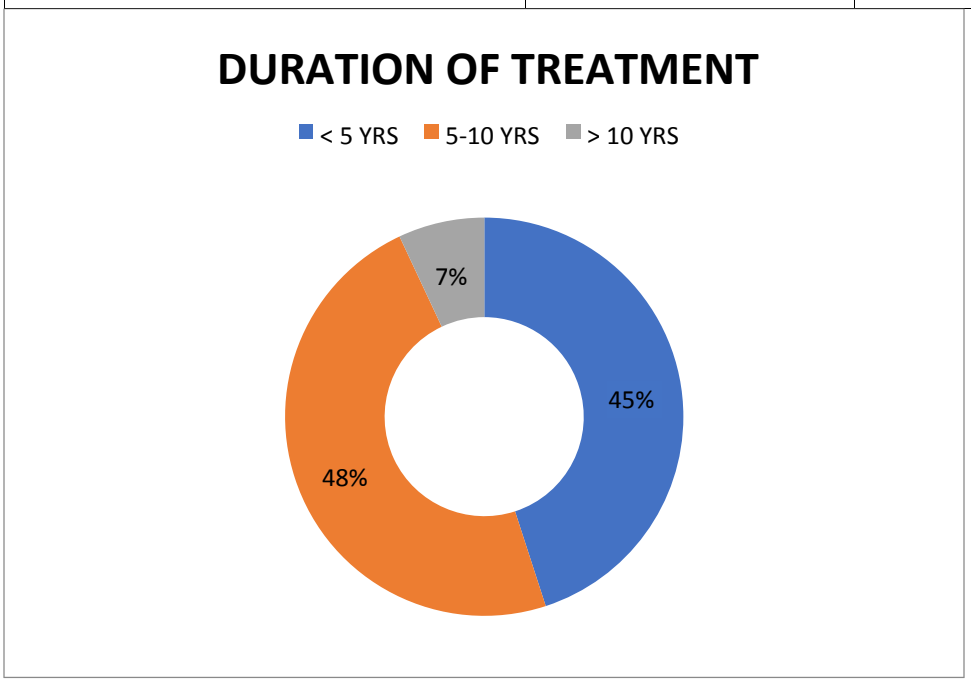


Table 9 Prevalence of abnormal PFT IN relation to treatment duration

DURATION OF TREATMENT	PFT	
	ABNORMAL	NORMAL
< 5 YRS	11	34
5-10 YRS	17	31
> 10 YRS	4	3
P VALUE - 0.176		
KRUSKAL WALLIS TEST		
NON SIGNIFICANT		

The p value by Kruskal Wallis test is 0.176 and is not significant.

Table10.DISTRIBUTION OF PATIENTS IN RELATIONS TO JOINT INVOLVED

JOINTS INVOLVED	NO OF PATIENTS	PERCENTAGE
MCP	98	98%
PIP	82	82%
WRIST	67	67%
ELBOW	21	21%
ANKLE	16	16%
KNEE	9	9%
SHOULDER	2	2%

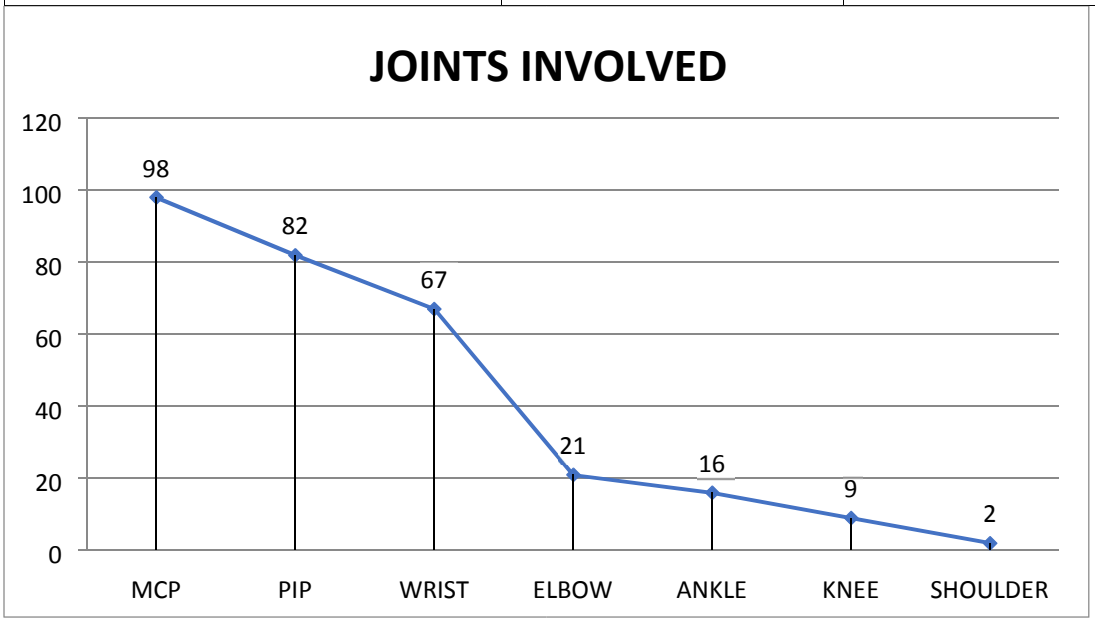
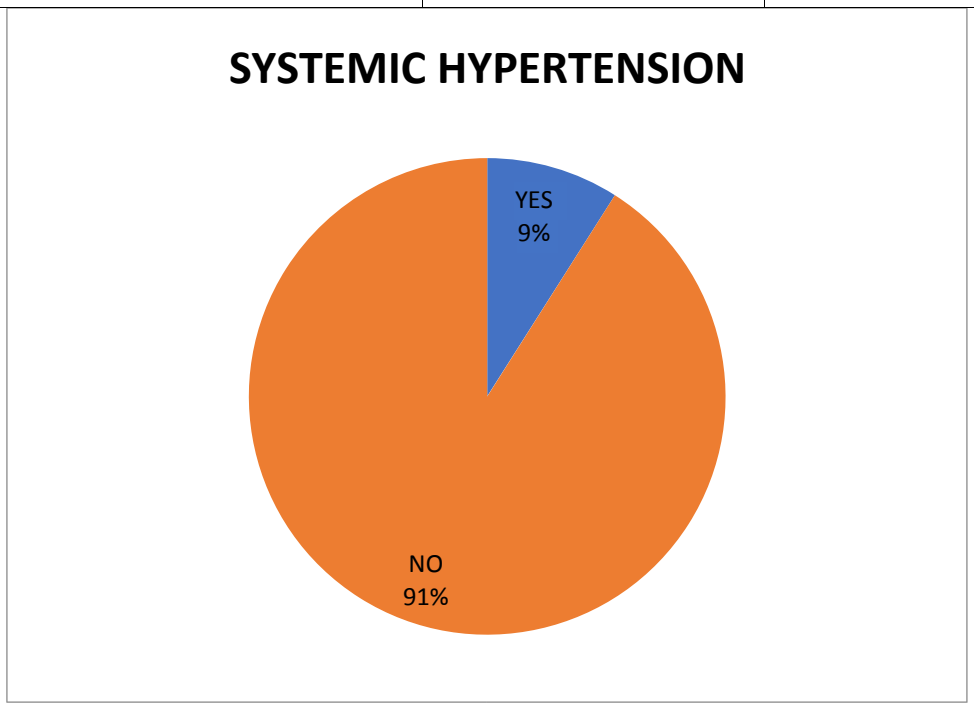
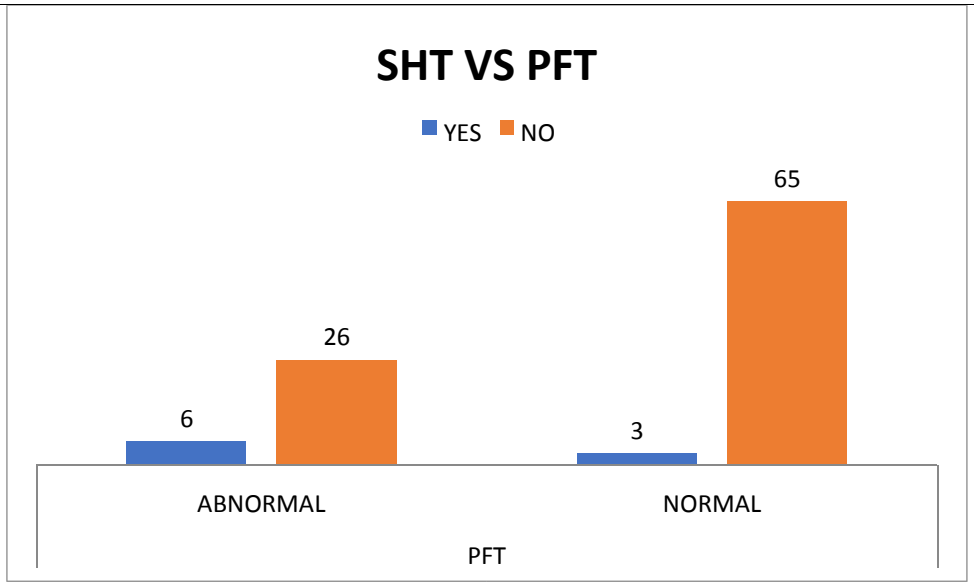


Table 11 SYSTEMIC HYPERTENSION

SHT	NO OF PATIENTS	PERCENTAGE
YES	9	9%
NO	91	91%



SHT	PFT	
	ABNORMAL	NORMAL
YES	6	3
NO	26	65
P VALUE - 0.019		
MANN WHITNEY U TEST		
SIGNIFICANT		

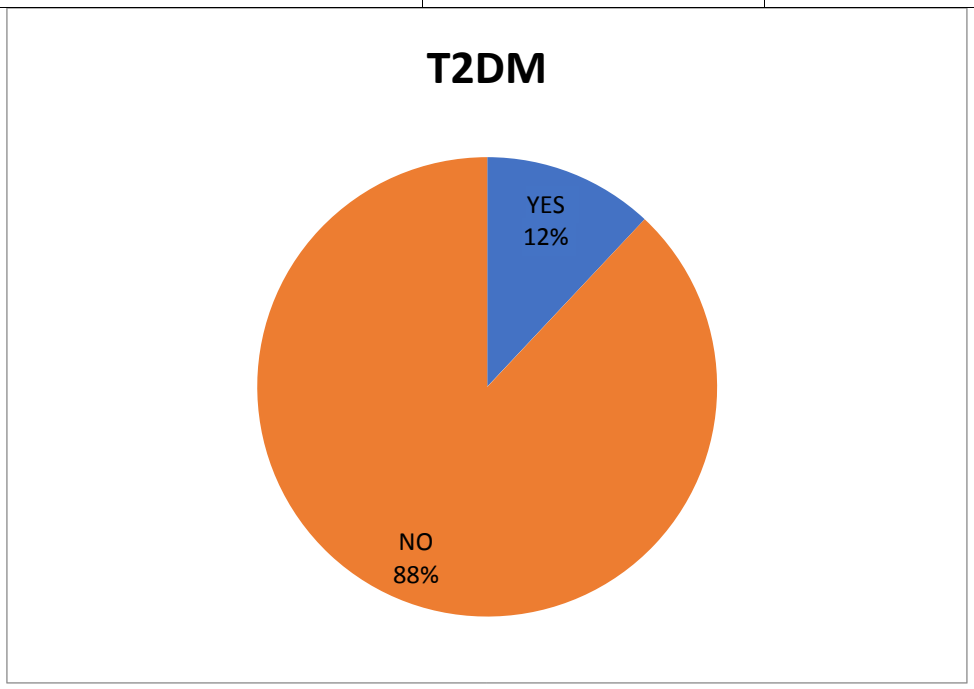


Systemic hypertension as a risk factor with abnormal PFT is seen in 6%

and the p value is 0.019 and is significant

Table 12 TYPE 2 DM

T2DM	NO OF PATIENTS	PERCENTAGE
YES	12	12%
NO	88	88%

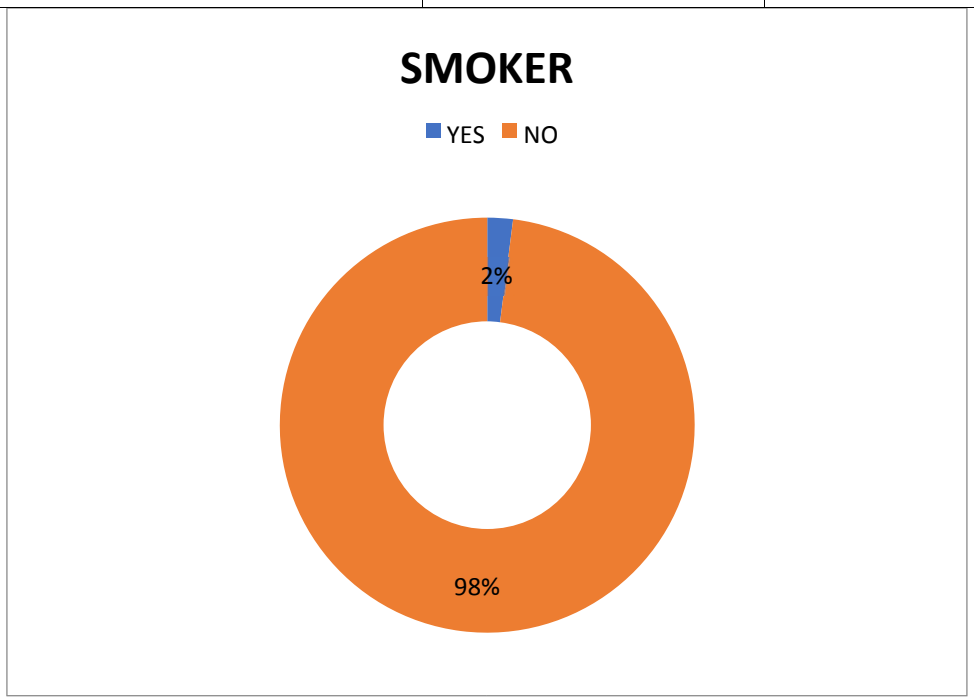


T2DM	PFT	
	ABNORMAL	NORMAL
YES	9	3
NO	23	65
P VALUE - 0.001		
MANN WHITNEY U TEST		
SIGNIFICANT		

In relation to diabetes as the risk factor in Rheumatoid arthritis the pulmonary abnormalities is found in 9% with p value 0.001 and is significant by Mann Whitney U test.

Table 13. SMOKER

SMOKER	NO OF PATIENTS	PERCENTAGE
YES	2	2%
NO	98	98%



SMOKER	PFT	
	ABNORMAL	NORMAL
MALE	1	1
FEMALE	31	67
P VALUE - 0.581		
MANN WHITNEY U TEST		
NON SIGNIFICANT		

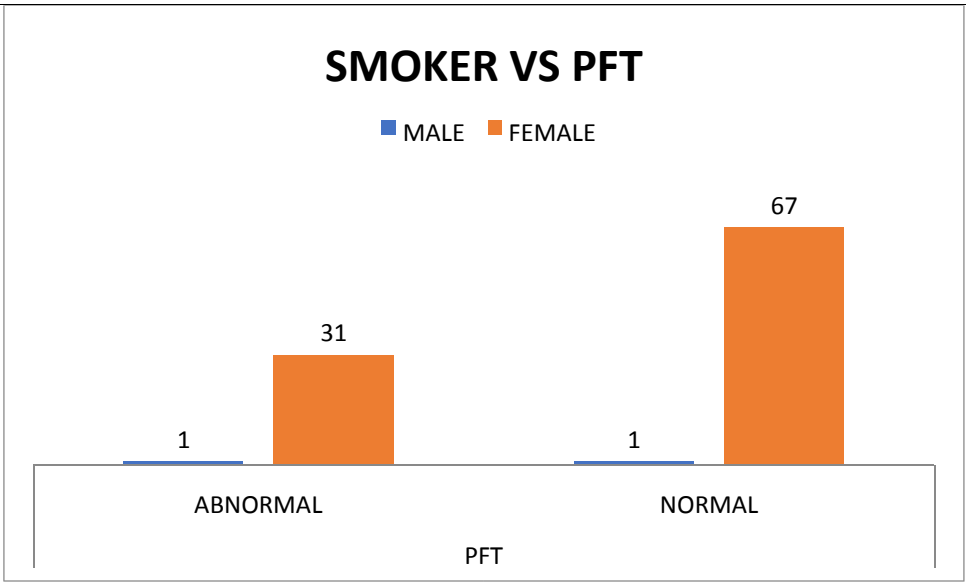
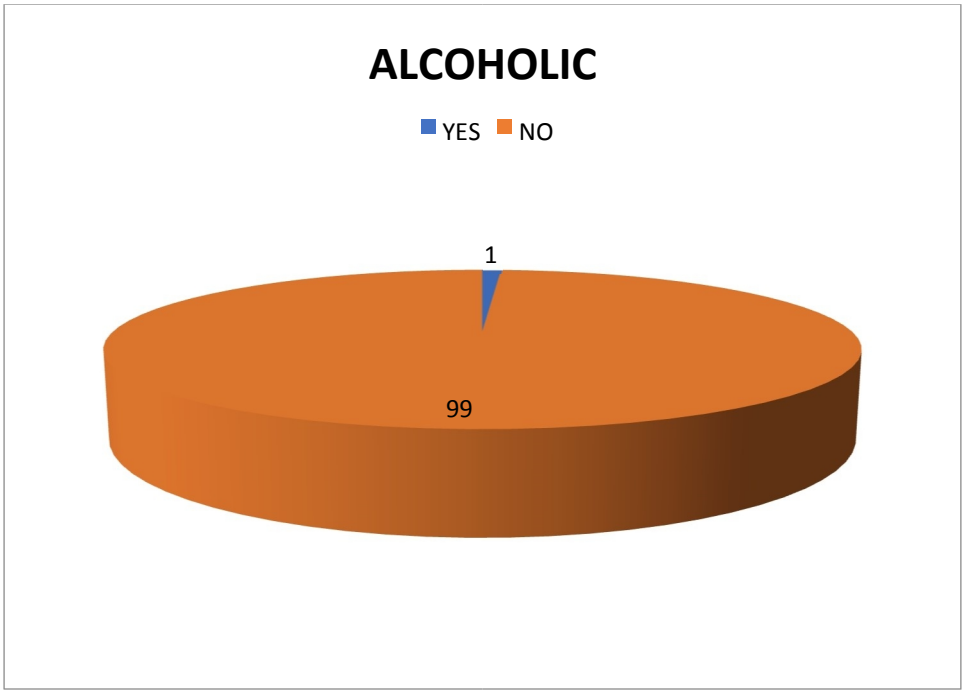


Table 14. ALCOHOLIC

ALCOHOLIC	NO OF PATIENTS	PERCENTAGE
YES	1	1%
NO	99	99%



Only 1% of study population is alcoholic.

ALCOHOLIC	PFT	
	ABNORMAL	NORMAL
YES	1	0
NO	31	68
P VALUE - 0.143		
MANN WHITNEY U TEST		
NON SIGNIFICANT		

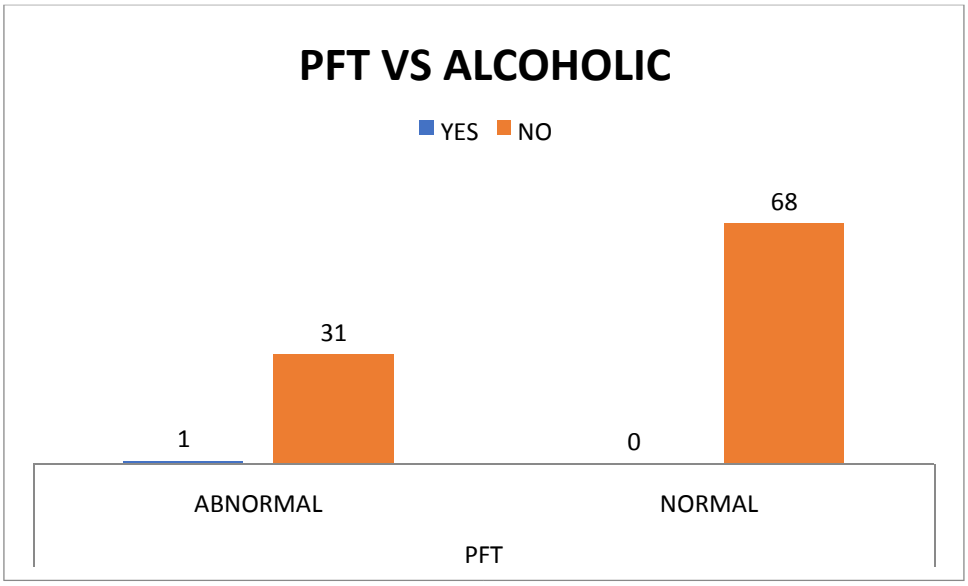
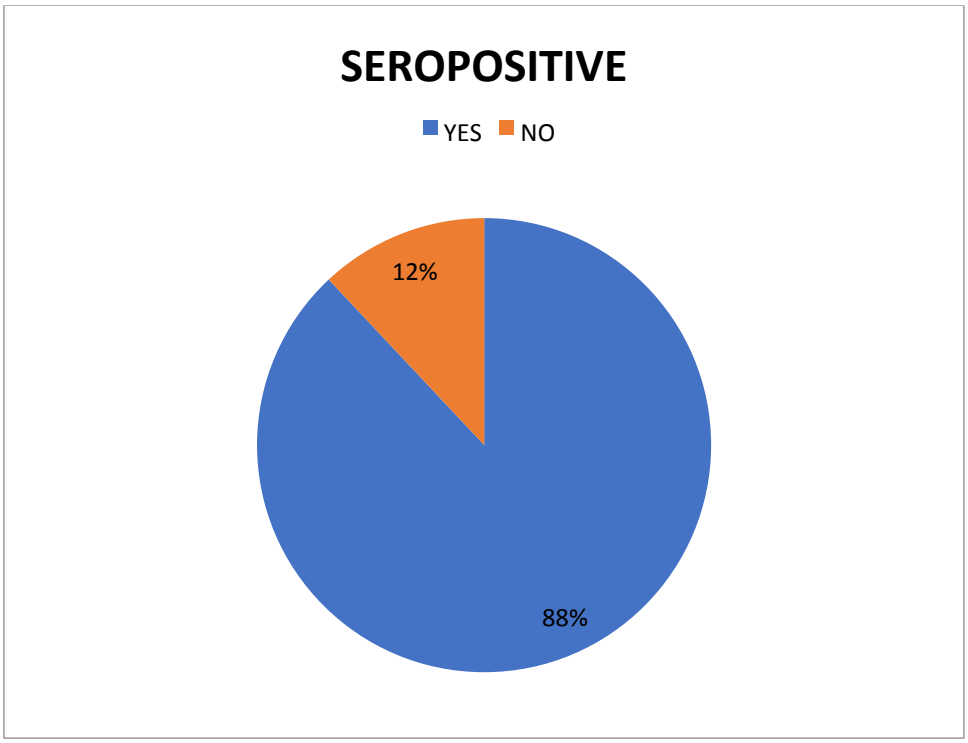


Table 15. SEROPOSITIVITY

SEROPOSITIVE	NO OF PATIENTS	PERCENTAGE
YES	88	88%
NO	12	12%



SEROPOSITIVE	PFT	
	ABNORMAL	NORMAL
YES	28	60
NO	4	8
P VALUE - 0.916		
CHI SQUARE TEST		
NON SIGNIFICANT		

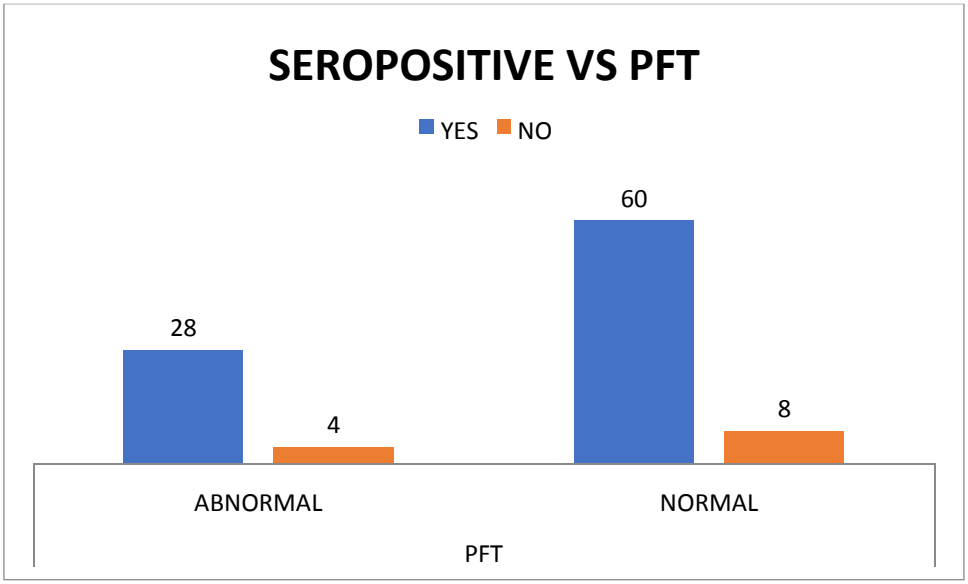
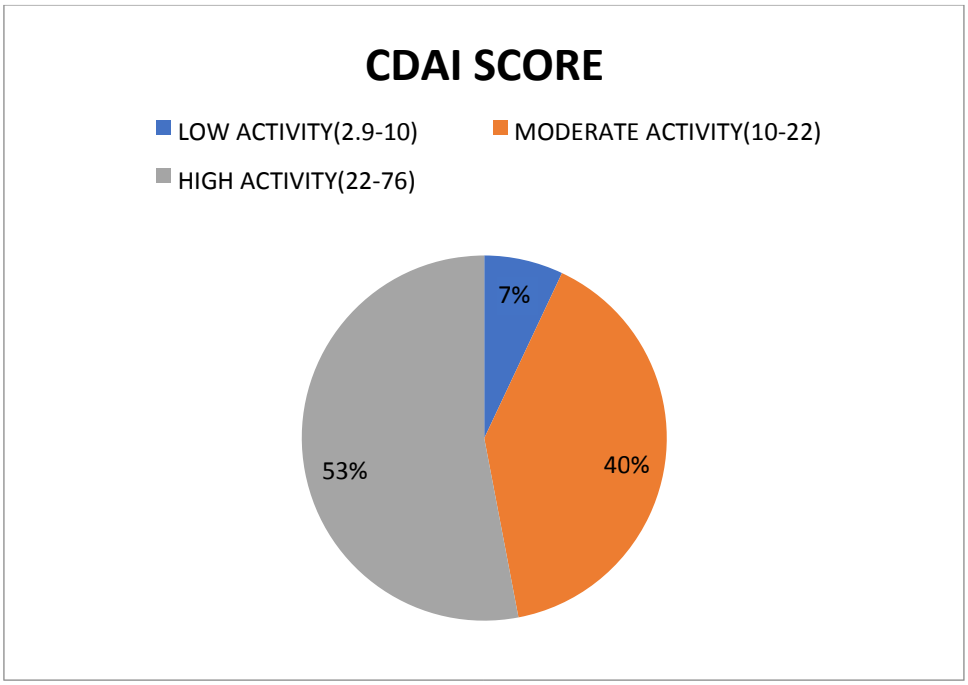


Table 16 CDAI SCORE

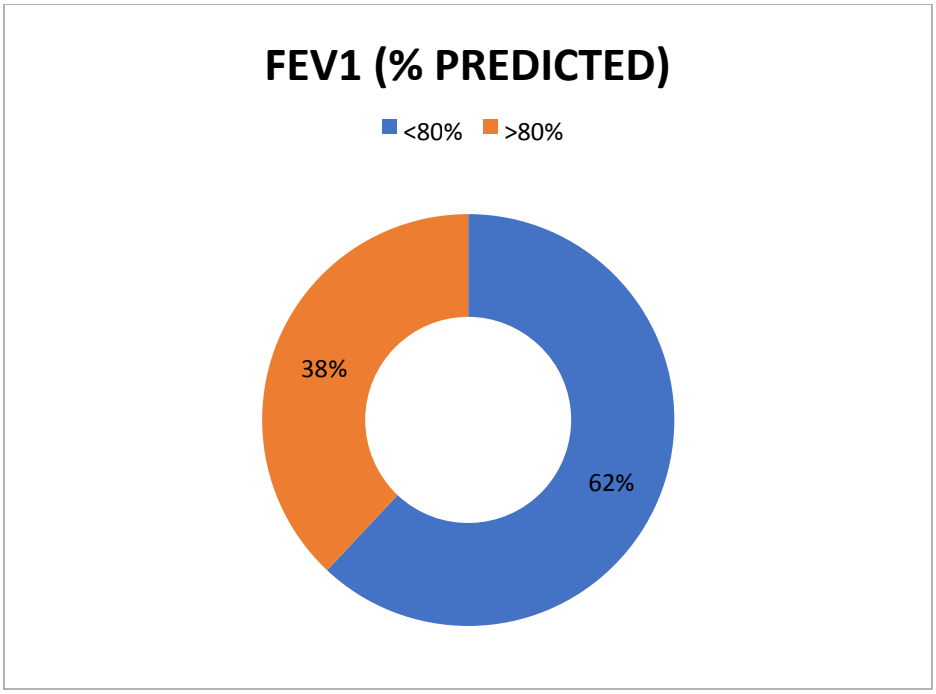
CDAI SCORE	NO OF PATIENTS	PERCENTAGE
LOW ACTIVITY(2.9-10)	7	7%
MODERATE ACTIVITY(10-22)	40	40%
HIGH ACTIVITY(22-76)	53	53%



53% of the patients had high disease activity.

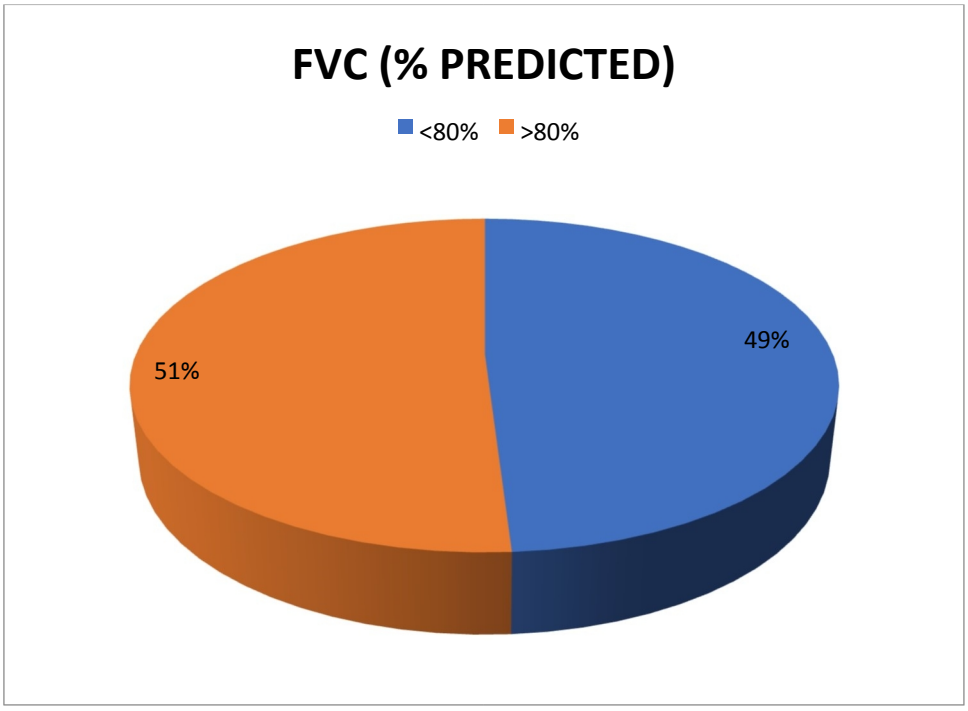
Table 17. FEV(% PREDICTED)

FEV1(% PREDICTED)	NO OF PATIENTS	PERCENTAGE
<80%	62	62%
>80%	38	38%



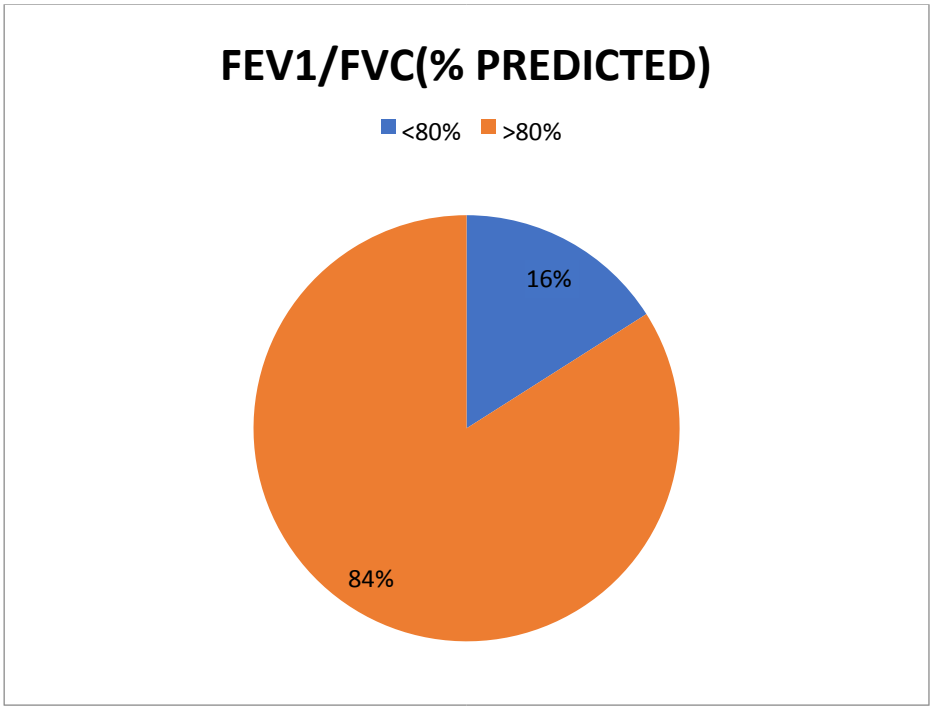
62% patients had FEV1 less than 80% **Table 18.FVC (% PRDEICTED)**

FVC(% PREDICTED)	NO OF PATIENTS	PERCENTAGE
<80%	49	49%
>80%	51	51%



49% of the study population had Forced vital capacity less than 80% **Table 19 FEV1/FVC(% PREDICTED)**

FEV1/FVC(% PREDICTED)	NO OF PATIENTS	PERCENTAGE
<80%	16	7%
>80%	84	40%

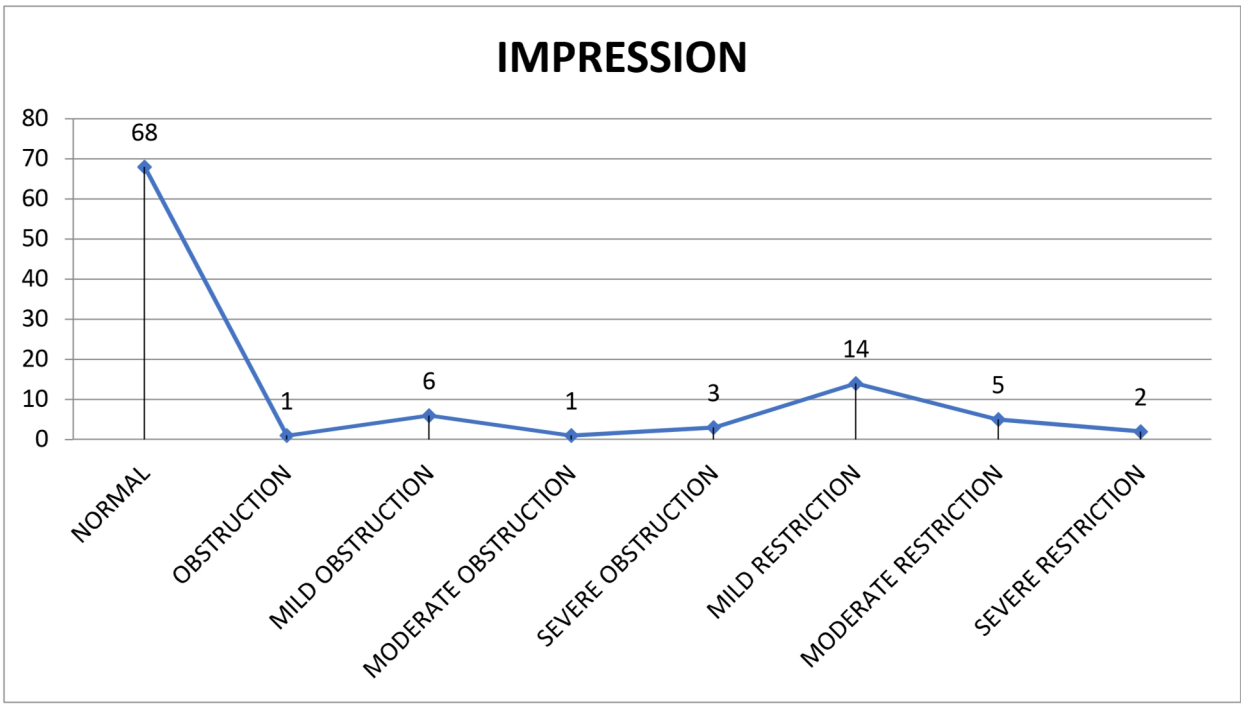


7% of the patients had abnormal FEV1/FVC ratio.

PREVALENCE OF VARIOUS TYPES OF ABNORMAL PFT IN PATIENTS WITH RHEUMATOID ARTHRITIS

TABLE 20 IMPRESSION

IMPRESSION	NO OF PATIENTS	PERCENTAGE
NORMAL	68	68%
MILD OBSTRUCTION	7	7%
MODERATE OBSTRUCTION	1	1%
SEVERE OBSTRUCTION	3	3%
MILD RESTRICTION	14	14%
MODERATE RESTRICTION	5	5%
SEVERE RESTRICTION	2	2%


IMPRESSION
80
70
60
50
40
30
20
10
0
68
1
6
1
3
14
5
2
NORMAL
OBSTRUCTION
MILD OBSTRUCTION
MODERATE OBSTRUCTION
SEVERE OBSTRUCTION
MILD RESTRICTION
MODERATE RESTRICTION
SEVERE RESTRICTION

PFT	DURATION OF DISEASE	
	MEAN	SD
ABNORMAL	7.14	4.56
NORMAL	8.18	3.39
P VALUE - 0.025		
UNPAIRED TEST		
SIGNIFICANT		

Abnormal PFT in relation to duration of disease is significant with p value 0.025 by Unpaired test method

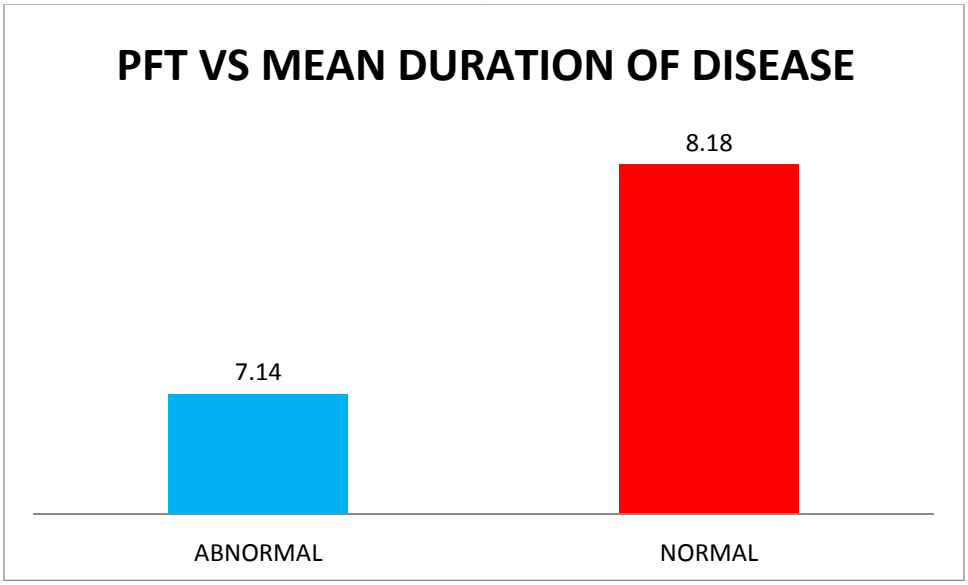


Table 21

PFT	DURATION OF TREATMENT	
	MEAN	**SD**
ABNORMAL	6.26	4.22
NORMAL	7.18	2.93
P VALUE - 0.273		
UNPAIRED TEST		
NON SIGNIFICANT		

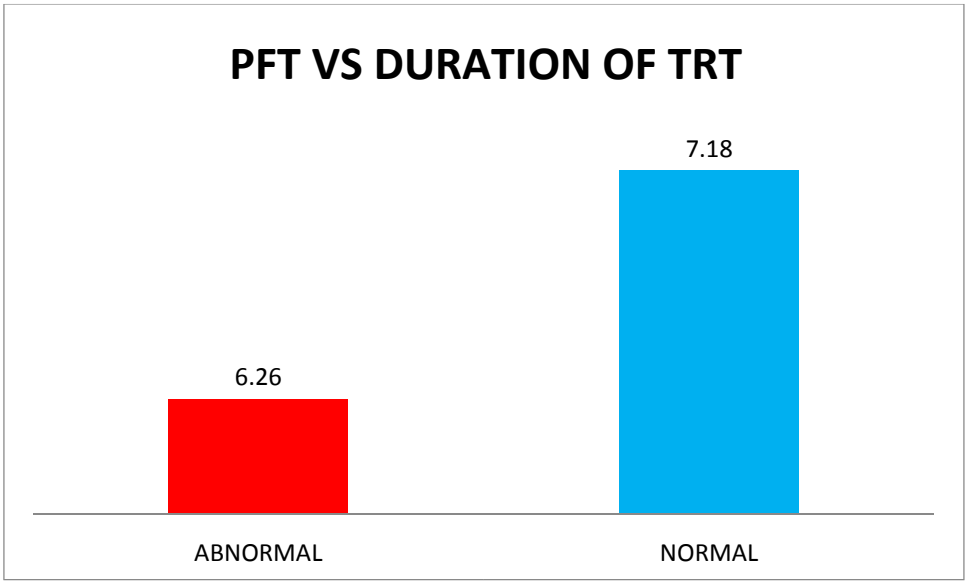


Table 22 PFT in relation to CDAI SCORE

PFT	CDAI SCORE	
	MEAN	SD
ABNORMAL	23.51	8.19
NORMAL	24	8.18
P VALUE - 0.783		
UNPAIRED TEST		
NON SIGNIFICANT		

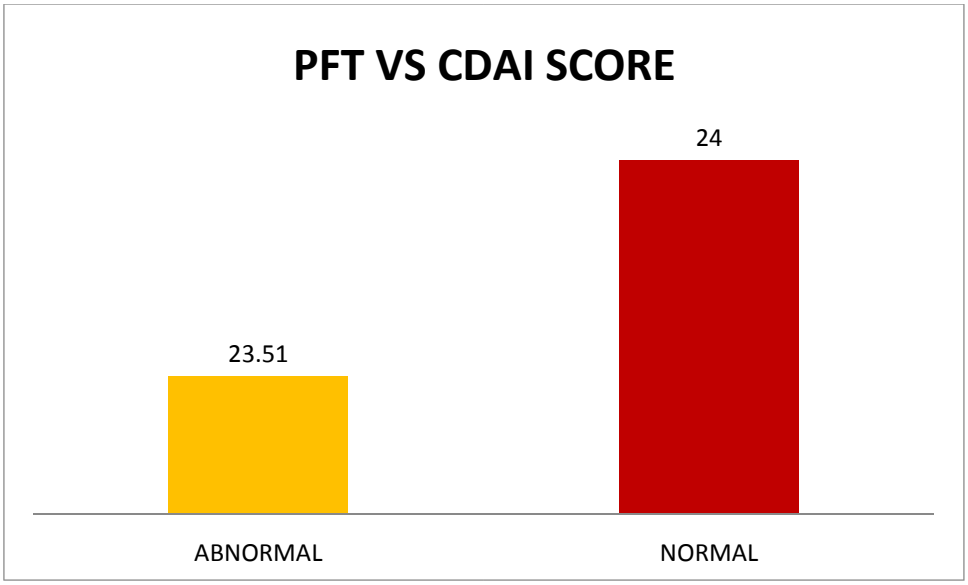


Table 23 Prevalence of abnormal PUT in relation to duration of disease

PFT	DURATION OF DISEASE		
	<5 YRS	5-10 YRS	> 10YRS
MEAN FEV1	2.12	2.23	1.79
MEAN FVC	2.77	2.59	2.08
MEAN FEV/FVC	0.77	0.78	0.84
MEAN PEF	3.67	3.52	3.19

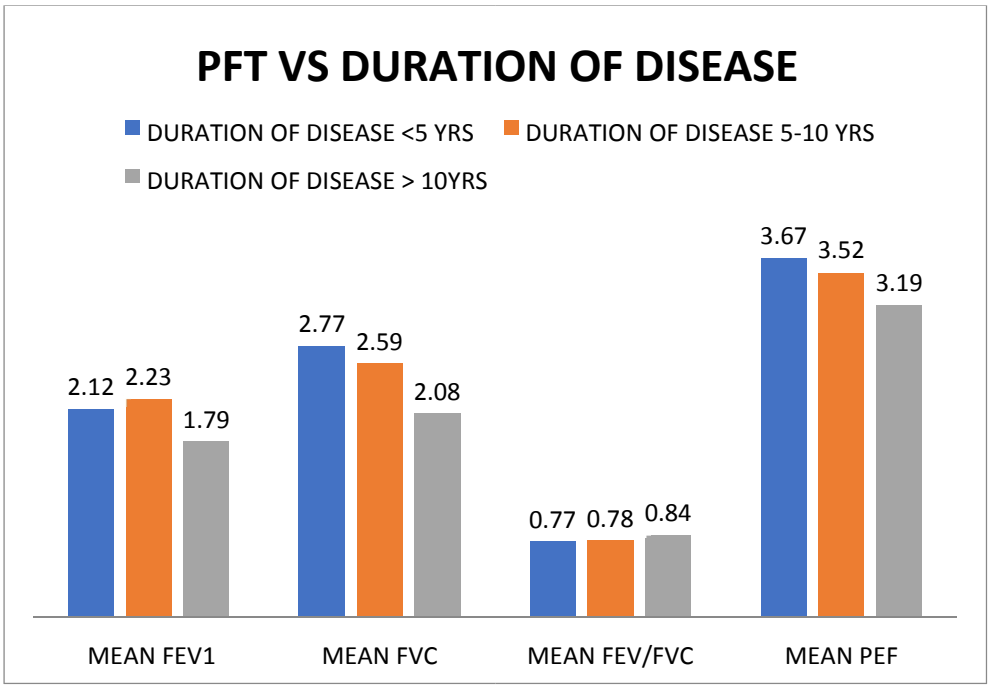


Table 24

PFT	DURATION OF DISEASE		
	<5 YRS	5-10 YRS	> 10YRS
MEAN FEV1 %	79.65%	78.36%	70.53%
MEAN FVC %	75.60%	73.65%	68.69%
MEAN FEV/FVC %	91.02%	89.54%	84.95%
MEAN PEF %	64.80%	62.69%	58.33%

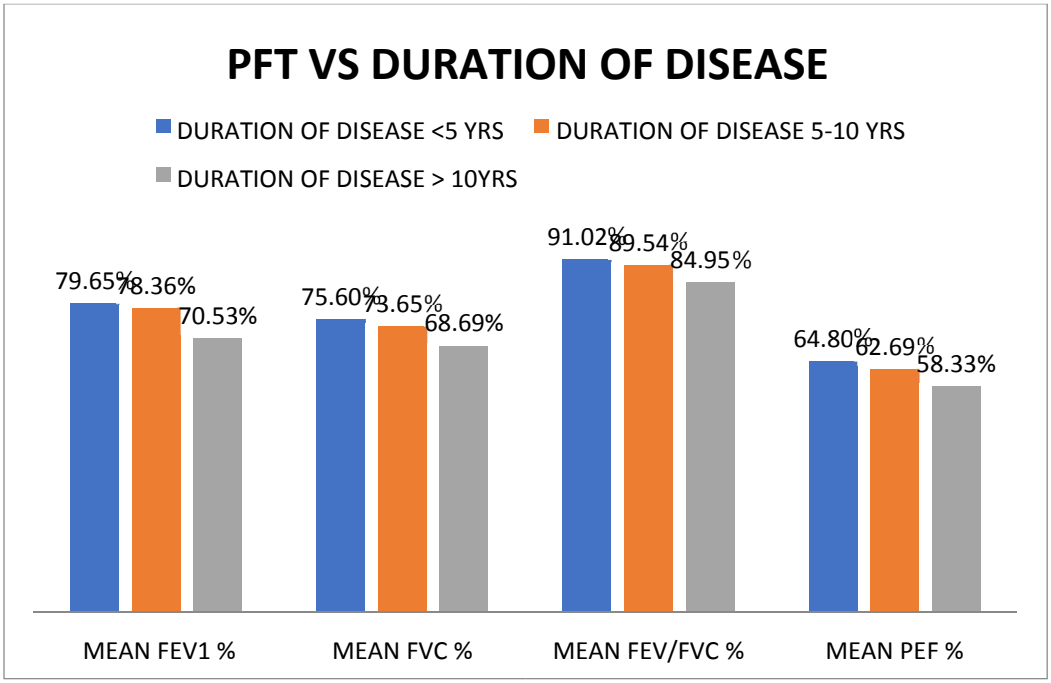


Table 25

PFT	DURATION OF TREATMENT		
	<5 YRS	5-10 YRS	> 10YRS
MEAN FEV1	2.16	2.14	1.92
MEAN FVC	2.85	2.41	2.32
MEAN FEV/FVC	0.77	0.79	0.87
MEAN PEF	3.63	3.48	2.97

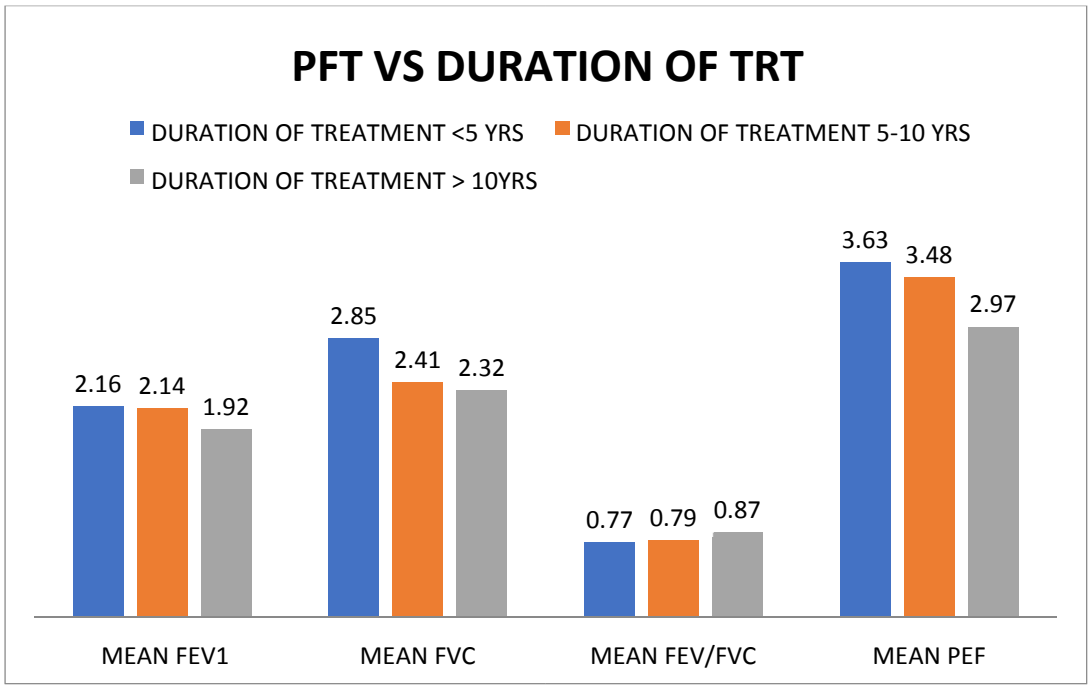


Table 26

PFT	DURATION OF TREATMENT		
	<5 YRS	5-10 YRS	> 10YRS
MEAN FEV1 %	75.62%	73.62%	64.00%
MEAN FVC %	80.75%	76.72%	66.14%
MEAN FEV/FVC %	89.86%	91.45%	94.43%
MEAN PEF %	64.80%	61.88%	57.57%

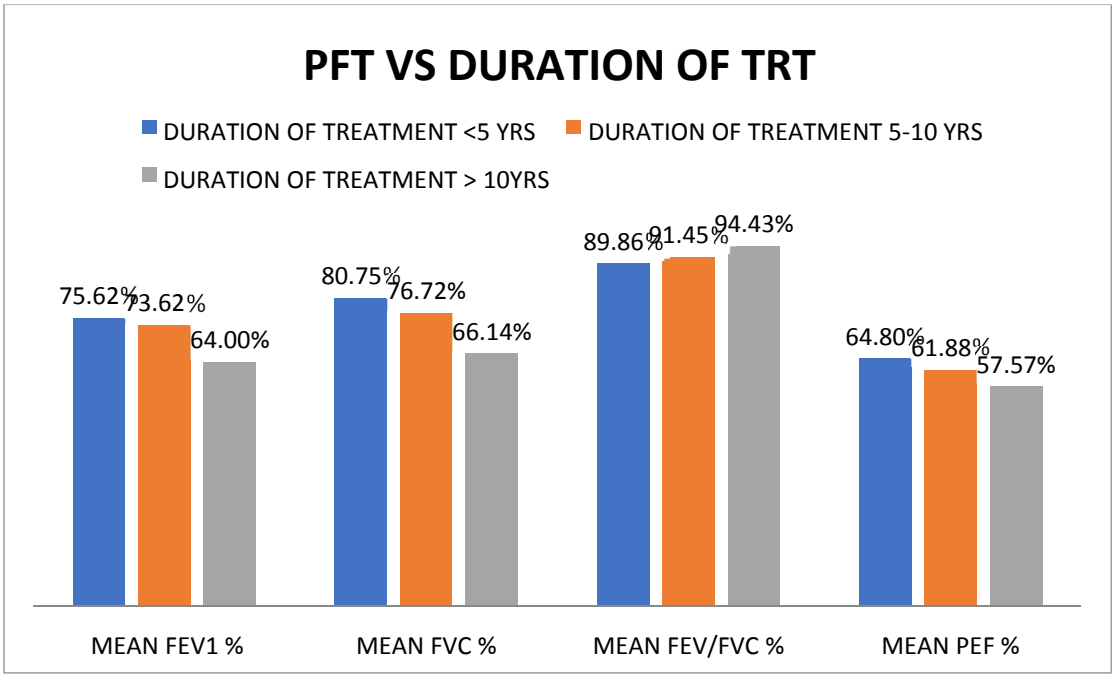


Table 27

PFT	SEROPOSITIVITY	
	POSITIVE	NEGATIVE
MEAN FEV1	2.09	2.44
MEAN FVC	2.58	2.68
MEAN FEV/FVC	0.77	0.81
MEAN PEF	3.54	3.46

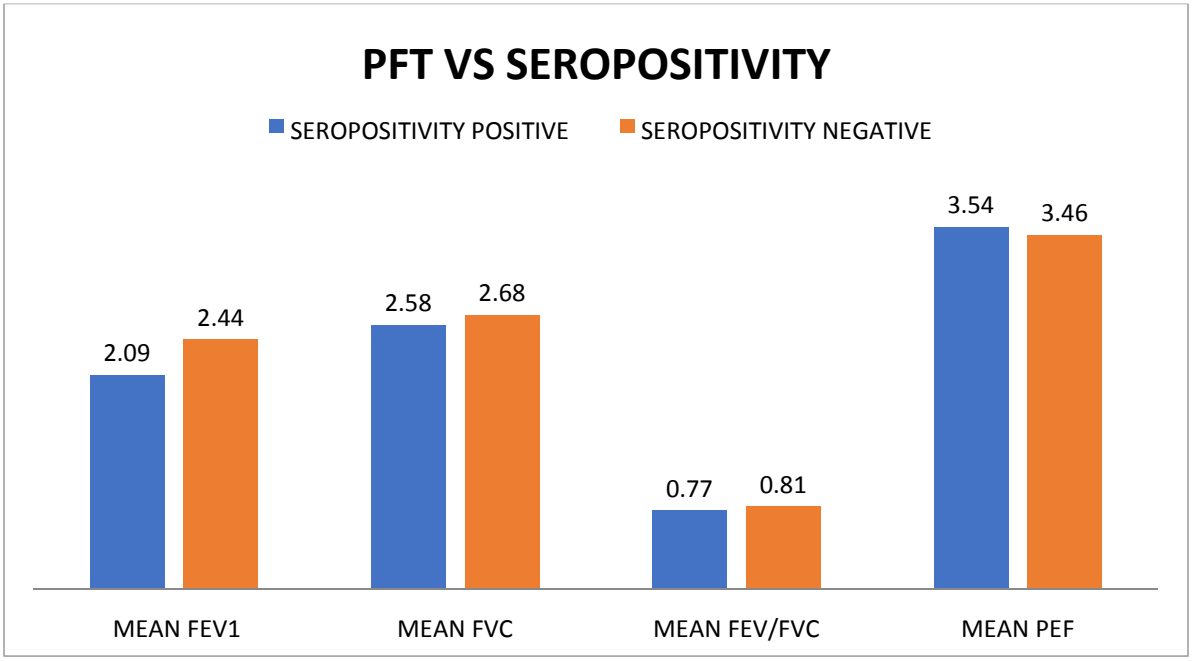
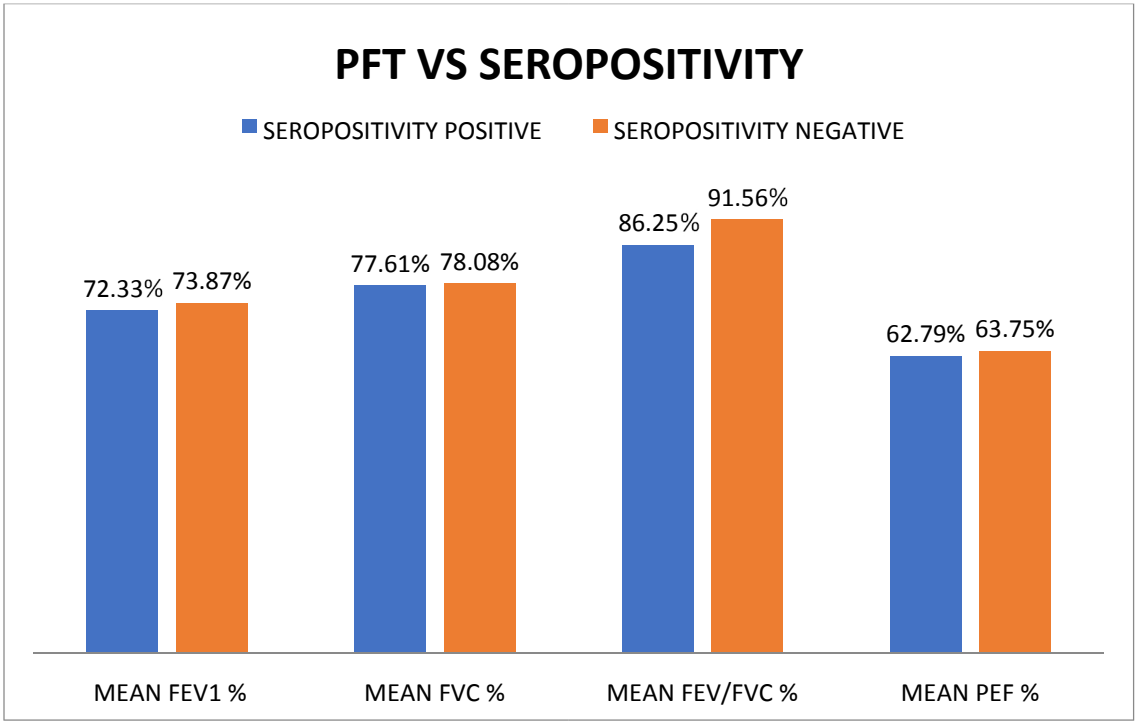


Table 28

PFT	SEROPOSITIVITY	
	POSITIVE	NEGATIVE
MEAN FEV1 %	72.33%	73.87%
MEAN FVC %	77.61%	78.08%
MEAN FEV/FVC %	86.25%	91.56%
MEAN PEF %	62.79%	63.75%



DISCUSSION

The aim of this study is to find the pulmonary function test abnormality in RA patients without pulmonary symptoms attending Rheumatology clinics in Tirunelveli medical college hospital.

In this study patients attending Rheumatology outpatient clinic who met the Rheumatology criteria for Rheumatoid arthritis and were receiving standard treatment were recruited and included 100 patients. Among them 83 were females and 17 were males.

The mean age of the study population was between 31 to 40 years as expected because the onset of rheumatoid arthritis is from third to fifth decade of life. The mean age in years for patients with abnormal pulmonary function is 45.81 . Age is a predictive of ILD in studies by multivariate analysis of other cofounders by Bilgici A et al [22].

Females were commonly affected by the disease (83%) and 17%males . This was similar to a study done by Owino et al [29]. (2009) which included 86% females and 14% males. Bongartz T et al studies shows male sex has been associated with development of RA ILD [23] .The disease concordance is 12 to 20% in monozygotic twins and 2% to 4% in fraternal twins as evidenced by Twin

studies. It is also found that first degree relative of the individuals with RA are 2 to 3 times more prone to develop the disease.

Pulmonary involvement in rheumatoid arthritis is associated with worse prognosis. It is seen that studies using respiratory symptoms as a trigger for screening underestimates the prevalence in particular with severe articular disease and limited mobility. The duration of disease is less than 5 years in 35% patients , 5 to 10 years in 52% and more than 10 years in 13% patients. The duration of the disease with abnormalities in pulmonary function tests ($p = 0.163$) by Kruskal Wallis Test was not significant. Multiple studies like Gochuico BR et al reveal that duration of RA is not a risk factor for pulmonary involvement[24]. The duration of RA influences the presence of clinical versus subclinical disease.

In our study disease activity was assessed by CDAI Score . About 53% was found to have high disease activity, 40 % had moderate activity and 7 % had low disease activity . The measure of RA disease activity has been associated with presence of pulmonary involvement as evidenced by

Koduri G et al [25].

In our study the duration of treatment was less than 5 years in 45% , 5 to 10 years was 48% and more than 10 years was seen in about 7% . Most of the patients were on DMARDs and remaining were on steroid therapy . Methotrexate

is well known to cause lung disease . In one study by Saag KG et al it has been found that methotrexate use associated with decline in pulmonary functions.[26]

Among the risk factors associated with RA , Diabetes mellitus , Systemic hypertension , Smoking and Alcohol were studied. In our study , diabetes was prevalent in 12 % patients among which 9 % had pulmonary abnormalities (p value 0.0001) and found to be significant by Mann whitney U test . Systemic hypertension was seen in 9% of which 6% (p value 0.0001) showed abnormal lung function tests and found to be significant by Mann Whitney U test.

Our study had only less number of male patients (17%) . Among them only 2% were indulged in smoking and 1 % is found to be alcoholic. A multivariate analysis of risk factors for physiologic or radiographic abnormalities suggestive of ILD in RA found that pack years of smoking was correlated with decline in FVC and DLCO as well as interstitial changes in chest X ray .

The pulmonary function test as measured by spirometry were found to be abnormal in 32% of the RA patients studied and all our patients did not carry any prior pulmonary disease diagnosis. This was similar to study by Madhavan et al . [27]

The predominant pattern of abnormalities in our study was mild restriction 14% followed by mild restriction 7 % . Other patterns include

moderate obstruction in 1% , Severe obstruction in 3% , moderate restriction in 5% and severe restriction in 2% . In addition to parenchymal lung disease, the presence of airway disease is also seen in high incidence in RA patients. It can involve both large airways (e.g. Bronchiectasis) and small airways (e.g. Asthma , COPD , bronchiolitis.

Airway abnormalities can be diagnosed using pulmonary function test and HRCT chest . The prevalence of obstructive airways abnormalities in RA is reported to be about 15 to 44% . In a study by Geddes DM et al [28] screening PFTs revealed 32% of patients with airflow obstruction as measured by decreased FEV1/FVC or forced expiratory flow at 25% to 75% of FVC. Amir et study showed mixed restrictive and obstructive pattern as commonest followed by restrictive pattern which is in contrast to our study . The reason for abnormal pulmonary function test in our study is due to disease activity. Injury to the alveoli by climatic factor, environmental pollution and presence of communicable diseases predisposes the patient to frequent chest infections . Initially the inflammation may be self limiting in normal persons but proceeds to fibrosis in RA patients . It can be prevented by incorporation of pneumococcal vaccine in all RA patients.

CONCLUSION

Our study highlighted the pulmonary function abnormalities in RA population without any pulmonary disease. The commonest defect pattern seen is mild restrictive pattern followed by obstructive pattern . In most patients the ventilatory defects were mild . There was increased prevalence of abnormal pulmonary function test in patients with additional risk factor like diabetes and hypertension. Rheumatoid disease activity by CDAI score

, Age , Duration of disease , Duration of treatment , Diabetes , Hypertension and Smoking were predictors of pulmonary impairment as determined by Spirometry.

LIMITATION

1. The study population was small and does not include the symptomatology of respiratory disease.
2. PFTs are not as sensitive as High resolution chest tomography in detecting respiratory disease.

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PROFORMA

NAME:

Age/Sex:

Address:

HISTORY OF ILLNESS:

DURATION OF RHEUMATOID ARTHRITIS:

DURATION OF TREATMENT:

RISK FACTORS, if any:

GENERAL EXAMINATION:

JOINTS INVOLVED: TENDER JOINTS:

SWOLLEN JOINT:

DEFORMITIES, if any:

SYSTEMIC EXAMINATION:

CVS:

RS:

P/A:

CNS:

CLINICAL DISEASE ACTIVITY INDEX SCORE(CDAI) :

INVESTIGATIONS:

CBC: TC

DC:

Hb:

Platelet count:

RBS:

RFT:

LFT:

SERUM ELECTROLYTES:

ESR:

CRP:

RA FACTOR/ANTI-CCP ANTIBODY:

CHEST X-RAY PA VIEW:

PULMONARY FUNCTION TEST:

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

Sl. No.	Name	Age	Sex	Duration of Disease	Duration of Treatment	Joints Involved	Prence of other risk factors				seropositivity	CDAI Score	FEV1(L)	FVC(L)	FEV1/FCV	FEV1,%	FVC%	FEV1/FVC%	PEF	PEF%	Impression
							SHT	T2Dm	Smoker	Alcoholic											
1	Ponmari	48	F	7	5	MCP,PIP	No	no	no	no	yes	34	2	2.55	0.784	81	90	90	3.61	58	Normal
2	Arockiyamuthu	36	F	6	5	MCP , PIP , , wrist	No	no	No	No	yes	34	2.1	2.56	0.82	82	93	96	3.55	52	Normal
3	Packiyalakshmi	34	F	6	5	MCP jts alone	no	no	no	no	yes	23	1.05	1.27	0.827	51	51	99	3.52	54	Moderate restriction
4	Petchiamammal	21	F	2	1	MCP, wrist, elbow, knee	No	no	no	no	no	34	2.23	2.12	0.7	70	65	69	3.19	74	Normal
5	Vijaya	45	F	2	0.5	MCP wrist	no	no	no	no	yes	15	2.12	3.04	70	72	83	84	4.71	71	Normal
6	pooranam	50	F	8	8	MCP, elbow, wrist	no	no	no	no	yes	21	2.11	2.55	0.78	80	90	90	3.51	55	Normal
7	Muniyamal	60	F	5	4	PIP, Ankle,knee	no	no	no	no	yes	6	1.58	1.8	0.87	66	59	111	3.74	61	Mild restriction
8	Subbaiah	65	M	10	8	MCP jts alone	no	no	no	no	yes	5	0.96	2.42		31	63	40	0.33	9	Severe obstruction
9	Amutha	55	F	7	5	MCP jts alone	no	no	no	no	yes	15	3.07	3.78		84	87	81	2.85	64	Normal
10	Ramalakshmi	40	F	6	4	MCP , PIP jts	no	no	no	no	yes	22	1.87	2.12		59	65	88	3.19	74	Moderate Obstruction
11	Marudhathal	49	F	8	4	MCP, PIP, elbow, wrist	no	No	no	no	no	29	2.57	6.97	0.45	63	102	53	4.14	68	Mild Obstruction
12	Kokilamal	52	F	4	2	MCPPIPWrist elbow shoulde kneeankle	No	No	no	no	yes	35	3.04	2.02	0.7	83	72	84	3.73	63	Normal
13	Anish baby	35	F	5	4	MCP , PIP, Wrist	no	no	no	no	yes	31	2.11	2.5	0.78	82	90	90	3.13	58	Normal

14	Chandu	40	F	8	6	MCP, PIP, wrist, elbow	no	no	no	no	yes	27	1.57	2.25	0.699	72	73	97	5.6	97	Mild restriction
15	Mohana	25	F	1	1	Wrist, MCP, PIP, wrist	no	No	no	no	yes	34	0.77	0.77	1	31	25	125	2.11	68	Moderate restriction

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							SHT	T2Dm	Smoker	Alcoholic	seropositivity										
16	Sudalaivadivu	35	F	7	5	MCP, PIP,Wrist,ankle, knee	no	no	No	no	yes	42	3.06	3.77		84	86	81	2.85	64	Normal
17	Jayakani	27	F	5	4	MCP, PIP. Ankle, wrist	No	no	no	no	yes	28	2.01	2.93		66	83	69	1.32	15	Obstruction
18	Sankaran	50	M	10	10	MCP, wrist	no	no	no	no	no	17	3	2.12	0.7	86	72	84	4.71	71	Normal
19	Rajakumari	39	F	8	8	MCP , PIP, Wrist	no	no	no	no	yes	38	0.75	1.94		25	55	38	0.27	7	Severe obstruction
20	Vellathai	60	F	20	14	mcp, wrist,knee, ankle	no	no	no	no	yes	36	1.5	1.74		40	40	87	2.3	49	Severe Restriction
21	Balasundari	22	F	2	2	MCP, wrist	No	no	no	no	no	10	2.02	2.45	0.824	81	88	83	3.65	68	Normal
22	Banu	39	F	9	8	MCP joints alone	no	No	no	no	yes	9	2.14	3.02	0.714	66	88	84	3.13	71	Normal
23	Jameena	38	F	8	8	MCP, PIP, wrist, elbow	No	no	no	no	yes	16	3.06	3.53	0.812	83	66	69	1.32	32	Mild Obstruction
24	Bhagavathiammal	65	F	3	3	MCP, PIP, wrist	no	no	no	no	yes	16	3.11	3.76	0.861	84	86	81	2.85	64	Normal
25	Sneha	20	F	1	0.6	PIP.knee jt	no	no	no	no	yes	20	2.12	3.04	0.706	72	83	84	4.71	71	Normal

26	Muthulaxmi	37	F	5	5	MCP, PIP, wrist	no	no	no	no	yes	18	3.55	5.35	0.684	81	99	81	2.41	50	Mild Obstruction
27	Piramu	60	F	9	8	MCP, PIP, Wrist, elbow	No	no	no	no	yes	18	1.33	1.72	0.77	75	79	94	2.79	59	Normal
28	Selvaraj	60	M	10	6	RA hand, MCP, PIP	no	no	no	no	yes	32	1.6	1.68	0.955	62	58	108	3.12	54	Mild restriction
29	Fathimarose	35	F	4	2	PIP, MCP	no	no	no	no	no	24	1.32	1.7	0.776	75	78	96	2.76	56	Normal
30	kala	30	F	4	3	MCP, PIP	no	no	no	no	yes	20	2.52	3.12	0.818	72	86	99	3.62	66	Normal
31	Muthumalai	50	F	12	10	MCP jt, PIP, wrist, elbow, ankle	no	no	no	no	yes	39	1.45	1.86	0.779	68	76	91	2.86	53	Normal

Sl. No.	Name	Age	Sex	Duration of Disease	Duration of Treatment	Joints Involved	Prence of other risk factors				seropositivity	CDAI Score	FEV1(L)	FVC(L)	FEV1/FCV	FEV1,%	FVC%	FEV1/FVC%	PEF	PEF%	Impression
							SHT	T2Dm	Smoker	Alcoholic											
32	Karupasamy	20	M	3	1	MCP jts alone	no	no	no	no	yes	23	1.99	2.43	0.818	84	84	102	4.62	67	Normal
33	Krishnaveni	23	F	3	3	MCP jts alone	no	no	no	no	yes	15	2.57	6.89	0.455	99	53	112	2.86	53	Normal
34	Pandi	40	M	15	10	MCP, wrist, elbow, knee	no	no	no	no	yes	34	1.33	1.72	0.77	75	78	94	2.79	59	Normal
35	Mani	50	M	10	8	RA hand, MCP, PIP, wrist	no	No	no	no	yes	34	1.44	1.86	0.779	68	76	91	2.84	53	Normal
36	Lakshmi	38	F	18	10	MCP, PIP,Wrist,ankle, knee	no	no	No	no	yes	42	1.9	2.8	0.678	90	99	74	5.62	74	Normal

37	Balamal	60	F	10	9	MCP joints alone	no	No	no	no	yes	10	3.04	2.1	0.704	83	74	84	3.92	64	Normal
38	Murugan	30	M	9	8	MCP, PIP, wrist, elbow	No	no	no	no	yes	29	2.6	3.2	0.818	74	90	97	2.89	78	Normal
39	Jesi	43	F	6	6	MCP, PIP, wrist	no	no	no	no	yes	16	2.4	2.68	0.895	88	84	102	5.84	88	Normal
40	Nanthinatchiyar	45	F	12	10	MCP, PIP. Ankle, wrist	No	no	no	no	no	28	1.62	1.66	0.955	62	58	106	3.12	54	Normal
41	Yovan	46	M	10	10	MCP, wrist	no	no	no	no	yes	17	1.09	3.33	0.329	48	130	37	2.41	45	Severe obstruction
42	Parvathy	40	F	10	8	MCP, PIP, Wrist, elbow	No	no	no	no	yes	38	1.45	1.86	0.77	68	76	91	2.79	59	Normal
43	Mariamal	45	F	8	6	RA hand, MCP, PIP	no	no	no	no	yes	32	1.46	2.11	0.691	70	78	78	3.12	54	Normal
44	Manjula	35	F	5	5	PIP, MCP	no	no	no	no	yes	24	1.57	2.25	0.69	72	73	97	5.6	90	Normal
45	Ponesaki	49	F	12	10	MCP jt, PIP, wrist, elbow, ankle	no	no	no	no	no	40	1.99	2.42	0.82	84	84	100	2.56	57	Normal

Sl. No.	**Name**	**Age**	**Sex**	**Duration of Disease**	**Duration of Treatment**	**Joints Involved**	**Prence of other risk factors**					**CDAI Score**	**FEV1(L)**	**FVC(L)**	**FEV1/FCV**	**FEV1,%**	**FVC%**	**FEV1/FVC%**		**PEF%**	**Impression**
							SHT	**T2Dm**	**Smoker**	**Alcoholic**	**seropositivity**								**PEF**		
46	Santhanalakshmi	43	F	6	6	MCP jts alone	no	no	no	no	yes	24	1.58	1.8	0.877	66	59	112	3.72	60	Mild restriction
47	Rajendran	47	M	6	2	MCP, PIP	no	no	no	no	yes	15	2.88	3.56	0.808	74	84	88	2.88	66	Normal

48	Chandra	35	F	9	7	MCPPIPWrist elbow shoulde kneeankle yes	No	No	no	no	yes	38	1.36	2.34	0.883	67	60	106	4.27	60	Mild restriction
49	Athikani	40	F	9	8	MCP , PIP, Wrist	no	no	no	no	yes	12	2.12	2.55	0.831	82	86	96	3.61	58	Normal
50	Pushpa	45	F	8	7	MCP jt, PIP, wrist, elbow, ankle	no	no	no	no	yes	15	1.54	1.85	0.832	66	68	96	2.89	54	Mild restriction
51	Muthuraku	40	F	12	11	MCP , PIP, Wrist	no	yes	no	no	yes	32	1.6	1.42	0.883	67	60	99	4.27	60	Mild restriction
52	Meena	31	F	5	4	MCP jt, PIP, wrist, elbow, ankle	no	no	no	no	yes	22	2.13	3.02	0.704	73	84	84	4.62	64	Normal
53	Murugamal	39	F	10	10	MCP , PIP jts	no	no	no	no	yes	15	3.32	3.72	0.88	99	96	104	5.21	66	Normal
54	Ponessaki	44	F	9	8	MCP , PIP , , wrist	no	no	no	no	yes	23	1.96	3.28	0.597	94	112	74	4.14	70	Normal
55	bazeer	20	M	2	2	MCP , PIP, Wrist	no	no	no	ni	yes	32	2.42	2.68	0.88	86	86	100	5.34	84	Normal
56	Saraswati	47	F	10	9	MCP , PIP jts	no	no	no	no	no	20	1.78	1.88	0.946	84	80	102	3.42	61	Normal
57	chandrapushpam	69	F	30	30	MCP , PIP , , wrist	no	no	no	no	yes	25	1.46	1.88	0.776	70	82	90	2.86	53	Normal
58	revathi	40	F	10	9	MCP , PIP, Wrist	no	no	no	no	yes	24	1.99	2.44	0.81	84	84	99	4.51	64	Normal

Sl. No.	**Name**	**Age**	**Sex**			**Joints Involved**	**Prence of other risk factors**								**FEV1/FVC%**		**PEF%**	**Impression**

				Duration of Disease	Duration of Treatment		SHT	T2Dm	Smoker	Alcoholic	seropositivity	CDAI Score	FEV1(L)	FVC(L)	FEV1/FCV	FEV1,%	FVC%		PEF		
59	Kanaga	23	F	2	2	MCP jts alone	no	no	no	no	yes	23	1.68	2.33	0.721	82	78	88	4.68	70	Normal
60	Maragatham	43	F	3	3	MCP , PIP, Wrist	no	no	no	no	yes	22	1.36	1.78	0.77	76	82	94	2.78	60	Normal
61	Fathima	38	F	5	5	MCP , PIP jts	no	no	no	no	no	30	2.12	3.03	0.699	72	96	74	3.77	78	Normal
62	Jeyamary	45	F	9	9	MCP , PIP , , wrist	yes	no	no	no	yes	31	2.32	2.12	1.09	74	65	120	3.19	74	Normal
63	Ayesha	50	F	10	10	MCP jt, PIP, wrist, elbow, ankle	no	yes	no	no	yes	27	1.26	1.29	0.969	57	56	112	3.59	62	Moderate restriction
64	Murugapan	60	M	10	10	MCP , PIP , , wrist	no	Yes	no	no	yes	26	1.36	2.35	88.3	69	65	105	3.69	68	Moderate restriction
65	Lakshmi	49	F	5	5	MCP , PIP, Wrist	no	no	no	no	yes	21	1.33	1.8	0.738	75	82	90	2.78	59	Normal
66	Vanaja	26	F	2	2	MCP joints alone	no	no	no	no	yes	23	2.1	2.4	0.875	88	90	99	4.34	64	Normal
67	Chermakani	42	F	5	5	MCP , PIP , , wrist	no	no	no	no	yes	26	3.07	3.76	0.816	60	65	88	3.19	74	Normal
68	Shanmugathai	36	F	5	5	MCP , PIP jts	no	no	no	no	no	28	2.51	4.28	0.586	63	88	64	4.14	70	Mild obstruction
69	Lakshmi	40	F	6	6	MCP , PIP, Wrist	no	no	no	no	yes	19	3	3.68	0.812	84	86	86	2.84	65	Normal
70	Baskar	42	m	5	5	MCP , PIP jts	no	no	no	no	yes	22	1.44	1.82	0.791	76	82	86	2.82	63	Normal
71	Kanaga	32	F	3	3	MCP , PIP , , wrist	no	no	no	no	yes	24	2.12	2.42	0.876	88	84	96	4.58	64	Normal
72	Chelladurai	40	M	6	6	MCP , PIP, Wrist	no	no	no	no	yes	20	1.54	1.85	0.833	66	68	96	2.75	82	Mild restriction

73	Ahamed	54	M	9	9	MCP , PIP, Wrist	no	no	no	no	yes	19	3.4	3.62	0.944	99	94	108	5.1	65	Normal

Sl. No.	Name	Age	Sex	Duration of Disease	Duration of Treatment	Joints Involved	Prence of other risk factors				seropositivity	CDAI Score	FEV1(L)	FVC(L)	FEV1/FCV	FEV1,%	FVC%	FEV1/FVC%	PEF	PEF%	Impression
							SHT	T2Dm	Smoker	Alcoholic											
74	Thenamal	32	F	3	3	MCP , PIP jts	no	no	no	no	yes	10	1.32	1.72	0.776	75	79	95	2.86	53	Normal
75	Mari	40	M	5	5	MCP , PIP, Wrist	no	no	no	no	yes	19	2.2	2.23	0.991	70	65	112	3.14	72	Normal
76	Subulaxmi	39	F	6	5	MCP , PIP, Wrist	no	no	no	no	yes	21	2	3.33	0.664	96	128	72	5.82	88	Normal
77	Regina	45	F	8	8	MCP , PIP, Wrist	no	no	no	no	yes	24	2.42	2.73	0.88	87	86	100	5.36	85	Normal
78	Ratnasamy	67	M	5	5	MCP , PIP jts	yes	yes	yes	yes	no	18	1.6	1.68	0.955	62	58	108	3.12	54	Mild restriction
79	Mariyammal	46	F	6	6	MCP , PIP, Wrist	no	yes	no	no	yes	21	3.07	3.77	0.814	84	87	81	2.85	64	Normal
80	Piramachi	55	F	8	8	MCP , PIP, Wrist	yes	yes	no	no	yes	23	1.58	1.8	0.876	66	59	111	3.74	61	Mild restriction
81	Mariyammal	37	F	5	5	MCP , PIP , , wrist	no	no	No	no	yes	22	1.91	3.47	0.77	92	136	68	5.84	88	Mild obstruction
82	Joseph	46	M	9	9	MCP , PIP jts	no	no	yes	no	yes	21	2.44	2.73	0.88	87	86	100	5.35	84	Normal
83	Guruvamma	45	F	6	6	MCP , PIP jts	no	no	no	no	yes	26	1.6	1.67	0.955	62	58	108	3..12	54	Mild restriction
84	Sulochana	45	F	9	9	MCP , PIP, Wrist	no	yes	no	no	yes	25	1.34	1.72	0.776	74	79	94	4.61	66	Normal
85	Eswari	38	F	5	5	MCP , PIP jts	no	no	no	no	yes	21	3.32	3.72	0.866	99	96	106	5.1	65	Normal
86	Muthulaxmi	39	F	6	6	MCP , PIP jts	no	no	no	no	yes	20	2.23	2.68	0.834	70	82	83	2.7	63	Normal

87	vigneshwari	40	f	8	7	MCP , PIP, Wrist	no	no	no	no	yes	24	6.97	2.57	0.455	102	63	53	4.14	74	Normal
88	Mohaidan meeral	39	F	4	4	MCP, PIP, elbow, wrist	no	no	no	no	yes	25	3.17	3.26	0.856	65	59	85	3.19	74	Normal

Sl. No.	Name	Age	Sex	Duration of Disease	Duration of Treatment	Joints Involved	Prence of other risk factors					CDAI Score	FEV1(L)	FVC(L)	FEV1/FCV	FEV1,%	FVC%	FEV1/FVC%	PEF	PEF%	Impression
							SHT	T2Dm	Smoker	Alcoholic	seropositivity										
89	Anthonyammal	48	F	10	10	MCP jt, PIP, wrist, elbow, ankle	yes	yes	no	no	no	29	6.54	1.85	0.836	66	68	96	2.89	54	Mild restriction
90	Bakyalaxmi	53	F	13	13	MCP , PIP, Wrist	yes	yes	no	no	yes	30	3.06	3.16	0.968	84	87	96	2.76	60	Normal
91	Tamilarasi	45	F	8	8	MCP , PIP jts	yes	no	no	no	yes	21	3	3.78	0.799	80	87	79	3.19	74	Normal
92	Shankuntala	58	F	13	13	MCP jt, PIP, wrist, elbow, ankle	yes	yes	no	no	yes	32	1.87	2.12	0.882	59	65	88	3.19	74	mild Obstruction
93	Yesumariyal	45	F	8	7	MCP , PIP , , wrist	no	no	no	no	yes	21	3.07	3.78	0.818	84	87	97	2.85	64	Normal
94	Chinnathai	57	F	11	11	MCP , PIP, Wrist	yes	yes	no	no	yes	23	1.5	1.74	0.874	40	40	87	2.3	49	Severe Restriction
95	Annal	49	F	8	5	MCP , PIP, Wrist	yes	no	no	no	yes	20	1.42	1.6	0.887	67	60	110	4.27	60	Mild restriction
96	Gomathy	51	F	15	14	MCP , PIP , , wrist	no	no	no	no	yes	15	2.5	2.8	0.891	88	89	112	3.14	58	Normal
97	Radha	30	F	3	3	MCP , PIP jts	no	no	no	no	yes	6	2.1	2.53	0.834	80	88	99	3.68	62	Normal
98	Madathy	46	F	12	10	MCP , PIP, Wrist	no	yes	no	no	yes	22	1.58	1.8	0.846	66	59	111	3.74		Mild restriction

99	Jeyalakshmi	35	F	8	8	MCP jt, PIP, wrist, elbow, ankle	no	no	no	no	yes	12	1.25	1.29	0.968	57	56	112	3.61	64	Moderate restriction
100	Manesha	28	F	2	2	MCP,PIP,wrist,elbow	no	no	no	no	yes	28	2	3.04	0.721	74	83	83	3.55	55	Normal