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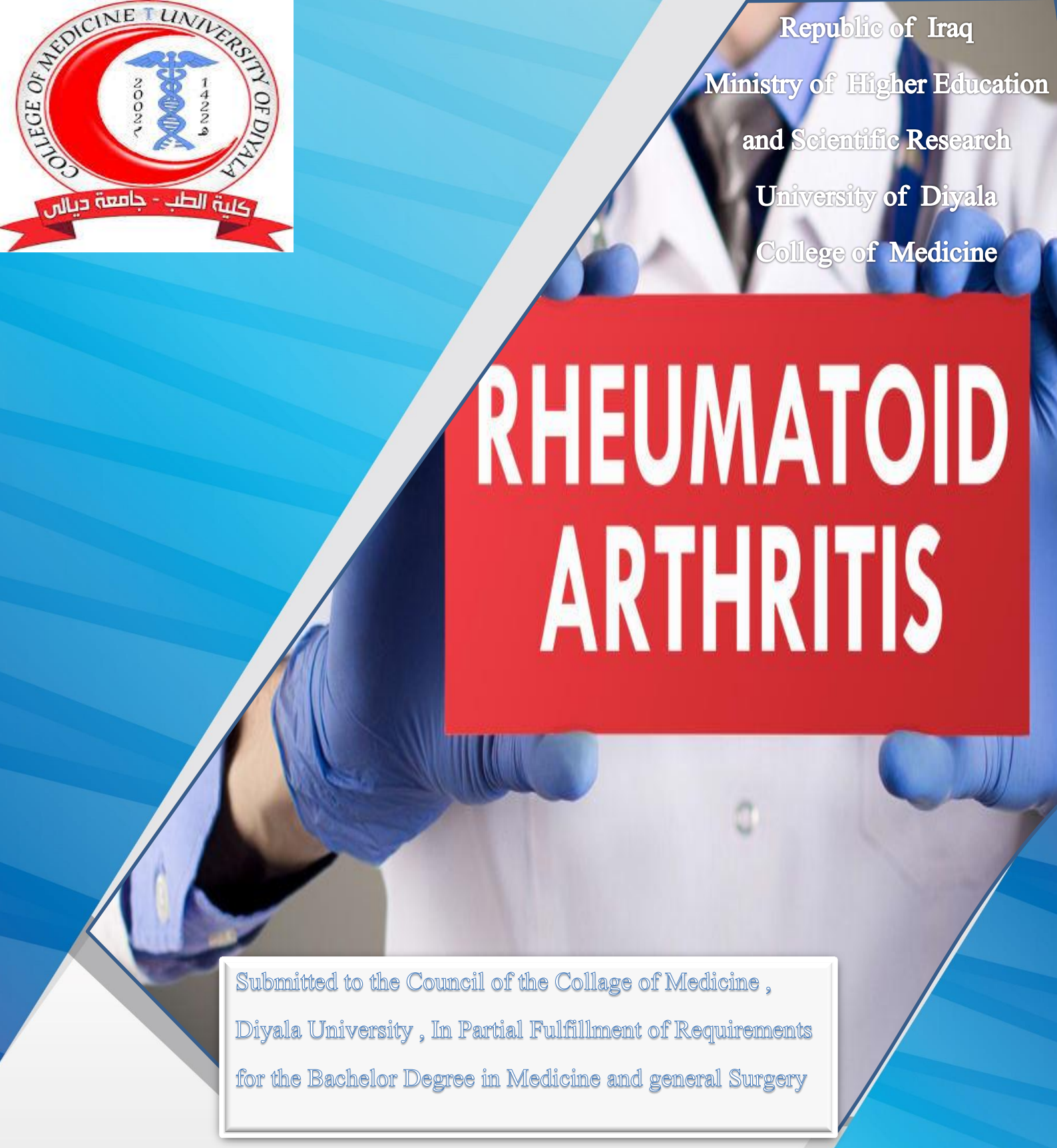

RHEUMATOID ARTHRITIS

Submitted to the Council of the Collage of Medicine , Diyala University , In Partial Fulfillment of Requirements for the Bachelor Degree in Medicine and general Surgery

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بسم الله الرحمن الرحيم

(يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ)

[المجادلة: ١١]

Contents :

Acknowledgement

By the name of Allah ,we start our project and we are thankful to Allah for helping us to complete this project .

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Abstract

Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic autoimmune disease, affecting the joints with varying severity among patients. The risk factors include age, gender, genetics, and environmental exposure (cigarette smoking, air pollutants, and occupational). Many complications can follow, such as permanent joint damage requiring arthroplasty, rheumatoid vasculitis, and Felty syndrome requiring splenectomy if it remains unaddressed. As there is no cure for RA, the treatment goals are to reduce the pain and stop/slow further damage. Here, we present a brief summary of various past and present treatment modalities to address the complications associated with RA.

INTRODUCTION

Rheumatoid arthritis (RA) is a common form of inflammatory arthritis, occurring throughout the world and in all ethnic groups. The prevalence of RA is approximately 0.8–1.0% in Europe and the Indian subcontinent, with a female-to-male ratio of 3 : 1. The prevalence is lower in South-east Asia (0.4%). The highest prevalence in the world is in Pima Indians (5%). It is a chronic disease characterised by a clinical course of exacerbations and remission

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder of unknown etiology that primarily involves synovial joints. It typically starts in small peripheral joints, is often symmetric, and progresses to involve proximal joints if not treated.Joint inflammation over time leads to the destruction of the joint with cartilage and bone erosion. RA with a symptom duration of fewer than six months is defined as early RA, and when the symptoms have been present for more than six months, it is defined as established RA.

There is no pathognomonic laboratory test for rheumatoid arthritis, which makes the diagnosis of this disease challenging. An astute and comprehensive clinical approach is required to make the diagnosis and prevent debilitating joint damage. The treatment of patients with rheumatoid arthritis requires both pharmacological and non-pharmacological therapy. Today, the standard of care is early treatment with disease-modifying anti-rheumatic drugs. Despite treatment, many patients progress to disability and suffer significant morbidity over time. A comprehensive pharmacological and non-pharmacological support

(physical therapy, counseling, and patient education) is required to improve clinical outcomes.

Pathophysiology

RA is a complex disease with both genetic and environmental components. The importance of genetic factors is demonstrated by higher concordance of RA in monozygotic (12–15%) compared with dizygotic twins (3%), and an increased frequency of disease in first-degree relatives of patients. Genome-wide association studies have detected nearly 100 loci that are associated with the risk of developing RA. The strongest association is with variants in the HLA region. Recent studies have shown that the association with HLA is determined by variations in three amino acids in the HLA-DRβ1 molecule (positions 11, 71 and 74) and single variants HLA-B (at position 9) and HLA-DPβ1 (at position 9). The non-HLA loci generally lie within or close to genes involved in regulating the immune response. It is currently believed that RA occurs when an environmental stimulus, such as infection, triggers autoimmunity in a genetically susceptible host by modifying host proteins through processes like citrullination so that they become immunogenic. However, no single specific pathogen has been identified as a cause. An important environmental risk factor is cigarette smoking, which is also associated with more severe disease and reduced responsiveness to treatment. Remission may occur during pregnancy and sometimes RA first presents post-partum. This is likely to be due to suppression of the immune response during pregnancy but hormonal changes may also play a role.

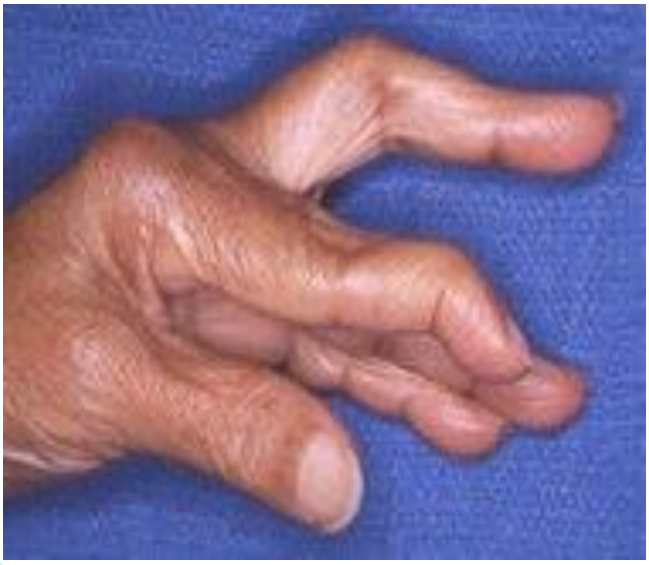
Clinical features

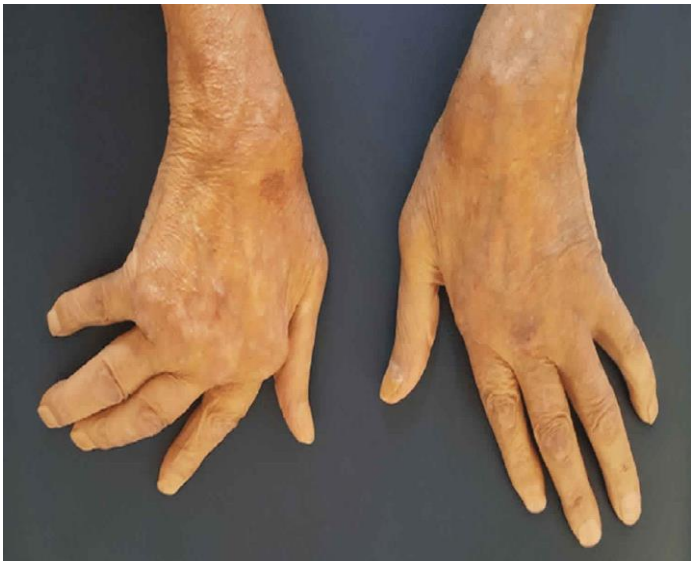
The typical presentation is with pain, joint swelling and stiffness affecting the small joints of the hands, feet and wrists in a symmetrical fashion. Large joint involvement, systemic symptoms and extra-articular features may also occur.

Sometimes RA has an acute onset, with severe early morning stiffness, polyarthritis and pitting oedema. This occurs more commonly in old age. Another presentation is with proximal muscle stiffness mimicking polymyalgia rheumatica . Occasionally, the onset is palindromic, with relapsing and remitting episodes of pain, stiffness and swelling that last for only a few hours or days.

Examination typically reveals swelling and tenderness of the affected joints. Erythema is unusual and its presence suggests coexistent sepsis.

Characteristic deformities may develop with long-standing uncontrolled disease, although these have become less common over recent years with more aggressive management. They include ulnar deviation of the fingers, ‘swan neck’ deformity, the boutonnière or ‘button hole’ deformity, and a Z deformity of the thumb . Dorsal subluxation of the ulna at the distal radio-ulnar joint may occur and contribute to rupture of the fourth and fifth extensor tendons. Triggering of fingers may occur because of nodules in the flexor tendon sheaths. Subluxation of the MTP joints of the feet may result in ‘cock-up’ toe deformities, causing pain on weight-bearing on the exposed MTP heads and the development of secondary adventitious bursae and callosities. In the hindfoot, a valgus deformity of the calcaneus may be observed as the result of damage to the ankle and subtalar joints. This is often associated with loss of the longitudinal arch (flat foot) due to rupture of the tibialis posterior tendon. Popliteal (Baker’s) cysts may occur in patients with knee synovitis, in which synovial fluid communicates with the cyst but is prevented from returning to the joint by a valve-like mechanism; this is not specific to RA. Rupture may be induced by knee flexion, leading to calf pain and swelling that may mimic a deep venous thrombosis (DVT). These joint deformities tend to be observed in older patients with long-standing disease but are becoming much less common with more aggressive treatment of RA in its early stages.





24.53 Extra-articular manifestations of rheumatoid disease

Systemic
- Fever
- Weight loss
- Fatigue
- Susceptibility to infection

Musculoskeletal
- Muscle-wasting
- Tenosynovitis
- Bursitis
- Osteoporosis

Haematological
- Anaemia
- Thrombocytosis
- Eosinophilia

Lymphatic
- Felty's syndrome (see Box 24.54)
- Splenomegaly

Nodules
- Sinuses
- Fistulae

Ocular
- Episcleritis
- Scleritis
- Scleromalacia
- Keratoconjunctivitis sicca

Vasculitis
- Digital arteritis
- Ulcers
- Pyoderma gangrenosum
- Mononeuritis multiplex
- Visceral arteritis

Cardiac
- Pericarditis
- Myocarditis
- Endocarditis
- Conduction defects
- Coronary vasculitis
- Granulomatous aortitis

Pulmonary
- Nodules
- Pleural effusions
- Fibrosing alveolitis
- Bronchiolitis
- Caplan's syndrome (p. 611)

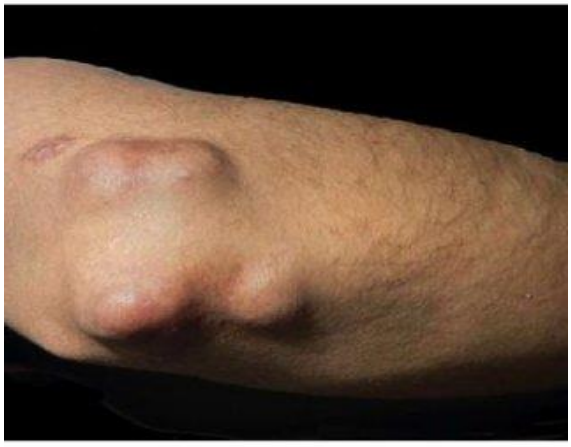
Neurological
- Cervical cord compression
- Compression neuropathies
- Peripheral neuropathy
- Mononeuritis multiplex

Amyloidosis (p. 81)

Systemic features

Anorexia, weight loss and fatigue may occur throughout the disease course. Osteoporosis is a common complication and muscle-wasting may occur as the result of systemic inflammation and reduced activity. Extra-articular features are most common in patients with long-standing seropositive erosive disease but may occasionally occur at presentation, especially in men. Most are due to serositis, granuloma and nodule formation or vasculitis .

1. **Nodules Rheumatoid nodules**
2. **Ocular involvement**
3. **Cardiac involvement**
4. **Pulmonary involvement**
5. **Peripheral neuropathy**
6. **Spinal cord compression**



Nodules

7. Other complications

Amyloidosis is a rare complication of long-standing disease that usually presents with nephrotic syndrome. Microcytic anaemia can occur due to iron deficiency resulting from NSAID induced gastrointestinal blood loss, whereas normochromic, normocytic anaemia with thrombocytosis occurs in patients with active disease. Felty's syndrome is a rare complication of seropositive RA in which splenomegaly occurs in combination with neutropenia and thrombocytopenia (Box 24.54). Localised or generalised lymphadenopathy can occur in patients with active disease but persistent lymphadenopathy may indicate the development of lymphoma, which is more common in patients with long standing RA .

24.54 Felty's syndrome

Risk factors

- Age of onset 50–70 years
- Female > male
- Caucasians > blacks
- Long-standing rheumatoid arthritis
- Deforming but inactive disease
- Seropositive for rheumatoid factor

Common clinical features

- Splenomegaly
- Lymphadenopathy
- Weight loss
- Skin pigmentation
- Keratoconjunctivitis sicca
- Vasculitis, leg ulcers
- Recurrent infections
- Nodules

Laboratory findings

- Normochromic, normocytic anaemia
- Neutropenia
- Abnormal liver function
- Thrombocytopenia
- Impaired T- and B-cell immunity

Investigation

Approach Considerations

No test results are pathognomonic for rheumatoid arthritis (RA); instead, the diagnosis is made by using a combination of clinical, laboratory, and imaging features. Bone scanning findings may help distinguish inflammatory from non-inflammatory changes in patients with minimal

swelling, and densitometry findings are useful for helping diagnose changes in bone mineral density that are indicative of osteoporosis.

Laboratory Studies

Routine viral screening by serologic testing does not significantly facilitate the diagnosis of RA in patients with early RA, nor is it helpful as a potential identifier of disease progression.Potentially useful laboratory studies in suspected RA fall into 3 categories—markers of inflammation, hematologic parameters, and immunologic parameters—and include the following :

- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP) level
- Complete blood count (CBC)
- Rheumatoid factor (RF) assay
- Antinuclear antibody (ANA) assay

Anti−cyclic citrullinated peptide (anti-CCP) and anti−mutated citrullinated vimentin (anti-MCV) assays (currently used in the 2010 American College of Rheumatology [ACR]/European League Against Rheumatism [EULAR] classification criteria)

Markers of inflammation

The ESR and the CRP level are associated with disease activity. The CRP value over time correlates with radiographic progression.

Hematologic parameters

The CBC commonly demonstrates anemia of chronic disease and correlates with disease activity; it improves with successful therapy. Hypochromic anemia suggests blood loss, commonly from the gastrointestinal (GI) tract (associated with the use of nonsteroidal anti-inflammatory drugs [NSAIDs]). Anemia may also be related to disease-modifying antirheumatic drug (DMARD) therapy.

Thrombocytosis is common and is also associated with disease activity. Thrombocytopenia may be a rare adverse event of therapy and may occur in patients with Felty syndrome. Leukocytosis may occur but is usually mild. Leukopenia may be a consequence of therapy or a component of Felty syndrome, which may then respond to DMARD therapy

Immunologic parameters

Immunologic parameters include autoantibodies (eg, RF, anti-CCP antibodies, and ANAs). RF is an immunoglobulin (Ig) M antibody directed against the Fc fragment of IgG that is present in approximately 60-80% of patients with RA over the course of their disease (but in fewer than 40% of patients with early RA). RF values fluctuate somewhat with disease activity, though titers of RF generally remain high even in patients with drug-induced remissions.

RF is not specific for RA but is also present in other connective tissue diseases, infections, and autoimmune disorders, as well as in 1-5% of healthy people. The presence of RF predicts radiographic progression of bone erosions, independent of disease activity.

Although ANAs are present in approximately 40% of patients with RA, test results for antibodies to most nuclear antigen subsets are negative.

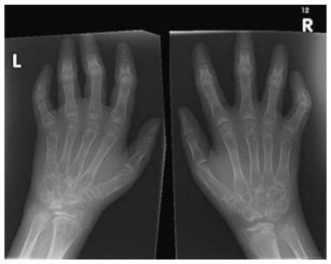
Assays for anti-citrullinated protein antibody (ACPA; often tested as anti-CCP) are now being used clinically for diagnosing RA. ACPA-positive and ACPA-negative RA may be 2 distinct disease subsets, with different underlying pathogeneses and risks for developing RA.[44, 45]ACPA-positive patients may have a more erosive RA disease course than ACPA-negative patients.[46]However, a 2011 study suggests that reassessment of ACPA or IgM RF during the first year after onset of arthritis does not provide significant additional information.

The sensitivity of anti-MCV assays has been reported to be comparable to that of ACPA; however, other studies have found the specificity of anti-MCV to be slightly lower than that of ACPA.Anti-MCV and anti-CCP levels may correlate with disease activity.

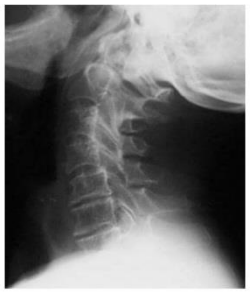
Studies of anti-CCP antibodies suggest a sensitivity and specificity equal to or better than those of RF, with an increased frequency of positive results in early RA; the presence of both anti-CCP antibodies and RF is highly specific for RA. Additionally, the presence of anti-CCP antibodies, like that of RF, indicates a worse prognosis.

Radiography

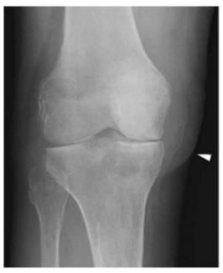
Radiography remains the first choice for imaging in RA; it is inexpensive, readily available, and easily reproducible, and it allows easy serial comparison for assessment of disease progression.Views of the hands, wrists, knees, feet, elbows, shoulders, hips, cervical spine, and other joints should be assessed with radiography when indicated (see the images below). Erosions may be present in the feet, even in the absence of pain and in the absence of erosions in the hands .



Juvenile rheumatoid arthritis. Widespread osteopenia, carpal crowding (due to cartilage loss), and several erosions affecting the carpal bones and metacarpal heads in particular in a child with advanced juvenile rheumatoid arthritis (also known as juvenile idiopathic arthritis).



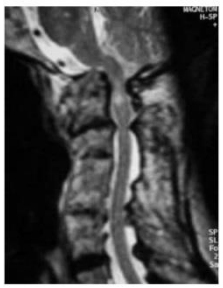
Rheumatoid arthritis. Lateral view of the cervical spine in a patient with rheumatoid arthritis shows erosion of the odontoid process.



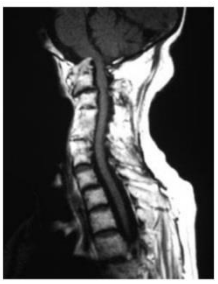
Rheumatoid arthritis. Anteroposterior radiograph of the knee shows uniform joint-space loss in the medial and lateral knee compartments without osteophytosis. A Baker cyst is seen medially (arrowhead).

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) provides a more accurate assessment and earlier detection of lesions than radiography does; however, the cost of the examination and the small size of the joints involved militate against its widespread use. MRI is used primarily in patients with abnormalities of the cervical spine (see the images below); early recognition of erosions on the basis of MRI images has been sufficiently validated.



Sagittal T2-weighted magnetic resonance image of cervical spine in same patient as in previous image. Compromised foramen magnum is easily appreciated, and there is increased signal intensity within upper cord; this is consistent with compressive myelomalacia. Further narrowing of canal is seen at multiple levels.

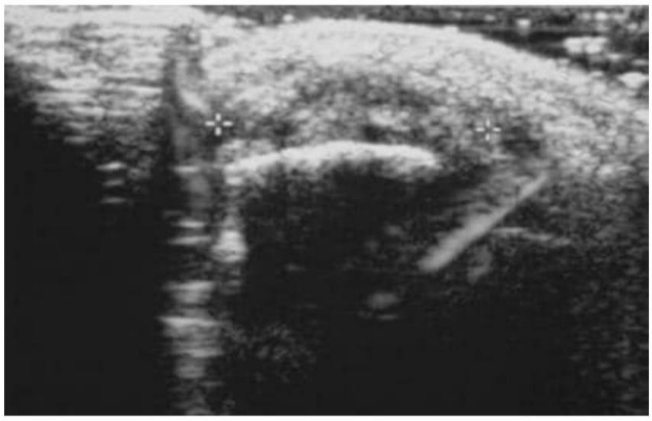


Rheumatoid arthritis. T1-weighted sagittal magnetic resonance image of the cervical spine shows basilar invagination with cranial migration of an eroded odontoid peg. There is minimal pannus. The tip of the peg indents the medulla, and there is narrowing of the foramen magnum due to the presence of the peg. Inflammatory fusion of several cervical vertebral bodies is shown.

Ultrasonography

Ultrasonography of joints (see the image below) is gaining increased widespread acceptance in clinical practice; however, its use in RA is not yet the standard of care.Ultrasonography allows recognition of effusions in joints that are not easily accessible (eg, the hip and, in obese patients, the shoulder) and of cysts (Baker cysts). In addition, high-resolution

sonograms allow visualization of tendon sheaths, changes and degree of vascularization of the synovial membrane, and even erosions. Ultrasonography can often be done in the office.



Rheumatoid arthritis. Ultrasonography-guided synovial biopsy of the second metacarpophalangeal joint of the right hand in a patient with rheumatoid arthritis of the hands. The biopsy needle is seen as a straight echogenic line on the left side of the image in an oblique orientation.

Treatment / Management

The goal of treatment in patients with RA is early diagnosis and early initiation of treatment to prevent irreversible damage to the joints. The International Task Force Guidelines published in 2014 make the following recommendations regarding treatment of RA.
The primary goal of treatment is to achieve long-term clinical remission and optimize quality of life with the absence of signs and symptoms associated with inflammatory disease activity.
If clinical remission cannot be achieved, low disease activity is an acceptable alternative.

Disease activity should be assessed every month in patients with moderate to severe disease activity.
In patients with low disease activity or clinical remission, disease activity should be assessed every 3 to 6 months.
Multiple clinical assessment tools have been developed to assist clinicians in determining the disease activity of patients with RA. An

updated recommendation from the American College of Rheumatology (ACR) in 2019 recommended using the following assessment tools because they met the minimum standard for evaluation per their recommendation:

- Clinical Disease Activity Index (CDAI)
- Disease Activity Score (DAS)
- Disease Activity Score 28 Joints (DAS28-ESR/CRP)
- Patient-Derived DAS28
- Hospital Universitario La Princesa Index (HUPI)
- Multi-Biomarker Disease Activity Score (MBDA score, VECTRA DA)
- Rheumatoid Arthritis Disease Activity Index (RADAI)
- Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)
- Routine Assessment of Patient Index Data 3 (RAPID3)
- Routine Assessment of Patient Index Data 5 (RAPID5)
- Simplified Disease Activity Index (SDAI)

Disease-modifying antirheumatic drugs (DMARDs)

typically used in treating RA include methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide. Anti-TNF-alpha agents include etanercept, infliximab, adalimumab, golimumab, and certolizumab pegol. Non-TNF biologic DMARDs include interleukin (IL) 6 receptor antagonists such as tocilizumab and sarilumab, T-cell blockers such as abatacept (CTLA4-Ig), and the anti-CD20 B-cell depleting monoclonal antibody such as rituximab. Other synthetic DMARDs include Janus kinases (JAK) inhibitors such as tofacitinib, baricitinib, and upadacitinib.
DMARD therapy, including biologic agents and targeted therapy agents (tofacitinib), should be temporarily held in patients with a serious active infection. They can be resumed after the infection has resolved and

antimicrobial treatment has been completed.It is essential to remember that all patients starting treatment for RA should be screened for hepatitis B and C and tuberculosis. Methotrexate should be avoided in patients with liver damage. Patients with latent tuberculosis should complete treatment for at least one month before the initiation of biologic agents. If patients cannot take or complete treatment for latent tuberculosis, conventional DMARD therapy should be used.In patients with underlying skin cancer and lymphoproliferative disorders, biologic agents should be avoided except for rituximab in patients with lymphoproliferative disorders as there is evidence of benefit from B-cell suppression in these cases.A, patients should receive vaccination for pneumococcus, hepatitis, influenza, human papillomavirus (HPV), and herpes zoster virus (HZV).

Nonbiologic DMARDs

This category includes hydroxychloroquine (HCQ), azathioprine (AZA), sulfasalazine, methotrexate, leflunomide, and cyclosporine. Methotrexate is the initial drug of choice for patients with RA. The recommended treatment plan recommends an initial dose of 15 mg/week of methotrexate with an escalation of 5 mg/month and a target dose of 25 to 30 mg/week. In patients who do not have an adequate response to oral administration, subcutaneous administration can be tried.

TNF inhibitors

The TNF inhibitors include etanercept, infliximab, adalimumab, certolizumab, and golimumab. The ACR does not recommend the use of TNF inhibitors until a nonbiologic DMARD has been tried.However, studies have shown that the addition of TNF inhibitors in patients who have failed methotrexate therapy is better than adding another nonbiologic DMARD. The most concerning adverse effect of these agents is opportunistic infections and reactivation of latent tuberculosis. There is some concern about the generation of antibodies against these agents, which may decrease their efficacy over time; however, the use of methotrexate in combination with these agents has been shown to decrease this complication. Acute infection, advanced heart failure, and recent malignancies are a contraindication for using these agents.

Rituximab

Rituximab is a biologic non-TNF DMARD that can be added for the treatment of RA if patients have uncontrolled RA and who did not improve with TNF therapy. Rituximab suppresses CD20+ B-cells and decreases the immune response to vaccines in patients receiving rituximab. As stated above, it is a preferred agent in patients with underlying lymphoproliferative disorders.

Abatacept

Abatacept inhibits T-cell activation by binding to CD80 and CD86. It is administered as a monthly intravenous infusion or as a weekly subcutaneous injection. Patients with uncontrolled RA, who have shown an inadequate response to methotrexate and TNF inhibitor therapy, benefit from abatacept therapy with proven efficacy from 6 months to 5 years of therapy.

Interleukin 6 Inhibitors

Tocilizumab, an IL-6 receptor inhibitor, is indicated for moderate-to-severe active RA in adults who have had an inadequate response to TNF inhibitor therapy. These patients develop clinically meaningful improvement with the use of tocilizumab. Sarilumab is another agent in this category that has been shown to improve clinical outcomes in patients with uncontrolled RA despite TNF inhibitor therapy.

Janus kinase (JAK) Inhibitors

JAK is a group of tyrosine kinases that participate in intracellular signal transduction for hematopoiesis and immune cell function. JAK inhibitors (such as tofacitinib) reduce the production of cytokines and are approved as second-line agents for the treatment of RA.

ACR and EULAR Treatment Guidelines

According to the ACR treatment guidelines for early RA, patients who have not taken disease-modifying antirheumatic drug (DMARD) therapy should start DMARD therapy regardless of the activity level.

In patients with low disease activity and early disease, monotherapy with methotrexate is the preferred treatment.

Leflunomide or sulfasalazine are the first-line treatment in patients with a contraindication to methotrexate or intolerance to it.

If monotherapy with DMARD does not control disease activity (regardless of concomitant glucocorticoid use), therapy should be altered. Methotrexate can be continued or discontinued at this point. Additional therapy options after failed monotherapy with DMARD are recommended as either dual traditional/nonbiologic DMARD therapy, tumor necrosis factor (TNF) inhibitors, or non-tumor necrosis factor biologic agents.
In patients with established RA, who are DMARD naive, methotrexate is the preferred agent for initial monotherapy, regardless of the disease activity level.
If monotherapy with DMARD does not control disease activity in established RA (regardless of concomitant glucocorticoid use), dual DMARD therapy, a TNF inhibitor, a non-TNF biologic agent, or tofacitinib therapy can be added.
If disease activity remains high on TNF inhibitor monotherapy, DMARD therapy should be added in addition to the TNF inhibitor.
If disease activity remains high despite anti-TNF inhibitor switch to a non-TNF biologic agent with or without methotrexate
If disease activity remains high despite a trial of anti-TNF and non-TNF agents, use another non-TNF biologic agent before considering tofacitinib.
If still uncontrolled despite the above trials, use tofacitinib
If disease activity remains high despite the above combination therapies, short-term low-dose glucocorticoid therapy should be added.
TNF inhibitors should be avoided in patients with congestive heart failure.
Patients with hepatitis C who have not been treated or are currently not on treatment for it should receive nonbiologic DMARD therapy rather than TNF inhibitors.

Materials and Methods

Patients diagnosed with RA and admitted to hospital . Data including age, gender, chief complaint, and physical examination findings were all recorded.

Also, patients were interrogated regarding comorbidities such as hypertension, cardiac diseases, thromboembolic events, diabetes mellitus, and past surgical history.

Study Design

Case control study included 30 patients with RA who were admitted to hospital . Their ages range between 29-75 years old, 8 were males and 22 were females. The diagnosis of each case was established using clinical diagnosis and radiological study. A careful case history was taken from each patient using formula sheet .

Results

Distribution of study population according to Gender

Table 1-1

Gender	Patients NO (%)
Male	8 (26 %)
Female	22 (74 %)
Total	30 (100%)

Distribution of study population according to Age

Table 1.2

Age group years	Patients No (%)
29-50	10 (33,33%)
50-75	20 (66,67%)
Total	30 (100%)

Distribution of study population according to presence of Chronic Disease

Table 1.3

Chronic Disease	Patients No (%)
Diabetes Mellitus	5 (16,67%)
Hypertension	12 (40%)
No Chronic Disease	16 (53,3%)
Total	30 (100%)

Distribution of study population according to smoking habit :

Table 1.4

smoking habit	Patients No (%)
Smokers	7 (23,33%)
Non-Smokers	23 (76,67%)
Total	30 (100%)

Distribution of study population according to joint involvement :

Table 1.5

joint involvement	Patients No (%)
Wrist	25 (83,33%)
PIP (Proximal Interphalangial Joint)	21 (70%)
Knee	17 (56,67%)
MTP (MetaTarso Phalangeal Joint)	9 (30%)
Shoulder	4 (13,33 %)
Elbow	2 (6,67 %)

Distribution of study population according to treatment :

Table 1.6

Treatment	Patients No (%)
Methotrexate	18 (60%)
Hydroxychloroquine	10 (33,33%)
Prednisolone	9 (30%)
Leflunmide	4 (13,33%)
Salfasalazine	3 (10 %)
Physiotherapy	3 (10 %)

Distribution of study population according to Family History :

Table 1.7

Family History	Patients No (%)
Family History (+)	5 (16,67%)
Family History (-)	25 (83,33%)

Discussion

The data from the 30 patients in this study demonstrate not only the extent of RA in population, but also the potential causal links between RA and many factors . It is important that the major findings of this report are confirmed across the 4 study centers, even though centers differed geographically and in the content of patients (tertiary centers, rheumatology practice, and community sample), among other factors. This important diversity and the concordance of results were among the reasons that led us to report the data from the centers individually.

In the 3 centers that reflected community and practice data, The total number of the patients was 30 , the most of them was female , as shown in table 1-1 .

Minimum age group was 29 years old and maximum age group was 75 years old. The highest number of patients 20 were in age group 50-75 years old, followed by 10 cases in age group 29-50 years old, as shown in table 1-2 .

Out of 30 patients with RA , 5 were diabetic , 12 were hypertensive and 16 have no any chronic disease , as shown in table 1.3 .

The highest incidence rate was noticed among non-smoking patients (23 cases) , in compare to smokers (7 cases) . as shown in table 1.4 .

There is many join involvement among the patients , which was mostly wrist joint which was 83.33 % , followed by proximal Interphalangial Joint which was 70% , Knee joint which was %56.67 , MetaTarso Phalangeal Joint which was 30% , Shoulder joint which was 13.33% and Elbow joint which was 6.67% . as shown in table 1.5 .

There are many drugs used , most of them was methotrexate 60% followed by hydroxychloroquine 33,33% , prednisolone 30% , leflunmide 13,33% and Salfasalazine 10 % .

We also noted that mortality in RA increases at an accelerated rate over time. This important finding, which had not been noted in a number of previous shorter studies, suggests that it is not merely having RA that is bad, but it is the progressive burden of disability, decrepitude, pain, treatment, and treatment side effects, operating over time, that increasingly leads to death in RA patients.

Conclusions

Significant variations of RA incidence and prevalence have been observed among different populations. It seems that there is a relative decrease in the disease occurrence during the last decades. There is a general consensus that RA is a multifactorial disease, resulting from the interaction of both genetic and expression . Several risk factors for RA have been suggested. They include genetic susceptibility, sex, age…etc .

The pathogenetic advances described herein have paralleled the introduction of new, effective therapies and remarkable improvement in clinical outcomes. Severe disease manifestations, such as vasculitis, nodule formation, scleritis, and amyloidosis, that are associated with persistent, uncontrolled inflammation have become rare. A rich pipeline of biologic and small-molecule agents, and of potential clinical biomarkers, exists that will add to our therapeutic armamentarium. In time, this should render remission achievable in increasing numbers of patients.

However, much remains to be resolved. We need to understand the factors that lead to loss of tolerance and that cause localization of inflammation in the joint. We need to find ways to promote immunologic resolution or homeostasis and repair of damaged joints. We must elucidate the mechanisms driving the various systemic disorders that contribute substantially to reductions in the quality and length of life. Ultimately, we must strive to develop curative and preventive therapeutics that will transform the notion of rheumatoid arthritis as a chronic disease.

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