A Review on: Rheumatoid Arthritis

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***Abstract*—Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease that primarily affects the lining of the synovial joints and is associated with progressive disability, premature death, and socioeconomic burdens. The disease is three times more common in women as in men. It affects people of all races equally. Genetic factors may play some role in RA either in terms of increasing susceptibility to developing the condition or by worsening the disease process. The main genetic marker identified with rheumatoid arthritis is HLA. Candidate genes responsible for rheumatoid arthritis are HLA-DRB1, HLA-DRB4, PTPN22, and PAD I4. Alteration of these genes results in production of inflammatory cells. The symptoms include fatigue, lack of appetite, low-grade fever, muscle and joint aches, and stiffness. Tissue inflammation may lead to pericarditis, shortness of breath followed by chest pain.**

It is characterized by persistent inflammation that primarily affects the peripheral joints. It usually starts as an insidious symmetrical arthritis and has an unpredictable and variable course, although pain and disability can be minimized if the condition is recognized early and treated promptly and appropriately.

***Index Terms*—Rheumatoid arthritis, Autoimmune**

I. INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder caused in many cases by the interaction between genes and environmental factors, including tobacco, that primarily involves synovial joints. It typically starts in small peripheral joints, is usually symmetric, and progresses to involve proximal joints if left untreated. Joint inflammation over time leads to the destruction of the joint with loss of cartilage and bone erosions. 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. RA, if untreated, is a progressive disease with morbidity and increased mortality.

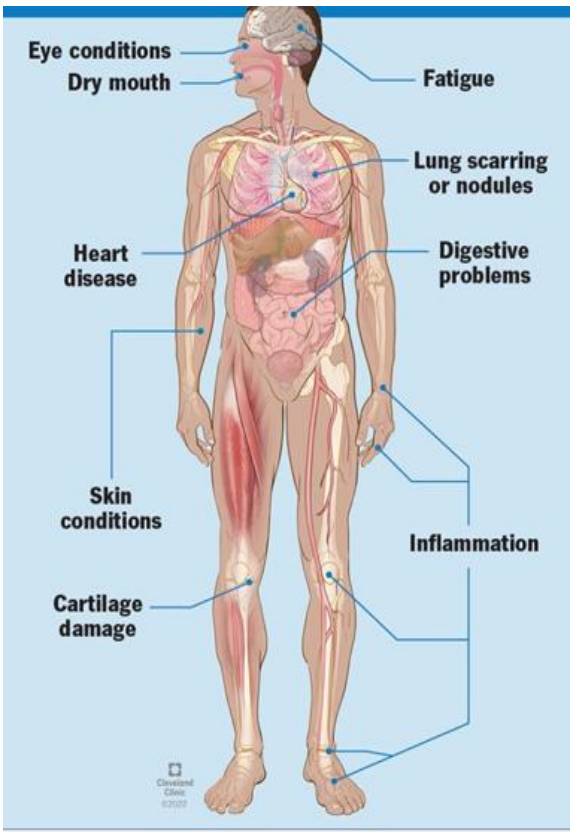
Along with joint pain, many people with RA experience fatigue, loss of appetite and low-grade fever. Joint stiffness is usually worse in the morning and lasts more than 30 minutes. Symptoms may come and go. A period of high disease activity is called a flare. Ongoing high levels of inflammation can cause problems throughout the body. Because RA can affect many parts of your body, it is called a systemic disease. Here are some of the ways RA can affect the body beyond the joints: Eyes. Dryness, pain, redness, sensitivity to light and impaired vision. Mouth. Dryness and gum irritation or infection. Skin. Rheumatoid nodules small lumps under the skin over bony areas. Lungs. Inflammation and scarring in the lungs, leading to shortness of breath. Cardiovascular. Increase in the risk of cardiovascular disease, including heart attack and stroke. Blood vessel inflammation, leading to nerve, skin and other organ damage. Blood Anemi a lower-than-normal number of red blood cell

II. HISTORY

As many chronic diseases, the history of rheumatoid arthritis started around 1500 BC when Ebers Papyrus also describes a condition similar to rheumatoid arthritis. Several reports suggest that mommies from different eras have deformities that are pathognomonic of arthritis, however, was not until later 1800 where this chronic condition was named by Garrod rheumatoid arthritis, replacing the terms arthritis deformans and rheumatic gout. Thomas Sydenham and later on, Beauvais pointed out that RA has a chronic progressive course especially in the tendon sheaths and bursa causing damage of the bone and cartilage.

In developing countries such as India data on prevalence are scarce and are under reported at between 0.28% to 0.7% of the general population.

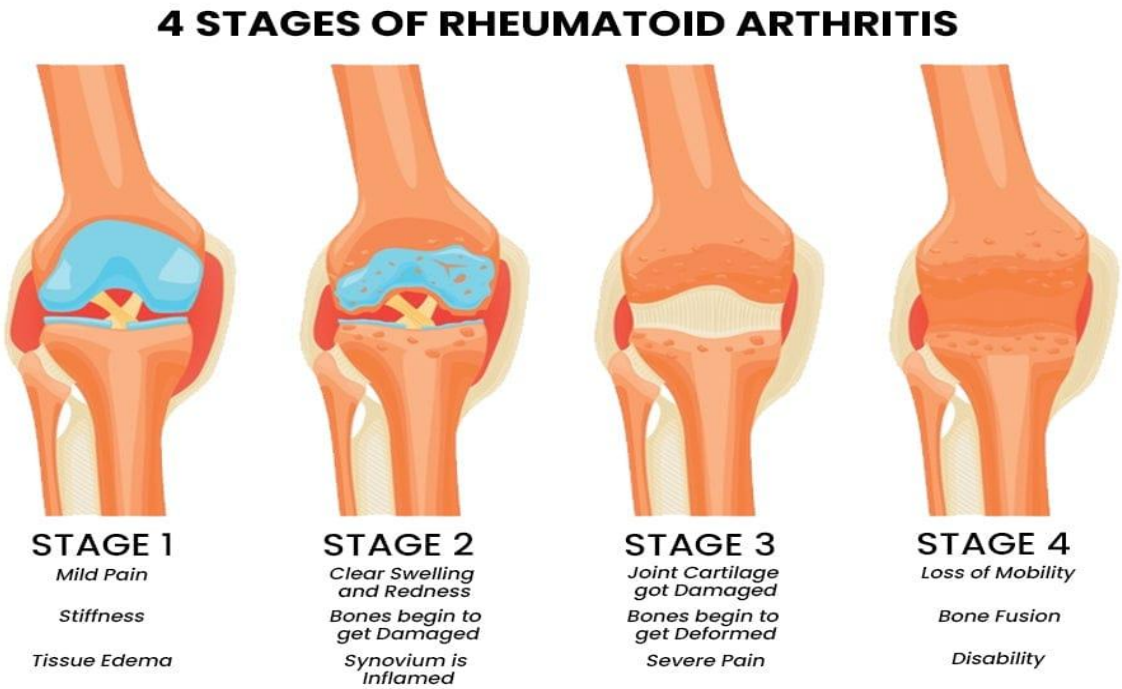
III. EFFECT ON THE BODY



STAGES OF RA :

The four stages of rheumatoid arthritis are:

- Stage 1: In early-stage RA, there's inflammation in the tissue around your joint(s). You may have some joint pain and stiffness. If your provider orders X-rays, they won't see destructive changes in your bones.
- Stage 2: The inflammation has begun to damage the cartilage in your joints. You might notice stiffness and a decreased range of motion.
- Stage 3: The inflammation is so severe that it damages your bones. You'll have more pain, stiffness and even less range of motion than in stage 2. You may start to see physical changes.
- Stage 4: In this stage, the inflammation stops but your joints keep getting Loss of mobility, Bone Fusion, Disability.

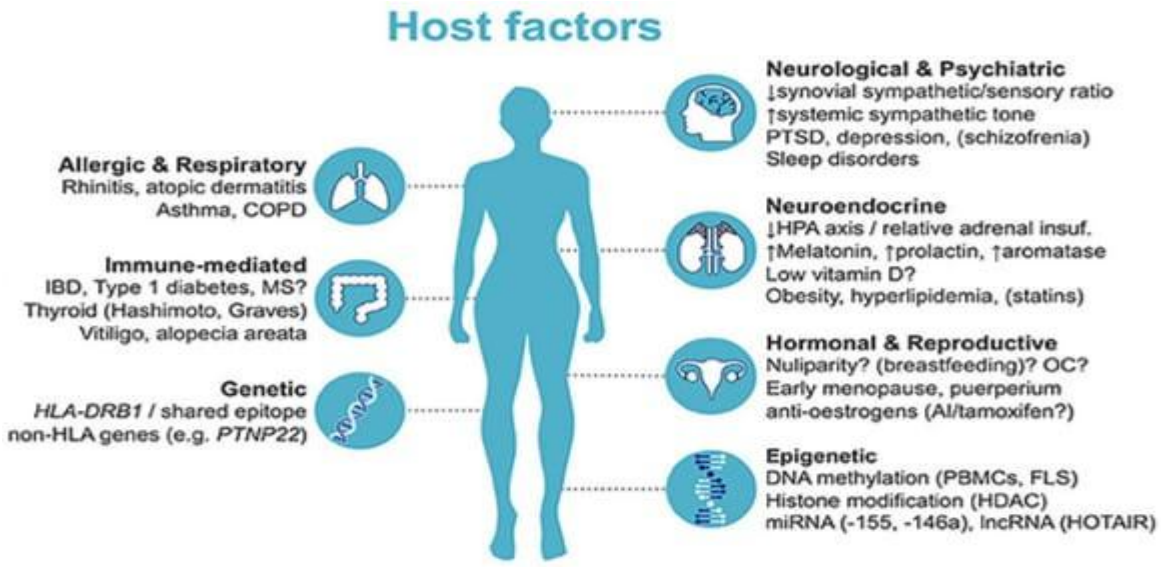


IV. SYMPTOMS AND EFFECT

Along with joint pain, many people with RA experience fatigue, loss of appetite and low-grade fever. Joint stiffness is usually worse in the morning and lasts more than 30 minutes. Symptoms may come and go. A period of high disease activity is called a flare. Ongoing high levels of inflammation can cause problems throughout the body. Because RA can affect many parts of your body, it is called a systemic disease. Here are some of the ways RA can affect the body beyond the joints:

- Eyes. Dryness, pain, redness, sensitivity to light and impaired vision. Mouth. Dryness and gum irritation or infection.
- Skin. Rheumatoid nodules small lumps under the skin over bony areas.
- Lungs. Inflammation and scarring in the lungs, leading to shortness of breath.
- Cardiovascular. Increase in the risk of cardiovascular disease, including heart attack and stroke.
- Blood vessels. Blood vessel inflammation, leading to nerve, skin and other organ damage. Blood anaemia, a lower-than-normal number of red blood cell.

V. RISK FACTOR OF RA



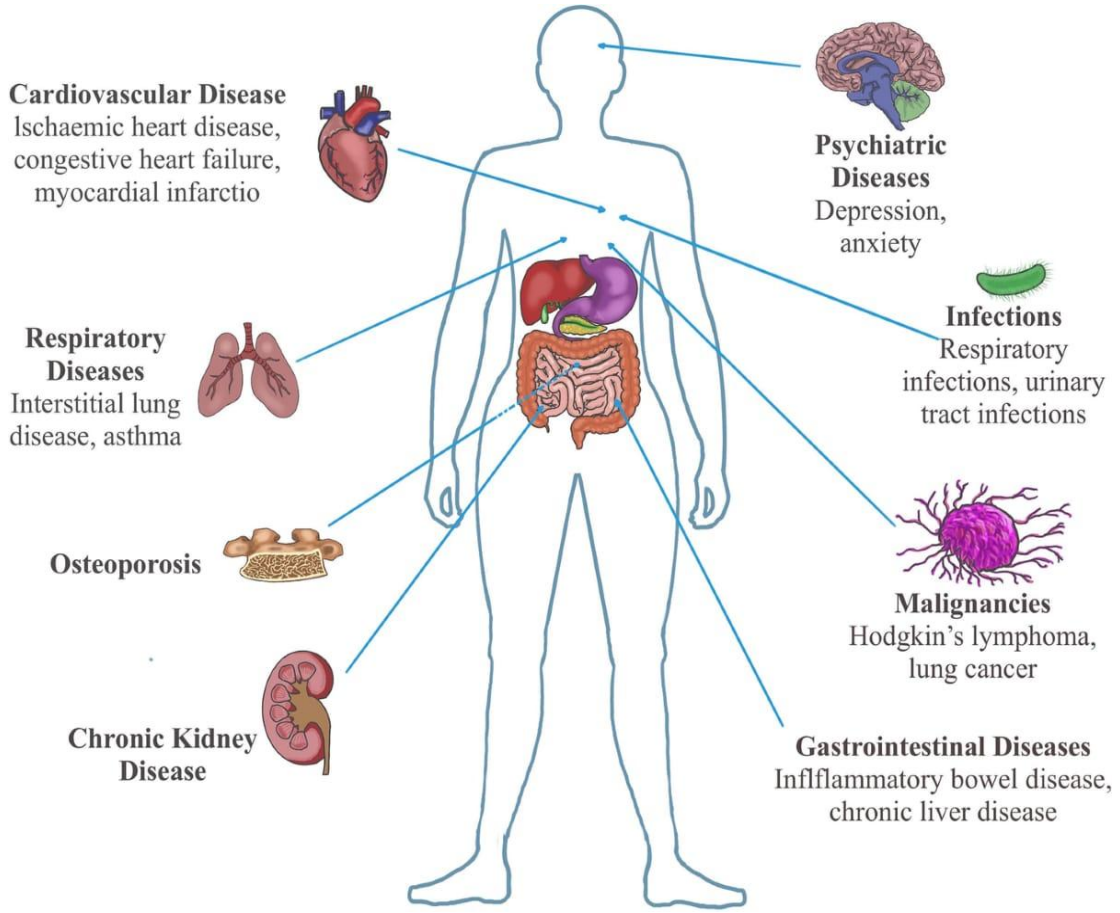
ENVIRONMENTAL FACTORS OF RA

Following factor may increase risk of developing the condition of the rheumatoid arthritis:

- Age: Rheumatoid arthritis can affect at any age, but most people are diagnosed between the ages of 40 and 60.
- Sex: Rheumatoid arthritis is two to three times more common among women than men. We don't know why. It may be because of the hormone oestrogen but the link hasn't been proven.
- Genes: There's no single gene that causes rheumatoid arthritis, although, there's some evidence that suggests that rheumatoid arthritis can run in families. However, the risk of inheriting rheumatoid arthritis is thought to be low, because genes are thought to only play a small role in developing the condition.
- Excess Weight: People who are overweight appear to be at somewhat higher chance of developing rheumatoid arthritis than a healthy weight person. Eating a balanced diet and exercising is a good way to manage weight.
- Smoking: Some research suggests that people who smoke have a greater risk of developing rheumatoid arthritis. Stopping smoking can be tough. But it could really improve your condition.

Complications:

- Infection
- Chronic anaemia
- Gastrointestinal cancers
- Pleural effusion
- Osteoporosis
- Heart disease
- Sicca syndrome
- Felty syndrome
- Lymphoma
- Side effect from treatment and medication
- Ocular complications
- Neurological complications
- General deconditioning



VI. DRUGS USED IN RHEUMATOID ARTHRITIS

1. Disease-Modifying Antirheumatic Drugs (DMARDs)

This slow disease progression and prevent joint damage.

- Methotrexate (most commonly used, first-line)
- Sulfasalazine
- Leflunomide
- Hydroxychloroquine

2. Biologic DMARDs

Used when conventional DMARDs are inadequate.

- TNF-α inhibitors: Etanercept, Infliximab, Adalimumab
- IL-6 inhibitors: Tocilizumab
- B-cell inhibitor: Rituximab
- T-cell costimulation blocker: Abatacept

3. Targeted Synthetic DMARDs (JAK inhibitors)

- Tofacitinib
- Baricitinib
- Upadacitinib

4. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

For pain and inflammation (do not alter disease course).

- Ibuprofen
- Naproxen
- Diclofenac

5. Corticosteroids

For short-term control of flares.

- Prednisone
- Methylprednisolone

VII. TREATMENT

FIRST-LINE MANAGEMENT:

NSAIDS and Corticosteroids:

NSAIDS and Corticosteroids the overall goal of first-line treatment is to relieve pain and decrease inflammation. Medications, considered to be fast-acting, are nonsteroidal anti-inflammatory drugs (NSAIDs) including acetylsalicylate (Aspirin), naproxen (Naprosyn), ibuprofen (Advil and Motrin), and etodolac (Lodine). Aspirin is an effective anti-inflammatory for RA when used at high doses, due to the inhibition of prostaglandins.

It is one of the oldest NSAIDs used for joint pain. Side effects of aspirin at high doses include tinnitus, hearing loss, and gastric intolerance. There are other NSAIDs that are newer on the market than aspirin and just as effective. In addition, these drugs require fewer doses per day. NSAIDs work by inhibiting cyclo-oxygenase to prevent the synthesis of prostaglandins, prostacyclin, and thromboxane's. Common side effects are nausea, abdominal pain, ulcers, and gastrointestinal (GI) bleeding. These symptoms can be reduced if taken with food, antacids, proton pump inhibitors, or misoprostol (Cytotec); an even newer NSAID called celecoxib (Celebrex) is a selective Cox-2 inhibitor that has less risk of GI side effects

Corticosteroids are a more potent anti-inflammatory medication than NSAIDs, but they come with greater side effects. For this reason, they are only indicated for a short period of time at low doses, during exacerbations or flares of RA. Intra-articular injections of corticosteroids can be used for the local symptoms of inflammation

SECOND-LINE MANAGEMENT:

Disease Modifying Anti Rheumatic Drugs (DMARDs):Disease-Modifying Anti rheumatic Drugs the overall goal of second-line treatment is to promote remission by slowing or stopping the progression of joint destruction and deformity. Medications are considered to be slow-acting because they take from weeks to months to be effective. Disease-modifying anti rheumatic drugs (DMARDs) can also reduce the risk of developing lymphoma that can be associated with RA

DIAGNOSIS CRITERIA:

In typical outpatient practice, a definitive diagnosis using these criteria may be difficult to obtain early in disease process. During the initial visit, patient should be asked about degree of pain, duration of stiffness and fatigue, and functional limitation. A careful joint examination.

Table No: 1 Revised American Rheumatism Association Criteria for Classification of Rhematoid Arthritis

SIGN AND SYMPTOM	DEFINITION
Morning stiffness	Stiffness in or around the affected joints for at least 1 hour after initiating movement
Arthritis on three or more joint area	Three or more joints noted to be fluid-filled: wrist, elbow, knee, and ankle.
Hand Joint involvement	Wrist, MCP, or PIP joints among the symptomatic joints observed.
Symmetric arthritis	Right or left joint involved for one or more of the following: wrist, PIP, MCP, elbow, knee, and ankle.
Rheumatoid nodules	Subcutaneous nodules in region surrounding joints, extensor surface, or bony prominences.
Serum rheumatoid factor positive	Positive result with >95% PPV; no more than 5% false positive.
Radiographic changes	Hand & wrist films show erosion or loss of density adjacent to affected joints.

LR+: Positive like hood ratio

LR-: Negative like hood ratio

PIP: Proximal Interphalangeal

MCP: Metacarpophalangeal

DIFFERENTIAL DIAGNOSIS:

Rheumatoid arthritis must be differentiated from a number of other disorders. Infection related reactive arthropathies, Seronegative Spondyloarthropathies, and other connective tissue disease such as systemic lupus erythematosus may have symptom in common with rheumatoid arthritis, as may an array of endocrine and other disorder (table no-2).

Table no.2: Differential Diagnosis of Rheumatoid Arthritis

DIAGNOSIS	COMMENT
A connective tissue disease	Such as scleroderma and lupus
Fibromyalgia	Evaluate for trigger point
Hemochromatosis	Iron studies & skin colour changes helpful
Infectious Endocarditis	Rule out murmurs, high fever, IV drug use
Polyarticular gout	Red, swollen joints; podagra; may coexist with RA
Polymyalgia Rheumatica	Unlike RA, rarely presents with pain only in proximal joints
Sarcoidosis	Granulomas, hypocalcaemia, chest film abnormalities
Seronegative Spondyloarthropathies / Reactive Arthritis	Asymmetric; spine involvement; related to psoriasis, Reiter's, IBD
Still’s Disease	High fever, leucocytosis, sore throat, rash, liver dysfunction
Thyroid Disease	Check TSH depending on symptoms
Viral Arthritis	Consider parvovirus, hepatitis B
Diagnosis	Comment
A connective tissue disease	Such as scleroderma and lupus
Fibromyalgia	Evaluate for trigger point

DIAGNOSTIC TEST:

No single diagnostic test definitively confirms the diagnosis of rheumatoid arthritis. How ever several tests can provide objective data that increase diagnostic certainty and allow disease progression to be followed. The American college of Rheumatology subcommittee on rheumatoid arthritis (ACRSRA) recommends that baseline laboratory evaluation include a complete blood cell count with differential, rheumatoid factor, and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Baseline evaluation of renal and hepatic function also is recommended because these findings will guide medication choice.

Table no.3: Laboratory and Imaging Finding Associated with Rheumatoid Arthritis.

LABORATORY TEST	ASSOCIATED FINDINGS
C-Creative Protein	Typically ↑ >0.7 Pg/ml; useful for monitoring
Erythrocyte Sedimentation Rate	Often ↑ >30 mm/hr; monitoring
Haemoglobin / Haematocrit	Slightly decreased (≈10 g/dl); may be normocytic
Liver Function	Normal or slightly ↑ alkaline phosphatase
Platelets	Usually increased
Radiographic Findings	May be normal or show osteopenia/erosion; baseline for comparison
Rheumatoid Factor	Negative in 30% early; may repeat; false positives possible
White Blood Count	May be increased
Anti-CCP Antibody	Correlates with progression; more specific than RF (90% vs 80%)
Antinuclear Antibody	Limited value for RA screening
Complement Level	Normal or elevated
Immunoglobulin	Elevated alpha-1 & alpha-2 globulin possible
Joint Fluid Evaluation	Straw-coloured; 5,000–25,000 WBC/mm³; mostly PMNs; glucose low in RA
Urinalysis	Microscopic haematuria/proteinuria in connective tissue disease

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