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Review on Patients with Rheumatoid Arthritis: Management and Survival in the Current Era with Biological Basis

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Abstract: Rheumatoid arthritis (RA) is an autoimmune disease that mostly affects tiny peripheral limbs and is a persistent, systemic, inflammatory condition. Age, heredity, gender, environmental exposure, tobacco, smoking, pollution, and heavy occupational stress are among the risk factors. In the US, there is an average of 0.5 instances of RA for every 1000 persons annually. The ratio of men to women is 3:1. Ages 20 to 60 are when the condition first manifests. An arthritic patient has skeletal muscle distortion. The current review covers the etiology, histology and pathogenesis, clinical consequences, signs and symptoms, diagnosis, therapy, and a few patents and applications related to RA. Rheumatoid arthritis is a chronic illness that lasts a lifetime. However, symptoms might go away for a while before returning. Arthritis has no known cure and will only worsen in the absence of medical intervention, potentially leading to permanent impairment. A healthy way of living, exercise, weight loss, physical therapy, medications, paracetamol, non-steroidal anti-inflammatory drugs, steroid injections, etc. are the most effective combinations of treatment techniques.

Keywords: Rheumatoid arthritis, TNF-α, IL, Inflammation, Synovium, Nonsteroidal anti-inflammatory medicines, Steroid injections, Tumor necrosis factor

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Introduction

Rheumatoid Arthritis (RA) is mainly a severe inflammatory disorder characterized by the destruction of cartilage and bone, stiffness, and bumping off of the joint. Dependent T-cells and major histocompatibility complex molecules are linked to the illness. This condition more seriously impacts women than men and older people are more affected (Radu and Bungau, 2021). This bodily joint deterioration leads to deformities and skeletal erosion, often far more painful for the

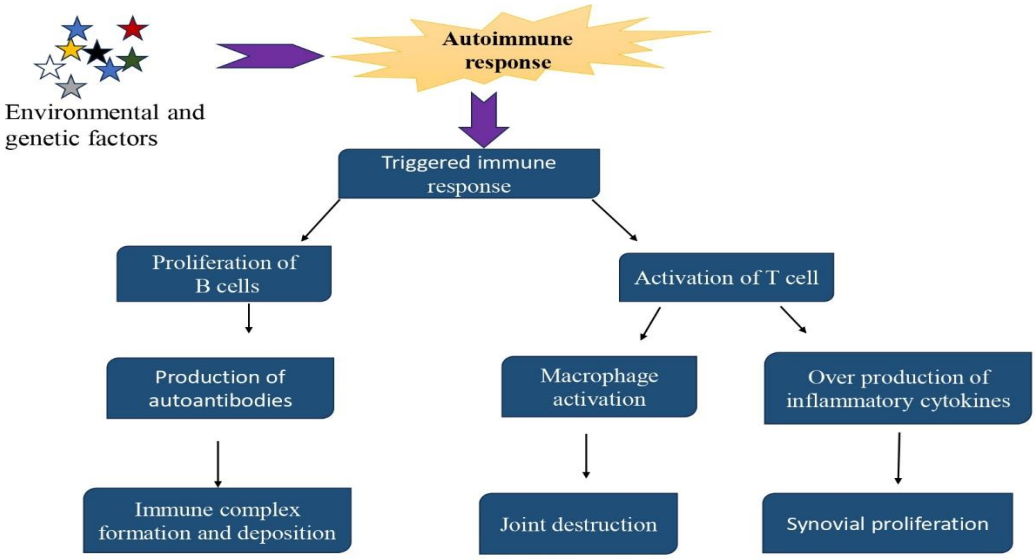

Fig. 1: Stages of rheumatoid arthritis.

patient. The most prevalent signs of a disease called rheumatoid arthritis (RA) include fatigue, tenderness under the skin, fever, weight loss, aching joints, swollen and hot joints, and morning stiffness of the affected joints lasting longer over thirty minutes. Between the ages of 35 and 60, this ailment frequently first appears, with intervals of improvement and worsening. Comparable to RA, juvenile RA (JRA) can also strike young children under the age of sixteen and lack the rheumatoid factor. Different stages of rheumatoid arthritis is shown in Figure 1.

The prevalence of RA in India is around 0.75%, greater than in China, Indonesia, the Philippines, and rural Africa, but comparable to wealthy nations. When it comes to arthritis, malfunctioning joints are the main cause of pain. Numerous factors can cause the condition to flare up, including (i) potential cartilage injury; (ii) a lack of synovial fluid; (iii) an autoimmune reaction; and (iv) infections (Weyand and Goronzy, 2021). Arthritis is a varied disease, these are a few of the typical ones: Osteoarthritis (OA), Gout, Ankylosing Spondylitis (AS), Infectious arthritis (IA), Rheumatoid Arthritis (RA), Lupus arthritis (LA), Juvenile arthritis (JA), Psoriatic arthritis (PA), and Fibromyalgia, these are the top nine diseases affecting the musculoskeletal system. The majority of outbreaks occur with OA, RA, gout, and occasionally AS; the other conditions are less common (Aletaha and Smolen, 2018). Because osteoarthritis is more common as people age (Alivernini *et al.*, 2022), the cost of treating this condition will only rise as the population becomes older. Walking difficulties are most commonly caused by osteoarthritis of the knee and hip (ACRSRAG, 2002).

RA is commonly characterized by stiffness in the affected joints in the morning lasting more than thirty minutes, as well as weariness, weight loss, sensitive joints, fever, swollen and heated joints, and subcutaneous nodules of rheumatoid. This illness often manifests between the ages of 35 to 60, and it can have remissions and flare-ups. Juvenile RA (JRA) may also affect young children below the age of 17. JRA is comparable with RA, but it does not have the rheumatoid factor (Bullock *et al.*, 2019). It is estimated that the prevalence of RA is 1% globally and 1-2% in the West (Bullock *et al.*, 2019). A chronic condition that can affect several distinct organs is rheumatoid arthritis. Most typically, the little joints within hands and feet are where rheumatoid arthritis first manifests. Most often, the same joints on both sides of the body are impacted. For instance, there is discomfort as well as swelling in

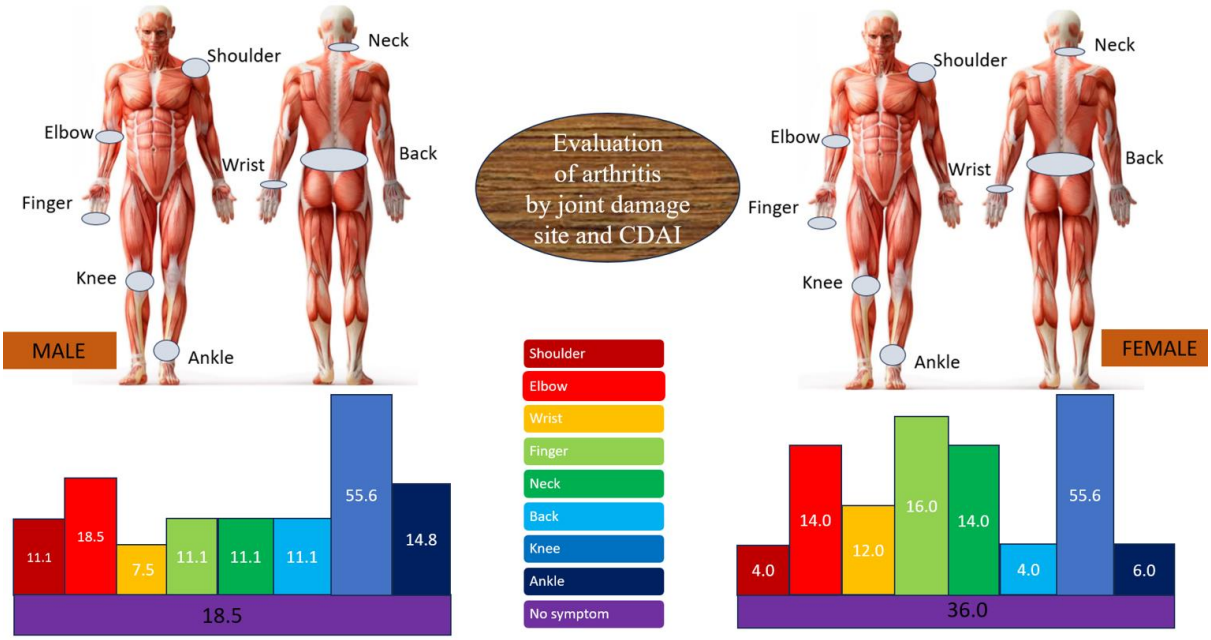

Fig. 2: Evaluation of arthritis by joint damage site and CDAI.

left knee if symptoms occur in right knee. Several joints are frequently impacted simultaneously. All the sign and symptoms are shown in Figure 2.

Anatomy

The body has a coating called synovium covering its joints, which lubricates the joints and facilitates movement. The lining swells as a result of rheumatoid arthritis, which makes the joint painful and rigid.

How it takes place: It is an autoimmune condition, rheumatoid arthritis. This indicates that the tissues are attacked by the immune system. The immune system starts to create chemicals that damage the joint and the muscles, ligaments, and tendons that support it when someone has rheumatoid arthritis, rather than defending the joint itself. Joint abnormalities, such as twisted or gnarled fingers, and mobility loss may arise from this.

Signs and symptoms: The whole body is affected by autoimmune illnesses. In addition to joint pain and stiffness, RA can also result in fever, appetite loss, and exhaustion. Rheumatoid arthritis is a lifelong affliction since it is a chronic illness. However, symptoms could go away for a while before returning.

Sign, symptoms, and features of several common arthritis

Osteoarthritis (*OA*): The cartilage stiffens and progressively deteriorates due to a loss of elasticity (Burmester and Pope, 2017). It can no longer serve as an appropriate shock absorber as a result. The discomfort begins with the stretching that occurs as ligaments deteriorate over time. Because of this, the pain increases when the bones begin to rub against one another. The joint gets increasingly damaged and inflamed as the symptoms gradually get worse over time. Patients experience pain during and following the movement of joints. Joint aches can be caused by any sudden movement and usually occur first in the morning. The beginning of stiffness is usually a prevalent indication. The condition gets worse as people get older (Deighton *et al.*, 1989). As it progresses, patients feel a grating sensation and lose flexibility while bending their joints. A sign that the joints being targeted, including the hands, knees, hips, or spines, have hard lumps or spikes in the bone (Emery, 2006).

Rheumatoid Arthritis (*RA*): RA is prevalent painful and inflammatory condition. In Rheumatoid arthritis, the synovium becomes inflamed as a result of an auto-immune reaction, which eventually causes stiffness, edema, pain, and deformity (Finckh *et al*., 2022). Between the ages of 40 and 60, women are three times more likely than males to get RA, while the disease seldom affects children (Finckh *et al*., 2022). The knees, legs, wrists, arms, and fingers are the joints affected. Joint swelling brought on by inflammation makes joints stiff, especially first thing in the morning. Patients' afflicted regions are red or swollen, and they feel irritating when touched. Patients often experience fatigue and weight loss. Multiple sites may experience simultaneous development of the sickness, advancing from small to bigger joints, and ankles, such as the feet, and wrists, to the shoulders, elbows, knees, hips, or necks.

Gout: It is an alternative term for the form of arthritis that impacts the bone joints, particularly the farthest points, such as the toes. Oestrogen is thought to be a main factor in avoiding the illness, as it is more frequent in males but levels out when women reach menopause (Gabriel, 2001). Deposition of uric acid or urate crystal in the joints, such as the fingers, toes, or ankles, is the usual cause of gout, which is a painful and incapacitating ailment. Diminished renal filtration and acute pain and suffering, which also causes inflammation, are the major reasons for the rise in uric acid levels that lead to its deposit. Inappropriate purine metabolism results in hyperuricemia or improper uric acid/urate excretion (Gaffo *et al.*, 2006).

Ankylosing spondylitis (*AS*): Alternate descriptions of it include inflammatory and autoimmune spinal joint illnesses or the area between the pelvis and spine (Grassi *et al.*, 1998). With time, the agonizing and heavy pain brought on by the inflamed joints grows worse. Along the route, the spine stiffens because of the bone's fusion. Though the main reason is yet unknown, speculation points to a potential hereditary component illness that often affects people between the ages of 20 and 40, with males being more impacted than females (Harris Jr, 1990). Even if they are less intense over the day when physical activity is done, acute pain and stiffness usually happen in the morning or at night. The sacroiliac joints, located in the spine and pelvis, are initially impacted by the ailment before it extends to other parts of the body. Lower back pain and trouble opening their chests for deep breathing are experienced by patients. Uveitis (eye swelling), hip, heel, or other joint pain accompanied by a low-grade temperature, an appetite decrease, and weight loss are additional symptoms (Harris Jr, 1990).

Arthritis lupus (*LA*): This systemic autoimmune disease has been identified in about 1.5 million population in the US only(Majithia and Geraci, 2007). Ninety per cent of patients who are facing lupus illness reported having muscle and joint pain, and around thirty-five per cent have LA (McInnes and O'Dell, 2010). The disease produces edema and joint pain in addition to morning stiffness. At the enlarged joints, fluid might accumulate sometimes. Apart from serious injury, it results in deformities and pain but has little effect on the neck or spine. The elbows, knees, feet, toes, fingers, wrists, and hands are among the distant portions of the body that sustain injuries the most frequently. Because the same joints on both sides of the body are affected by LA, treatment has a symmetrical influence. Studies indicate that its occurrence can be related to anti-histone antibodies (Scherer *et al.*, 2020).

Infectious arthritis (*IA*): A bacterial, fungal, or viral infection within the synovium causes infectious arthritis (IA). The virus first affects the bloodstream and then progresses to the joints. It would worsen the symptoms of arthritic patients, who are already more vulnerable to it. It could be the cause of the frequent infections that exacerbate arthritis in those who have it. Joint pain, edema, and inflammation are the common first symptoms, which are followed by recurrent fever. Among the areas targeted are the knee, shoulder, ankle, wrist, finger, elbow, etc. IA,

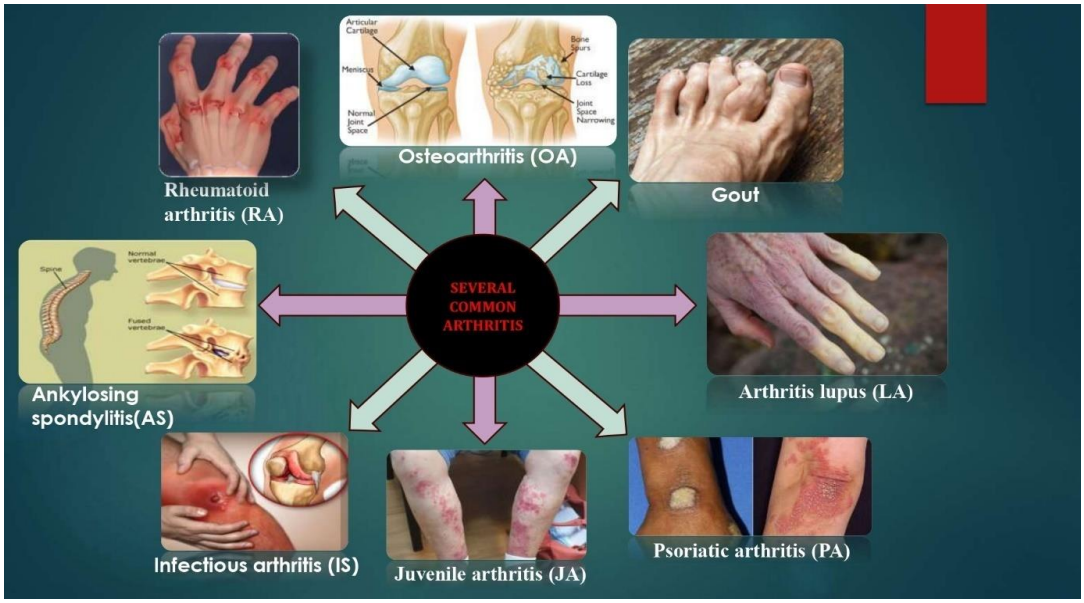

Fig. 3: Types of arthritis.

however, is limited to one joint (Smith and Berman, 2022).

Juvenile arthritis (*JA*): The patient is a young person. The symptoms include decreased appetite, rare evening fever, and reduction in weight with rashes on the arms and legs. In addition to limping, the patients usually have discomfort in their fingers, wrists, or knees. Affected joints look larger because of the swelling. Among the symptoms are stiffness and soreness in the hips and neck. Anaemia is also often shown to develop (Fig. 3) (Smolen *et al.*, 2007).

Psoriatic arthritis (*PA*): In general, 1-3% of individuals who identify as white Europeans have psoriasis, a well-known inflammatory skin disorder. In 15% of psoriasis patients, human leukocyte antigen (HLA), more precisely HLA-B27, is expressed (Steinbrocker *et al.*, 1949). T cells are presented with an antigenic peptide by the Class-I surface antigen HLA-B27, which is encoded by the B locus of the Major Histocompatibility Complex (MHC) on chromosome 6. The AS and HLA-B27 are closely linked. Studies show that individuals with inflammatory bowel disease and Crohn's disease had much higher rates of psoriasis and PA. Innate and adaptive immunity, in addition to genetic susceptibility, are involved in the pathophysiology of both PA and psoriasis (Weyand and Goronzy, 2021). Particularly important in this respect is TNF-α involvement, as it greatly exacerbates the illness. Given that finding, several anti-TNF-α therapeutic alternatives are being investigated for potential use. Treatments for psoriasis that are not successful include monoclonal antibodies and fusion proteins that express soluble TNF-α – R (TNF-α receptors) (Aho *et al.*, 1991). Pediatric pain is frequently accompanied by edema, stiffness, and warmth or redness in the joints. The fingertips and toes are where sausage-like swellings are most evident. In addition, tendinitis can occasionally occur at the Achilles tendon. Often, discomfort isfelt in the lower back too or tailbone (Aho and Heliövaara, 2004).

Fibromyalgia: Physical discomfort and exhaustion are the causes of this disorder. Many believe that the pain feeling is exaggerated compared to how one typically perceives it. This ailment is often associated with physical trauma, psychological stress, or disease. Studies show that females are more likely than males to get injured. Apart from tension headaches, a significant percentage of fibromyalgia sufferers also experience anxiety, sadness, and irritable bowel syndrome. Since the disease seems to run in families, genetic defects might be a major factor. Patients suffering from RA or those suffering from post-traumatic stress

disorders often play a role in the illness's progression (Alamanos and Drosos, 2005).

Epidemiology of Arthritis:

Many researches have been undertaken to investigate the prevalence of different types of arthritis in the western and eastern hemispheres. There has not been a clear explanation found for why environmental stimuli or genetic predisposition matters. 46.4 million persons in the US alone, or more than 21% of the population, have been diagnosed with arthritis. Additionally, according to data from 2008, 1.3 million Americans have RA, which is a little fewer than the 2.1 million projected in 1995. According to the report, the number of AS patients varies from 0.6 - 2.4 million, while the number of LA patients is between 161,200 and 322,300. For JA, the figure is around 294,000. Additionally, the study reveals that around 27 million Americans have clinical OA, an increase from 21 million in 1995. In contrast, 3.0 million people have gout (increased from 2.1 million in 1995) and approximately 5.0 million have fibromyalgia (Chaudhari *et al.*, 2016). About 15% of people worldwide suffer from some kind of arthritis, according to recent Canadian research (Fig. 4). There are 51.2% female victims and 48.8% male victims. The argument that the difference is considerable is backed by further research that indicates that women are more affected by this issue. According to the survey, white Europeans and Caucasians make up a larger percentage of Canadian citizens (19.17%) than Asians (5.15%) or other ethnic groups (8.9%, which include African people and other non-Caucasians). In addition, many similar research supports the notion that Asians, regardless of age, sex, or educational attainment, had reduced rates of arthritis (Conigliaro *et al*., 2019). Although a precise consensus about ethnicity and arthritis has not been achieved in the US, certain research indicates that ethnicity does have a discernible role in certain types of arthritis. For example, the average incidence of RA is believed to be somewhat higher in the Hispanic community (Deane and Holers, 2019). Previous decades have seen arthritis ranked as the 40th biggest cause of non-fatal burden worldwide. According to the World Health Organization (WHO) Report, RA is expected to be the 31st main reason for YLD worldwide in the ensuing ten years, with a proportion of 0.7% rising to more than >1% (Firestein and McInnes, 2017). Caucasians are more likely than Asians, especially when compared to the Japanese, to have osteoarthritis (OA) in their hip joints (Hastings *et al.*, 1975). Research conducted in the 1990s spanning the previous three decades shows that the prevalence of RA in emerging Asian countries is around similartothat in Western countries (0.76%), but it is somewhat lower in the case of India or Pakistan, at roughly 0.55% (Hastings *et al*., 1975). Even for Indonesia and China which include both rural and urban populations, the result is very low (0.4%) (Imboden, 2009). It is interesting to note that while RA is very high in Latin American countries (1.5%) and Jamaica (2%) it is rather low in rural African nations (McInnes and Schett, 2011). These discrepancies are thought to be mostly caused by ecological variables or genetic variants. Numerous studies indicate that West Africans and Asians had somewhat lower rates of RA or a milder form of the disease (McInnes and Schett, 2017). Research carried out in the US with a global emphasis just on RA revealed that the prevalence is significantly greater in North America and Europe than in any developing country (Myasoedova *et al.*, 2010). The bulk of the data for developing nations was gathered by the International League Against Rheumatism (ILAR), mostly from Malaysia, Indonesia, China, the Philippines, and South Africa (not from Pakistan or India) (Okada *et al.*, 2019).There is still doubt about the statistics from Pakistan or India. Certain studies claim that there is no discernible difference between it and the countries of Western Europe (Oliver and Silman, 2006). India and Pakistan share a common genetic profile linked to RA, although Chinese and other South Asians do not. The fundamental cause is thought to be the variations in the HLA motif (Pincus and Callahan, 1993).

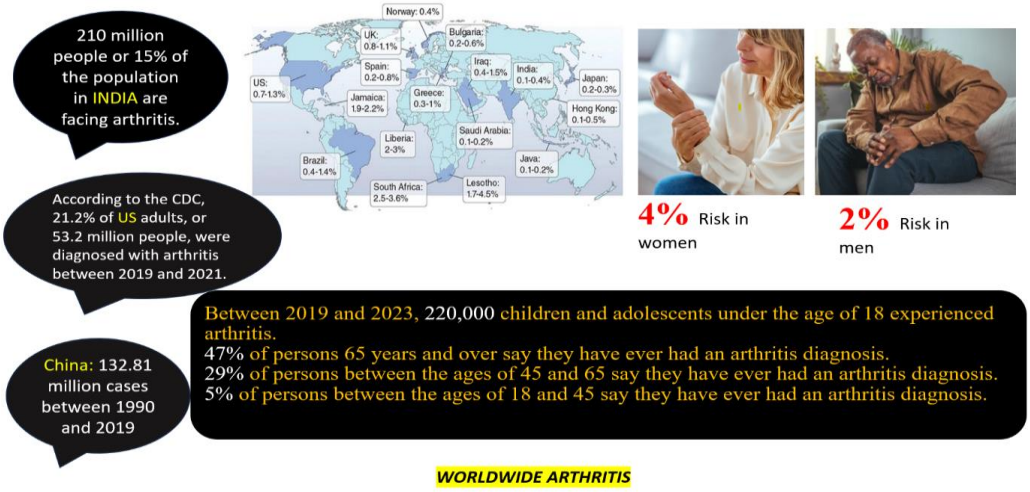

Fig. 4: Worldwide arthritis.

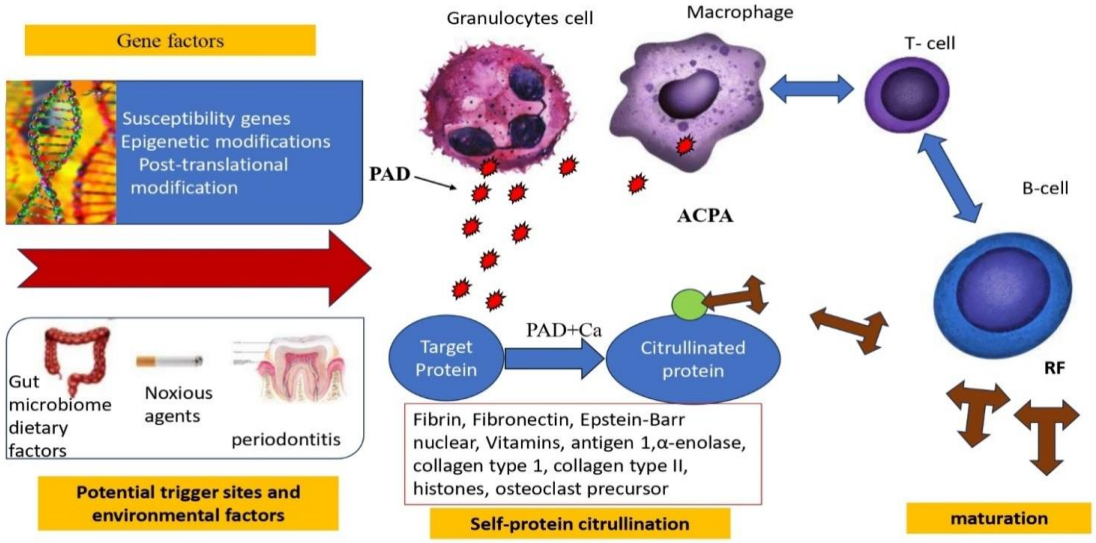

Fig. 5: Pathophysiology.

Pathophysiology:

In joints and other organs where it appears, RA mostly begins as a state of chronic cellular activity that results in autoimmunity and immune complexes. Joint destruction and inflammation of the synovial joints are the main clinical symptoms of the illness, and fibroblast-like synoviocytes are essential to these pathogenic processes. The development of RA occurs in three stages: an amplification phase brought on by T cell activation, an initiation phase caused by non-specific inflammation, and a chronic inflammatory phase characterized by tissue damage brought on by the cytokines IL-1, TNF-alpha, and IL-6. Complex autoimmune and inflammatory functions involving elements of the innate and adaptive immune systems lead to swelling, synovitis, and joint destruction that define active RA. When genes and environment combine in a vulnerable person, resistance to self-proteins containing citrulline residues is lost. The enzyme peptidyl arginine deiminase converts arginine residues to citrulline residues post-translationally to produce these proteins. Patients who share epitopes produce citrullinated peptides that the immune system no longer recognizes as "self," which causes the immune system to create ACPAs against the patients. The results of synovial

membrane biopsies and magnetic resonance imaging (MRI) in both healthy individuals and patients positive for ACPA and/or RF indicate that the production of systemic autoantibodies takes place before the formation of adhesion molecules and inflammation in the synovium, implying that the initiation of the synovium's involvement in RA may require a secondary event (Scutellari and Orzincolo, 1998). In RA patients, the onset of RF and ACPA was shown to occur a median of 4.5 years before clinical RA affecting the synovium. The development of RA illness and immune activation are intricate processes involving interactions between elements of the innate and adaptive immune pathways. The local cytokine and chemokine milieu of the synovium in which these interactions occur has a significant effect on their nature. Many inflammatory cell types fill the synovial membrane in established RA, and they cooperate to destroy joints (Fig. 5).

Factors linked to the pathogenicity of RA:

• Too much smoking Cigarettes.

• TNF-a (Tumour necrosis factor) activity.

• Aberrant production of antibodies, or inappropriate and atypical B-lymphocyte activity. •Finding circulating autoantibodies against IgFc, sometimes referred to as "rheumatoid factor," may contribute to B cells presenting antigens to the T cells incorrectly.

• Unwanted activation of certain signaling pathways, such as the Wnt signaling pathway, which is connected to embryonic development and cell renewal, in synovial tissue. RA patients' synovial cells have been shown to have aberrantly high Wnt gene activity in addition to several other genes that encode chemokines, cell adhesion molecules, and cytokines.

• Serum RF levels are one way to diagnose rheumatoid arthritis (Seyler *et al.*, 2005). Morning stiffness that lasts for an hour or more, six weeks or more; arthritis in three or more joints; symmetrical arthritis that lasts for six weeks or more; rheumatoid nodules; and the use of hand radiographs to observe changes, erosion, or obvious decalcification of the bone.

The general connection between arthritis and inflammation:

While no two family members suffer arthritis in the same way, it is widely accepted to be an inflammation of the bone joints. The bulk of symptoms associated with RA, PA, GA, LA, and AS stem from inflammation resulting from an inflammatory reaction; OA and fibromyalgia are two different illnesses. These both only produce signs of inflammation after they have been caused (Silman *et al.*, 2002). Conversely, with auto-immune disorders, the immune system of the body inadvertently attacks the healthy tissues. If it affects the tissues of the joints, it is known as inflammatory arthritis, a condition that includes RA and its analogs. Because of joint deterioration from bone erosion and inflammation, these disorders produce chronic pain (Smith and Haynes, 2002). By using radiography or other diagnostic methods, RA is identified in patients. Initially, there is not much damage that is visible, but with time, that changes (Van Vollenhoven, 2009).

Which are the standard treatments?

Arthritis has no known cure and will only worsen in the absence of medical intervention, perhaps leading to permanent impairment. To develop an efficient treatment plan that can easily adhere to, the patient must collaborate closely with doctor. Most people discover that a certain mix of therapeutic techniques is most effective.

Lifestyle modifications: To preserve joints and halt the disease's progression, the doctor can advise making adjustments to the way of living.

Exercise: Getting regular exercise helps strengthen the muscles that support joints and reduce stiffness. The weight-bearing joints will be less stressed if converted to low-impact exercises from high-impact ones, like jogging. Low-impact exercises like cycling, swimming, and walking are recommended.

Losing weight: Losing a few pounds can have a

significant impact on how much stress is placed on weight-bearing joints if the patient is overweight. Additionally, losing weight might help stay independent and move more easily.

Physical therapy: The patient can increase the range of motion in afflicted joints by performing certain exercises. With their ability to lessen joint tension, braces, splints, and shoe inserts can also help ease the symptoms of arthritis.

Medication: Many medications can reduce pain and inflammation. For mild cases of arthritis pain, acetaminophen is a common treatment. Ibuprofen and aspirin are two examples of pharmaceuticals that reduce pain and swelling.

Steroid injections: Cortisone is a potent anti-inflammatory drug that can be injected into a sore joint or taken orally.

Anti-rheumatic medications that treat the disease: These medications are used to reduce the rate at which rheumatoid arthritis progresses. Gold injections, sulfasalazine, and methotrexate are among the medicines that are intended to prevent the body's immune system from damaging the joints.

Surgery: If the pain becomes more severe and hinders the activity, the doctor may recommend surgery. Osteotomy involves cutting and realigning the bones comprising a joint, such as the knee.

Synovectomy: To lessen discomfort and swelling, the rheumatoid arthritis-related diseased and damaged joint lining is removed. This reduces discomfort and stops joint mobility. Joint replacement surgery involves replacing it with a synthetic one and taking out the damaged joint.

Having arthritis: Apart from the plethora of therapy alternatives available for arthritis, there are measures to mitigate the disease's effects on the life.

Consult physician: The patient can discuss treatment plan with the doctor if symptoms get worse or if it is difficult to manage (Fig. 6).

Physical therapist for advice: The patient can learn exercises to increase strength and flexibility from a physical therapist. Seeking fresh approaches to routine tasks can also be facilitated by a therapist. Pain relief from joint strain can be greatly enhanced by little adjustments, such as reaching down to pick up objects that are low to the ground. The therapist could recommend railings, a raised toilet seat, and a shower bench for bathroom (Fig. 6).

Get lots of sleep: Arthritis can exacerbate tiredness and weariness itself to increase arthritis symptoms. Aim for a full night's sleep, and if necessary, take short naps during the day.

Talk the doctor about alternative medicine: Some alternative treatments seem to relieve arthritic symptoms. Consult physician before beginning any alternative medical regimen. They can obstruct your course of treatment.

More Current medicines:

Leflunomide is an oral drug that prevents the synthesis of pyrimidine, uridine monophosphate, and ribonucleotide by changing it into malononitrilamide. It slows the progression of the disease and decreases RA symptoms. Although it is advisable to use it in conjunction with MTX, people who do not respond to MTX may benefit from using it alone. Hypertension, neuropathy, dermatitis, liver damage, gastrointestinal distress, leukopenia, interstitial lung disease, and bone marrow loss are a few of the negative symptoms (Whalley *et al.*, 1997). Biologics, or biological disease-modifying antirheumatic medications, are highly successful in halting the advancement of RA-induced joint deterioration. It is believed that their therapeutic strategy is more "direct, defined, and targeted". However, a major drawback of biologics is their potential for serious side effects, like an elevated risk of infections. Other typical side effects are neurological conditions including multiple sclerosis and lymphoma (Wolfe and Hawley, 1998). Joint inflammation is facilitated by a messenger protein called tumor necrosis factor (TNF). TNF inhibitors work fast to reduce

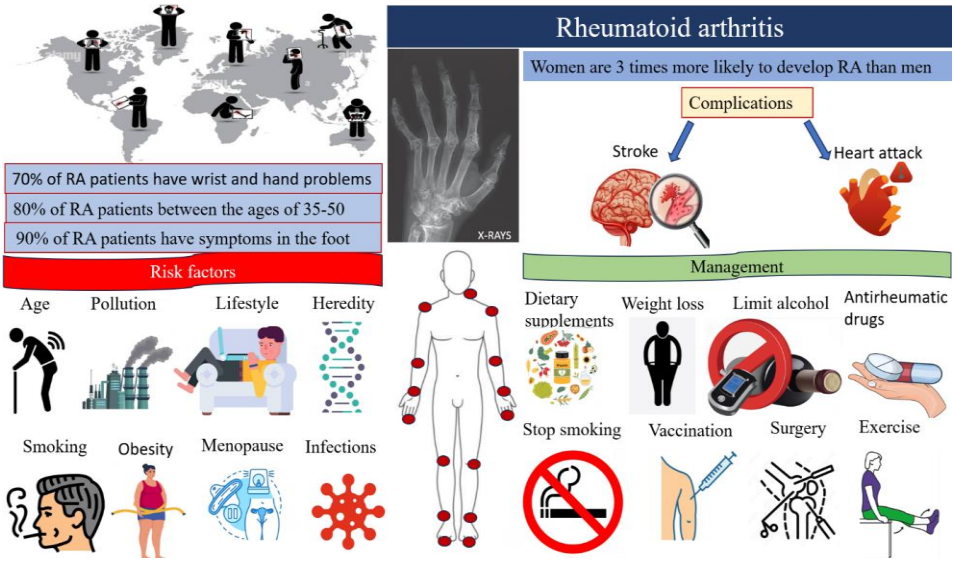

Fig. 6: Common risk and Prevention for arthritis.

inflammation and stop the recruitment of new immune cells. Etanercept (Enbrel), adalimumab (Humira), infliximab (Remicade), golimumab (Simponi), and certolizumab pegol (Cimzia) are a few examples of these inhibitors. They are suggested if other second-line drugs do not work. Unfortunately, research is still being done to assess how well these medications treat patients with different stages of RA and different mechanisms of action, and they can be rather expensive at times. They frequently work in tandem with other DMARDs, particularly MTX. TNF inhibitor usage is not advised in patients with demyelinating diseases that cause congestive heart failure. Each biological drug is delivered in a unique way (Kellgren and Lawrence, 1957). The medication anakinra (Kineret) is subcutaneously injected once a day. It binds to the inflammatory signaling molecule IL-1 to initiate its action. It is not used as frequently as other biologics because of its low response rate (McInnes and Schett, 2007). It can be used either on its own or in conjunction with other DMARDs. Rituximab, also known as Rituxan, helps people with RA by reducing the number of B cells that trigger inflammation and the production of erroneous antibodies. This medication, which is frequently used to treat lymphomas, can also be used to treat RA when TNF inhibitors are ineffective. Two other side effects of RA that have been successfully treated with rituximab are cryoglobulinemia and vasculitis. Every six months, it is injected intravenously in two doses separated by two weeks (O'Dell, 2004). A biological drug called abatacept (Orencia) stops T-cell activation. This is administered subcutaneously once a week or pumped intravenously once a month. Patients who have not responded appropriately to conventional DMARD treatment are given it (Padyukov, 2022). A functional biologic is Actemra's tocilizumab. via inhibiting the inflammatory chemical messenger IL-6. A weekly subcutaneous injection regimen or a monthly intravenous infusion is used. Patients who have not reacted well to conventional DMARD therapy may also be treated with it (Paliard *et al*., 1991). The inflammatory enzymes known as Janus kinases are prevented from being released by the cell. It is referred to as a JAK inhibitor as a result. Patients for whom MTX has not proven to be an effective therapy are given this drug. Oral tofacitinib is administered twice a day, either by itself or in conjunction with MTX. Neither conventional biologic drugs nor any other strong immunosuppressants should be taken with it (Suarez-Almazor *et al*., 1996). In 1990s, there was a significant jump in the number of RA

patients undergoing joint surgery.

Conclusion

RA is a debilitating, inflammatory, chronic disease that can cause joint deterioration and long-term disability. Timely diagnosis and treatment are essential to prevent serious injury and the loss of essential physiological functions. The treating physician may want to consider adhering to the treat-to-target (T2T) principles, which dictate that goals should be defined before procedures are implemented to achieve and assess them (McInnes and Schett, 2007). Furthermore, early professional referral may ensure better therapy outcomes. Thanks to advances in molecular medicine, now there is an improved comprehension of disease processes, which can aid in the creation of more effective treatments. There have been both fresh and enhanced iterations of therapeutic approaches developed. Gene array analysis is being used to assist in identifying patients who will respond better to specific treatments. Customization throughout the trial phase will enable speedier treatment and lower the risk of illness progression when determining the appropriate drug for a particular patient. The gene-array analysis is also being used to find individuals who could be more vulnerable to more severe forms of RA. It is expected that considerable progress will be made in RA management techniques.

Conflict of Interest

The authors declare no conflicts of interest.

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