



"Rheumatoid Arthritis in India: Epidemiology, Impact, and Care Perspectives"

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Abstract

All joint-related conditions are often referred to as having arthritis. The joints in the body, which include the wrists, fingers, toes, hips, and knees, are the places where bones connect. Rheumatic diseases are the general term used to describe these disorders. Unintentionally attacking its own tissues by the immune system is how rheumatoid arthritis, an autoimmune disease, arises. Rheumatoid arthritis affects 0.92% of adult Indians. The primary reasons for the increasing incidence of RA in India are most likely an ageing population, changes in lifestyle, and increased stress levels. Many RA patients may have delayed or inappropriate treatment as a consequence of an incorrect or mistaken diagnosis. Due to the lack of trained medical practitioners with RA specialty in India, patients find it difficult to get specialist therapy. The pathophysiology of RA is largely dependent on genetic predisposition, environmental factors, and cytokines. NSAIDs, Disease-Modifying Anti rheumatic Drugs (DMARDs) such as methotrexate, and biological DMARDs are among the treatment choices available for improved results. In situations of severity, surgical procedures become required. Research advances and treatment improvements are driving growth in the market for RA medications, according to market trends.

Key Words: Autoimmune disease, Prevalence, Biological DMARDs, Patient care, Global Market trend.

Introduction - The term arthritis is derived from the Greek phrase meaning "disease of the joints." Acute or chronic joint inflammation that commonly coexists with pain and structural damage is its defining feature.¹ Joint inflammation is often used to refer to any disease affecting the joints, even though it is more accurately described as a symptom or sign than an actual diagnosis. The joints, which include the knees, wrists, fingers, toes, and hips, are the places where bones link together in the body. Under the general heading of rheumatic disorders, multiple conditions fall. These illnesses are defined by swelling and a reduction in the functionality of one or more bodily structures that link or support other systems. Joints, tendons, ligaments, bones, and muscles are particularly affected. Severe pain, edoema, and stiffness are typical indications. Worldwide, millions of individuals have been affected by over 100 different rheumatic illnesses.²⁻⁴ Joint pain is the primary and sometimes the most prominent symptom of a number of disorders. The term "arthritis" usually refers to one of the following conditions: rheumatoid arthritis, osteoarthritis, pseudo-gout, gout, ankylosing spondylitis, juvenile idiopathic arthritis, still's disease, and septic arthritis. In addition, some disorders may present with joint discomfort. Psoriasis (Psoriatic arthritis), reactive arthritis, and other conditions are examples of conditions in which the arthritis is seen as a subsequent complaint to the primary illness.⁴⁷ Women are also more prone to get arthritis, which is increasingly frequent as people age, with the majority of cases starting in their 60s and 70s¹⁴.

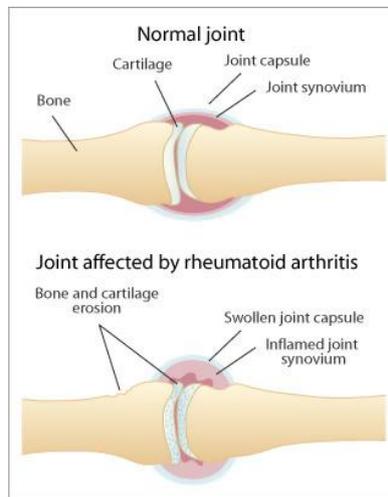


Figure 1: Represents the difference between normal joints and RA affected joints.⁵³

Types of Arthritis

- **Rheumatoid arthritis** - Rheumatoid arthritis is a long-term inflammatory illness that affects more than only our joints. Certain people may suffer harm to several bodily systems, such as the heart, blood vessels, lungs, skin, and eyes. A condition known as rheumatoid arthritis arises when the immune system of the body mistakenly attacks its own tissues.¹¹
- **Fibromyalgia** - The disorder known as fibromyalgia (FM) can be defined by persistent pain in the musculoskeletal system. Muscle and joint stiffness, weariness, sleeplessness, mood swings, cognitive impairment, anxiety, depression, general sensitivity, and the incapacity to perform regular daily tasks are the primary symptoms of this illness^{16,17}. FM has also been linked to certain illnesses, including rheumatic diseases, diabetes, infections, and neurological or psychiatric conditions¹⁸.
- **Systemic lupus erythematosus** - An autoimmune condition known as systemic lupus erythematosus (SLE) is marked by periods of symptoms and cures and has the potential to seriously harm a wide range of organs and tissues. The kidneys, neurological system, joints, and skin are the organs most commonly impacted by SLE. The development of circulating autoantibodies, immune complexes that form in arteries, and strong inflammatory reactions that ultimately cause damage to several organs are the defining characteristics of systemic lupus erythematosus (SLE).^{19,20}
- **Osteoarthritis** - Millions of individuals worldwide are afflicted with osteoarthritis, the most prevalent kind of arthritis. It is caused by the progressive degradation of the cushioning cartilage at the ends of the bones. Although osteoarthritis may harm any joint, it often affects the hands, knees, hips, and spine joints.⁸
- **Ankylosing spondylitis** – It is an inflammatory disease that may finally cause certain vertebrae, or spine bones, to fuse together. This fusion may result in a hunched posture and decreased lumbar flexibility. If the ribs are affected, deep breathing might be difficult.⁵
- **Gout** - Everyone is at risk for gout, a frequent and complicated kind of arthritis. It is described by unexpected, strong symptoms of redness, swelling, pain, and tenderness in multiple joints, usually the big toe.⁶
- **Juvenile idiopathic arthritis** - Children under the age of sixteen most commonly suffer with juvenile idiopathic arthritis, formerly known as juvenile rheumatoid arthritis. An ongoing source of joint discomfort, swelling, and stiffness is juvenile idiopathic arthritis. While some children may only have symptoms for few weeks or months, others may have them for several years.⁷
- **Psoriatic arthritis** - A skin condition known as psoriasis, which is characterised by red skin areas covered in silvery scales, may cause psoriatic arthritis in some people. Psoriasis is the most common ailment to manifest before psoriatic arthritis is identified. However, sometimes, skin patches develop first or even concurrently with joint issues. One cannot cure psoriatic arthritis. The primary goals of treatment are to prevent joint degradation and control symptoms. The discomfort from psoriatic arthritis may be excruciating if therapy is not administered.⁹

- **Reactive arthritis** - Reactive arthritis refers to swelling and discomfort in the joints that are caused by an infection in another area of the body, usually the urinary system, genitalia, or intestines. Typically, this illness affects the feet, ankles, and knees. Additionally susceptible to inflammation include the skin, eyes, and urethra, the tube that exits the body carrying pee. Reiter's syndrome was a former term for reactive arthritis.¹⁰
- **Septic arthritis** - A nasty infection in a joint, septic arthritis can be caused by bacteria that enter our circulatory system from another area of our body. Additionally, penetrating injuries (such animal bites or traumas) that allow bacteria to enter the joint directly might cause septic arthritis. Septic arthritis is more common in older persons and infants. Septic arthritis can also strike people with prosthetic joints. Prompt treatment is essential because the infection can quickly and severely destroy the bone and cartilage within the joint.¹²
- **Thumb arthritis** - Thumb arthritis is frequently associated with ageing and arises from the wear and tear of cartilage from the ends of the bones that make up the carpometacarpal (CMC) joint, which is located at the base of your thumb. Simple actions like opening jars and turning doorknobs can become challenging due to the acute discomfort, swelling, and reduced strength and range of motion caused by thumb arthritis.¹³

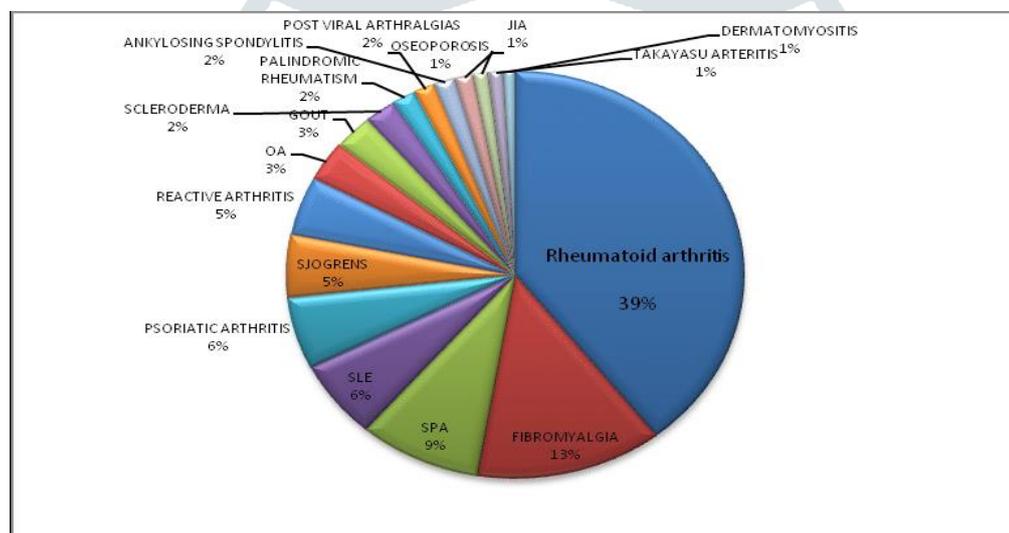


Figure 2: Represents the distribution of different types of arthritis.¹⁵

Prevalence of RA in India

About 0.92% of Indian adults suffer from rheumatoid arthritis (RA). It is a kind of systemic autoimmune illness that causes inflammation and swelling in different joints. Internal joint destruction from the swelling results in long-term abnormalities. For this prevalent illness, there are already efficient therapies available. Most of the time, severe treatment combined with early diagnosis may avoid extending damage. Unfortunately, rare instances like this occur. Every year, there are between 20–40 new cases per Lac population, and females are more likely to get the illness.⁴⁵ An ageing population, lifestyle variables, and rising stress levels are probably the main causes of the rising prevalence of RA in India, especially in metropolitan areas. RA has a big financial impact on India as it has an effect on both the whole healthcare system and the productivity and incomes of people who are effected. Treatment for RA may be expensive, including both medicine and medical care, and many RA patients in India might not have access to reasonably priced, efficient care. The absence of understanding and an awareness of RA in India presents significant treatment challenges. A mistake or improper diagnosis may result in delayed or unsuitable therapy for a large number of persons with RA. Patients find it challenging to get specialised treatment due to the scarcity of qualified medical professionals in India with RA specialisation.⁴⁶ Women are also more prone to get arthritis,⁴⁶ which is increasingly frequent as people age, with the majority of cases starting in their 60s and 70s¹⁴

Sr. no.	Age group (Year)	Male (%)	Female(%)
1	≤ 19	0.5	1.3
2	20-29	2.2	5.7
3	30-39	3.2	13.4
4	40-49	5.4	22.3
5	50-59	4.6	21.9
6	60-69	3.7	12.0
7	70-79	0.9	2.5
8	≥ 80	0.0	0.4

Table-1: Age-wise distribution of rheumatoid arthritis patients⁵¹

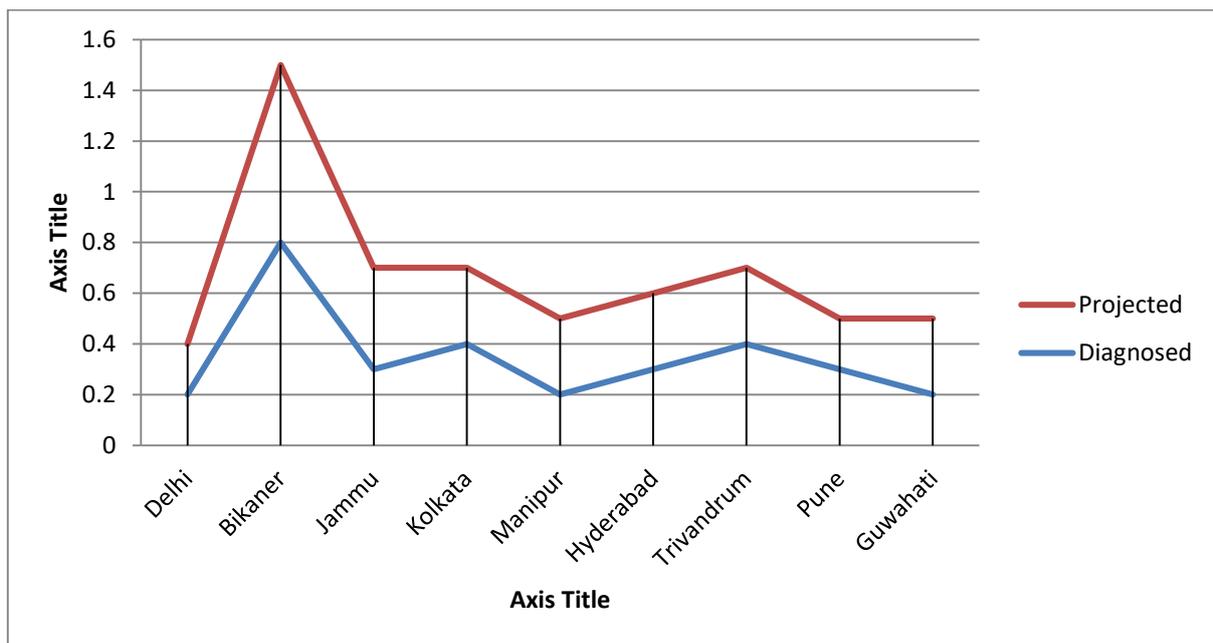


Figure 3: % prevalence of RA diagnosed and future projections in different regions of India.⁵²

Symptoms of RA - The primary characteristics of the condition, as previously established by the American College of Rheumatology, are swelling of three or more joints, involvement of tiny hands and wrist joints, symmetry of joint involvement, and morning stiffness lasting more than an hour.⁴⁵

Epidemiology and pathogenesis of RA

- Genetic factors** - The development of RA is mostly determined by genetic predisposition; in particular, the human leukocyte antigen (HLA) region, and specifically the HLA-DRB1 alleles, are highly correlated with the susceptibility to the illness. Further genetic variations beyond the HLA area that have been found by genome-wide association studies (GWAS) increase the risk of RA^{21,22}.
- Environmental triggers** - Genetically sensitive people may develop RA as a result of environmental factors such as smoking, microbial infections, and hormone changes. One major environmental risk factor that has been repeatedly found to be associated with the start and progression of RA is smoking^{23,24}.
- Immunological Factors** - RA is characterised by dysregulated immune systems, which lead to the generation of autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs). Through specifically attacking self-antigens, these autoantibodies cause harm to the joints and lead to persistent inflammation.^{25,26}

4. **Synovial inflammation and joint damage** - Tumor necrosis factor-alpha (TNF- α), interleukin-1 (IL-1), and interleukin-6 (IL-6) are pro-inflammatory cytokines that cause the distinctive synovial inflammation linked to the pathophysiology of RA. This ongoing inflammation leads to the formation of pannus, hyperplasia of the synovium, and ultimately, the deterioration of bone and cartilage²⁷.

Causes of RA - Although the exact origins of RA are unclear, a number of different factors might raise the probability of getting the disease.⁵⁰

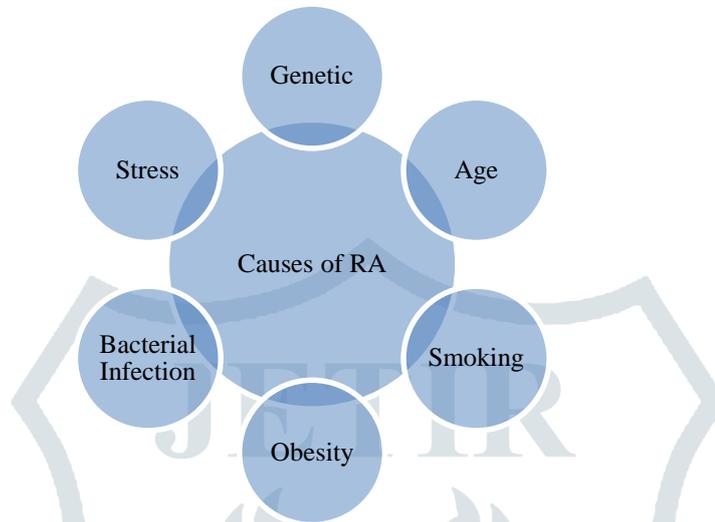


Figure 4: Represents the main causes of RA prevalence.³⁴

Diagnosis of RA - A history and physical examination may be used to diagnose or rule out a number of rheumatic illnesses. Additionally, clinical observations serve as the foundation for determining whether diagnostic laboratory testing are necessary to confirm RA or clear the other rheumatic disorders.⁴⁹

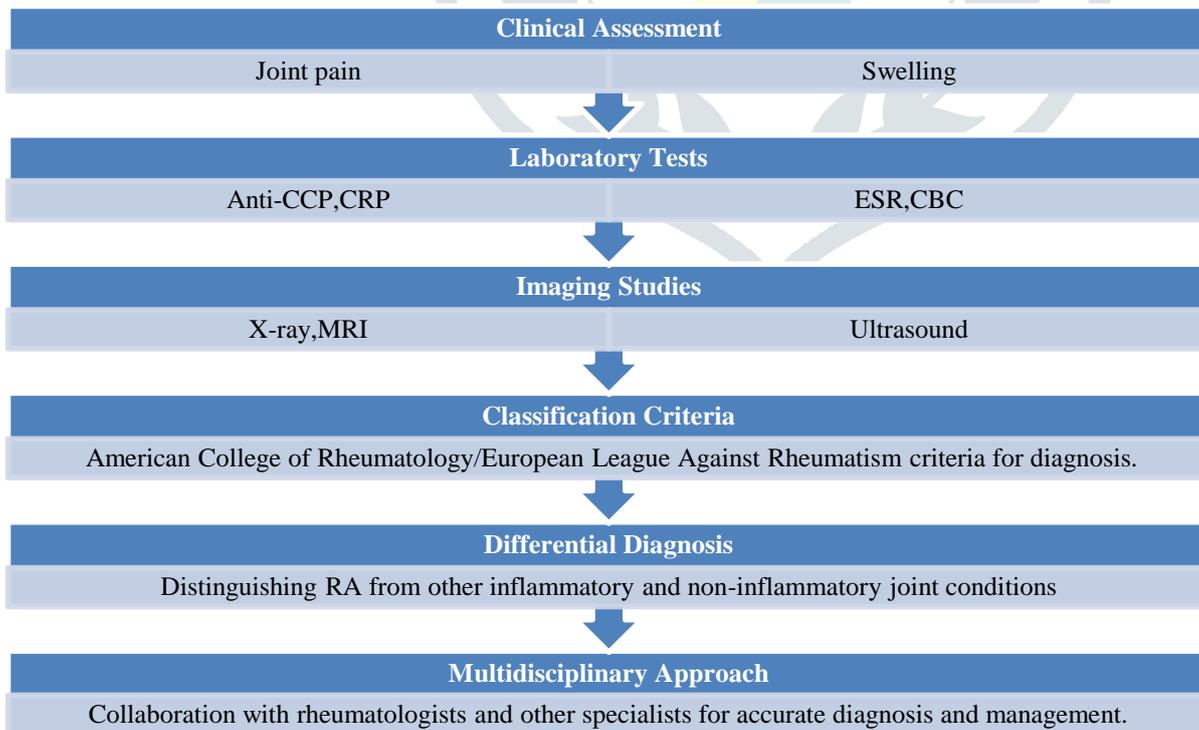


Figure 5: Represents the various approaches for RA diagnosis.²⁸⁻³³

Prevention of RA - Many significant preventative methods have been proposed to halt the progression of rheumatoid arthritis and avoid it completely.

1. Minimizing exposure to inhaled dust, silica, and occupational hazards.
2. Give up smoking
3. Maintaining a nutritious diet
4. Maintaining a healthy weight and exercising⁴⁴

Treatment of RA - The major objectives of RA therapy are to limit long-term consequences, minimize symptoms, avoid joint and organ damage, enhance physical function, and control inflammation early in the disease's course.⁴⁸

1. Modern Treatment:

- **NSAIDs:** (NSAIDs), include acetylsalicylate (Aspirin), ibuprofen (Advil and Motrin), naproxen (Naprosyn), and etodolac (Lodine). By preventing prostaglandin formation, aspirin significantly lowers inflammation in RA when taken in high doses. This is one among the first NSAIDs for the treatment of joint pain. Tinnitus, stomach distress, and hearing loss are adverse consequences of high aspirin doses. There are other NSAIDs that are available that are more current and just as effective as aspirin. Moreover, lower daily doses are needed for these drugs. NSAIDs inhibit cyclo-oxygenase, which prevents prostaglandins, prostacyclin, and thromboxanes from being formed. Common side effects include nausea, upset stomach, ulcers, and gastrointestinal (GI) bleeding. These symptoms may subside if misoprostol (Cytotec), antacids, proton pump inhibitors, or meals are taken concurrently. An even more contemporary NSAID is celecoxib (Celebrex), a selective Cox-2 inhibitor with a decreased risk of GI side effects.³⁵
- **Corticosteroids:** Nonsteroidal anti-inflammatory medications (NSAIDs) have lower efficacy as anti-inflammatory agents compared to corticosteroids. However, corticosteroids are associated with a higher incidence of side effects. Therefore, it is advisable to take them just briefly and in modest amounts, especially during episodes of RA flare-ups or exacerbations. Corticosteroid intra-articular injections may be used to alleviate localised inflammatory symptoms. They operate by inhibiting the production of phospholipids and suppressing eosinophil activity, hence reducing inflammation.³⁶

2. Conventional Treatment

- **Synthetic DMARDs:** The rheumatologist will generally prescribe a disease-modifying anti-rheumatic medication (DMARD), ideally within three months of the beginning of symptoms. DMARDs are immunosuppressive medications that inhibit inflammation, which slows the deterioration of joint tissue. Methotrexate, leflunomide, sulfasalazine, and hydroxychloroquine are a few examples. When the therapeutic goal has been achieved, the DMARD dose is gradually raised, if tolerated, under close observation. Remission or decreased disease activity are the usual therapy goals. A combined approach of DMARDs may be used if there is proof of poor prognostic indicators.³⁷
 - **Biological DMARDs:** When a patient's reaction to a synthetic DMARD is insufficient, biological DMARDs are chosen. In Japan, injectable or drip infusion are available for TNF-targeting medications (such as infliximab, etanercept, adalimumab, golimumab, and certolizumab), IL-6-targeting medications (such as tocilizumab and sarilumab), and the T cell-selective co-stimulation modulator abatacept. Each of these medications has immediate and significant therapeutic benefits. About 50% of cases can be brought into remission when used in alongside methotrexate. For extended periods of time, biological DMARDs can also stop joint degeneration and dysfunction from worsening.³⁸
3. **Surgery:** The final option for treating RA is surgery. When all nonsurgical methods have been exhausted, indications may include unbearable joint pain or functional loss brought on by joint damage.
 - **Tenosynovectomy:** A tenosynovectomy is the removal of inflammatory tendon sheaths or the healing of a recently ruptured tendon, usually in the hand.³⁹
 - **Radiosynovectomy:** An alternative to surgical synovectomy is radio synovectomy, which is less expensive, treats many joints at once, and requires intra-articular injection of tiny radioactive particles.⁴⁰

- **Osteotomy:** Weight-bearing bones are realigned during this surgery in order to fix valgus or varus abnormalities, which are most frequently in the knee.⁴¹

Strategies for Improving RA Care in India

Rheumatology fellowship training is given by around ten centres of excellence, with twenty training spots available annually.⁵⁴ In a recent poll, doctors in practice were asked to rate their confidence in their ability to diagnose and treat rheumatic disorders as well as the quality of their training and exposure to these conditions throughout their undergraduate and postgraduate medical education in India. This study produced some very interesting results: throughout UG training, more than 75 percent of the 333 physicians surveyed said they had not received enough exposure or prior instruction in rheumatic disorders. In addition, 99% of the respondents said that further exposure to and instruction in rheumatic disorders was necessary for UG and PG students.⁵⁵ A lack of exposure, inadequate curricular revisions, and poorly planned medical education are some of the present gaps that have resulted in unmet needs related to rheumatic diseases, as this research and others have noted. These factors collectively have led to medical learners in India having little interest in rheumatology as a career path.^{54,56}

Challenges in the Management of RA In India

The first significant issue is the lack of rheumatologists, which causes a delay in receiving the right therapy and diagnosis. The APLAR standards also made reference to this difficulty.⁵⁷ In fact, governmental financing for RA is frequently redirected to other conditions (such as infectious diseases, diabetes, hypertension, and cancer) and there are no national initiatives for arthritis in India.⁵⁸

The second obstacle is putting into practice the treat-to-target (T2T) strategy, which is the gold standard for managing RA and places a priority on achieving treatment objectives and individualised care. Nevertheless, most rheumatologists in the nation's public health system—regardless of their financial status—do not have enough consultation time to put a T2T strategy into practice. The lack of rheumatologists, the lack of facilities for routine follow-up, and the opposition to therapy progression worsen this.⁵⁹⁻⁶²

Global Rheumatoid Arthritis Drugs Key Market Trends

Rheumatoid arthritis is becoming more common in the senior population. In addition, the market for rheumatoid arthritis medications is expanding due to a change from treating symptoms to delaying the disease's development. The lack of a 100% cure is fuelling the market for medications that can be used to manage and control the progress of illness. Growing investments by the majority of the top players in R&D activities for the development of innovative treatments and biosimilars, along with the rising introduction of novel medicines such monoclonal antibodies for rheumatoid arthritis, are expected to boost the expansion of the worldwide market for rheumatoid arthritis medications⁴².

Rheumatoid Arthritis Drugs Market size was valued at USD 59.031 billion in 2019 and is poised to grow from USD 60.02 billion in 2023 to USD 70 billion by 2031, growing at a CAGR of 1.72% in the forecast period (2024-2031)⁴³.

Conclusion

In India, the incidence of rheumatoid arthritis (RA) is gradually increasing, posing a considerable health burden. RA has an influence on people's quality of life and healthcare resources in addition to causing physical suffering. Even with improvements in care, getting access to care is still difficult. The burden of RA in India may be reduced by increasing early identification, access to cost-effective treatment choices, and awareness. Better RA treatment and a higher standard of living for those impacted in India also depend on encouraging interdisciplinary methods and making investments in infrastructure and research.

Conflicts of interest

There are no conflicts of interest.

Abbreviations

RA – Rheumatoid Arthritis

FM – fibromyalgia

SLE - Systemic lupus erythematosus

NSAIDs - Non-steroidal anti-inflammatory drugs

DMARDs - Disease-modifying antirheumatic drugs

APLAR - The Asia Pacific League of Associations for Rheumatology

T2T – Treat-to-target

Declarations

Ethics approval and consent to participate

Not applicable, as this research did not involve human participants.

Consent for publication

Not Applicable

Availability of data and materials

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

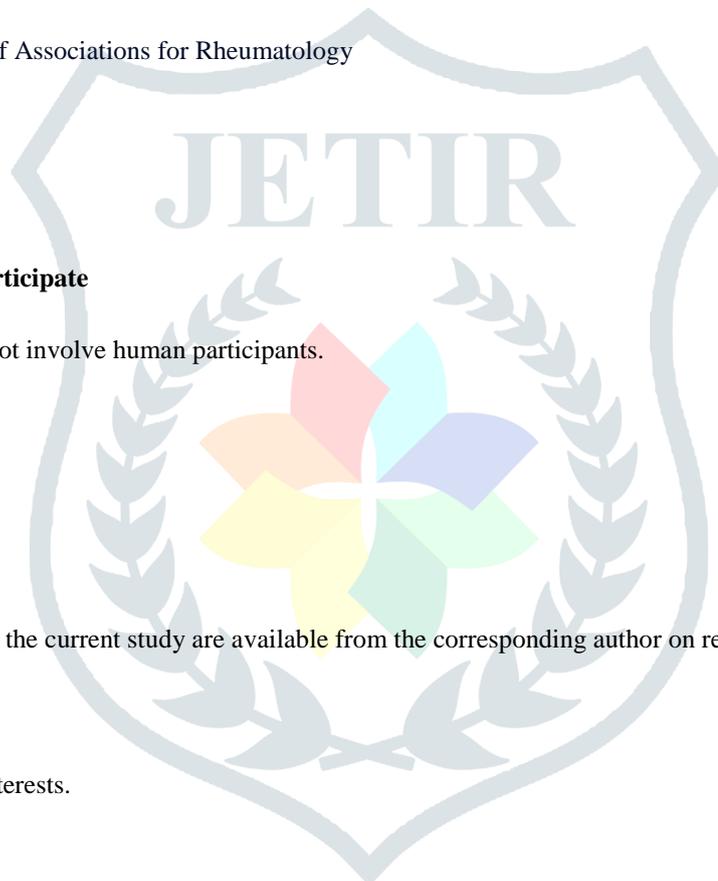
The authors declare no competing interests.

Authors' contributions

All authors contributed to the writing and editing of this paper.

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