PATIENT INFORMATION LEAFLET

Dr Saira Khan
Consultant Rheumatologist

Rheumatoid Arthritis

Understanding RA — the most common inflammatory arthritis, and how to treat it

www.lahore-rheumatology.com

Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis worldwide — an autoimmune disease in which the body's own immune system attacks the lining of the joints, causing pain, swelling, stiffness and, if untreated, permanent joint damage. The good news is that the past two decades have transformed the outlook for patients with RA: with early diagnosis and modern treatment, the majority can achieve disease remission and live full, active lives. This leaflet explains what RA is, how and why it develops, how it is diagnosed, and how it is treated today — guided by the EULAR 2022/2025 recommendations. It is intended to complement, not replace, your consultation with your rheumatologist.

3:1	0.5–1%	40–60
Female : male ratio in adult RA	Estimated global prevalence in adults	Typical age of onset (years)

What this leaflet covers

1. What is rheumatoid arthritis?
2. How common is it? — global and Pakistani data
3. Why does it happen? — pathogenesis explained
4. Recognising the symptoms
5. How the diagnosis is made
6. Treatment — the modern step-up approach
7. Living well with rheumatoid arthritis
8. When to seek urgent advice

1. What is rheumatoid arthritis?

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease in which the immune system mistakenly attacks the synovium — the thin membrane that lines the joints. The result is inflammation of the joint lining (*synovitis*), which over time can erode bone and destroy cartilage, leading to deformity and disability if untreated.

RA is far more than 'joint pain'. It is a true systemic illness that can affect the lungs, heart, eyes, skin and blood vessels, and it carries a measurable increase in cardiovascular risk. The hallmark of the disease is **symmetrical** inflammation of the small joints of the hands and feet, accompanied by **prolonged early-morning stiffness** lasting longer than 30 to 60 minutes.

Key features at a glance

Feature	Typical pattern in RA
Joint distribution	Symmetrical; small joints of the hands (MCPs and PIPs), wrists, feet (MTPs); larger joints (knees, shoulders, ankles) affected later.
Sparing	The distal interphalangeal (DIP) joints and the lower back are characteristically spared (helping distinguish RA from osteoarthritis and spondyloarthritis).
Stiffness	Marked early-morning stiffness lasting more than 30–60 minutes, improving with activity.
Course	Insidious onset over weeks to months; persistent and relapsing rather than self-limiting.
Systemic features	Fatigue, low-grade fever, weight loss, depression; extra-articular features in up to 40% of patients.

Seropositive versus seronegative RA

About **70–80%** of patients have **seropositive RA** — that is, blood tests show rheumatoid factor (RF) and/or anti-citrullinated protein antibodies (anti-CCP). These patients tend to have more aggressive disease and a higher risk of joint erosion and extra-articular features. The remaining 20–30% have **seronegative RA**, where both antibodies are negative — the diagnosis is then made on clinical and imaging grounds, and the disease course is generally (though not always) milder.

2. How common is rheumatoid arthritis?

Global figures

RA is the most prevalent chronic inflammatory rheumatic disease. The best available evidence — including the Global Burden of Disease study and large national registries — provides the following figures:

- **Global prevalence** is estimated at approximately **0.5–1.0% of the adult population**, affecting around 18 million people worldwide.
- **Annual incidence** is approximately **20 to 50 new cases per 100,000 adults per year**, with variation between populations.
- Women are affected approximately **two to three times more often than men** in younger age groups; after the age of 60, the sex ratio narrows toward 1:1.
- Peak age at onset is between **40 and 60 years**, but RA can begin at any age — including in childhood (juvenile idiopathic arthritis) and in the elderly ('elderly-onset RA').
- Prevalence is highest in Northern Europe and North America (around 1%) and somewhat lower in much of Asia and Africa (0.3–0.5%), although figures are influenced by case-finding methods.

- RA significantly shortens life expectancy if untreated, primarily through accelerated cardiovascular disease — a risk now substantially reduced by modern DMARD therapy.

Data from Pakistan

Rheumatoid arthritis is one of the most common reasons for attendance at rheumatology clinics in Pakistan. Several robust local studies provide insight into how the disease behaves in our population:

- A landmark community survey of **1,997 adults in north Pakistan** (*Farooqi & Gibson, Rheumatology, 1998*) estimated a **population prevalence of RA of around 0.5%**, similar to that of Pakistanis living in England — confirming that RA is a significant public health problem locally.
- In a large hospital-based series from Liaquat National Hospital, Karachi (*Hameed et al., 2008*), **RA accounted for 12.9% of all rheumatology clinic attendances**, with a female-to-male ratio of **4:1** and a mean age of onset of **38.5 years in women and 44.8 years in men** — younger than typical Western cohorts.
- A prospective study of **500 Pakistani RA patients** (*Akhter et al., 2016*) confirmed the female predominance (3:1 overall), with peak prevalence in the **45–60 year age group**, and disease severity increasing with age.
- A recent systematic review and meta-analysis (*Naqvi et al., 2019*) found that Pakistani RA patients have high rates of **low disease knowledge (74.5%)**, **poor DMARD adherence (23%)**, and limited access to specialist care — all modifiable factors that worsen long-term outcomes.
- Extra-articular manifestations appear **less common in Pakistani cohorts than in Western ones**, but cardiovascular comorbidity remains an important contributor to morbidity and mortality.
- Analysis of GBD data from 1990 to 2021 (*Scientific Reports, 2025*) shows that the burden of RA in Pakistan has risen steadily over three decades, particularly among women — reflecting both an ageing population and improved diagnosis.

> **A note on local awareness**
>
> Many Pakistani patients first attend a general physician for 'joint pain' that is labelled as gout, age-related wear, or muscular strain. Persistent symmetrical small-joint swelling, prolonged morning stiffness, or unexplained fatigue with joint pain should prompt early rheumatology referral. The earlier RA is treated, the better the long-term outcome — the so-called 'window of opportunity' is the first three to six months from symptom onset.

3. Why does rheumatoid arthritis happen?

The precise cause of rheumatoid arthritis is unknown, but it develops through a well-characterised sequence of events — a complex interplay between **genetic susceptibility**, an **environmental trigger**, and a self-sustaining autoimmune response that ultimately targets the joint lining.

The key steps in pathogenesis

1 **Genetic susceptibility**

The strongest genetic risk factor is the 'shared epitope' — a sequence found in certain HLA-DRB1 alleles (notably HLA-DRB1*04 and *01). Non-HLA genes (PTPN22, STAT4, PADI4, TNFAIP3) and a positive family history all contribute to risk.

2 **Environmental trigger**

Smoking is the strongest established environmental risk factor, particularly for seropositive RA — it interacts with the shared epitope to dramatically increase risk. Other triggers include silica exposure, periodontal disease (*Porphyromonas gingivalis*), gut microbiome disturbance, and possibly some viral infections.

3 **Citrullination and loss of tolerance**
Inflammation at mucosal sites — the lungs (from smoking), gums (from periodontitis) and gut — generates 'citrullinated' self-proteins. In genetically susceptible individuals, the immune system loses tolerance to these modified proteins.

4 **Autoantibody production**
B cells produce **anti-citrullinated protein antibodies (anti-CCP)** and **rheumatoid factor (RF)**. These antibodies can appear in the blood years before any joint symptoms develop — the 'pre-clinical RA' phase.

5 **Synovitis**
T cells, B cells, macrophages and dendritic cells infiltrate the joint synovium. Pro-inflammatory cytokines — particularly **TNF-α, IL-6, IL-1 and GM-CSF** — drive synovial proliferation, producing the swollen, boggy, painful joint typical of RA.

6 **Pannus formation and joint destruction**
Inflamed synovium thickens to form a 'pannus' that invades adjacent cartilage and bone. Osteoclasts are activated, producing the characteristic bony erosions seen on X-ray. Once destruction occurs, it is irreversible.

7 **Systemic and cardiovascular effects**
Circulating inflammation accelerates atherosclerosis, contributing to the elevated cardiovascular risk in RA. The same cytokines drive fatigue, anaemia of chronic disease, and the extra-articular manifestations seen in some patients.

Smoking and RA — a critical message

Smoking roughly **doubles** the risk of developing rheumatoid arthritis, and far more so in people who carry the shared epitope. In patients who already have RA, continued smoking reduces the response to methotrexate and biologic therapy, worsens lung complications, and accelerates cardiovascular disease. **Stopping smoking is the single most important lifestyle change a person with RA can make.**

4. Recognising the symptoms

RA usually develops gradually over weeks to months. Symptoms fall into two broad categories: **articular** (joint-related) and **extra-articular** (affecting other organs and the whole body).

Articular (joint) symptoms

- **Symmetrical joint pain and swelling** — typically beginning in the small joints of the hands (knuckles and finger joints), wrists, and feet (toe joints).
- **Early-morning stiffness** lasting **more than 30–60 minutes**, easing with movement — a defining feature that distinguishes RA from osteoarthritis (in which stiffness is brief and worsens with use).
- **Warmth, tenderness and visible swelling** of affected joints — the swelling is soft and 'boggy' (synovitis), not bony.
- **Reduced grip strength and difficulty with fine tasks** such as buttoning, opening jars, or holding utensils.
- **Late deformities** if untreated — ulnar deviation of the fingers, swan-neck and boutonnière deformities, hammer toes, and 'Z-thumb'. With early modern treatment, these are now uncommon.
- **Cervical spine** involvement — particularly atlantoaxial subluxation — is an important but often unrecognised complication, especially before any surgery requiring neck manipulation.

Extra-articular and systemic manifestations

Around **40%** of patients with RA develop one or more features outside the joints. These are more common in seropositive disease and untreated, severe RA.

System	Common manifestations
General	Profound fatigue (often the most disabling symptom), low-grade fever, unintentional weight loss, depression.
Skin	**Rheumatoid nodules** — firm, painless lumps over pressure areas (elbows, fingers, Achilles tendon); rheumatoid vasculitis (rare but serious).
Lungs	Interstitial lung disease, pleural effusion, pulmonary nodules, bronchiectasis. Smoking and anti-CCP positivity are the main risk factors.
Heart and vessels	Accelerated coronary artery disease (the leading cause of death in RA), pericarditis, and small-vessel vasculitis.
Eyes	Dry eyes (secondary Sjögren's syndrome), episcleritis, scleritis (may threaten vision).
Blood	Anaemia of chronic disease, thrombocytosis; **Felty's syndrome** (RA + splenomegaly + neutropenia) is now rare.
Bone	Increased risk of osteoporosis and fragility fractures, exacerbated by steroid use and reduced mobility.
Nerves	Carpal tunnel syndrome (very common), peripheral neuropathy, cervical myelopathy in advanced disease.

Cardiovascular risk in RA — a hidden danger

Patients with RA have approximately a **50% higher risk** of heart attack and stroke than the general population, comparable to the risk associated with diabetes. This is driven by chronic systemic inflammation. Aggressive treatment of RA, control of blood pressure, lipids and weight, and stopping smoking are all essential parts of modern RA care.

5. How the diagnosis is made

There is no single test that diagnoses rheumatoid arthritis. The diagnosis is built from a careful clinical history, joint examination, blood tests and imaging. In specialist practice, the **2010 ACR/EULAR classification criteria** are used both to support diagnosis and to confirm eligibility for research and clinical trials.

The diagnostic workup

- **Clinical history and joint examination** — pattern, number and distribution of affected joints; duration of symptoms; presence of synovitis (soft, warm, tender swelling).
- **Inflammatory markers** — ESR (erythrocyte sedimentation rate) and CRP (C-reactive protein) are usually elevated in active disease, although a normal value does not exclude RA.
- **Rheumatoid factor (RF)** — positive in 60–80% of patients, but also in many other conditions and in 5% of healthy people; alone it is not diagnostic.
- **Anti-citrullinated protein antibody (anti-CCP)** — more specific than RF (specificity around 95%); a positive result strongly supports RA and predicts more aggressive disease.
- **Antinuclear antibody (ANA)** — to help exclude lupus and overlap connective-tissue diseases.

- **Plain X-rays** of the hands and feet — to look for periarticular osteopenia, joint space narrowing and characteristic **bony erosions**; may be normal in very early disease.
- **Ultrasound and MRI** — far more sensitive than X-ray for detecting early synovitis and erosions; increasingly used to confirm the diagnosis in seronegative or early disease.
- **Baseline screening** — full blood count, liver and kidney function, hepatitis B and C, tuberculosis screen, and fasting lipids — all required before starting DMARD therapy.

The 2010 ACR/EULAR classification criteria — at a glance

The criteria are applied to patients with at least one swollen joint not better explained by another disease. A score of ≥ **6 out of 10** classifies the patient as having definite RA.

Domain	Score
A. Joint involvement (any swollen or tender joint, excluding DIPs, first CMC, first MTP)	**0–5**
1 large joint	**0**
2–10 large joints	**1**
1–3 small joints	**2**
4–10 small joints	**3**
> 10 joints (at least 1 small)	**5**
B. Serology — RF and anti-CCP	**0–3**
Both negative	**0**
At least one low-positive	**2**
At least one high-positive (> 3× upper limit)	**3**
C. Acute-phase reactants (CRP and ESR)	**0–1**
Both normal / abnormal	**0 / 1**
D. Duration of symptoms	**0–1**
< 6 weeks / ≥ 6 weeks	**0 / 1**

Source: Aletaha D et al. Arthritis Rheum 2010;62:2569–2581.

> **The 'window of opportunity'**
>
> RA responds best to treatment in the **first three to six months** after symptom onset. Patients who reach a rheumatologist and start a disease-modifying drug within this window are far more likely to achieve sustained remission and avoid joint damage. This is why we say: **persistent joint swelling lasting more than six weeks deserves a rheumatology assessment**.

6. Treatment

Treatment of rheumatoid arthritis has been transformed over the past 25 years. The modern approach — endorsed by the **EULAR 2022/2025 recommendations** — is built on three principles: **treat early, treat to target, and treat aggressively**. The goal is sustained **remission** (or, in long-standing disease, low disease activity), measured by composite scores such as the DAS28 or SDAI.

The step-up DMARD strategy

Disease-modifying anti-rheumatic drugs (DMARDs) are the cornerstone of treatment. They slow or halt joint damage rather than simply relieving symptoms. Therapy follows a stepwise pathway:

Step	Treatment
Step 1 — First line	**Methotrexate** (oral or subcutaneous, 15–25 mg once weekly) is the anchor drug for almost all patients. Folic acid 5 mg weekly reduces side effects. A short course of low-dose prednisolone may be used to bridge until methotrexate takes effect (8–12 weeks).
Step 1 alternatives	If methotrexate is not tolerated or is contraindicated: **sulfasalazine**, **leflunomide**, or **hydroxychloroquine** (typically reserved for milder disease or as part of combination therapy).
Step 2 — Inadequate response	If the disease remains active after three to six months of optimal csDMARD therapy, treatment is escalated to a **biologic DMARD (bDMARD)** or **targeted synthetic DMARD (tsDMARD)** — usually in combination with methotrexate.
Biologic DMARDs	• **TNF inhibitors** — adalimumab, etanercept, infliximab, certolizumab, golimumab • **IL-6 inhibitors** — tocilizumab, sarilumab • **B-cell depletion** — rituximab • **T-cell co-stimulation blocker** — abatacept
Targeted synthetic DMARDs	**JAK inhibitors** — tofacitinib, baricitinib, upadacitinib, filgotinib. Highly effective oral drugs, but EULAR 2022/2025 advises that they should be used with caution in patients aged ≥ 65, smokers, or those with significant cardiovascular or malignancy risk, given concerns from the ORAL Surveillance trial. Biologics are preferred first in these groups.
Step 3 — Sustained remission	If a patient is in sustained remission for at least six months, careful, gradual tapering of glucocorticoids first, then biologic or tsDMARD doses, may be considered. Methotrexate is usually continued as a 'maintenance' DMARD.

Other important components of treatment

- **Pain relief** — paracetamol and short courses of NSAIDs for symptomatic relief (with PPI cover where appropriate); these do not modify disease and should not replace DMARDs.
- **Glucocorticoids** — useful as short-term 'bridging' therapy at the start of treatment, for flares, and as intra-articular injections. EULAR strongly advises minimising long-term use because of metabolic, bone and infection risks.
- **Physiotherapy and occupational therapy** — preserve joint function, teach joint protection, provide splints and aids.
- **Vaccinations** — influenza, pneumococcal, and (where appropriate) shingles and COVID-19 vaccines are recommended; live vaccines need discussion before starting biologic therapy.
- **Screening before treatment** — tuberculosis (chest X-ray, IGRA), hepatitis B and C, and varicella status are checked before starting biologic or JAK-inhibitor therapy. This is particularly important in Pakistan, where latent TB is common.
- **Cardiovascular risk management** — annual review of blood pressure, lipids, diabetes, and weight; smoking cessation; statin therapy where indicated.
- **Surgery** — joint replacement and tendon repair remain valuable in advanced disease, although the need for major surgery has declined dramatically in the biologic era.

Treat to target

Modern RA care is guided by the 'treat-to-target' strategy: at every clinic visit, disease activity is measured using a composite score (such as the DAS28). If the patient is not in remission or low disease activity, treatment is escalated. This structured approach, repeated every one to three months in active disease, is what has driven the dramatic improvement in RA outcomes over the past two decades.

7. Living well with rheumatoid arthritis

RA is a long-term condition, but with modern treatment most patients can lead full and active lives. A few practical principles make a real day-to-day difference.

- **Take your DMARD reliably** — methotrexate and other DMARDs work over weeks and months, not hours. Adherence is the single biggest predictor of long-term outcome.
- **Stop smoking** — smoking worsens RA and reduces the response to every available treatment. This is the single most important lifestyle change you can make.
- **Stay active** — graded aerobic exercise (walking, swimming, cycling) and muscle-strengthening exercises preserve joint function, reduce pain, lift mood and lower cardiovascular risk. Rest swollen joints during a flare, but resume activity as soon as possible.
- **Eat well** — a Mediterranean-style diet rich in fruit, vegetables, fish, olive oil and whole grains has modest anti-inflammatory benefit. Maintain a healthy weight.
- **Look after your bones** — calcium, vitamin D, and bisphosphonates where indicated. Long-term steroid users need particular attention.
- **Look after your heart** — blood pressure, cholesterol, weight and diabetes monitoring; statin therapy where indicated. RA itself is a cardiovascular risk factor.
- **Look after your teeth** — periodontal disease and RA are linked; regular dental review and good oral hygiene matter.
- **Vaccinations** — annual influenza and pneumococcal vaccines are recommended, particularly while on biologic or JAK-inhibitor therapy. Live vaccines need to be discussed first.
- **Pregnancy and family planning** — RA is compatible with successful pregnancy, but methotrexate and leflunomide must be stopped well before conception (men and women). Many biologics are now considered safe in pregnancy — please plan with your rheumatologist.
- **Mental wellbeing** — depression, anxiety and fatigue are common in RA and treatable. Please raise these concerns; support groups, counselling and good disease control all help.
- **Attend your reviews** — regular clinic appointments allow disease activity to be measured and treatment adjusted in time. Blood-test monitoring of methotrexate and other DMARDs is mandatory and not optional.

8. When to seek urgent advice

Please contact the clinic, or attend a hospital, promptly if you experience any of the following:

- **A high temperature, severe shivering, or feeling unwell** while on methotrexate, a biologic or a JAK inhibitor — possible serious infection
- **A new persistent cough or breathlessness** — possible drug-induced lung disease or tuberculosis
- **A sudden severe headache, blurred vision, weakness or speech change**
- **Severe chest pain or new shortness of breath**
- A **red, painful or visually disturbing eye** — possible scleritis
- **Sudden severe pain or weakness in the neck**, or pins-and-needles in the arms or legs — possible cervical instability
- **Unusual bleeding, bruising or persistent mouth ulcers** — possible methotrexate toxicity
- **A new hot, swollen, very painful single joint** — septic arthritis must be excluded urgently

A word from your rheumatologist

Rheumatoid arthritis is a serious condition, but it is also one of the great success stories of modern medicine. Patients diagnosed today have access to treatments and outcomes that were unimaginable a generation ago — sustained remission, normal joint function, and the chance to lead an active life are now realistic goals. The single most important factor in achieving this is partnership: between you, your family and your rheumatology team. Please bring this leaflet to your next appointment, mark anything that resonates with your own experience, and we will go through it together.

— Dr Saira Khan, Consultant Rheumatologist

Selected references

1. Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis 2023;82(1):3–18.

2. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62(9):2569–2581.

3. Smolen JS, Aletaha D, Barton A, et al. Rheumatoid arthritis. Nat Rev Dis Primers 2018;4:18001.

4. Sparks JA. Rheumatoid arthritis. Ann Intern Med 2019;170(1):ITC1–ITC16.

5. Farooqi A, Gibson T. Prevalence of the major rheumatic disorders in the adult population of north Pakistan. Br J Rheumatol 1998;37(5):491–495.

6. Hameed K, Bowman S, Kondeatis E, et al. Epidemiology of rheumatoid arthritis in a tertiary care unit, Karachi, Pakistan. J Pak Med Assoc 2011;61(2):123–126.

7. Naqvi AA, Hassali MA, Aftab MT. Epidemiology of rheumatoid arthritis, clinical aspects and socio-economic determinants in Pakistani patients: a systematic review and meta-analysis. J Pak Med Assoc 2019;69(3):389–398.

8. Charles-Schoeman C, Buch MH, Dougados M, et al. Risk of major adverse cardiovascular events with tofacitinib versus tumour necrosis factor inhibitors (ORAL Surveillance). Ann Rheum Dis 2023;82(1):119–129.

***Important note:** This leaflet is for general information only and does not replace personal medical advice. Every patient is different; please discuss any questions or concerns directly with Dr Saira Khan or another qualified rheumatologist. Version 1.0 — May 2026.*