Natural Resources for Human Health
eISSN: 2583-1194

Original Research

**Received** 03 May 2026
**Revised** 04 June 2026
**Accepted** 16 June 2026

Natural Resources for Human Health 2026, Vol. 6 (5): 602–613

**KEYWORDS**:
Rheumatoid arthritis; renal involvement; glomerulonephritis; amyloidosis; chronic kidney disease; risk factors

# Clinical and Morphological Manifestations and Risk Factors for Renal Involvement in Rheumatoid Arthritis

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## ABSTRACT:

**Background**: Renal involvement is an underrecognized but clinically important extra-articular manifestation of rheumatoid arthritis (RA).

**Objectives**: To review the clinical and morphological manifestations and identify major risk factors for renal involvement in RA.

**Materials and Methods:** Published clinical and renal biopsy studies were reviewed, focusing on epidemiology, clinical presentation, histopathological patterns, pathophysiological mechanisms, and risk factors associated with renal impairment.

**Results**: Reported prevalence of renal involvement ranges from approximately 1% to more than 50%, depending on diagnostic criteria and detection methods. Renal biopsy studies identify mesangial and immunoglobulin A-dominant glomerulonephritis, membranous nephropathy, and AA amyloidosis as major histopathological patterns. Clinically, renal involvement most commonly presents with microalbuminuria or subnephrotic proteinuria, while nephrotic syndrome, haematuria, and declining estimated glomerular filtration rate may also occur. Older age, hypertension, dyslipidaemia, prolonged and highly active RA, extra-articular manifestations, and nephrotoxic drug exposure are important risk factors.

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**Conclusion**: Renal involvement in RA has diverse clinical and morphological manifestations. Early screening, monitoring of renal function and proteinuria, effective control of systemic inflammation, and management of modifiable risk factors are essential for early detection and nephroprotection.

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that affects approximately 0.5% to 1% of adults worldwide and is characterised primarily by symmetrical polyarthritis, synovial inflammation, and progressive joint destruction [3]. Beyond the joints, RA has protean extra-articular manifestations involving the skin, eyes, lungs, heart, nervous system, and kidneys [4]. Whereas renal involvement in connective tissue disease has traditionally been studied predominantly in the context of systemic lupus erythematosus, kidney disease in RA has received comparatively less attention despite carrying substantial clinical significance, since it worsens the overall course of the disease and contributes meaningfully to excess mortality [2,4].

Historically, renal disease in RA was attributed largely to nephrotoxicity from disease-modifying antirheumatic drugs (DMARDs) such as gold compounds and D-penicillamine, or to nonsteroidal anti-inflammatory drug (NSAID) exposure, together with secondary (AA) amyloidosis arising from long-standing, poorly controlled systemic inflammation [2]. The widespread adoption of biologic and, more recently, targeted synthetic DMARDs has transformed this landscape: tighter control of inflammation has been associated with a marked decline in amyloidosis and gold-induced membranous nephropathy, while the relative contribution of immune-complex glomerulonephritis, cardiometabolic comorbidity, and drug-related effects of newer agents has come into sharper focus [1].

Contemporary epidemiological data indicate that chronic kidney disease (CKD) is a frequent comorbidity in RA, with prevalence estimates ranging from roughly 20% to 50% depending on cohort characteristics and case definitions [1], and that RA carries an independently increased risk of incident reduced kidney function, end-stage renal disease (ESRD), and specific glomerular diseases such as immunoglobulin A (IgA) nephropathy [6,7,34]. Renal involvement is frequently silent, detected only through routine laboratory screening, yet even low-grade albuminuria below conventional microalbuminuric thresholds has been linked to excess mortality in RA [1], underscoring the value of proactive surveillance.

This review synthesises current evidence on the epidemiology, clinical manifestations, morphological and histopathological spectrum, pathophysiological mechanisms, and risk factors for renal involvement in RA, drawing on renal biopsy and necropsy series, population-based cohorts, and case reports spanning nearly four decades. The aim is to provide clinicians with an integrated, practical framework for recognising, investigating, and managing renal disease in patients with RA.

## METHODS

A narrative literature review was conducted using PubMed/MEDLINE, Scopus, and Google Scholar for articles published between 1987 and 2026, using combinations of the terms "rheumatoid arthritis," "renal involvement," "kidney," "nephropathy," "glomerulonephritis," "amyloidosis," "chronic kidney disease," and "risk factors." Original articles, cross-sectional and cohort studies, case series, case reports, and narrative or systematic reviews reporting clinical, histopathological, or epidemiological data on renal involvement in RA were eligible for inclusion. Studies addressing renal involvement in juvenile idiopathic arthritis and overlap connective tissue disease syndromes were also reviewed where they provided relevant comparative insight. Forty sources meeting these criteria were retained and synthesised narratively. Given the marked heterogeneity of study designs, populations, case definitions, and eras of RA management represented in the available literature, this is a narrative rather than a systematic review; the quantitative comparisons presented in Figures 2 and 3 are descriptive syntheses of the reviewed literature rather than pooled meta-analytic estimates, and are intended to illustrate patterns rather than to provide precise effect sizes.

### Epidemiology and Burden of Renal Involvement in Rheumatoid Arthritis

Estimates of the prevalence of renal involvement in RA vary widely, reflecting differences in case definition (histological, biochemical, or clinical), study setting, and era of treatment. Early hospital-based series relying on clinical detection reported prevalence figures as low as 1% to 5% [4], whereas more recent studies incorporating estimated glomerular filtration rate

(eGFR) and albuminuria screening report considerably higher rates, with CKD prevalence of roughly 20% to 50% in contemporary RA cohorts [1].

Population-based comparative studies provide the strongest evidence that RA confers an independent excess renal risk beyond that of the general population. In a retrospective cohort of 813 incident RA cases matched with 813 non-RA comparators followed over two decades, the cumulative incidence of an eGFR below 60 mL/min/1.73 m² was significantly higher among patients with RA (25% versus 20%) [6]. A large Korean nationwide study of nearly 930,000 individuals found that RA was associated with a more than two-fold increase in the adjusted risk of incident ESRD, an effect that was proportionally greater among younger and otherwise healthier individuals [7]. Similarly, a Japanese nationwide database study of over four million adults demonstrated a significantly higher incidence of IgA nephropathy among individuals with RA compared with those without (hazard ratio 1.50) [34].

A large Austrian population-based study found that CKD prevalence was nearly double in RA compared with controls (11.8% versus 6.7%), with albuminuria at preserved eGFR representing the dominant renal phenotype; notably, the association between RA and CKD was substantially attenuated after adjustment for metabolic comorbidities, suggesting that much of the excess renal risk in this cohort was mediated by shared cardiometabolic factors rather than by inflammation per se [5]. This finding illustrates an important and recurring tension in the literature, discussed further below, between an inflammation/immune-complex-driven renal phenotype and a cardiometabolic/vasculopathic phenotype of renal involvement in RA.

**Clinical Manifestations**

Renal involvement in RA spans a broad clinical spectrum, from entirely asymptomatic laboratory abnormalities to overt nephrotic syndrome and renal failure. Renal damage in RA is often mild to moderate in severity and clinically silent, being detected chiefly through routine investigation rather than through symptoms [4]. Microalbuminuria, reflecting increased renal vascular permeability, has been identified in around 30% of unselected patients with RA in one hospital-based study and correlated significantly with markers of inflammatory activity such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [4], supporting its use as a sensitive early marker of subclinical renal involvement.

Where clinically apparent renal disease occurs, the presenting pattern is heterogeneous. In a large Egyptian cohort of RA patients with renal involvement, presentations included nephrotic syndrome (33.5%), acute nephritis (23.9%), persistent proteinuria with recurrent haematuria (13.3%), persistent subnephrotic proteinuria (12.2%), isolated recurrent haematuria (7.4%), and elevated serum creatinine above 1.5 mg/dL (10.6%) [19]. In an Argentinian biopsy series spanning four decades, nephrotic syndrome was the most common clinical indication for biopsy overall (60%), followed by haematuria with or without proteinuria (46%) [18].

A recurring and clinically important observation is that clinical parameters alone, including the degree of proteinuria, the presence of an active urinary sediment, and overt symptoms, do not reliably predict the underlying renal histology in RA [16,26]. This poor clinicopathological correlation is central to the rationale for renal biopsy discussed later in this review.

Uncommon but diagnostically important presentations include renal involvement as part of overlapping or coexisting autoimmune processes. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) may develop in patients with established RA, typically years after the articular diagnosis, and the kidney is the most frequently affected extra-articular organ in this setting (74.5% of cases), usually manifesting as microscopic polyangiitis with pauci-immune crescentic glomerulonephritis [28]. Patients with AAV superimposed on RA are more likely to be asymptomatic at presentation than those with isolated AAV, which may delay recognition [28]. Rare case reports further illustrate the diagnostic complexity of renal disease in RA, including simultaneous ANCA-associated crescentic glomerulonephritis with autoimmune hepatitis [29], an overlap "Rhupus" syndrome combining features of RA and lupus nephritis [30], isolated IgA nephropathy discovered during treatment escalation for active RA [31], and rheumatoid nodule formation within the renal parenchyma itself, a rare diagnosis of exclusion [32].

**Pathophysiological Mechanisms**

The diverse morphological spectrum of renal involvement in RA reflects at least five overlapping pathophysiological pathways (Figure 1). First, persistent systemic inflammation drives sustained hepatic production of serum amyloid A protein, which is deposited as insoluble amyloid fibrils in the mesangium, vessel walls, and tubular basement membranes, producing

AA (secondary) amyloidosis; this pathway is strongly time- and inflammation-dependent, explaining the association of amyloidosis with long-standing, poorly controlled disease and its decline in the era of effective biologic inflammation control [1,18].

Second, immune-complex and autoantibody-mediated processes, involving rheumatoid factor and citrullinated peptide antibody-containing complexes together with complement activation, underlie mesangial, IgA-dominant, and membranous glomerulonephritis, and, less commonly, ANCA-associated pauci-immune crescentic glomerulonephritis when vasculitic transformation supervenes [16,28]. Third, pharmacological nephrotoxicity remains an important and partly modifiable pathway: gold compounds and D-penicillamine are classically associated with immune-complex membranous nephropathy, NSAIDs with interstitial nephritis and haemodynamically mediated acute kidney injury, and calcineurin inhibitors such as cyclosporine with dose-dependent nephrotoxicity and arteriolopathy; targeted synthetic agents such as Janus kinase inhibitors are not classically nephrotoxic but require dose adjustment and heightened infection vigilance in the presence of reduced kidney function [1,2].

Fourth, cardiometabolic comorbidity, including hypertension, dyslipidaemia, and obesity, contributes to arteriolar nephrosclerosis and vascular renal injury largely independent of RA-specific immune mechanisms [5,8,9]. Fifth, ageing and cumulative disease duration compound the effects of the pathways above by reducing renal functional reserve over time. A study using intrarenal resistive index as a marker of renal vascular involvement found that cumulative structural joint damage, assessed by the Sharp/van der Heijde score, correlated significantly with renal vascular parameters, carotid intima-media thickness, and composite cardiovascular risk, providing direct evidence that sustained systemic inflammation simultaneously drives joint destruction and vascular renal injury through a shared pathway [35].

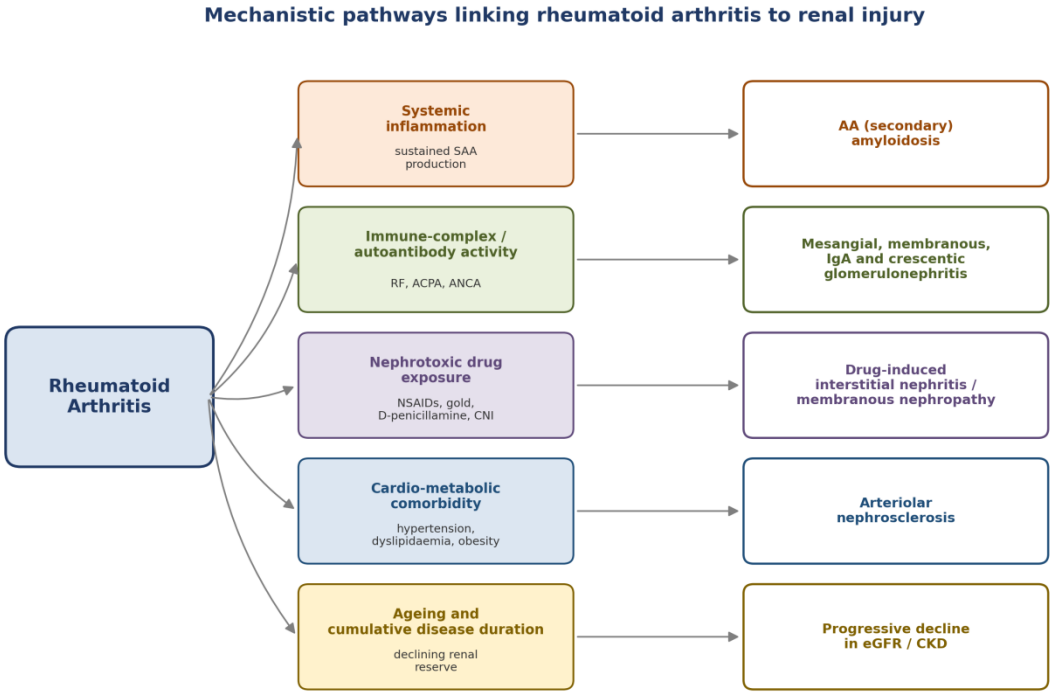


**Figure 1.** Mechanistic pathways linking rheumatoid arthritis to renal injury, spanning systemic inflammation, immune-complex/autoantibody activity, nephrotoxic drug exposure, cardiometabolic comorbidity, and ageing/cumulative disease duration.

## MORPHOLOGICAL AND HISTOPATHOLOGICAL SPECTRUM

Renal biopsy series accumulated from the 1980s to the present demonstrate that RA-associated nephropathy encompasses a wide and evolving spectrum of glomerular, tubulointerstitial, and vascular lesions (Table 1, Figure 2). In one of the earliest large biopsy series (n = 110), mesangial glomerulonephritis was the most common finding (36%), followed by amyloidosis

(30%), membranous glomerulonephritis (17%), focal proliferative glomerulonephritis (4%), and minimal-change nephropathy (3%); membranous glomerulonephritis was closely linked to gold or D-penicillamine therapy, whereas mesangial glomerulonephritis appeared related to RA itself [16].

A Japanese series of 100 renal biopsies found membranous nephropathy to be the single most common lesion (31%), followed by mesangial proliferative glomerulonephritis (21%, including both IgA and non-IgA forms), minor glomerular changes (17%), amyloidosis (11%), and interstitial nephritis (9%); amyloidosis was strongly associated with longer RA duration, and 82% of patients with amyloidosis progressed to renal failure, underscoring its poor prognosis relative to other histological patterns [17].

A four-decade Argentinian series (1976 to 2015, n = 65) illustrated a clear temporal shift in the histopathological landscape: amyloidosis was the leading diagnosis overall (31%), but its relative dominance declined over time, while mesangial glomerulonephritis reached parity with amyloidosis in the most recent era (2003 to 2015); gold-associated membranous nephropathy, present in 45% of membranous cases, likewise declined in frequency after 1990, coincident with declining use of gold salts, and the overall frequency of renal biopsy fell by 40% in the final study period [18]. A comparable pattern was reported from Bulgaria (n = 48 biopsies drawn from 275 patients with RA), where amyloidosis again predominated (27%), membranous glomerulonephritis was linked to gold exposure and declined after 2001, mesangioproliferative glomerulonephritis was the leading lesion between 2002 and 2011, and focal segmental sclerosis predominated between 2012 and 2022; biologic-treated patients had a lower risk of progressive renal function decline than those receiving synthetic DMARDs alone [22].

Substantial regional variation is evident. In a Chinese cohort of 56 patients with RA and renal involvement, IgA nephropathy was unexpectedly the dominant lesion (48%), followed by membranous nephropathy (23%) and focal segmental glomerulosclerosis (20%); renal dysfunction was concentrated mainly among patients with IgA nephropathy and correlated with the degree of glomerulosclerosis and interstitial fibrosis at biopsy [20]. By contrast, a large Egyptian series (n = 376) found amyloidosis to be most common (28%), followed by mesangioproliferative glomerulonephritis (19%) and focal segmental glomerulosclerosis (19%); specific drug exposures showed distinct histological associations, with leflunomide and hydroxychloroquine linked to membranous nephropathy, infliximab linked to focal segmental sclerosis and tubulointerstitial-pattern amyloidosis, and etanercept appearing unrelated to any renal lesion [19]. A Russian cohort similarly identified amyloidosis as the leading histological variant (50%), followed by chronic glomerulonephritis (predominantly mesangial, 30%) and tubulointerstitial nephritis (20%), with amyloidosis specifically associated with longer disease duration and higher CRP levels [11,14].

Necropsy-based data offer a complementary, unselected perspective. In 132 autopsied patients with RA, nephrosclerosis was found in 90% of cases, considerably more common than amyloidosis (11%), membranous glomerulopathy (8%), or focal glomerular disease (8%), highlighting that much of the renal pathology accumulated over a lifetime with RA reflects vascular ageing and shared cardiovascular disease rather than RA-specific immune injury [23]. Consistent with this, an early biopsy series of patients with only mild urinary abnormalities found no histological abnormality in the majority of cases, with the remainder showing only minor mesangial changes, suggesting that overt clinical renal disease represents the more advanced end of a continuum of largely subclinical glomerular change [25].

Biopsy series in broader non-lupus rheumatic disease cohorts, in which RA patients form a subset, corroborate the centrality of amyloidosis and immune-complex glomerulonephritis but also demonstrate disease-specific patterns: amyloidosis was most frequent overall in a Turkish cohort (37%), driven particularly by a very high rate among patients with familial Mediterranean fever, while IgA nephropathy was disproportionately frequent in psoriatic arthritis [21]; in an Indian cohort, pauci-immune crescentic glomerulonephritis was the most common lesion overall, reflecting a predominance of ANCA-associated vasculitis in that series, with RA contributing a smaller proportion of cases [24]. Together, these findings indicate that the histopathological spectrum of renal involvement in RA is shaped by an interplay of disease duration and activity, drug exposure, era of treatment, and population-specific factors, and cannot be reliably inferred from the underlying rheumatological diagnosis alone.

**Table 1.** Selected renal biopsy and necropsy series describing the histopathological spectrum of renal involvement in rheumatoid arthritis

| Study (first author, year) | Country | Sample (n) | Most common lesion(s) | Key observations |
|---|---|---|---|---|
| Boers, 1987 [23] | Netherlands (necropsy) | 132 | Nephrosclerosis 90%; amyloidosis 11%; membranous glomerulopathy 8%; focal glomerular disease 8% | Unselected necropsy series; vascular/age-related change dominates over RA-specific glomerular lesions |
| Helin, 1995 [16] | Finland | 110 | Mesangial GN 36%; amyloidosis 30%; membranous GN 17%; focal proliferative GN 4%; minimal-change 3% | Membranous GN linked to gold/D-penicillamine; mesangial GN linked to RA itself |
| Makino, 2002 [17] | Japan | 100 | Membranous nephropathy 31%; mesangial proliferative GN 21% (IgA 12%, non-IgA 9%); amyloidosis 11% | 82% of amyloidosis cases progressed to renal failure; DMARDs correlated with membranous nephropathy |
| Vinicki, 2015 [18] | Argentina | 65 | Amyloidosis 31%; mesangial GN 18%; membranous nephropathy 17%; extracapillary proliferative GN 15% | Temporal decline in amyloidosis and gold-associated membranous nephropathy after 1990; biopsy frequency fell 40% by 2003–2015 |
| Fayed, 2019 [19] | Egypt | 376 | Amyloidosis 28%; mesangioproliferative GN 19%; FSGS 19%; crescentic GN 17% | Leflunomide/hydroxychloroquine linked to membranous nephropathy; infliximab linked to FSGS/amyloidosis |
| Zhang, 2020 [20] | China | 56 | IgA nephropathy 48%; membranous nephropathy 23%; FSGS 20% | Renal dysfunction concentrated in IgA nephropathy; correlated with sclerosis/fibrosis burden |
| Chebotareva, 2020 [11,14] | Russia | 86 (biopsied subset) | Amyloidosis 50%; chronic (mainly mesangial) GN 30%; tubulointerstitial nephritis 20% | Amyloidosis associated with disease duration and CRP level |
| Monova, 2023 [22] | Bulgaria | 48 | Amyloidosis 27%; mesangioproliferative/tubulointerstitial nephritis 15% each; membranous GN 19% | Mesangioproliferative GN peaked 2002–2011, FSGS 2012–2022; biologics associated with lower risk of GFR decline |
| Sezen, 2026 [21] | Türkiye | 139 non-lupus (RA n=46) | Amyloidosis 37%; FSGS 19%; tubulointerstitial nephritis 9%; IgA nephropathy 8% | Cohort-wide figures across five non-lupus rheumatic diseases; amyloidosis highest in familial Mediterranean fever |

*GN, glomerulonephritis; FSGS, focal segmental glomerulosclerosis; IgA, immunoglobulin A; CRP, C-reactive protein; DMARDs, disease-modifying antirheumatic drugs; GFR, glomerular filtration rate.*

Natural Resources for Human Health
eISSN: 2583-1194

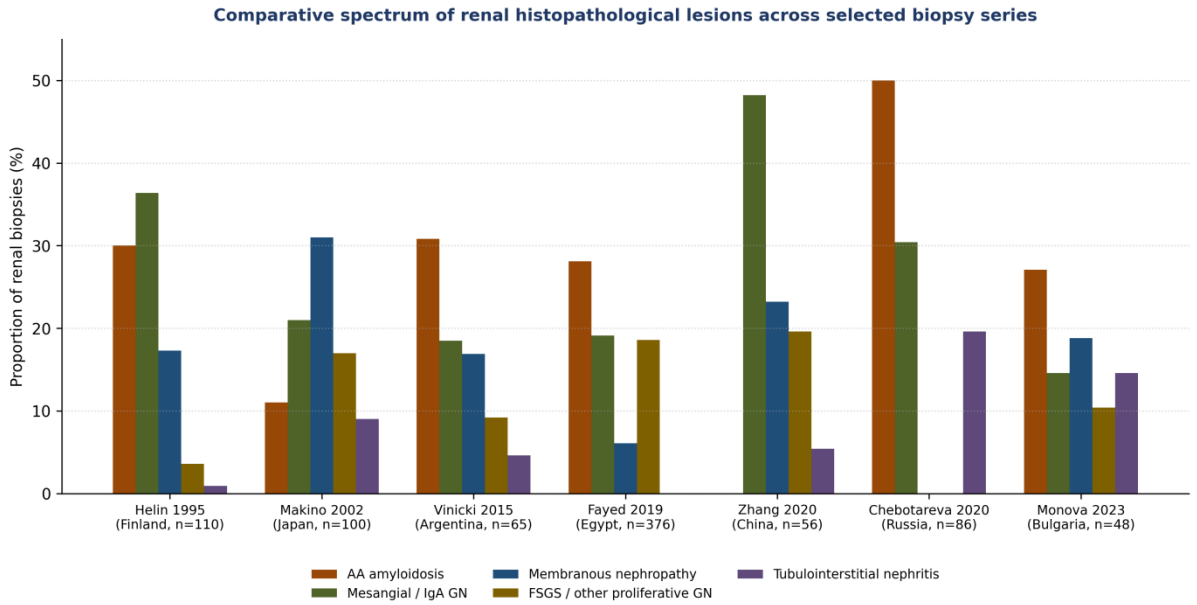


**Figure 2.** Comparative spectrum of renal histopathological lesions across seven selected renal biopsy series in rheumatoid arthritis, expressed as the percentage of biopsies showing each lesion category.

**Risk Factors for Renal Involvement**

Risk factors for renal involvement and CKD in RA identified across the reviewed literature fall broadly into four categories: demographic, cardiometabolic, RA-specific, and drug-related factors (Table 2, Figure 3).

Among demographic and cardiometabolic factors, older age is the most consistently reported risk factor, identified as an independent predictor of reduced eGFR or CKD in multiple cohorts [6,9,10,11,37]. Hypertension is similarly consistently implicated [9,10,11,15], as are dyslipidaemia and hypercholesterolaemia [8,11,5] and elevated serum uric acid [8]. The direction of the association with sex is less consistent: one Japanese community-based study found female sex to be an independent risk factor for reduced eGFR [10], whereas an Iranian cohort found male sex associated with a three-fold higher risk of renal failure [37], a discrepancy likely reflecting differences in case-mix, comorbidity profile, and renal function definitions between populations.

RA-specific factors show a more heterogeneous evidence base. Several studies report that longer disease duration and higher disease activity, reflected by elevated ESR, CRP, or Disease Activity Score in 28 joints (DAS28), are independently associated with CKD or declining eGFR [6,11,4], and extra-articular disease has similarly been linked to renal dysfunction [8]. However, other well-conducted cross-sectional studies found no significant independent association between renal impairment and disease activity, duration, or severity after adjustment for cardiovascular risk factors [8,9,10]. This apparent contradiction likely reflects the coexistence of at least two distinct renal phenotypes in RA: an inflammation- and immune-complex-driven phenotype, in which glomerulonephritis and amyloidosis track with disease activity and duration, and a cardiometabolic/vasculopathic phenotype, in which albuminuria and declining eGFR track with classical cardiovascular risk factors largely independent of joint disease activity [5]. Both phenotypes may coexist within the same patient population, and their relative contribution may vary by cohort, era, and treatment exposure.

Drug-related factors include historical exposure to gold compounds and D-penicillamine, consistently linked to membranous nephropathy across multiple biopsy series [16,18,19], and NSAID use, which has shown inconsistent associations with renal dysfunction, being significant in some cohorts [5,13] but not others [8]. Conversely, treatment with biologic DMARDs has been associated with a lower risk of progressive renal function decline in several studies, including a reduced hazard of glomerular filtration rate decline in adults [22] and reduced risk of ESRD when preferentially considered in at-risk patients [7], suggesting a renoprotective effect mediated through more effective and sustained control of systemic inflammation.

A comparative paediatric perspective from juvenile idiopathic arthritis (JIA) reinforces several of these themes. Among 376 children with JIA, renal involvement occurred in 8.5% overall but varied markedly by subtype, from 16.2% in systemic JIA to

3.4% in rheumatoid factor-negative polyarticular disease; elevated CRP, higher juvenile arthritis disease activity score, and longer duration of active disease independently predicted renal involvement, while biologic therapy was protective (hazard ratio 0.394) [38]. Systemic JIA with renal involvement was characterised by proteinuria and high serum amyloid A, consistent with an amyloidogenic mechanism, whereas enthesitis-related arthritis was associated with haematuria and elevated IgA, suggestive of IgA nephropathy; these subtype-specific patterns closely mirror the heterogeneity of mechanisms described in adult RA [38].

**Table 2.** Reported risk factors for renal involvement and chronic kidney disease in rheumatoid arthritis, by category

| Category | Risk factor | Reported association | Representative studies |
|---|---|---|---|
| Demographic | Older age | Independent risk factor for reduced eGFR/CKD in most cohorts | [6,9,10,11,37] |
| Demographic | Sex | Inconsistent: female sex (Japan) vs male sex (Iran) reported as risk factor | [10,37] |
| Cardiometabolic | Hypertension | Consistently associated with renal impairment | [9,10,11,15] |
| Cardiometabolic | Dyslipidaemia / hypercholesterolaemia | Independently associated with reduced eGFR/CKD | [8,11,5] |
| Cardiometabolic | Elevated serum uric acid | Independently associated with reduced eGFR | [8] |
| Cardiometabolic | Metabolic syndrome / obesity | Associated with CKD; mediates much of RA–CKD association in one cohort | [5,10] |
| RA-related | Longer disease duration | Associated with CKD/amyloidosis in several cohorts; not confirmed in others | [6,11,18] |
| RA-related | High disease activity (ESR, CRP, DAS28) | Associated with CKD in several cohorts; no association after adjustment in others | [4,6,11,8,9] |
| RA-related | Extra-articular disease / seropositivity | Associated with renal dysfunction | [8] |
| Drug-related | Older DMARDs (gold salts, D-penicillamine) | Consistently linked to membranous nephropathy | [16,18,19] |
| Drug-related | NSAID exposure | Inconsistent association across cohorts | [5,13,8] |
| Drug-related | Biologic DMARD therapy | Associated with lower risk of progressive renal function decline (reno-protective) | [22,7,38] |

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eISSN: 2583-1194

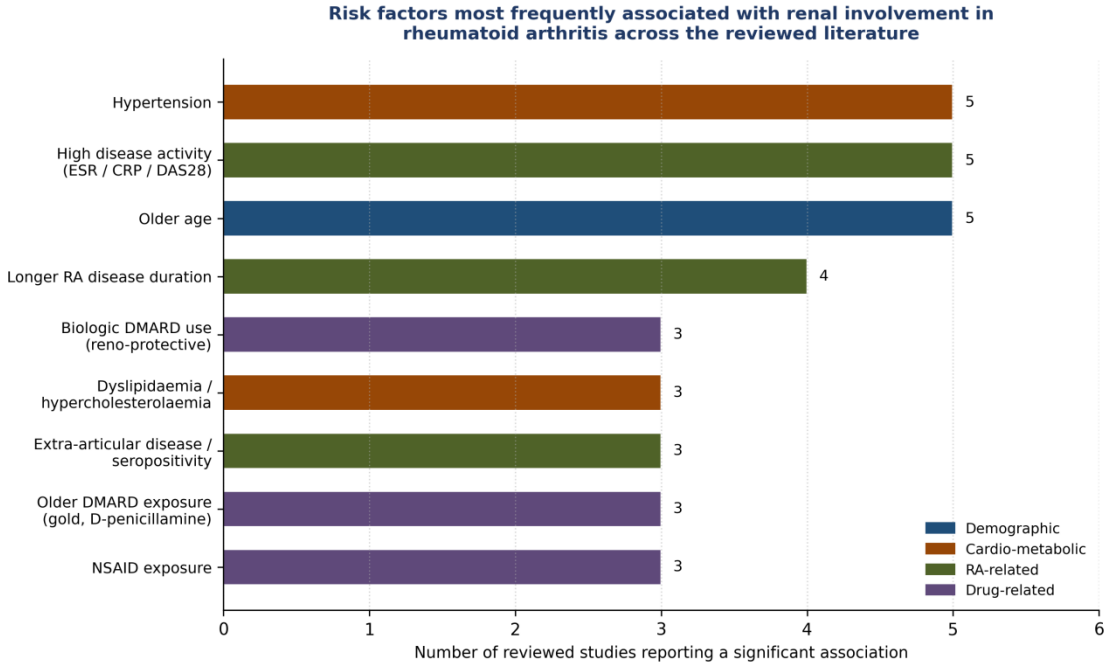


**Figure 3.** Risk factors most frequently reported as significantly associated with renal involvement in rheumatoid arthritis across the reviewed literature, grouped by category.

## DIAGNOSTIC EVALUATION AND SCREENING

Given the largely silent clinical course of renal involvement in RA and the poor correlation between clinical presentation and underlying histology, a proactive screening strategy is warranted. Baseline and periodic assessment of serum creatinine with eGFR estimation, urinalysis for proteinuria and haematuria, and quantification of the urinary albumin-to-creatinine ratio are recommended, since microalbuminuria may be present in a substantial proportion of patients even when disease appears well controlled and correlates with markers of inflammatory activity [4,1]. Systematic albuminuria screening has been specifically advocated even in patients with preserved eGFR, since this appears to be the dominant renal phenotype in some populations [5].

Renal biopsy remains the definitive investigation when clinically indicated, including in the setting of persistent or nephrotic-range proteinuria, an active urinary sediment with haematuria, an unexplained rise in creatinine, or when the clinical picture is atypical or suggestive of an overlap syndrome. Because clinical features cannot reliably predict the underlying histology [16,26], biopsy provides essential information for differential diagnosis, prognostication, and treatment decision-making, including distinguishing RA-related nephropathy from drug-induced nephrotoxicity, unrelated intercurrent renal disease, or overlap with lupus nephritis or ANCA-associated vasculitis, the latter requiring correlation with serological testing (antinuclear antibody, anti-double-stranded DNA antibody, ANCA, and complement levels) and immunofluorescence and electron microscopy of biopsy tissue [29,30].

### Management Implications and Prognosis

Effective control of systemic inflammation with contemporary DMARD strategies, including biologic and targeted synthetic agents, appears to confer a degree of renoprotection, most plausibly by reducing the amyloidogenic burden of serum amyloid A and by allowing reduction in exposure to nephrotoxic conventional agents such as NSAIDs and older DMARDs [1,22,7]. Where feasible, chronic NSAID use should be minimised, and clinicians should remain alert to the renal effects of calcineurin inhibitors when used, while targeted synthetic agents such as Janus kinase inhibitors require dose adjustment and increased vigilance for infection in the presence of reduced kidney function [1].

Amyloidosis carries a disproportionately poor renal prognosis relative to other histological patterns, with the majority of affected patients progressing to renal failure in some series [17], reinforcing the importance of early recognition and aggressive, sustained control of inflammatory activity as the principal preventive strategy. Because CKD in RA is strongly linked to

cardiovascular risk, serious infection, and all-cause mortality [1,6,35], multidisciplinary care involving both rheumatology and nephrology is advisable for patients with biopsy-proven renal disease or progressive CKD, with attention to cardiovascular risk reduction alongside renal and articular disease management.

**Limitations of the Current Evidence**

The evidence base summarised in this review has several limitations. Most renal biopsy series are retrospective and derived from single centres, introducing referral and selection bias toward patients with clinically overt disease, while subclinical renal involvement is likely under-represented. Definitions of CKD and renal involvement vary considerably between studies, limiting direct comparability, and few prospective, biopsy-based studies have been conducted in the contemporary era of widespread biologic and targeted synthetic DMARD use. Data from African populations remain particularly sparse in the existing literature, despite the substantial burden of RA and its comorbidities across the continent, highlighting an important gap for future regional research.

**Future Directions**

Future research priorities include prospective cohort studies incorporating both non-invasive renal markers, such as urinary albumin-to-creatinine ratio and intrarenal resistive index, and biopsy or histological correlation, in patients receiving contemporary RA therapy; mechanistic studies to clarify the basis of the reported association between RA and IgA nephropathy; generation of epidemiological and histopathological data from underrepresented African and other low- and middle-income country populations; and development of RA-specific renal risk stratification tools that integrate disease activity, comorbidity burden, and drug exposure to guide individualised screening and nephroprotective strategies.

## CONCLUSION

Renal involvement in rheumatoid arthritis is common, frequently clinically silent, and pathologically heterogeneous, encompassing immune-mediated glomerulonephritis, AA amyloidosis, drug-induced nephropathy, and cardiometabolic-driven nephrosclerosis. The relative frequency of these entities has evolved substantially with contemporary RA therapy, with declining amyloidosis and gold-induced membranous nephropathy but a persisting burden of chronic kidney disease driven in part by shared cardiovascular risk factors. Routine screening with eGFR and albuminuria testing, judicious use of nephrotoxic agents, sustained control of disease activity, a low threshold for renal biopsy in atypical presentations, and close collaboration between rheumatology and nephrology together form the foundation of an approach aimed at improving renal and overall outcomes in patients with rheumatoid arthritis.

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