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Review

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# Acute Kidney Injury in Autoimmune-Mediated Rheumatic Diseases

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## Abstract

Acute kidney injury (AKI) is increasingly affecting hospitalized patients worldwide. Patients with inflammatory rheumatic diseases, although primarily impacted by functional impairment and sometimes structural damage to joints, bones, and muscle tissue, may also develop AKI during the course of their disease. This narrative review aimed to summarize potential causes of AKI and the associated disease patterns. The following databases were searched for references: PubMed, Web of Science, Cochrane Library, and Scopus. The search period covered from 1958 to 2024. Certain inflammatory rheumatic diseases increase the risk of AKI due to specific types of kidney disease. However, the most common conditions, such as rheumatoid arthritis and spondylarthritis, rarely cause AKI directly. Among the medications used for pain and sometimes disease activity control, nonsteroidal anti-inflammatory drugs (NSAIDs) can potentially induce AKI, even progressing to acute tubular necrosis. There is evidence that certain rheumatic diseases are associated with increased risk of AKI, independently of directly affecting kidney function or structure. However, the data on this topic are quite limited. AKI is a potentially significant issue for patients with inflammatory rheumatic diseases. Additional data on the increased risk of AKI, independent of direct kidney involvement, are needed.

**Keywords:** AKI; Rheumatic disease; Glomerulonephritis; NSAID; DMARD therapy

## Introduction

Acute kidney injury (AKI) is a growing concern for hospitalized and non-hospitalized patients worldwide. The incidence of AKI ranges from 5% to over 30%, depending on the region, medical specialty, and the specific medical circumstances (e.g., Eastern Asia 14.7%, Western Europe 20.1%, Southern Europe 31.5%; community-acquired 8.3%, all hospital acquired 20.9%, critical care 31.7%) [1, 2]. Patients receiving intensive care are affected in 50% or more [3], depending on the underlying disease and its treatment. An almost 100% mortality rate has been observed in patients with hematologic malignancies, chemotherapy-induced sepsis, and AKI requiring kidney replacement therapy (KRT) [4]. The diagnosis of AKI is still based on the 2012 revised "Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines for acute kidney injury" [5], which provide cutoff values for changes in serum creatinine levels over time. Recent advancements in AKI biomarker research are expected to lead to a revised definition of the syndrome, which will likely involve the integration of so-called damage biomarkers [6].

Individual AKI episodes increase the risk of developing chronic kidney disease (CKD) [7-11]. In 2014, Rewa et al [12] published a review of the long-term survival of patients with AKI, highlighting the strongest reduction in probability of survival for patients with CKD stage 5D (dialysis requirement). The life expectancy of individuals with pre-existing CKD who also developed AKI was almost equally reduced. The study also found that even individuals without pre-existing CKD who experienced a single episode of AKI faced a reduced life expectancy, with the greatest decline occurring for more severe episodes (RIFLE criteria [13]). Back in 2013, Lewington et al already demonstrated that annually more people worldwide die from the direct and indirect consequences of AKI than from the combined conditions of diabetes mellitus, heart failure, breast cancer, and prostate cancer [14]. Finally, it is important to note that elderly individuals with AKI have a reduced likelihood of renal recovery when compared to younger subjects [15]. This phenomenon is presumably attributable to the elevated average morbidity observed in the elderly population. Comparable observations on renal recovery were made in the gender comparison: women have a higher risk of non-recovery than men [16]. The second aspect is relevant insofar as many inflammatory rheumatic diseases manifest themselves more frequently in women than in men, namely rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

The most common cause of AKI is transient renal hypoperfusion, leading to either pre-renal or, in prolonged cases, intra-renal AKI [17]. The latter is characterized by structural abnormalities of the tubular epithelium. In a clinical setting,

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renal hypoperfusion often occurs due to worsening heart failure, sepsis, and fluid or blood loss. AKI can also result from specific glomerular or tubulointerstitial diseases, especially those with a sudden onset. Obstruction of the ureters or bladder is the least common cause [18]. Several risk factors can increase the susceptibility to AKI, including pre-existing conditions such as hypertension, diabetes mellitus, heart failure, and others. The highly complex pathogenesis of AKI has been addressed by excellent review articles [6].

Autoimmune inflammatory rheumatic diseases are represented by four main groups: RA, seronegative spondyloarthritides, collagenoses, and vasculitides. Medical attention, especially among rheumatology specialists, often focuses on the impact of the disease processes on the function and structure of the musculoskeletal system. However, defined collagenoses and vasculitides are disproportionately associated with severe kidney diseases. Furthermore, it is well known that chronic inflammatory autoimmune diseases significantly increase the cardiovascular disease risk [19], ultimately also increasing the risk for CKD and potentially susceptibility to AKI. Finally, a wide range of, at times very specific, medications are meanwhile used in the treatment of inflammatory rheumatic diseases. Some of these are well-known risk factors for AKI (e.g., nonsteroidal anti-inflammatory drugs (NSAIDs) [20]), while others have been sporadically linked with the syndrome mechanistically.

The aim of the current article is to discuss the epidemiology and etiology of AKI in inflammatory rheumatic diseases. Three perspectives will be highlighted: the impact of the underlying disease itself, the potential effects of medication therapy, and the risk of AKI in the context of latent systemic inflammation.

## Methods

The following databases were searched for references: PubMed, Web of Science, Cochrane Library, and Scopus. The period lasted from 1958 until 2024. The following article types were considered: prospective, randomized and controlled clinical trials, original experimental studies, retrospective observational cohort studies, case reports, systematic and non-systematic reviews, and specific guidelines.

The following terms were utilized: 1) group 1: disease-related "inflammatory rheumatic diseases" OR "autoimmune-mediated rheumatic diseases" OR "rheumatoid arthritis" OR "spondylarthritis" OR "ankylosing spondylitis" OR "arthritis psoriatica" OR "collagenoses" OR "vasculitis" OR "vasculitides" OR "SLE" OR "systemic lupus erythematosus" OR "Sjogren's syndrome" OR "inflammatory myopathy" OR "ANCA-associated vasculitis" OR "granulomatosis with polyangiitis" OR "microscopic polyangiitis" OR "cryoglobulinemia" OR "Henoch-Schonlein purpura" OR "IgA vasculitis" OR "polyarteriitis nodosa" OR "Behcet's disease" OR "giant cell arteriitis"; 2) group 2: therapy-related (in variable combinations with group 1 and 3 terms): "NSAID" OR "cDMARDs" OR "bDMARDs" OR "bsDMARDs" OR "tsDMARDs"; 3) group 3: AKI-related (in variable combinations with group 1 and 2 terms) "acute renal failure" OR "acute kidney injury" OR "AKI" OR "glomerulonephritis" OR "GN" OR "ATN" OR "papillary necrosis". Additional terms were "anti-IL6" OR "anti-IL12" OR "anti-IL12/-23" OR "anti-IL17" AND "AKI" and "oral health" OR "periodontitis"; 4) group 4: cytokine and oral health-related (predominantly in variable combinations with group 1 terms).

## AKI Resulting From the Underlying Disease

This section will only discuss literature on AKI as a direct manifestation of an inflammatory rheumatic disease. References will be listed chronologically, from oldest to most recent dates, if not specified otherwise. The article does not refer to rare entities (polyarteritis nodosa, Behcet's syndrome, etc.).

### RA

RA is the most common singular entity in the realm of inflammatory rheumatic diseases, affecting approximately 2% of adults in Central Europe [21]. The primary feature of the disease process is chronic inflammation of the synovial membrane in the joints. Reports of acute deteriorations in excretory kidney function were already published in the 1980s; however, these are reports or case studies. In 1986, Bar et al [22] reported on a patient with AKI complicating RA-associated amyloidosis, while Wegelius et al [23] published a report on two patients with severe interstitial kidney edema. Interestingly, the two latter individuals did not exhibit a specific glomerular or tubular damage pattern. Instead, they showed an accumulation of hyaluronic acid (HA) in the interstitial space. This accumulation could potentially have been responsible for edema formation, as HA has a significant water-binding capacity. In conclusion, the accumulation of HA was considered to directly indicate impaired connective tissue homeostasis in RA. Another case report from 2009 [24] identified focal-segmental proliferative glomerulonephritis as the leading cause of AKI. Renal biopsy investigation did not reveal any interstitial inflammation or renal amyloidosis. A somewhat similar case was published in 2010 [25], reporting on a 40-year-old woman with RA who developed acute, oliguric kidney injury. Histologically, there were no specific tubular or interstitial abnormalities, but there was an edematous thickening of the vascular intima, accompanied by signs of ischemic damage to the glomeruli. In summary, RA can sometimes lead to AKI. The patterns of kidney damage are generally nonspecific, though glomerulonephritis may occasionally occur.

### Spondylarthritis (SpA)

SpA encompasses five distinct entities: ankylosing spondylitis (AS), psoriatic arthritis, reactive arthritis, enteropathic arthritis, and undifferentiated SpA. Collectively, the prevalence of this group is comparable to that of RA. SpA, in general, [26] and AS, in particular, have occasionally been reported to coincide with immunoglobulin (Ig)A nephritis [27]. The pat-

 

tern of IgA mesangioproliferative glomerulonephritis is also typically diagnosed in Henoch-Schonlein purpura (HSP), where extracapillary inflammation may require treatment with cyclophosphamide, as seen in other vasculitides (see "Vasculitides"). However, extracapillary proliferative glomerulonephritis, whether or not associated with mesangial IgA, is likely negligible as a cause of AKI in AS. Only 1% of all AS patients with renal involvement exhibit extracapillary changes [28]. The literature provides minimal evidence for specific kidney disease patterns in other types of spondyloarthritis. However, there are numerous references regarding kidney-related side effects of drugs used for managing disease activity and progression in SpA (see "AKI Resulting From the Anti-Rheumatic Therapy").

## Collagenoses

Collagenoses, particularly SLE, are significantly associated with AKI. The literature on potential kidney involvement in SLE is indeed so extensive that a comprehensive review here is hardly feasible. We must refer to relevant review articles, setting aside hundreds of original manuscripts [29-32]. Lupus nephritis (LN) is likely one of those complications of inflammatory rheumatic diseases that the vast majority of physicians will be familiar with. Up to 50% of all SLE patients experience kidney involvement during the course of the disease [31]. According to the revised International Society of Nephrology/Renal Pathology Society classification for LN, LN classes III and IV are characterized by endocapillary hypercellularity and crescent formation in less than 50% (focal - class III) or more than 50% (diffuse - class IV) of all glomeruli examined by a pathologist [33]. The clinical spectrum of renal involvement in LN can encompass virtually all patterns of acute or chronic glomerular damage: isolated glomerular hematuria or proteinuria, nephrotic and nephritic syndrome, the latter with a rapid course AKI, renal hypertension, and progressive CKD [34]. Nephritic manifestations, including the potential development of AKI, are predominantly observed in LN classes III and IV [31]. These two forms also require intensified immunosuppression. The most recently updated KDIGO guidelines from 2024 [35] currently offer four distinct therapeutic regimens for remission induction in this situation, with the inclusion of belimumab as a potential first-line treatment option. Primary Sjogren's syndrome is classically associated with dryness of the eyes and mouth, caused by autoimmune inflammation of the exocrine glands in the head region [36]. In addition to articular, cutaneous, and pulmonary complications, affected individuals are potentially at risk for renal manifestations. While renal tubular dysfunctions (such as renal tubular acidosis (RTA) types 1 and 2) are predominant, proliferative glomerulonephritis including AKI have also been reported. In 2015, the EULAR-SS Task Force Group summarized potential kidney damage patterns [37]. The prevalence of RTA was estimated at 9%, while the prevalence of all glomerulonephritides was 4%. The publication also lists the findings from 149 reported cases of glomerulonephritis associated with Sjogren's syndrome. Crescentic rapidly progressive glomerulonephritis, typically associated with AKI, was identified in only nine individuals. A 2019 case series on patients with primary Sjogren's syndrome and kidney involvement (n = 20) did not identify any cases of AKI, although glomerulonephritis was diagnosed in six individuals [38].

In contrast to the relatively low incidence of AKI as a direct consequence of primary Sjogren's syndrome, systemic sclerosis, particularly the diffuse variant, is associated with a significantly increased AKI risk. The term renal crisis describes the concurrence of AKI and the histopathological finding of obliterative endarteritis within the kidney itself [39]. The vascular obstructions result from intimal hyperplasia and fibrinoid media degeneration. Serologically, affected patients are characterized by the association with RNA polymerase 3 antibodies [40]. Before the availability of angiotensin-converting enzyme (ACE) inhibitors, the mortality rate of renal crisis was high. In 2019, classification criteria for this condition were published [41]. The criteria also include possible accompanying phenomena such as thrombotic microangiopathy, which can clinically aggravate the course. Several case reports have already been published on this topic [42-44]. The combined manifestation of systemic sclerosis and anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis has also been documented in the literature, although such cases are likely to be rare [45]. Other sporadic manifestations include the pattern of membranoproliferative glomerulonephritis [46] and pauci-immune glomerulonephritis in systemic sclerosis without skin involvement [47].

Inflammatory myopathies include the following entities: idiopathic dermatomyositis (DM), juvenile dermatomyositis (jDM), idiopathic amyopathic DM (often associated with anti-MDA5), idiopathic polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), anti-synthetase syndrome (ASys), paraneoplastic idiopathic poly-/dermatomyositis, inclusion body myositis, and overlap myositis [48]. Other, even rarer types have also been identified. Although glomerulonephritis has been described in a few cases of inflammatory myopathies [49], these diseases primarily pose a risk of AKI due to rhabdomyolysis [50, 51]. The unusual manifestation of thrombotic microangiopathy in PM was reported in 2021 [52].

The issue of AKI is most significant in SLE and less so in other types of collagenoses. In Sjogren's syndrome, systemic sclerosis, or inflammatory myopathies, glomerulonephritis can cause AKI. In inflammatory myopathies, rhabdomyolysis must also be considered. In all affected patients, side effects of medication or other causes must always be considered.

## Vasculitides

Similar to the group of collagenoses, vasculitides often present an interdisciplinary challenge for rheumatologists and nephrologists. This is particularly true for ANCA-associated vasculitides (AAV), namely granulomatosis with polyangiitis and microscopic polyangiitis. The 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis distinguishes between five disease stages: nonse-

**Table 1.** Patterns of Kidney Damage Associated With AKI in Patients With Inflammatory Rheumatic Diseases

| Entity | Possible pattern of kidney disease associated with AKI |
|---|---|
| Rheumatoid arthritis (RA) | Focal-segmental proliferative glomerulonephritis [24] (sporadic) |
| | Interstitial or vascular wall edema (case reports) [23, 25] |
| Spondylarthritis | |
| Ankylosing spondylitis (AS) | IgA nephropathy, occasionally associated with extracapillary proliferation [27, 28] |
| Other | No specific patterns |
| Collagenoses | |
| Systemic lupus erythematosus (SLE) | Lupus nephritis (50% of all individuals), classes I to VI according to ISN/RPS classification; classes III and IV associated with extracapillary pathology [31, 33] |
| Sjogren's syndrome (SS) | Extracapillary proliferative glomerulonephritis possible although rare [37] |
| Systemic sclerosis (SSc) | Obliterative endarteritis +/- thrombotic microangiopathy [41] |
| | Case reports on obliterative endarteritis and membranoproliferative or extracapillary proliferative glomerulonephritis [42-45] |
| Inflammatory myopathy (IIM - idiopathic inflammatory myopathy) | Rhabdomyolysis [50] |
| | Case reports on glomerulonephritis [49] and thrombotic microangiopathy [52] |
| Vasculitides | |
| ANCA-associated vasculitis (AAV) | Cause of the most common type of extracapillary proliferative glomerulonephritis [55] |
| IgA vasculitis | IgA nephropathy, extracapillary proliferation possible [59, 60] |
| Cryoglobulinemia (CG) | Extracapillary proliferative glomerulonephritis in 20-50% of type 2 CG [58] |

AKI: Acute kidney injury; ANCA: anti-neutrophil cytoplasmic antibodies; ISN/RPS: International Society of Nephrology/Renal Pathology Society; Ig: immunoglobulin.

vere, severe, active, refractory, remission, and relapse [53]. Extrapapillary proliferative glomerulonephritis, with either focal or diffuse manifestation, is a common AAV-associated complication that was nearly always fatal before the availability of cyclophosphamide [54]. Among the types of extrapapillary proliferative glomerulonephritis, the ANCA-associated variant is the most common, accounting for 70% of cases. Immunofluorescence histology does not reveal a specific finding, which explains the term pauci-immune. It is estimated that 70-100% of all AAV patients develop a prognostically significant renal involvement over the course of the disease [55]. Clinically, most affected patients suffer from AKI.

A similar pattern of glomerular injury (extrapapillary proliferative glomerulonephritis) may occur in cryoglobulinemia (CG) of either primary or secondary origin. Immunofluorescence staining reveals granular glomerular deposition of immune complexes [56]. CG is represented by three types, with type 3 being the most prevalent [57]. Type 2 immune complexes contain monoclonal antibodies that interact with pre-existing polyclonal immunoglobulins. A significant percentage of affected patients test positive for hepatitis C [58]. Approximately 20-50% of all type 2 CG patients develop extrapapillary proliferative glomerulonephritis [58], usually resulting in AKI.

Another specific type of small-vessel vasculitis, HSP, also referred to as IgA vasculitis, is typically characterized by IgA mesangioproliferative glomerulonephritis [59]. The disease can be interpreted as a systemic form of IgA nephropathy [60]. Comparable to IgA nephropathy, kidney involvement in the context of HSP can be associated with extracapillary proliferations [60]. Clinically, this may sometimes manifest as AKI, although despite the histological findings, milder consequences of glomerular damage are also possible, such as isolated proteinuria or a non-rapidly progressive course [61].

Table 1 summarizes all discussed types of rheumatic diseases and respective risk and mechanism of kidney involvement [23-25, 27, 28, 31, 33, 37, 41-45, 49, 50, 52, 55, 58-60].

## AKI Resulting From the Anti-Rheumatic Therapy

### NSAIDs

Several potential NSAID side effects can impact kidney function and structure. Some of these effects are dose-dependent, while others are not. Acute adverse events include reversible pre-renal failure, which may progress to acute tubular necrosis (ATN), acute interstitial nephritis (AIN), renal vasculitis (rare),

and acute papillary necrosis [62-64]. In theory, papillary necrosis can potentially cause AKI by leading to bilateral ureteral obstruction. The most common type of NSAID-induced AKI results from diminished intrarenal blood flow due to inhibited prostaglandin synthesis. This particularly affects patients whose renal blood flow is stabilized by increased intrarenal prostaglandin synthesis. This occurs in situations characterized by latent reduced blood flow to the entire body, including the kidneys, such as heart failure, sepsis, and advanced atherosclerosis with manifestation in the organ itself [65]. NSAIDs exhibit varying selectivity for cyclooxygenase (COX)-1 and COX-2 enzymes. Non-selective drugs include ibuprofen and ketoprofen, while meloxicam, diclofenac, and celecoxib show intermediate COX-2 selectivity. Highly COX-2 selective substances include rofecoxib and etoricoxib. However, it would be incorrect to assume that COX-2 selective medications do not increase the risk of AKI. Huerta et al [66] reported a threefold increase in AKI risk in patients receiving diclofenac, ibuprofen, ketoprofen, or meloxicam compared to those not on such therapies. The overall risk increased with longer duration of therapy and higher doses. This dose-dependent effect was further confirmed by Fine et al [20], who found a 2.3-fold higher AKI risk with the use of conventional NSAIDs, including a 2.42-fold risk increase with naproxen. Rofecoxib also posed a higher risk, with a 2.31-fold increase [20]. The risk of AKI increases significantly when NSAIDs are taken in combination with certain other drugs. Specifically, diuretics, ACE inhibitors, and angiotensin receptor blockers can substantially elevate the risk when used with NSAIDs [67]. Due to the almost routine use of NSAIDs in individuals with various forms of inflammatory rheumatic diseases, the issue of NSAID-induced AKI remains highly relevant both epidemiologically and prognostically. Other potential side effects are not even mentioned, such as an increase in cardiovascular risk and gastrointestinal bleeding.

### Conventional disease-modifying anti-rheumatic drugs (cDMARDs)

Methotrexate is the drug of first choice for RA patients requiring disease-modifying therapy. It has also been proven effective in psoriatic arthritis [68, 69]. When considering the kidney-related side effects of methotrexate, the required dose for disease control must be taken into account. In patients with hematologic-oncologic disorders, the drug dosage ranges from 1 to 15 g/m$^2$, which can lead to AKI due to acute crystalline nephropathy [70]. However, for rheumatic diseases, methotrexate is used as an anti-inflammatory and anti-progressive drug, with doses typically between 10 and 20 (up to 25) mg per week [71]. Within this dosage range, the risk of adverse effects on kidney function and structure is almost negligible.

Renal adverse events associated with azathioprine (AZA) have been reported sporadically. Bir et al published a rare case of AZA-induced AIN, which was subsequently followed by rapidly progressive AKI [72].

Sulfasalazine has also been reported to occasionally induce AIN [73].

Calcineurin inhibitors (CNIs) can act as vasoconstrictors, reducing glomerular perfusion and potentially leading to AKI in severe cases [74]. These vascular effects are dose-dependent and can be mitigated by regular monitoring of CNI blood levels. In the long term, CNIs contribute to renal fibrogenesis. They have been shown to induce transforming growth factor (TGF)-beta, a well-known key mediator of fibroblast activity and epithelial-mesenchymal transition [75].

### Biological/biosimilar disease-modifying anti-rheumatic drugs (bDMARDs/bsDMARDs)

Kidney-related side effects of anti-tumor necrosis factor (TNF)-alpha are rare. Wei et al reported the uncommon occurrence of IgA nephropathy [76], while Kaneko et al [77] documented two cases of extracapillary necrotizing glomerulonephritis in patients treated with anti-TNF-alpha. Korsten et al [78] reported adalimumab-induced granulomatous interstitial nephritis in AS. Overall, the risk of renal adverse events induced by anti-TNF-alpha is considered low. The current literature search (as of May 2024) yields no official entries for the following search terms: "AKI" and "anti-IL6" or "anti-IL12" or "anti-IL12/-23" or "anti-IL17". The same applies to the terms "AKI" and "abatacept". Overall, the risk of AKI induced by biological DMARDs (bDMARDs) or their corresponding biosimilars (bsDMARDs) is effectively negligible.

### Other types of disease-modifying anti-rheumatic drugs

Targeted synthetic DMARDs (tsDMARDs) are a relatively new class of drugs, currently represented by JAK kinase inhibitors such as baricitinib, filgotinib, tofacitinib, and upadacitinib. Apremilast can also be included in this group, although it inhibits the activity of phosphodiesterase 4, leading to reduced production of TNF-alpha. The literature on JAK kinase inhibitors and AKI is sparse. However, in 2021, an experimental study using a lipopolysaccharide-induced AKI model was published [79]. This study demonstrated that kidney damage could be reduced with tofacitinib. Aside from this, no additional references can currently be identified using the terms "JAK kinase inhibitors" and "AKI".

## General AKI Susceptibility in Rheumatic Diseases

Initially, it seems plausible to assume that inflammatory rheumatic systemic diseases are associated with an increased risk of AKI. This theoretical increase should be suspected even if the underlying disease does not primarily involve specific renal complications. Given the data on the elevated cardiovascular risk in RA and seronegative spondyloarthropathies [19, 80], affected individuals are more likely to suffer from atherosclerosis more frequently and at an earlier stage. Atherosclerosis also affects the intrarenal arteries, potentially reducing the kid-

ney's overall stress tolerance. However, regarding the general risk of AKI in inflammatory rheumatic diseases, there are currently few significant references available. Levy et al [81] conducted a retrospective study on AS patients between 1996 and 2006, including 4,836 males and 3,780 females, to determine the prevalences of AKI, CKD, amyloidosis, and hypertensive renal disease. All predefined types of renal disease were 72% more prevalent in individuals with AS compared to healthy controls, particularly among younger individuals. The study does verify the hypothesis of an increased AKI risk, at least in AS patients; however, the investigation does not necessarily support the presumed association with heightened AKI susceptibility due to aggravated atherosclerosis. However, inflammatory rheumatic diseases can also contribute to morbidities beyond the cardiovascular system. These can be particularly relevant to nephrology and may increase the risk of AKI. Periodontitis for instance, a multifactorial inflammatory disease of the tissues surrounding the teeth [82], could be of particular interest. Periodontitis has been reported to be related to systemic rheumatic diseases, especially due to common risk factors [83]. Recent literature indicates potential bidirectional interrelationships between rheumatic diseases (especially RA) and periodontitis, such as the affected citrullination of antibodies caused by periodontal bacteria [84]. These bacteria, primarily *Porphyromonas gingivalis*, can promote autoimmune inflammatory diseases by inducing the activation of the inflammasome [85]. On the other hand, periodontal diseases are reported to be related to kidney diseases. Although not fully clarified, several mechanisms appear to connect periodontitis and chronic kidney failure [86], as supported by a recent meta-analysis [87]. Furthermore, oral bacteria can potentially cause intestinal nephritis, leading to AKI [88]. Therefore, oral and particularly periodontal inflammation might represent a further link between rheumatic diseases and kidney injury. This example highlights the potential relevance of inflammatory comorbidities and offers another field for future research. However, by applying the search terms "AKI risk" and "rheumatic diseases", a total of 18 references were found (as of May 2024). No study provides satisfactory conclusions on the subject. Undoubtedly, there is a significant data gap that needs to be addressed in the coming years.

## Conclusions

AKI is a potentially significant issue for patients with inflammatory rheumatic diseases. The risk of AKI is elevated not only due to possible direct kidney involvement from the underlying disease but also significantly due to the uncontrolled use of NSAIDs. It is suspected that individuals with inflammatory rheumatic diseases are already at risk of developing AKI resulting from the proatherogenic/inflammatory activity of the underlying condition itself. However, data on this latter aspect are still very limited.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

## Author Contributions

Daniel Patschan wrote the article. Gerhard Schmalz provided substantial information on oral health in rheumatic diseases. Wajima Safi, Friedrich Stasche, and Igor Matyukhin searched for references. Oliver Ritter assisted in writing. Susann Patschan designed the article, assisted in reference collection and writing.

## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

## Abbreviations

AAV: ANCA-associated vasculitis; AKI: acute kidney injury; ANCA: anti-neutrophil cytoplasmic antibodies; AS: ankylosing spondylitis; ATN: acute tubular necrosis; CG: cryoglobulinemia; CKD: chronic kidney disease; COX: cyclooxygenase; DMARDs: disease-modifying anti-rheumatic drugs; bDMARDs: biologic disease-modifying anti-rheumatic drugs; bsDMARDs: biosimilar disease-modifying anti-rheumatic drugs; tsDMARDs: targeted synthetic disease-modifying anti-rheumatic drugs; DM: dermatomyositis; GN: glomerulonephritis; HA: hyaluronic acid; HSP: Henoch-Schonlein purpura; IMNM: immune-mediated necrotizing myopathy; KDIGO: Kidney Disease Improving Global Outcomes; KRT: kidney replacement therapy; LN: lupus nephritis; NSAID: non-steroidal anti-inflammatory drugs; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; SpA: spondylarthritis

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