ORIGINAL ARTICLE

Acute interstitial nephritis in adults: A retrospective case series from a nephrology center in Tunisia

Néphrite interstitielle aiguë chez l'adulte : Une série de cas rétrospectifs d'un centre de néphrologie en Tunisie et revue de la littérature

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Abstract

Introduction-Aim: Acute interstitial nephritis (AIN) shows variability in incidence and etiology based on geography. The study aimed to understand the characteristics and root causes of AIN, its diagnosis methods, treatment strategies, and results within a Tunisian population.
Method: We retrospectively gathered data on biopsy-proven AIN from a Nephrology center over 16 years.
Results: We gathered 36 confirmed cases of biopsy-proven AIN. The average age of the patients was 50.58 years. The predominant clinical signs were fatigue (58%) and fever (22%). The mean level of creatinine was 691.58 µmol/l. Interstitial infiltrate was significant in 52.77% of cases, with eosinophils present in only 5.55% of cases and fibrosis noted in 27.77% of cases. Drug-related causes accounted for 46.66% of AIN cases, while infections and systemic diseases accounted for 16.66% and 11.11%, respectively. We have identified two exceptional causes of AIN, one associated with treatment with Rituximab and the other with a triple parasitic infection. Some cases (25%) lacked an identifiable cause. Corticosteroid treatment was recommended for 93.33% of cases. The median follow-up duration was 2.2 years. Seven patients required hemodialysis, and 71.42% recovered renal function. The presence of interstitial fibrosis correlated with the progression to chronic kidney disease.
Conclusion: AIN is a leading cause of acute kidney injury that can progress to chronicity. Interstitial fibrosis is associated with the progression of chronic kidney disease. The primary etiology is drug intake, and some causes are yet to be identified.

Key words: Nephritis, Acute kidney injury, Drug, Fibrosis, Acute interstitial nephritis

Résumé

Introduction-Objectif: La néphrite interstitielle aiguë (NIA) présente une variabilité géobraphique d'incidence et d'étiologie. Le but de ce travail était d'étudier les caractéristiques et les étiologies de la NIA, ses moyens diagnostics et thérapeutiques ainsi dans une population tunisienne.
Méthodes: L'étude était rétrospective incluant les cas de NIA prouvée par biopsie dans un centre de néphrologie sur une période de 16 ans.
Résultats: Nous avons recueilli 36 patients âgés en moyenne de50,58 ans. Les signes cliniques prédominants étaient la fatigue (58%) et la fièvre (22%). Le taux moyen de créatinine était de 691,58 µmol/l. L'infiltrat interstitiel était significatif dans 52,77% des cas, avec des éosinophiles présents dans 5,55% des cas et une fibrose notée dans 27,77% des cas. Les causes médicamenteuses représentaient 46,66 % des cas de NIA et les infections et les maladies systémiques étaient responsables de 16,66 % et 11,11 % des cas respectivement. Nous avons identifié deux causes exceptionnelles de NIA, l'une associée au traitement par Rituximab et l'autre à une triple infection parasitaire. Certains cas (25%) n'avaient pas de cause identifiable. Une corticothérapie a été recommandée dans 93,33% des cas. La durée médiane du suivi était de 2,2 ans. Sept patients ont dû être hémodialysés et 71,42 % ont récupéré leur fonction rénale. La fibrose interstitielle était corrélée à l'évolution vers une maladie rénale chronique.
Conclusion: La NIA est une cause majeure d'insuffisance rénale aiguë qui peut évoluer vers la chronicité. L'étiologie principale est médicamenteuse et certaines causes sont encore méconnues.

Mots clés: Néphrite, insuffisance rénale aiguë, médicament, fibrose, néphrite interstitielle aiguë.

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What is known: Acute interstitial nephritis is a curable cause of acute renal failure. The main cause is drug-induced.

What this article adds: The etiologies of acute interstitial nephriitis are not yet fully understood, although some causes are exceptional

Introduction

Acute interstitial nephritis (AIN) accounts for 2-3% of renal biopsies and up to 27% of biopsies for acute kidney injury (AKI) diagnosis [1]. Histopathological confirmation is often necessary [2].

Drug-related factors are the primary cause (70% of cases) [3,4]. AIN can also stem from infections, autoimmune conditions, or infiltrative diseases, rarely being idiopathic [5].

Several studies have demonstrated regional variations in the causes of AIN, possibly influenced by differences in infection rates and medication usage [6]. Additionally, an increasing number of cases among the elderly have been reported [7]. with notable changes in clinical manifestations and treatment approaches [8-10].

To address the lack of data on AIN in Tunisian adults, this study was conducted to provide insights into its characteristics, underlying causes, diagnostic processes, treatment approaches, and outcomes in a Tunisian population.

Methods

This study was a retrospective observational and analytic review conducted at a single Nephrology center. We investigated patients aged 15 years and above diagnosed with AIN based on renal biopsies of native kidneys spanning from January 1, 2006, to December 31, 2021, covering a 16-year period. The study involved gathering epidemiological, clinical, biological, and histological data, as well as details on treatment and patient outcomes. Information was obtained from patient records and the Pathology department's database, excluding cases with incomplete records.

Glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula, while acute kidney injury was determined based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria [11].

Recovery of renal function after an episode of AKI was assessed based on the eGFR. It could be complete, partial, or absent.

The stages of chronic kidney disease (CKD) were classified according to KDIGO recommendations as follows [12]:

Stage 1: Kidney damage with normal or increased GFR (> 90 mL/min/1.73 m2)

Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m2)

Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m2)

Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m2)

Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m2)

Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m2 or dialysis)

Proteinuria was considered positive at a level of 500 mg/d and nephrotic syndrome (NS) was defined as proteinuria was ≥ 3.5 g/day/1.73 m2 and blood albumin level was lower than 30 g/L.

The diagnosis of AIN relied on the presence of cellular infiltrate in histological analysis.

Statistical analyses were conducted using SPSS (Statistical Package for Social Sciences) software version 23. Qualitative variables were presented in frequencies and percentages. We analyzed quantitative variables by calculating their means, medians, standard deviations, and identifying extreme values.

The analytical study was conducted using the Chi-square test for comparing two percentages and the Student's t-test for comparing two means. The significance level was set at 5%.

For multivariate analysis, we included in the binary logistic regression the variables with a p-value < 0.2 in the univariate analysis. We retained the variables that were statistically significantly associated with a 5% error risk.

Results

A total of 40 cases of biopsy- proven AIN were collected between 2006 and 2021, representing 2.84% of all renal biopsies performed during this period, or a total of 1407 cases. In consideration of the inclusion and exclusion criteria, 36 cases of AIN were included in this study.

The mean incidence was 2.25 cases per year. The study population consisted of 21 females and 15 males, resulting in a sex ratio of 0.71. The mean age of the patients was 50.58 ± 17.76 years, with a range of 15 to 78 years.

Hypertension was the most common comorbidity among the patients. Fatigue was the predominant symptom reported at the initial presentation, while fever was the most frequently observed clinical sign during examination (see table 1).

Table1. Clinical data of patients with biopsy-proven AIN

	Number, %
Comorbidities	*HTN (n=11, 30.55%), diabetes mellitus (n=5, 13.88%), atopy (n=4, 11.11%), peripheral hypothyroidism (n=4, 11.11%), CKD (n=2, 5.55%), systemic sclerosis (n=1, 2.77%), mantle cell lymphoma (n=1, 2.77%), and IgA nephropathy (n=1, 2.77%)*
Initial clinical presentation	***Symptoms**: fatigue (n=21, 58%), inflammatory poly-arthralgia of the large joints (n=14, 38.9%), abdominal pain (n=12, 33.3%), anorexia (n=19, 52.8%), nausea and vomiting (n=13, 36.1%), dry cough (n=7, 22.2%), and xerostomia (n=6, 16.6%).*
	***Examination signs**: acute lung edema (n=1, 2.77%), hypertension (n=3, 8.33%), fever (8, 22%), urticaria (7, 19%), maculopapular lesions (1, 2.77 %), bilateral anterior uveitis (2, 5.54%), unilateral anterior uveitis (n=1, 2.77%), scleritis (n=1, 2.77%), hepatomegaly and splenomegaly (n=3, 8.33%), oligoanuria (n=5, 13.88%), polyuria (n=2, 5.54%) and peripheral edema (n=5, 13.88%)*

CKD: chronic kidney disease, **HTN**: arterial hypertension, **HSM**: Hepatosplenomegaly

Previous renal function was known in two cases, with one patient exhibiting CKD stage 2 and the other exhibiting CKD stage 3a. At presentation, the serum creatinine level was, on average, 691.583 ± 456.043 µmol/L.

Hyperkalemia was noted in three cases (8.33%), anemia in 30 (83.33%), eosinophilia in 14 (38.88%), biological inflammatory syndrome in 12 (33.33%), hepatic cytolysis in four (11.11%), leukocyturia in 21 (58.33%), and microscopic hematuria in nine (25%). A urinary infection was found in four patients and NS was defined in one patient (see Table 2).

Table 2. Biochemical features at presentation of patients with biopsy proven AIN

Parameter	Average	Range
Plasma Creatinine	691,58± 456,04 [141 ; 1949]	49-90 µmol/L
Urea	22,01 ± 10,84	2.8-7.2 mmol/L
Hemoglobin	10 ±1,89	12-16 g/dL
Eosinophils	481,66 ± 375,83 [20 ; 2160]	0,1-0,5 × 10^9/L
Plasma protein	70,18±11,27 [33 ; 88]	66-83 g/L
Plasma albumin	32,26±6,62 [10.5 ; 41.8]	35-52 g/L
C-reactive protein	66,51 [1 ; 218]	≤ 5 mg/L
Urinary albumin	1,02 ±1,17 [0,13 ; 5,2]	<0.3g/ d
Urinary leukocytes	113,13 [0 ; 1600]	< 10 mm^3
Urinary red blood cells	73 [0; 1400]	< 10 mm^3

Table 1 exposes the clinical para-clinical characteristics of the 15 patients.

The presence of antinuclear antibodies was evaluated in 22 patients, with positive results observed in three individuals (8.33%). Anti-SSA and anti-SSB antibodies were tested in four patients, with positive results observed in two cases (5.55%). Total immunoglobulin E (IgE) level was quantified in 10 patients, with elevated level observed in four of them. One patient underwent IgG level measurement, which returned elevated with a high IgG4.

Renal ultrasound revealed that four patients (11.11%) exhibited enlarged kidneys, while the remaining patients exhibited normal renal ultrasound findings.

The diagnosis of AIN was based on the results of a renal biopsy. The histological findings are detailed in Table 3.

Table 3. Histological findings in biopsy-proven AIN

	Number, %
Interstitial lesions	***Infiltrate:***
	-Intensity: Significant (n=19, 52.77%), moderate (n=16, 44.44%), discreet (1, 2.77%).
	-Cells: EOS (2, 5.55%), NEUT (n=20, 55.55%, LYMPH (N=5, 13.88%), plasma cells (n=15, 44.66%), histiocytes (n=4, 11.11%), polymorph (n=10, 27.77%)
	- Granulomatous (n=5, 13.88%)
	***Oedema** (n=25, 69.44%)*
	***Fibrosis:** discreet (n=2, 5.55 %), moderate (n=6, 16.66%), significant (n=2, 5.55)*
Tubular lesions	*ATN (n=4, 11.11%), tubulitis (n=4, 11.11%), tubular atrophy (n=8, 22.22%)*
Glomerular lesions	*Mesangial proliferation (n=1, 2.77%)*
Vascular lesions	*fibrous endarteritis (n=3, 8.33%)*
Immunofluorescence examination	*IgA (n=1, 2.77%)*
Immunohistochemistry examination	*IgG4 (n=1, 2.77%)*

EOS: eosinophils, **NEUT**: neutrophils, **LYMPH**: lymphocytes, **IgA**: Immunoglobulin A, **IgG4**: Immunoglobulin G4

The final clinical and histological diagnoses were primarily drug-induced AIN, observed in 15 patients (41.66%). Among the cases, one was identified as a non-immune-allergic drug reaction due to rituximab (anti-CD20 monoclonal antibody) in one patient. This was a sarcoidosis-like reaction, which was treated with r-CHOP (rituximab + cyclophosphamide, doxorubicin, vincristine, and prednisone) for mantle cell lymphoma.

Infection was identified in 16.66% of cases. In addition to acute bacterial pyelonephritis, AIN was para-infectious following a multiple parasitic infection. The patient was a 61-year-old individual who presented with a fever, a diffuse pruritic maculopapular rash, purpura in the lower extremities, and watery diarrhea. A stool parasitological examination revealed the presence of Giardia lamblia, Entamoeba coli, and Endolimax nana.

The various causes of AIN encountered in our series are presented in Table 4.

Table 4. Etiology of biopsy-proven AIN

Drugs (41.66%)	Immune allergic pathway (14*): NSAID (6), Amoxicillin-clavulanic acid (2), Amoxicillin (1), Cefixime (1), Gentamicin + NSAIDs (1), NSAIDs + Macrolide (1), Captoril (1), Acetaminophen (1)*
	Non immune-allergic pathway (1): *Rituximab (anti-CD20 monoclonal antibody)*
Infections (16.66%)	*Bacterial acute pyelonephritis (5): Escherichia coli (3) , Klebsiella pneumoniae (1), and Pseudomonas aeruginosa (1).*
Associated with systemic disease (11.11%)	*para-infectious parasitic AIN (1): Giardia lamblia + Entamoeba coli + Endolimax nana.*
	primary Sjögren's syndrome (1), SLE (1), systemic sarcoidosis (1), IgG4-related disease (1)
Paraneoplastic interstitial nephropathy (2.77%)	pancreatic neuroendocrine tumor (1)
TINU (2.77%)	
Idiopathic (25%)	

NSAID: nonsteroidal anti-inflammatory drug, **SLE**:Systemic lupus erythematosus, **TINU**: tubulointerstitial nephritis and uveitis syndrome

A review of the clinical and paraclinical presentations of patients with AIN based on the etiology revealed that fever was present in five patients with drug-induced immune-allergic AIN, one patient with an infectious cause, one patient with sarcoidosis, and one patient with idiopathic AIN. In all cases, urticaria was drug-induced immune-allergic, while the maculopapular rash was linked to a triple parasitic infection. The patient who had a NS had an NSAID-induced AIN. Enlarged kidneys were associated with infectious AIN, paraneoplastic AIN, and drug-induced immune-allergic AIN due to beta-lactam antibiotics. Patients with significant interstitial fibrosis had a known CKD.

Given that immune-allergic AIN was the most incriminated cause in AIN, we compared the epidemiological, clinical, biological, and anatomopathological data of patients with immune-allergic AIN with those of the rest of the patients. This comparison revealed that cutaneous signs, microscopic hematuria, and hypereosinophilia were significantly higher in patients with immune-allergic AIN with p-values of 0.002, 0.02, and 0.04, respectively. There was no significant difference for the remaining

parameters.
A total of seven cases (19.44%) required hemodialysis sessions during the acute phase of the disease.
For patients with drug-induced AIN, it was recommended that all patients discontinue any suspected medication. Corticosteroid therapy was indicated in 14 cases of them (93.33%), on average 10 days after the diagnosis of AIN, using oral prednisolone at a dose of 0.5 to 1 mg/kg/day for one month, followed by gradual tapering. In the case of the patient with drug-induced AIN and a sarcoid-like reaction, oral corticosteroid therapy was initiated at a dose of 1 mg/kg/day. Patients with AIN associated with systemic diseases and those of undetermined origin received oral corticosteroid therapy at a dose of 1 mg/kg/day and 0.5 mg/kg/day, respectively. The patient with IgG4-related AIN was administered 0.6 mg/kg/day of prednisone. Patients with infectious AIN were administered appropriate antibiotic therapy. Infections were observed in two patients receiving corticosteroid therapy. One patient developed herpetic uveitis, while the other developed a common bacterial pneumonia.
The median follow-up duration was 2.2 years. A total of five patients were lost to follow-up, representing 16.66% of the total number of patients. One patient died at home, the cause of death being undetermined.
The evolution of renal function was assessed according to eGFR in patients, after excluding known chronic renal failure patients, those lost to follow-up, and those who died. The mean creatinine level at the conclusion of the follow-up period was 176.77 µmol/l (range: 64–1000), with a median eGFR of 57.62 ml/min/1.73m2 (range: 4.1–124.6).
At the conclusion of the follow-up period in our study, 20 patients (71.42% of the total) demonstrated a recovery of renal function, with eGFR of at least 90 ml/min/1.73 m2 for 13 patients (46.42%) and an eGFR between 60 and 90 ml/min/1.73 m2 for seven patients (25%).
Eight patients (28.57%) did not regain normal renal function and progressed to chronic kidney disease (CKD). The distribution of these patients was as follows: Two patients exhibited CKD stage 3a, one patient exhibited CKD stage 3b, two patients exhibited CKD stage 4, and one patient exhibited CKD stage 5. Two patients required chronic hemodialysis (7.14%).
The predictive factors for progression CKD were determined using a univariate statistical study. We identified the interstitial fibrosis as the only predictor of progression to CKD (p=0.004). Multivariate analysis showed that interstitial fibrosis was an independent factor associated with CKD progression (OR=14.27; 95% CI=1.1-170.3; p=0.036).

Discussion

In this study, we reviewed all patients with biopsy-proven AIN followed at a single Tunisian adult Nephrology center. The prevalence of AKI (2.8% among all kidney biopsies) in this series was the same as that of other studies where it was 2-3% [1].
The mean age of our patients was 50.58 years. Our results are consistent with those documented in various studies, which show an average age range of 40 to 65 years [7,9]. The adult population, especially those aged 61 to 75 years, were most affected. This is consistent with similar observations in other studies [13]. This pattern may be related to the higher medication use of these patients and their increased life expectancy.
In our study, 22.2% of patients experienced fever, with a notable link to drug-induced causes. A skin rash was observed in 19.4% of our patients, and in 85.71% of cases, it was associated with immune-allergic AIN. These findings are consistent with other studies [14,15].
The gold standard for establishing a definitive diagnosis of AIN is renal biopsy [16]. Several studies in the literature have demonstrated the diagnostic value of renal biopsy in cases of unknown origin of acute kidney injury [7,13]. Recently, the urinary level of CXCL9 has been validated as a biomarker for the diagnosis of AIN [6] and it has also shown that some AIN etiologies can be detected by Positron-Emission Tomography-Computed Tomography Imaging [17,18].
An inflammatory infiltrate in the renal interstitium is a key indicator of this kidney disease, predominantly located in the renal cortex [4]. The distribution of the infiltrate and the dominant cell type varied in our study. Eosinophils (EOS) were found in only 5.55% of all biopsies in our study, they were associated with an immune-allergic etiology in 50% of cases. In the literature, the presence of EOS in histology ranges from 18 to 94% [9,19]. The presence of EOS in the inflammatory infiltrate in immune-allergic AIN suggests the involvement of allergic hypersensitivity mechanisms [20].
Histologic examination revealed interstitial fibrosis in 27.77% of patients. In fact, kidney damage during AIN progresses to fibrosis and this progression typically occurs within 7 to 10 days following the onset of the acute inflammatory process [3]. The development towards interstitial fibrosis and tubular atrophy can be prevented by avoiding the offending agent or promptly initiating steroid treatment [21]. Review of the histologic features of AIN in our series, led us to believe that renal biopsy remains an important tool in cases of AIN, because even if the diagnosis can be made by other means [6], evaluation of the renal parenchyma remains important for prognostic purposes, given the high number of biopsies containing interstitial fibrosis and the high number of associated tubular lesions found in our patients.
In our series, 41.66% of all patients had immune-allergic AIN. In our series, NSAID were the most common cause of immune-allergic AIN. Other authors reported that NSAID were the second most common cause after antibiotics in the etiology of immune-allergic AIN [9].
Our series included one patient who presented with an unusual drug-associated AIN. This was a renal sarcoid-like reaction associated with rituximab after r-CHOP treatment for mantle cell lymphoma [22].
In different studies, the frequency of infectious interstitial nephritis (IIN) ranged from 3% to 15% [14]. In our study, IIN accounted for 13.88% of cases. We observed a severe case associated with dermatitis and hemolytic anemia in a patient with a triple parasitic infection, a first reported

case [20].
NITU was diagnosed in only one of our patients. We believe that some of the idiopathic cases of AIN in our series are actually cases of TINU, since ocular abnormalities may appear later than renal damage [23]. Hence the importance of ophthalmological follow-up of patients with idiopathic AIN.
Discontinuation of the suspected causative medication is the primary approach in treating drug induced AIN [4]. If kidney function does not show signs of recovery within 5–7 days after discontinuing the suspected medication, studies recommend initiating treatment with steroids [4]. Prednisolone is consistently described as the reference molecule. The initial dose varies from 0.5 mg/kg/day to 1 mg/kg/day depending on the series [15,24]. However, intravenous methylprednisolone therapy at a dose of 500 mg/day for 3 days followed by oral corticosteroid therapy may be proposed [3]. In view of the rapid onset of interstitial fibrosis in AIN, as demonstrated in this series, we recommend early initiation of corticosteroid therapy in this etiology of AIN within no more than 7 days of diagnosis, since discontinuation of the drug alone would not be sufficient to repair the histological damage.
The time to renal recovery in AIN is often described in the literature as highly variable. In our series, the evolution of renal function was generally favorable. Twenty patients, or 71.42% of cases, achieved renal recovery. Our results are similar to those reported in the literature (18,25).
At the end of follow-up in our series, two of our patients were on end-stage hemodialysis. This result is comparable with those published in the literature, with a rate varying between 4% and 14% [9].
In the AIN, mortality is rarely linked to renal damage [26]. There were no deaths in the acute phase of AIN in our study. The only death was of undetermined cause remote from the AIN episode.

Strengths and limitations of the study
The limitations of our study were primarily the number of cases and the retrospective nature of our research. However, in the literature, most studies on AKI were retrospective and based on data from renal biopsy registries.
The main strengths were the diversity of pathological conditions associated with AIN including some exceptional causes.

Conclusion

This study confirms that AIN is a common cause of AKI and also a significant contributor to CKD. Our findings also confirmed that the clinical presentation of AIN can be misleading with nonspecific symptoms at times. In this series, the etiology of AIN was predominantly drug-induced immune-allergic; however, a significant rate of idiopathic AIN was identified. The etiological spectrum of AIN remains broad, including rare and likely still unrecognized causes. The anatomoclinical correlation in AIN underscores the crucial role of renal biopsy in diagnosis and prognostication of the disease. Initiating treatment promptly is advisable to improve prognosis and limit progression of histological lesions towards chronicity.

References

1. Perazella MA, Markowitz GS. Drug-induced acute interstitial nephritis. Nat Rev Nephrol. 2010;6(8):461-70.
2. Donati A, Krishnan N. Should Corticosteroids Be Used to Treat Biopsy-Proven Drug-Induced Acute Interstitial Nephritis?: PRO. Kidney360. 2022;3(8):1306-1309.
3. Praga M, González E. Acute interstitial nephritis. Kidney International.2010;77(11):956-61.
4. Caillard S, Moulin B. Néphropathie interstitielle immuno-allergiqueDrug-induced acute interstitial nephritis. Réanimation.2003;12(4):306-12.
5. Raghavan R, Shawar S. Mechanisms of Drug-Induced Interstitial Nephritis. Adv Chronic Kidney Dis.2017;24(2):64-71.
6. Moledina DG, Obeid W, Smith RN, Rosales I, Sise ME, Moeckel G, et al. Identification and validation of urinary CXCL9 as a biomarker for diagnosis of acute interstitial nephritis. J Clin Invest. 2023;133(13):e168950.
7. Goicoechea M, Rivera F, Lopez-Gomez JM, on behalf of all the members of the Spanish Registry of Glomerulonephritis. Increased prevalence of acute tubulointerstitial nephritis. Nephrology Dialysis Transplantation. 2013;28(1):112-5.
8. Roy S, Awogbemi T, Holt RCL. Acute tubulointerstitial nephritis in children- a retrospective case series in a UK tertiary paediatric centre. BMC Nephrol. 2020;21(1):17.
9. Muriithi AK, Leung N, Valeri AM, Cornell LD, Sethi S, Fidler ME, et al. Biopsy-Proven Acute Interstitial Nephritis, 1993-2011: A Case Series. American Journal of Kidney Diseases. 2014;64(4):558-66.
10. Praga M, Sevillano A, Auñón P, González E. Changes in the aetiology, clinical presentation and management of acute interstitial nephritis, an increasingly common cause of acute kidney injury. Nephrol Dial Transplant. 2015;30(9):1472-9.
11. Khwaja A. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. Nephron Clin Pract. 2012;120(4):c179-84.
12. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4S):S117-S314.
13. Davison A. Acute interstitial nephritis in the elderly: a report from the UK MRC glomerulonephritis register and a review of the literature. Nephrology Dialysis Transplantation. 1998;13(90007):12-6.
14. Muriithi AK, Leung N, Valeri AM, Cornell LD, Sethi S, Fidler ME, et al. Clinical characteristics, causes and outcomes of acute interstitial nephritis in the elderly. Kidney International. 2015;87(2):458-64.
15. Valluri A, Hetherington L, Mcquarrie E, Fleming S, Kipgen D, Geddes CC, et al. Acute tubulointerstitial nephritis in Scotland. QJM. 2015;108(7):527-32.
16. Kodner CM. Diagnosis and Management of Acute Interstitial Nephritis. 2003;67(12).
17. McCammack KC, Hawkes NC, Silverman ED, Paz DA. PET/CT appearance of acute pyelonephritis. Clin Nucl Med. 2013;38(7):e299-301.
18. Miao J, Alexander MP, Zoghby ZM. Acute Interstitial Nephritis on Positron-Emission Tomography-Computed Tomography Imaging. Kidney Medicine. 2022;4(11):100552.
19. Clarkson MR. Acute interstitial nephritis: clinical features and response to corticosteroid therapy. Nephrology Dialysis Transplantation.2004;19(11):2778-83.
20. Mrabet S, Romdhane W, Fradi A, Boukadida R, Azzabi A, Guedri Y, et al. Severe Acute Interstitial Nephritis, Dermatitis, and Hemolytic Anemia due to Polyparasitic Infection in an Immunocompetent Male Patient. Am J Mens Health. 2022;16(6):15579883221139914.
21. González E, Gutiérrez E, Galeano C, Chevia C, de Sequera P, Bernis

C, et al. Early steroid treatment improves the recovery of renal function in patients with drug-induced acute interstitial nephritis. Kidney International. 2008;73(8):940-6.

22. Mrabet S, Dahmene R, Fradi A, Jaziri A, Boukadida R, Azzebi A, et al. Sarcoid-Like Reaction in the Kidney Following Rituximab for Mantle Lymphoma in a 60-Year-Old Man. Am J Mens Heal th.2023;17(2):155798832311593.
23. Saarela V, Nuutinen M, Ala-Houhala M, Arikoski P, Rönnholm K, Jahnukainen T. Tubulointerstitial nephritis and uveitis syndrome in children: a prospective multicenter study. Ophthalmology. 2013;120(7):1476-81.
24. Prendecki M, Tanna A, Salama AD, Tam FWK, Cairns T, Taube D, et al. Long-term outcome in biopsy-proven acute interstitial nephritis treated with steroids. Clin Kidney J. 2016;sfw116.
25. Su T, Gu Y, Sun P, Tang J, Wang S, Liu G, et al. Etiology and renal outcomes of acute tubulointerstitial nephritis: a single-center prospective cohort study in China. Nephrology Dialysis Transplantation. 2018;33(7):1180-8.
26. Naqvi R, Mubarak M, Ahmed E, Akhtar F, Naqvi A, Rizvi A. Acute tubulointerstitial nephritis/drug-induced acute kidney injury; an experience from a single center in Pakistan. J Renal Inj Prev. 2016;5(1):17-20.