RESEARCH ARTICLE

Etiological spectrum and short-term outcomes of acute kidney injury in hospitalised patients of uncertain aetiology who underwent percutaneous renal biopsy

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Abstract_

Objective: To analyse the aetiological spectrum, clinical presentation and short-term renal outcomes of patients with acute kidney injury of uncertain aetiology subjected to percutaneous renal biopsy.

Method: The prospective, cohort study was conducted at the Sindh Institute of Urology and Transplantation, Karachi, from March 1 to October 30, 2024, and comprised hospitalised acute kidney injury patients of either gender aged 18-75 years who had been subjected to percutaneous renal biopsy. The patients were followed up for at least three months from the time of the biopsy. Data was analysed using SPSS 26.

Results: Of the 115 patients with mean age 32.61±10.20 years, 60(52.2%) were females and 55(47.8%) were males. The mean estimated glomerular filtration rate was 23.05±18.62ml/min/1.73m^2. Over half 62 (53.9%) required kidney replacement therapy at presentation. Most patients 104(90.4%) had renal involvement due to glomerulopathy, while the rest exhibited non-glomerular renal disease. The most common primary glomerular diseases were focal segmental glomerulosclerosis 26(22.6%), membranoproliferative glomerulonephritis 16(13.9%) and membranous nephropathy 4(3.5%). The leading secondary glomerular diseases were pauci-immune necrotising glomerulonephritis 18(15.7%), thrombotic microangiopathy 16(13.9%) and lupus nephritis 8(7.0%). At 3-month follow-up, 43(37.4%) achieved complete recovery, 34(29.6%) achieved partial recovery and 38(33%) showed no recovery, while 4(3.4%) patients from the no recovery group expired at the time of the last follow-up. Patients who required kidney replacement therapy on admission had lower rates of complete recovery ($p < 0.001$), with more patients progressing to end-stage kidney disease ($p=0.02$) and increased mortality ($p=0.08$).

Conclusion: Most biopsied acute kidney injury patients had coexisting glomerular disease with worse renal recovery, while acute tubular necrosis alone was less frequent.

Keywords: Acute kidney injury, End-stage kidney disease, Glomerular diseases, Kidney replacement therapy, Percutaneous renal biopsy. (JPMA 75: 25; 2025)

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Introduction

Acute kidney injury (AKI) is a multifaceted and varied clinical syndrome, characterised by a rise in serum creatinine levels, with or without decreased urine output, occurring over a period of hours to days.[1]

The extent of injury can range from mild impairment to severe kidney failure, sometimes necessitating dialysis.[2] AKI is closely linked to an increased risk of mortality, and is a significant risk factor for the development of chronic kidney disease

(CKD) and end-stage kidney disease (ESKD).[3] The diagnostic evaluation can be used to classify AKI as pre-renal AKI, which results from inadequate perfusion of the kidneys, and post-renal AKI, which results from obstruction to the flow of urine, and renal AKI, which can be due to injury or dysfunction of the renal glomeruli, tubules, interstitium or blood vessels.[4]

Most cases of AKI can be diagnosed through clinical history, physical examination, and urine, blood and radiology tests.[5-6] Recent studies have highlighted the use of novel kidney injury biomarkers to improve early diagnosis, and pinpoint the cause of AKI.[6] Establishing a specific cause of AKI can be challenging in complex clinical settings. When pre-renal and post-renal causes are ruled out and the intrinsic cause remains unclear, percutaneous renal biopsy (PRB) becomes a crucial diagnostic tool to determine the underlying aetiology.[7] PRB is essential for accurate diagnosis, treatment and prognosis prediction in AKI. Despite AKI being a common complication in 10-20% of hospital admissions, only a small proportion of cases undergo PRB.[8]

Patients undergoing PRB for AKI evaluation are at a higher

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risk of complications, particularly those with lower pre-biopsy haemoglobin (Hb) levels and higher baseline serum creatinine levels.[9] Clinicians must carefully consider the diagnostic uncertainty and potential therapeutic benefits of a PRB in patients with AKI, weighing these against the associated risks. It is also essential to implement all necessary precautions to prevent complications during the procedure.[10] Most existing literature primarily focusses on the frequency and outcomes of AKI, regardless of its underlying aetiology, whether pre-renal, renal or post-renal.[11] Additionally, some studies report only histopathological features of AKI without providing follow-up or outcome data[12], and those that do report outcomes are typically retrospective in nature.[13-14]

There is a knowledge gap due to the lack of prospective data on the topic. The current study was planned to address this gap by determining the aetiology of renal disease in hospitalised patients with AKI who underwent PRB, and to evaluate their short-term outcomes.

Patients and Methods

The prospective, cohort study was conducted at the Sindh Institute of Urology and Transplantation, Karachi, from March 1 to October 30, 2024. After approval from the institutional ethics review board, the sample size was calculated using the World Health Organisation (WHO) calculator[15] based on previous estimates[16] of 59.6% complete recovery (CR) with 5% margin of error and 95% confidence interval (CI). The sample was raised using consecutive sampling technique. Those included were hospitalised AKI patients of either gender aged 18-75 years who met the Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria[17] and were then subjected to PRB for histological diagnosis of their renal disease. The patients were followed up at the renal clinic for at least three months after PRB. Patients with pre-existing renal disease, prior imaging studies with contrast agents, those with pre-renal and post-renal AKI, or those who did not require renal biopsy were excluded. Written informed consent was obtained from each participant or their blood relative.

Demographic and clinical characteristics of the patients were collected at baseline using a predesigned proforma. The variables included age, gender, body mass index (BMI), duration of symptoms before presentation, the presence of hypertension (HTN), diabetes mellitus (DM) or cardiovascular disease (CVD), smoking status, obesity, autoimmune history, obstetric history, and family history of renal disease. Additionally, the use of nephrotoxic medications, extra-renal manifestations, as well as signs and symptoms on physical examination, such as HTN, oedema, rash, and other indicators, were recorded. Further data included the length of hospital stay (LOS), the requirement for mechanical ventilation (MV), plasmapheresis, inotropic support, and the need for kidney replacement therapy (KRT).

Laboratory parameters included serum creatinine and albumin levels, urine detailed report (DR), spot urine protein-to-creatinine ratio (UPCR), and 24-hour urinary protein. Serological examinations were performed when glomerulonephritis or vasculitis was suspected, which included tests for anti-nuclear antibody (ANA), anti-double-stranded deoxyribonucleic acid (dsDNA), serum complement levels C3 and C4 (expressed as low or normal), anti-phospholipid antibodies (APLA), extractable nuclear antigen (ENA), anti-phospholipase A2 receptor (anti-PLA2R) antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), anti-glomerular basement membrane (anti-GBM) antibodies, and anti-streptolysin O titer (ASOT). The estimated glomerular filtration rate (eGFR) was calculated using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation.[18] All patients underwent kidney and urinary tract ultrasonography, with the length of the kidneys recorded for each patient.

1. Two renal pathologists, one with over 20 years of experience and the other with 10 years, independently reported all histological diagnoses. In cases of discrepant results, they combined their findings to reach a consensus. Both the pathologists were blinded to patient outcomes. All cases were classified into three broad categories. The first category was primary glomerular diseases (PGD), including minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), immunoglobulin A (IgA) nephropathy (IgAN), membranous nephropathy (MN), membranoproliferative glomerulonephritis (MPGN) and others. The second category was secondary glomerular diseases (SGD), including pauci-immune necrotising glomerulonephritis (PING), lupus nephritis (LN), diabetic nephropathy (DN) and others. The third category was non-glomerular diseases, such as acute interstitial nephritis (AIN) and others including acute tubular necrosis (ATN).

Serum creatinine level and eGFR were evaluated upon admission, during hospitalisation, at 1 month, and 3 months after discharge. The reading that showed the lowest level during hospitalisation was considered the baseline serum creatinine level because laboratory data prior to hospitalisation was unavailable. The highest serum creatinine level during hospitalisation was used to diagnose AKI. Disease-specific treatment was administered based on the underlying cause of AKI. The management of AKI followed standard protocols, and short-term outcomes were recorded.

Recovery of the kidney function was assessed based on the latest eGFR value available within 3 months after PRB. CR was defined as eGFR >60mL/min/1.73m^2. Partial recovery (PR) was defined as eGFR 15-60mL/min/1.73m^2. No recovery (NR) was defined as eGFR <15mL/min/1.73m^2 or the need for maintenance dialysis.

Data was analysed using SPSS 26. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR). Categorical variables were expressed as frequencies and percentages. Parametric distribution was confirmed using the Shapiro-Wilk test. Independent t-test was used for inferential analysis, and the chi-square test was used for nominal variables. P< 0.05 was considered statistically significant.

Results

Of the 115 patients with mean age 32.61±10.20 years, 60(52.2%) were females and 55(47.8%) were males. The sample had a median symptom duration of 14 days (IQR: 3-45 days). Most patients 88(76.5%) had nephrotic-range proteinuria, and 48(41.7%) were oliguric. Over half 62 (53.9%) required KRT at presentation, and 67(58.2%) needed blood transfusion. The mean LOS was 13.5±9.47 days (Table 1).

Table-1: Baseline demographic and clinical characteristics of the patients.

Variables	n(%), mean ± SD, median (IQR) n= 115 (%)
Age (Years)	32.61 ± 10.20
Gender	
Male	55 (47.8)
Female	60 (52.2)
Body Mass Index (BMI) (Kg/m^2),	23.13 ± 3.39
Duration of symptoms before admission (days)	14 (IQR 3-45)
Comorbidities	
Hypertension	26 (22.2)
Diabetes	14 (12.2)
Cardiovascular disease	2 (1.7)
Obesity	14 (12.2)
History of Infection	44 (38.2)
History of smoking	2 (1.7)
History of Autoimmune Disease	8 (6.8)
Family history of renal disease	10 (8.7)
Obstetric complications	14 (12.2)
Oliguria at presentation	48 (41.7)
Oedema	115 (100)
Use of Nephrotoxic Drugs	11 (9.4)
eGFR (ml/min/1.732)	23.05 ± 18.62
Kidney Replacement Therapy (KRT) on admission	62 (53.9)
Plasmapheresis on admission	24 (20.9)
Need for mechanical ventilation	8 (7)
Need for blood transfusion	67 (58.2)
Need for Inotropes	21 (18.3)
Hospitalisation (Days)	13.50 ± 9.47

eGFR: Estimated glomerular filtration rate, SD: Standard deviation, IQR: Interquartile range

Table-2: Baseline laboratory characteristics of the patients.

Variables	n(%), mean ± SD)
ANA positive	14 (16.5)
Anti dsDNA positive	8 (6.9)
ENA positive	1 (0.8)
APLA positive	6 (5.2)
ANCA positive	
c-ANCA	2 (1.7)
p-ANCA	6 (5.2)
Anti-GBM positive	2 (1.7)
Anti-PLA2R positive	2 (1.7)
ASOT positive	2 (1.7)
Proteinuria (dipstick)	
1	2 (1.7)
2	25 (22.1)
3	36 (31.9)
4	52 (46)
Microscopic Haematuria	
1	10 (8.8)
2	6 (5.3)
3	16 (14.2)
4	7 (6.2)
Serum Creatinine (mg/dl)	6.11 ± 4.47
eGFR (ml/min/1.732)	23.05 ± 18.62
Serum albumin (g/dL)	2.53 ± 0.80
Spot UPCR (mg/mg) or 24 h Urinary Protein (g)	5.97 ± 4.36

SD: Standard deviation, ANA: Antinuclear antibodies, Anti-dsDNA: Anti double-stranded deoxyribonucleic acid, APLA: Antiphospholipid antibodies, ENA: Extractable nuclear antigen, Anti-PLA2R: Anti-phospholipase A2 receptor antibodies, ANCA: Anti-neutrophil cytoplasmic antibodies, Anti-GBM: Anti-glomerular basement membrane antibodies, ASOT: Anti-streptolysin O titer, eGFR: Estimated glomerular filtration rate, UPCR: Urine protein-to-creatinine ratio.

The mean eGFR was 23.05±18.62ml/min/1.73m^2. Other laboratory parameters were also noted in detail (Table 2).

Most patients 104(90.4%) had renal involvement due to glomerulopathy, while the rest exhibited non-glomerular renal disease. The most common primary glomerular diseases were FSGS 26(22.6%), MPGN 16(13.9%) and MN 4(3.5%). The leading secondary glomerular diseases were PING 18(15.7%), thrombotic microangiopathy (TMA) 16(13.9%) and LN 8(7.0%) (Table 3).

At 3-month follow-up, the mean eGFR improved from 23.05±18.62ml/min/1.73m^2 at presentation to (mg/mg) or 55.58±41.11ml/min/1.73m^2, and serum albumin increased from 2.53±0.08g/dL at 1 month to 3.20±0.91g/dL. Further, 43(37.4%) patients achieved CR, 34(29.6%) achieved PR and 38(33%) showed NR, while 4(3.4%) patients from the NR group expired at the time of the last follow-up. Patients who required KRT on admission had lower CR rate (p<0.001), with more patients progressing to ESKD (p=0.02) and increased mortality (p=0.08) (Table 4).

T**able-3:** Aetiological spectrum and outcomes of the patients.

Histological diagnosis	No. of patients n (%) n(%)	Required KRT on admission, n=62 n(%)	CR n=43 n(%)	PR, n =34	NR n=38	P-value
Primary						
MCD	2 (1.7)	0	0	2 (5.8)	0	0.08
FSGS	26 (22.6)	9 (14.5)	16 (37.2)	2 (5.8)	8 (21.0)	0.004
MN	4 (3.5)	0	4 (9.3)	0	0	0.027
MPGN	16 (13.9)	6 (9.67)	8 (18.6)	2 (5.8)	6 (15.7)	0.26
Chronic Sclerosing GN	2 (1.7)	2 (3.2)	0	0	2 (5.2)	0.14
Secondary						
PIGN	4 (3.5)	2 (3.2)	0	4 (11.7)	0	0.006
PING	18 (15.7)	12 (19.3)	1 (2.3)	8 (23.5)	9 (23.6)	0.002
Anti-GBM nephritis	2 (1.7)	0	0	1 (2.9)	1 (2.3)	0.08
LN Class IV	4 (3.5)	0	3 (6.9)	1 (2.9)	0	0.2
LN Class IV/V	4 (3.5)	2 (3.2)	2 (4.6)	2 (5.8)	0	0.31
MM	2 (1.7)	2 (3.2)	0	2 (5.8)	0	0.08
DN	2 (1.7)	2 (3.2)	0	2 (5.8)	0	0.08
TMA	16 (13.9)	14 (22.5)	2 (4.6)	4 (11.8)	10 (26.3)	0.028
Acute Pyelonephritis	2 (1.7)	2 (3.2)	0	2 (5.8)	0	0.08
AIN	1 (0.9)	1 (1.6)	0	1 (2.9)	0	0.28
ATN	10 (8.7)	10 (16.1)	7 (16.2)	1 (2.9)	2 (5.2)	0.06

KRT: Kidney replacement therapy, MCD: Minimal change disease, FSGS: Focal segmental glomerulosclerosis, MN: Membranous nephropathy, MPGN: Membranoproliferative glomerulonephritis, PING: Pauci-immune necrotising glomerulonephritis, PIGN: Post-infectious glomerulonephritis, Anti-GBM nephritis: Anti-glomerular basement membrane disease, GN: Glomerulonephritis, LN: Lupus nephritis, MM: Multiple myeloma, DN: Diabetic nephropathy, TMA: Thrombotic microangiopathy, AIN: Acute interstitial nephritis, ATN: Acute tubular necrosis.

T**able-4:** Renal outcomes at 3-month follow-up.

Histological diagnosis	n(%), mean ±SD Overall n=115	n(%), mean ±SD Required KRT on n=62	n(%), mean ±SD Not required KRT on n=53	p-value
Renal Outcomes, at 1 month				
Serum Creatinine (mg/dl)				<0.001
	4.47 ± 2.90	5.75 ± 3.05	2.98 ± 1.83	
Serum Albumin (g/dL)	2.53 ± 0. 80	3.14 ± 0.72	2.30 ± 0.72	<0.001
eGFR(ml/min/1.73^2)	28.36 ± 27.66	17.51 ± 13.89	41.05 ± 33.86	<0.001
CR	11 (9.6)	0	11 (20.7)	<0.001
PR	53 (45.3)	24 (38.7)	29 (54.7)	0.063
NR	51 (43.6)	38 (61.2)	13 (24.5)	<0.001
Renal outcomes at 3 months				
Serum Creatinine (mg/dl)				0.007
	3.71±3.73	4.58±3.61	2.70±3.66	
Serum Albumin (g/dL)	3.20 ± 0.91	3.35 ± 0.85	3.01 ± 0.95	0.04
eGFR(ml/min/1.73^2)	55.58 ± 41.11	41.48 ± 35.71	72.07 ± 41.18	<0.001
CR	43 (37.4)	14 (22.5)	29 (54.7)	<0.001
PR	34 (29.6)	22 (35.4)	12 (22.6)	0.09
NR	38 (33.0)	26 (41.93)	12 (22.64)	0.02
Mortality	4 (3.4)	4 (6.4)	0	0.081

SD: Standard deviation, KRT: Kidney replacement therapy, eGFR: Estimated glomerular filtration rate, CR: Complete recovery, PR: Partial recovery, NR: No recovery.

Discussion

AKI affects approximately one in five hospitalised patients based on KDIGO or equivalent criteria, as reported in meta-analyses published in 2013 and 2015.[8,19] Although PRB is crucial for evaluating complex AKI, few studies have focused on the pathological disease spectrum of AKI. This has led to a lack of understanding of glomerular disease-associated AKI (GD-AKI) since this patient population is often excluded from epidemiological studies on AKI. The current study aimed at analysing the aetiological range, clinical presentation, and short-term treatment outcomes of patients with AKI of uncertain aetiology who underwent PRB. The findings provided valuable insights for the diagnostic and prognostic management of this challenging patient population.

As reviewed by Waikar et al. in 2018[20], most histopathology reports of AKI date back to an earlier era when the term acute renal failure (ARF) was used. During that time, ARF was diagnosed in its most severe forms, such as sepsis, rhabdomyolysis and severe trauma, with ATN being the typical pathological presentation. These earlier renal biopsy reports did not adequately reflect the types of AKI treated by the clinicians today. With the new consensus on criteria and a deeper understanding of AKI, the condition is now monitored more frequently and diagnosed more promptly. The introduction of new procedures and agents has also contributed to the evolving landscape of AKI, further complicating our understanding of how the condition presents in modern clinical practice.[21,22]

In the present study, 90.4% patients had renal involvement primarily caused by glomerulopathy, while 9.5% exhibited non-glomerular diseases, like ATN or AIN. This aligned with recent studies where ATN or AIN alone was observed in less than 20% of biopsied AKI cases, whereas glomerulopathy was the most frequent cause in 50%

cases.[23-25] A 2023 study by Abuduwupuer et al.[26] reported glomerulopathy in 78.4% of biopsied AKI cases. Earlier studies[27-29] showed that ATN or AIN was observed in >45% of biopsy specimens for ARF. These discrepancies are due to the rapid evolution in the understanding of AKI over the past decades. In 2012, KDIGO standardised the definition and classification criteria, facilitating epidemiological studies of AKI.[17]

The current study also found that 43.4% patients had PGD, while SGD was found in 46.9% cases. The results were similar to those of Konigsfeld et al. in 2019[30] reporting FSGS as the most frequent PGD. However, this contrasted with Abuduwupuer et al. who in 2023 reported a higher prevalence of IgAN. Among the secondary diseases, PING had the highest prevalence in the current study, aligning with Haas et al. in 2000, but differing from a recent study that showed LN as the most common.[26] These findings reflect the changing histopathological landscape of AKI biopsies from ATN or AIN to GD over the decades.

The current demographic data aligned with other studies, indicating that an increasing number of young people are now developing AKI(1-2). The slight predominance of females may be attributed to gender-related factors that predispose women to unexplained AKI. Previous studies have suggested that autoimmune diseases, which more commonly affect female patients, could play a significant role in this trend.[3]

The present study identified infection and nephrotoxic drug exposure incidence rates at 38.3% and 9.6%, respectively. Both factors are well-known causes of renal injury, potentially leading to direct tubular toxicity or glomerular damage.[10-11] The relatively low frequency of nephrotoxic drug use observed in the current study might indicate improved medication management practices or could be due to underreporting of exposure.

Previous studies have found that, compared to non-AKI patients, those with AKI have a 13-fold increased risk of developing ESKD, and this risk is 40 times higher if the patients have underlying pre-existing renal disease.[3,10, 31] In the current study, overall recovery at 3 months was observed in 66.9% patients, with CR in 37.4% and PR in 29.6%. However, 33% patients had NR and progressed to ESKD. These findings were lower compared to a study from China[26], which reported that >70% patients had CR at the end of 3 months. The wide variation in recovery rates could be attributed to differences at the time of presentation, as more than half of the current patients required KRT on presentation, compared to only 15% of patients in the Chinese study.[26] Among patients with PGD, higher CR rates were observed in those with FSGS, followed by MPGN, compared to MN. Among patients with SGD, those with PING had the lowest CR rates. These findings are consistent with the study from China.[26]

The current study observed a mortality rate of 3.4% at 3 months mainly in the KRT group, which is similar to the rate reported by Konigsfeld et al. in 2019[30] at 12 months. This higher mortality rate could also be attributed to the greater requirement for KRT on admission due to late presentation.

The strength of the study lies in its prospective design, representing adult cohorts with biopsy-proven AKI from a developing South Asian country. Given the scarcity of data, particularly prospective data on AKI outcomes in this demographic, the study fills a critical gap in the literature. However, several limitations must be acknowledged. Firstly, the single-centre nature of the study may not fully represent the broader population of the country. Secondly, the small sample size may limit the generalisability of the findings. Thirdly, the absence of follow-up data beyond three months restricts the ability to evaluate long-term renal recovery.

Conclusion

Most biopsied AKI patients had coexisting GD, while ATN alone was seen less frequently. Overall, the crucial impact of coexisting GD on the prognosis of AKI patients with worse renal recovery was noted. In cases suspected of having GD-AKI, it is essential to promptly differentiate the underlying conditions of AKI through kidney biopsy. This timely differentiation can guide treatment decisions and help reduce the risk of disease progression.

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References

1. Thongprayoon C, Hansrivijit P, Kovvuru K, Kanduri SR, Torres-Ortiz A, Acharya P, et al. Diagnostics, Risk Factors, Treatment and Outcomes of Acute Kidney Injury in a New Paradigm. J Clin Med 2020;9:1104. doi: 10.3390/jcm9041104.
2. Kellum JA, Sileanu FE, Bihorac A, Hoste EA, Chawla LS. Recovery after Acute Kidney Injury. Am J Respir Crit Care Med 2017;195:784-91. doi: 10.1164/rccm.201604-0799OC.
3. Chawla LS, Bellomo R, Bihorac A, Goldstein SL, Siew ED, Bagshaw SM, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nat Rev Nephrol 2017;13:241-57. doi: 10.1038/nrneph.2017.2.
4. Thongprayoon C, Hansrivijit P, Kovvuru K, Kanduri SR, Torres-Ortiz A, Acharya P, et al. Diagnostics, Risk Factors, Treatment and

Outcomes of Acute Kidney Injury in a New Paradigm. J Clin Med 2020;9:1104. doi: 10.3390/jcm9041104.
5. Mercado MG, Smith DK, Guard EL. Acute Kidney Injury: Diagnosis and Management. Am Fam Physician 2019;100:687-94.
6. Kashani K, Al-Khafaji A, Ardiles T, Artigas A, Bagshaw SM, Bell M, et al. Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury. Crit Care 2013;17:R25. doi: 10.1186/cc12503.
7. Darmon M, Ostermann M, Cerda J, Dimopoulos MA, Forni L, Hoste E, et al. Diagnostic work-up and specific causes of acute kidney injury. Intensive Care Med 2017;43:829-40. doi: 10.1007/s00134-017-4799-8.
8. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, et al. World incidence of AKI: a meta-analysis. Clin J Am Soc Nephrol 2013;8:1482-93. doi: 10.2215/CJN.00710113.
9. Bhatraju PK, Zelnick LR, Chinchilli VM, Moledina DG, Coca SG, Parikh CR, et al. Association Between Early Recovery of Kidney Function After Acute Kidney Injury and Long-term Clinical Outcomes. JAMA Netw Open 2020;3:e202682. doi: 10.1001/jamanetworkopen.2020.2682.
10. Siew ED, Abdel-Kader K, Perkins AM, Greevy RA Jr, Parr SK, Horner J, et al. Timing of Recovery From Moderate to Severe AKI and the Risk for Future Loss of Kidney Function. Am J Kidney Dis 2020;75:204-13. doi: 10.1053/j.ajkd.2019.05.031.
11. Xu J, Xu X, Shen B, Zhuang Y, Liu L, Wang Y, et al. Evaluation of five different renal recovery definitions for estimation of long-term outcomes of cardiac surgery associated acute kidney injury. BMC Nephrol 2019;20:427. doi: 10.1186/s12882-019-1613-6.
12. Langenberg C, Bagshaw SM, May CN, Bellomo R. The histopathology of septic acute kidney injury: a systematic review. Crit Care 2008;12:R38. doi: 10.1186/cc6823.
13. Eadon MT, Schwantes-An TH, Phillips CL, Roberts AR, Greene CV, Hallab A, et al. Kidney Histopathology and Prediction of Kidney Failure: A Retrospective Cohort Study. Am J Kidney Dis 2020;76:350-60. doi: 10.1053/j.ajkd.2019.12.014.
14. Huang Y, Shi K, Zhu X, Yuan S, Chen X, Fu X, et al. Disease spectrum of 9 310 cases of renal biopsy pathological diagnosis from a single center in China. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2022;47:546-54. doi: 10.11817/j.issn.1672-7347.2022.210487.
15. Lwanga SK, Lemeshow S. Sample size determination in health studies: a practical manual. Geneva, Switzerland: World Health Organization; 1991 . [Online] 1991 [Cited 2024 December 10]. Available from URL: https://apps.who.int/iris/handle/10665/40062.
16. Xu J, Ruan M, Wu J, Huang L, Xue C, Chen S, et al. The Role of Renal Pathology in the Prognosis and Recovery of Community-Acquired Acute Kidney Injury. Nephron 2021;145:353-62. doi: 10.1159/000514287.
17. International Society of Nephrology (ISN), Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2012;2:1-138.
18. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12. doi: 10.7326/0003-4819-150-9-200905050-00006.
19. Mehta RL, Cerdá J, Burdmann EA, Tonelli M, García-García G, Jha V, et al. International Society of Nephrology's 0by25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology. Lancet 2015;385:2616-43. doi: 10.1016/S0140-6736(15)60126-X.
20. Waikar SS, McMahon GM. Expanding the Role for Kidney Biopsies in Acute Kidney Injury. Semin Nephrol 2018;38:12-20. doi: 10.1016/j.semnephrol.2017.09.001.
21. Eknoyan G. Emergence of the concept of acute kidney injury. Adv Chronic Kidney Dis 2008;15:308-13. doi: 10.1053/j.ackd.2008.04.010.
22. Nast CC. Medication-Induced Interstitial Nephritis in the 21st Century. Adv Chronic Kidney Dis 2017;24:72-9. doi: 10.1053/j.ackd.2016.11.016.
23. Thomas ME, Blaine C, Dawnay A, Devonald MA, Ftouh S, Laing C, et al. The definition of acute kidney injury and its use in practice. Kidney Int 2015;87:62-73. doi: 10.1038/ki.2014.328.
24. Haas M, Spargo BH, Wit EJ, Meehan SM. Etiologies and outcome of acute renal insufficiency in older adults: a renal biopsy study of 259 cases. Am J Kidney Dis 2000;35:433-47. doi: 10.1016/s0272-6386(00)70196-x.
25. Korbet SM, Gashti CN, Evans JK, Whittier WL. Risk of percutaneous renal biopsy of native kidneys in the evaluation of acute kidney injury. Clin Kidney J 2018;11:610-5. doi: 10.1093/ckj/sfy048.
26. Abuduwupuer Z, Lei Q, Liang S, Xu F, Liang D, Yang X, et al. The Spectrum of Biopsy-Proven Kidney Diseases, Causes, and Renal Outcomes in Acute Kidney Injury Patients. Nephron 2023;147:541-9. doi: 10.1159/000530615.
27. Mustonen J, Pasternack A, Helin H, Pystynen S, Tuominen T. Renal biopsy in acute renal failure. Am J Nephrol 1984;4:27-31. doi: 10.1159/000166768.
28. Solez K, Morel-Maroger L, Sraer JD. The morphology of "acute tubular necrosis" in man: analysis of 57 renal biopsies and a comparison with the glycerol model. Medicine (Baltimore) 1979;58:362-76.
29. Hida M, Saitoh H, Satoh T. Autopsy findings in postoperative acute renal failure patients, collected from the annuals of pathological autopsy cases in Japan. Tokai J Exp Clin Med 1984;9:349-55.
30. Konigsfeld HP, Viana TG, Pereira SC, Santos TOCD, Kirsztajn GM, Tavares A, et al. Acute kidney injury in hospitalized patients who underwent percutaneous kidney biopsy for histological diagnosis of their renal disease. BMC Nephrol 2019;20:315. doi: 10.1186/s12882-019-1514-8.
31. Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, et al. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol 2009;20:223-8. doi: 10.1681/ASN.2007080837.

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