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**ORIGINAL RESEARCH**

# Etiology, clinical profile and short-term outcome of acute kidney injury in pediatric population in a tertiary care hospital, KGH

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## ABSTRACT

**Introduction**: Acute Kidney Injury substituted the term Acute Renal Failure as the term failure reflects only part of the spectrum of damage to the kidney that occurs clinically. In most cases of damage, the reduction in kidney function is submissive. Moreover, the term renal is less recognized by the general population making communication with patients and family more challenging, hence "kidney" has replaced "renal"[2]. Pediatric AKI can present with a spectrum of clinical features ranging from minimal elevation inserum creatinine to anuric kidney failure with severely diminished eGFR manifesting aselectrolyte and acid-base disturbances, from various causes, and occurs in different clinicalsettings8. Knowledge of the burden of AKI etiology, clinical profile, and outcome of AKI is essential for thenitiation of preventive and therapeutic strategies. Given the limited data available on theetiology, clinical profile, and outcomes of pediatric AKI from Indian children, and the regionalvariations in the clinical profile of AKI, the present observational prospective study was conducted. **Material and Methods**: A total of 54 children who fulfilled standard clinical criteria for acute kidney injury, their clinical parameters and outcomes were studied between March 2023 –February 2024. **Results**: In the study based on outcome, 1.9% progressed to Chronic Kidney Disease, 77.8% had Complete Recovery, 1.9% lost follow up and 18.5% died. **Conclusions:** 54 patients enrolled in the study. Frequency of AKI was more common among males(59.3%) than females (40.7%). The mean age of the study is 94.42 months with most patients between 60-120 months. Among the study population, oliguria(85.2%) was the most common presenting symptom, followed by edema and fever. The most common etiology was Acute glomerulonephritis 31.5% of which 76.5% were cases of infection-related glomerulonephritis. The most common histological finding in renal biopsy was infection-related glomerulonephritis with an exudative endocapillary proliferative pattern on light microscopy and granular IgG and C3 deposits on immunofluorescence. In the study, 69.7% required RRT, in which 3.7% of cases had hemodialysis, and 63% had peritoneal dialysis. There was no significant association between dialysis and outcome. Out of 54 patients in the study, 43 patients (79.6%) recovered and 11 patients (20.4%) expired. A total of 43 children of the survivors with AKI 77.8% had complete renal recovery 1.9% werediagnosed with chronic kidney disease and 1.9% lost followup at the end of 3 months.

**Keywords:** acute kidney injury, Renal replacement therapy



## INTRODUCTION

Acute Kidney Injury (AKI) is defined as the abrupt loss of kidney function that results in a decline in glomerular filtration rate, retention of urea, and other nitrogenous waste products, and dysregulation of extracellular volume and electrolyte hemostasis[1].

Acute Kidney Injury substituted the term Acute Renal Failure as the term failure reflects only part of the spectrum of damage to the kidney that occurs clinically. In most cases of damage, the reduction in kidney function is submissive. Moreover, the term renal is less recognized by the general population making communication with patients and family more challenging, hence "kidney" has replaced "renal"[2]. Pediatric AKI can present with a spectrum of clinical features ranging from minimal elevation inserum creatinine to anuric kidney failure with severely diminished eGFR manifesting aselectrolyte and acid-base disturbances, from various causes, and occurs in different clinicalsettings8. Knowledge of the burden of AKI etiology, clinical profile, and outcome of AKI is essential for thenitiation of preventive and therapeutic strategies. Given the limited data available on theetiology, clinical profile, and outcomes of

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pediatric AKI from Indian children, and the regionalvariations in the clinical profile of AKI, the present observational prospective study was conduct.

## METHODOLOGY

- After obtainingapproval from the ethics committee,a single centre prospective observational study wasconducted on children aged below 13 yrs fulfilling the inclusion and exclusion criteria.
- A predesigned proforma was applied to record all the necessary information .
- Demographic data, relevant history, clinical examination,diagnosis at admission were noted.To assess the severity of general condition the following information was also collected which includes need for mechanical ventilation,usage of vasopressors,serum creatinine at admission, need for peritoneal dialysis, and presence of sepsis or septic shock was recorded for each patient.
- Relevant Laboratory data was collected which includes eCCL (estimated creatinine clearance) and patients were classified based on the pRIFLE criteria.A baseline eCCL was calculated using the Schwartz equation from a baseline serum creatinine derived from modifies Jaffes with an automated analyzer. Previous renal function was considered normal when this data was unavailable and a baseline serum creatinine clearance rate of 100ml/min/1.73 $m^2$ was taken.
- After the diagnosis of AKI and staging according to pRIFLE, detailed clinical history and examination were done and relevant investigations with respect to clinical features were collected to ascertain the etiology and clinical profile.
- Blood and urine cultures were sent if sepsis was suspected Ultrasound abdomen was done and noted.
- Malaria was diagnosed usingRDT followed by Qbc for malarial parasite,microscopy with visualization of Giemsa-stained malaria parasites in at least one blood sample with clinical correlation.
- Dengue Fever was diagnosed using IgM antibodies by ELISA against Dengue Virus with Clinical correlation.
- Poison-induced AKI was considered based on clinical history after ingestion of one of the poisonous substances in a previously healthy person.
- For all patients admitted with a history of envenomation with acute kidney injury, a detailed history was obtained from the patient's caretakers about the envenomation, time of the bite,site of bite, local examination for fang marks, and associated clinical features were noted.
- When Urine Output is less than 400ml/day patients are considered oligurucand when <100 mL per day patients considered as anuric.
- Further workup was done according to the need in individual cases like ANA, Complement levels, ASO titers, and renal biopsy for Light Microscopy and Immunofluorescence.

Renal biopsy (after excluding pre-renal and post-renal causes) was done in children with rapidly worsening renal function or non-recovering AKI (defined as acute kidney injury not improving or deteriorating based on Serum Creatinine and clinical examination after 21 days of onset of acute injury)

Renal biopsy was done in children with systemic lupus erythematosus who were suspected to have lupus nephritis assessed by proteinuria, active sediment, and/or renal dysfunction and classified according to the ISN/RPS classification.

Renal biopsy is not recommended for diagnosing children with PSGN and was performed only when other glomerular pathologies were suspected. A renal biopsy was done if there were:

1. Progressive decline in Renal function beyond 2 weeks
2. Anuric renal failure of more than 1 week
3. When there was no latent period between the acute glomerulonephritis and streptococcal infection
4. If the complement levels were normal or failed to normalize after 4weeks
5. When there was no rise in antistreptococcal antibodies Indications for renal replacement therapy was

1. anuria or oliguria for >24hrs
2. volume overload
3. refractory metabolic acidosis
4. severe dyselectrolemia
5. uremic encephalopathy

Renal replacement therapy in the form of peritoneal dialysis was done in the study population when indicated as the facility of hemodialysis in children was unavailable at our center. Hemodialysis was done if the child's weight was above 35 kgs.

For outcome, patients were followed till recovery or 3 months post-diagnosis date and categorized as

1. Recovered (eGFR >90ml/min) is defined as the return of creatinine to less than the threshold for RIFLE-R or within 50% of baseline.
2. CKD stage 2-4(eGFR 15-89ml/min) defined as persistently decreased eGFR <90ml/min beyond 3months
3. ESRD (eGFR<15 ml/min);
4. Death

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## RESULTS

**Table 1: Distribution of the study population based on Age**

| Age in months | Number of patients | Percentage |
|---|---|---|
| <12 months | 4 | 7.4% |
| 12 – 24 months | 1 | 1.9% |
| 24 – 60 months | 11 | 20.4% |
| 60 – 120 months | 24 | 44.4% |
| 120 – 180 months | 14 | 25.9% |
| Total | 54 | 100% |
| Mean ± SD | 94.42 ± 47.32 months | |

The mean age of the study population was 94.42 ± 47.32 months of which 7.4% belonged to <12 months, 1.9% belonged to 12-24 months, 20.4% belonged to 24-60 months, 44.4% belonged to 60-120 months, 25.9% belonged to 120-180 months.

**Table 2: Distribution of the study population based on Gender.**

| Gender | Number of patients | Percentage |
|---|---|---|
| Male | 32 | 59.3% |
| Female | 22 | 40.7% |
| Total | 54 | 100% |

In the study, 59.3% were males and 40.7% were females.

**Table 3: Distribution of Study population based on Etiology**

| Etiology | Frequency | Percentage |
|---|---|---|
| Nephritic syndrome | 17 | 31.5% |
| Malaria | 6 | 11.1% |
| Acute Gastroenteritis | 4 | 7.4% |
| Poisoning (paraquat) | 4 | 7.4% |
| Dengue Shock Syndrome | 3 | 5.6% |
| Sepsis (meningoencephalitis) | 3 | 5.6% |
| Snake envenomation | 3 | 5.6% |
| Malaria + Dengue | 2 | 3.7% |
| Poisoning (castor oil) | 2 | 3.7% |
| Poisoning (hog plum) | 2 | 3.7% |
| Septic shock | 2 | 3.7% |
| Bee sting | 1 | 1.9% |
| Dengue hemorrhagic fever | 1 | 1.9% |
| Diabetic ketoacidosis | 1 | 1.9% |
| Diabetic ketoacidosis with sepsis | 1 | 1.9% |
| Sepsis(bronchopneumonia) | 1 | 1.9% |
| Thrombotic microangiopathy | 1 | 1.9% |
| Total | 54 | 100.00% |

**Table 4: Distribution of study population based on P-RIFLE**

| P-RIFLE | No of patients | Percentage |
|---|---|---|
| Failure | 37 | 68.5% |
| Injury | 14 | 25.9% |
| Risk | 3 | 5.6% |
| Total | 54 | 100% |

Based on the P-RIFLE classification, Failure was noted in 68.5% of cases, Injury in 25.9% of cases, and Risk in 5.6% of cases.

**Table 5: Distribution of study population based on Clinical presentation**

| Clinical profile | No of patients | Percentage |
|---|---|---|
| Oliguria/Anuria | 46 | 85.2% |
| Fever | 34 | 63% |
| Edema | 44 | 81.5% |
| Vomiting | 24 | 44.4% |
| Dark urine | 29 | 53.7% |

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| | | |
|---|---|---|
| Diarrhea | 7 | 13% |
| Seizures | 10 | 18.5% |
| Rash | 14 | 25.9% |
| Jaundice | 20 | 37% |
| Cough | 18 | 33.3% |

- In the present study based on laboratory parameters, 24.1% had hemoglobin levels >10g/dl, 42.6% with Hb levels 7-10 g/dl, and 33.3% with Hb levels <6 g/dl.
- In the study, 38.9% had a normal total count, and 61.1% with an abnormal total count.
- In the study, 51.9% had normal platelet count, 61.1% with platelet count range between 50000 – 150000, and 7.4% with platelet count <50000.
- Based on urea levels, 7.4% had urea levels ranging between 20-50, 38.9% with levels between 51-100, and 53.7% with levels>100.
- 90.7% had normal sodium levels, 7.4% with Hyponatremia, and 1.9% with hypernatremia.
- Based on potassium levels, 61.1% had normal potassium levels, 3.7% with hypokalemia, and 35.2% with hyperkalemia.
- In the study, 63% had normal complement levels, 27.8% had low complement levels, and not done in 9.3%.
- In the study based on ASO Titres, 72.2% were found to be negative, 18.5% had ASO titers>200 and in 9.3% it was not done.
- In the study, 42.6% had proteinuria, and 77.8% had Fena>1.
- Based on culture, 14.8% had blood Cultures positive, 3.7% with urine culture positive, 13% with sputum culture positive, and 3.7% with stool culture positive.

**Table 6: Distribution based on creatinine.**

| Creatinine | Minimum | Maximum | Mean ± SD |
|---|---|---|---|
| At admission | 1.10 | 8.0 | 3.91 ±1.90 |
| At discharge | 0.40 | 2.0 | 0.86 ±0.33 |
| Mean difference = 2.80 ± 1.70, 95% CI = 3.33 – 2.28, p= 0.0001* Statistically significant | | | |

On renal Biopsy, 38.5% were diagnosed with IRGN (Infection Related Glomerulonephritis) with an exudative endocapillary proliferative pattern on light microscopy (LM) with immunofluorescence (IF) showed granular IgG and C3 deposits.

15.4% were diagnosed with Lupus nephritis.

15.4% with Acute Tubular Necrosis with LM showed flattened tubular epithelium, loss of brush border, vacuolization of cytoplasm, dilated tubules with normal IF pattern

TMA (thrombotic microangiopathy) was seen in 7.7% where LM showed fibrinoid necrosis with fibrin thrombi within the glomeruli and mesangium with nonspecific staining of IgM in glomeruli.

7.7% had ATIN (Acute tubulointerstitial nephritis), LM showed edematous interstitium with infiltration with macrophages, plasma cells with loss of brush border of tubular epithelium with normal IF.

7.7% with MPGN type 1 showed LM with lobular accentuation of glomeruli with focal duplication of basement membrane with hypercellularity of mesangium and endocapillary cells. IF showed peripheral coarse granular deposits of IgG and C3c with minimal deposits of IgM and IgA suggestive of immune complex-mediated MPGN type 1 7.7% with Lupus Nephritis( diffuse glomerulonephritis) with TMA

**Table 7: Renal Replacement Therapy**

| RRT | No of patients | Percentage |
|---|---|---|
| Peritoneal Dialysis | 34 | 63% |
| Hemodialysis | 2 | 3.7% |
| Total | 54 | 100% |

Distribution based on RRT shows, 63% underwent peritoneal dialysis, and 3.7% underwent hemodialysis.

| | | | | | |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 18 | 18 | 33.3% |
| 1 | 15 | 0 | 0 | 15 | 27.8% |
| 2 | 9 | 0 | 0 | 9 | 16.7% |
| 3 | 7 | 1 | 0 | 8 | 14.8% |
| 4 | 2 | 1 | 0 | 3 | 5.6% |
| 5 | 1 | 0 | 0 | 1 | 1.9% |
| Total | 34 | 2 | 18 | 54 | 100% |

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In the study based on several sessions of dialysis patients underwent, out of 34 cases who underwent peritoneal dialysis 15 cases had 1 session, 9 cases with 2 sessions, 7 cases with 3 sessions, 2 cases with 4 sessions, and 1 case with 5 sessions.
Out of 2 cases who underwent hemodialysis, 1 case had 3 sessions and 1 case had 4 sessions.

**Table 8: Outcome**

| | Frequency | Percentage |
|---|---|---|
| Survived | 43 | 79.6% |
| Expired | 11 | 20.4% |
| Total | 54 | 100% |

In the study, 79.6% survived and 20.4% expired.

**Table 9: Final outcome**

| | Frequency | Percentage |
|---|---|---|
| Chronic Kidney Disease | 1 | 1.9% |
| Complete Recovery (CR) | 42 | 77.8% |
| Death(D) | 10 | 18.5% |
| Lost Follow-Up (F/U) | 1 | 1.9% |
| Total | 54 | 100% |

In the study based on outcome, 1.9% progressed to Chronic Kidney Disease, 77.8% had Complete Recovery, 1.9% lost follow up and 18.5% died.

## DISCUSSION

The present study is a single-center observational study on the Etiology, Clinical Profile, and Short term outcome of Acute Kidney Injury in a Pediatric population of 54 cases that were diagnosed with AKI using the P-RIFLE criteria at the time of admission in the nephrology department, KGH.

In the present study, the mean age of the study population was 94.42 ± 47.32 months. The majority of the cases in our study belonged to the 60-120 months group. 7.4% belonged to <12 months, 1.9% belonged to 12-24 months, 20.4% belonged to 24-60 months, 44.4% belonged to 60-120 months, 25.9% belonged to 120-180 months

Most of the studies listed above observed a mean age-wise incidence to be between 40 months to 90 months.

In the present study, based on Etiology Nephritic syndrome(Acute glomerulonephritis) 31.5% of which post-infectious glomerulonephritis(PIGN) was the most common cause followed by Malaria at 11.1%, Acute Gastroenteritis at 7.4%, Paraquat Poisoning at 7.4%, Dengue shock syndrome at 5.6%, Sepsis (meningoencephalitis) at 5.6%, Snake envenomation at 5.6%, Malaria+Dengue at 3.7%, Castor Poisoning at 3.7%, Hog Plum poisoning at 3.7%, Septic shock at 3.7%, Bee sting at 1.9%, Dengue hemorrhagic fever at 1.9%, Diabetic keto acidosis at 1.9%, DKA sepsis at 1.9%, Sepsis (Bronchopneumonia) at 1.9%, Thrombotic microangiopathy at 1.9%. Our study findings were in concordance with Yan Cao[143] et al and Christopher[148] et al.

This finding of increased incidence of PIGN in our study shows this etiology is a major contributing factor of AKI in developing countries like India where poor socioeconomic status, overcrowding, and poor sanitation are still rampant making children susceptible to streptococcal infections.

The next common etiology in our study was severe complicated malaria affecting 11.1% as malaria is endemic in the districts of coastal Andhra Pradesh and may be one of the probable reasons for malaria being the next common etiology.

The etiology of AKI due to snake bites and bee stings was also present in our study as India is a tropical country encounters with animals and insects are common, due to their ubiquitous distribution. Snakebite is an important cause of death in rural areas of developing countries and is a neglected public health issue[151] Moreover, many bites in rural areas are initially treated by 'tantriks', snake charmers, or religious men who either chant 'mantras' or use herbal remedies, further contributing to morbidity.Snakebite is very common in school-age children, adolescents, and young adults. It accounts for 3% of all deaths in children of ages 5–14years[152]

Another etiology in our study was dengue and its complications.Dengue fever is one of the most common causes of “undifferentiated tropical fevers” in hospitalized children across India[149].In a prospective multicenter study done in 34 ICUs across India, dengue (23%) was found to be the most common etiological diagnosis in patients presenting with acute febrile illness and systemic manifestations

In our study, AKI in children was also due to castor oil and hog plum consumption showing the various herbal practices followed in remote areas of India for treating minor ailments. There was no literature reported regarding these substances causing AKI but the AKI could be due to unknown adulterants in castor oil. These etiologies were considered as there was a clear history of oliguria following consumption of these agents followed by a deranged renal profile.

The exact etiology of biopsy-proven TMA seen in 1 case in the present study could not be established due to inconclusive results from the investigations done to

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zero in on a particular etiology and unavailability of the expensive tests (WES genetic tests, ADAMTS 13 levels, or antibody, anti-factor H antibody) at our center that could point towards an exact cause. The patient had no history of diarrhea, stool culture was negative and renal dysfunction persisted for more than 4 weeks suggesting an atypical etiology of TMA[153]

## CONCLUSION

1. This dissertation has added to the literature regarding the etiology, clinical profile, and short-term outcome of acute kidney injury in children diagnosed with AKI.
2. 54 patients enrolled in the study.
3. Frequency of AKI was more common among males(59.3%) than females (40.7%)
4. The mean age of the study is 94.42 months with most patients between 60-120 months.
5. Among the study population, oliguria(85.2%) was the most common presenting symptom, followed by edema and fever.
6. The most common etiology was Acute glomerulonephritis 31.5% of which 76.5% were cases of infection-related glomerulonephritis.
7. The most common histological finding in renal biopsy was infection-related glomerulonephritis with an exudative endocapillary proliferative pattern on light microscopy and granular IgG and C3 deposits on immunofluorescence.
8. In the study, 69.7% required RRT, in which 3.7% of cases had hemodialysis, and 63% had peritoneal dialysis. There was no significant association between dialysis and outcome.
9. Out of 54 patients in the study, 43 patients (79.6%) recovered and 11 patients (20.4%) expired.
10. A total of 43 children of the survivors with AKI 77.8% had complete renal recovery 1.9% were diagnosed with chronic kidney disease and 1.9% lost followup at the end of 3 months.
11. There was no significant association between gender, P-RIFLE category, type of AKI, blood pressure, urine output, and requirement of RRT with the outcome.
12. Duration of hospital stay was significantly high in the expired group compared to the recovered group.
13. The number of patients requiring inotropic support was significantly higher in the succumbed group compared to the recovered group.
14. Significant number of patients who required mechanical ventilation eventually were lost.
15. Anemia and/or thrombocytopenia were significantly higher in the critically ill group who subsequently expired.

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