

# Profile of Acute Kidney Injury in Children Hospitalized with Nephrotic Syndrome: An Observational Study from Bihar, India

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**Abstract:** *The study aimed to assess the characteristics of AKI in children hospitalized with nephrotic syndrome. The present study was conducted on n=271 children aged <15 years admitted due to nephrotic syndrome. An information regarding demography, clinical and physical, haematological examination were recorded. The responsiveness of the disease to first line therapy of oral steroids was assessed and categorized. Total duration of hospital stay was also recorded. Among n=271, n=66 patients were diagnosed with AKI. The prevalence of AKI was found to be 24.35%. The age of onset of AKI was 3 - 5 years in 31.25% of children followed by it was <3 years, >10 years, and 5 - 10 years in 27.54%, 25%, and 16.33% of children respectively suggesting no association (P=0.1177). AKI was associated with response to steroid, albumin, cholesterol, hypertension, and urine infection (P<0.05). The duration of hospital stay in AKI patients was significantly more than their counterparts (11.09±5.04 days vs 6.89±2.96 days, P<0.00001). Response to steroids, use of nephrotoxic medications, hypertension, urine infection, increased total cholesterol level, and low serum albumin concentration were the main risk factors of AKI.*

**Keywords:** Acute kidney injury, childhood nephrotic syndrome, nephrotic syndrome, risk factors,

## 1. Introduction

One of the most typical kidney illnesses encountered in children is nephrotic syndrome (NS). Increased glomerular filtration barrier permeability causes the kidney condition known as nephrotic syndrome. Proteinuria, hypoalbuminemia, edema, and hyperlipidaemia are its four main clinical features, which are used to make the diagnosis. [1] Children of any age can develop nephrotic syndrome, but school - aged children and adolescents are the most frequently affected. With an incidence of 2 to 7 cases per 100, 000 children, there are nearly 16 cases per 100, 000 children worldwide. [1] Without quick identification and treatment, children with NS can experience a range of acute consequences that have the potential to be serious and even fatal. Acute kidney injury (AKI), thromboembolism (TE), and infection are three of the main complications of NS.

“Acute kidney injury (AKI) ” is a rapid failure in renal excretory mechanism characterized by a temporary rise in blood creatinine and nitrogenous by - product concentration, frequently accompanied by a reduction in urine production, and by the kidney's incapability to regulate “fluid and electrolyte homeostasis”. [2] Childhood nephrotic syndrome patients may develop acute kidney injury (AKI), which is a rare but deadly consequence brought on by intravascular volume loss, acute tubular necrosis, interstitial nephritis, bilateral renal venous thrombosis, or rapid advancement of underlying glomerular disease. [3] Important risk factors for

AKI in children with childhood nephrotic syndrome include sepsis, shock, peritonitis, severe hypoalbuminemia, exposure to nephrotoxic medications, and steroid resistance. [4 - 7]

Even though several studies have examined the risk factors for AKI in children with NS, there is a paucity of information on factors that predict both the recovery and recurrence of AKI in this population. Thus, to establish a clear connection between several risk factors and AKI, a detailed study of risk factor is required. The study was aimed to assess the characteristics of acute kidney injury in children hospitalized with nephrotic syndrome.

## 2. Material and Methods

The present prospective observational study was conducted at the department of paediatrics Indira Gandhi institute of medical sciences, Patna after obtaining ethical approval. A sum of 271 children aged <15 years admitted due to nephrotic syndrome were recruited in the study post obtaining informed consent from the parents. Whereas, children with congenital nephrotic syndrome, and CKD ≥ III at admission were excluded from the study.

A detailed history was obtained including age of first onset of disease, the responsiveness of the disease to the first line therapy of oral steroids classifying them as frequent relapses if two or more relapses occurred in the initial 6 months or four or more relapses in any twelve months, also they were

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grouped into steroid dependant if two consecutive relapses happened while on alternate day steroids or within 17 days of its discontinuation. If remission could not be achieved despite daily prednisolone at a dose of 2 mg/kg/day for 4 weeks, they were grouped into steroid resistant.

Thorough clinical examination was done. Daily vitals and nephrotic charting including daily weight, urine output, and urinary dipstick were monitored. Throughout the hospital stay patient was closely observed for response to therapy or any worsening if present.

Blood investigations including kidney function test, total cholesterol, serum albumin, TSH, urine investigation consisting of spot urine protein creatinine ratio was sent and reports recorded for analysis. Total duration of hospital stay was also recorded to enable us to understand the effect acute kidney injury on the length of hospital stay. Any patient who had oliguria was designated to have developed AKI as per AKIN criteria and those in whom urine output could not be monitored, any clinical suspicion of AKI prompted us to send a blood sample for kidney function test and label them as AKI if the creatinine report fulfilled AKIN criteria. Those who had AKI, BUN: serum creatinine was used to differentiate between pre - renal and renal AKI. Serum creatinine values within 6 months before admission or the lowest creatinine value during hospital stay were considered as baseline serum creatinine. Patients were followed up at 1 month and 3 months for progression to chronic kidney disease. Bedside eGFR was calculated to stage CKD based on NKF KDOQI guidelines.

**Statistical analysis**

Data were collected in approved proforma and entered into a Microsoft excel sheet. Data were analyzed using the SPSS IBM V 20 software. Continuous variables were expressed in terms of mean±SD whereas, categorical variables were expressed in percentage and frequency. Logistic regression analysis was used to find the association between AKI and its risk factors. P value was determined using the chi - square test. P value <0.05 was considered statistically significant.

**3. Results**

In this study majority of participants were male (57.93%). Among n=271 study subjects, n=66 patients were diagnosed with AKI. The prevalence of AKI was found to be 24.35%. The AKI and CKD stages are shown in table 1.

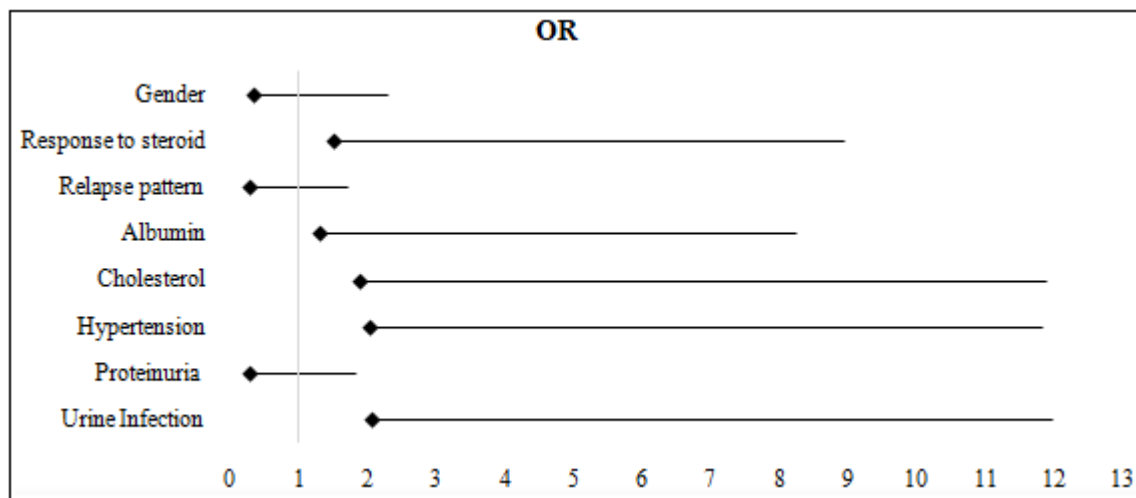
**Table 1:** Distribution of subjects according to AKI and CKD stages

AKI stages	Frequency (n)	Percentage (%)
1	24	36.36
2	17	25.76
3	25	37.88
Total	66	100
Stages of CKD	Frequency (n)	Percentage (%)
Stage 2	4	6.06
Stage 3	2	3.03
No CKD	60	91.01
Total	66	100

The age of onset of AKI was 3 - 5 years in 31.25% of children followed by it was <3 years, >10 years, and 5 - 10 years in 27.54%, 25%, and 16.33% of children respectively. There was no association between age of onset and AKI (P=0.1177). AKI was found to be associated with response to steroid, albumin, cholesterol, hypertension, and urine infection (P<0.05) (table 2 and figure 1). The mean duration of hospital stay in patients with AKI was significantly more compared to patients without AKI (11.09±5.04 days vs 6.89±2.96 days, P<0.00001).

**Table 2:** Odds ratio of the study variables

Variable	OR	Lower Limit	Upper Limit	P - Value
Gender	0.8331	0.4764	1.4566	0.5217
Response to steroid	2.2917	0.7886	6.6593	0.00061
Relapse pattern	0.5769	0.2907	1.1448	0.1157
Albumin	2.9389	1.6242	5.3178	0.0004
Cholesterol	4.1988	2.2962	7.6778	< 0.0001
Hypertension	3.6000	1.5720	8.2440	0.0024
Proteinuria	0.6519	0.3595	1.1821	0.1587
Urine Infection	3.5741	1.5197	8.4054	0.0035



**Figure 1:** Odds ratio of the study variables

#### 4. Discussion

The present study was intended to assess the characteristics of acute kidney injury in children hospitalized with nephrotic syndrome. In this study, a total of n=271 children <15 years of age presented with nephrotic syndrome were studied. The significant findings of the study were the incidence of AKI was found to be 24.35%. AKI was found to be significantly associated with response to steroids, use of nephrotoxic medications, hypertension, urine infection, increased total cholesterol level, and low serum albumin concentration. The duration of hospital stay was significantly more in AKI children compared to those without AKI patients.

AKI is a rare complication associated with nephrotic syndrome. The exact pathophysiology is not known however, it may be resulting from acute tubular necrosis. [8] The possible aetiopathogenesis of AKI in NS includes acute tubular necrosis from hypovolaemia and infection, renal interstitial oedema with vascular congestion, bilateral renal vein thrombosis, acute pyelonephritis, rapid progression of the original glomerular disease, and exposure to nephrotoxic medications. [9 - 11] A report has suggested that the incidence of AKI increased from 3.3% to 8.5% in a decade. [6] Various other studies have reported different rates of incidence ranging from 11% to 51%. [4, 6, 8, 12 - 16] The differences in the incidence of AKI may be due to differences in the AKI definition, study setting, and design.

Younger age children are more prone to NS. In most patients with NS, hospitalization is required during the initial years of the disease due to recurrent relapse and infection. [1, 17] In this study, the age of onset of AKI in the majority of patients was 3 - 5 years, followed by <3 years, 5 - 10 years, and >10 years. These findings are comparable with the study of Kumar R. et al. [18] These findings suggested that the relapse decreases as age increases. Furthermore, age and sex were not significantly associated with AKI which is similar to the findings of Anigilaje EA, and Ibraheem I. [19] However, Sutherland et al. reported that the incidence of AKI was more in 15 - 18 - year - old hospitalized children [20]. While Kim et al. showed a significant association between AKI and age  $\geq 9$  years [15]. The difference in the results may be due to the difference in the AKI definition, study setting, and design. Here, a total of n=27 patients had severe steroid - dependent nephrotic syndrome, n=26 patients had steroid - resistant nephrotic syndrome, and n=217 had steroid - sensitive nephrotic syndrome. Among these patients n=10, n=18, and n=38 patients had AKI respectively. We found a significant association between AKI and resistance to steroids ( $P < 0.0001$ ). These findings are comparable with the study of Prasad et al and Beins NT. et al. [12, 21]

Previous reports showed that exposure to ACE inhibitors, calcineurin inhibitors, and antibiotics was associated with an increased risk of AKI. [8, 12 - 15, 22] Similarly, in this study a total of n=18 (6.64%) patients had antibiotics among these patients n=9 (50%) were found to have AKI. ACEI use was reported in n=123 (45.39%) patients including n=39 (31.71%) patients with AKI and n=84 (68.29%) patients without AKI. In n=7 (2.58%) patients with a history of

tacrolimus, AKI was found in n=5 (71.43%) patients. A significant association was found between AKI and nephrotoxic drugs ( $P=0.0419$ ). Moreover, in the patients with AKI, n=44 (66.67%) had hypertension. A significant association was observed between hypertension and AKI ( $P=0.00026$ ) which was in line with the result shown by Sharma et al. [14]

Albumin is proposed as a tubular toxin linked to increased intracellular stress, apoptosis, and heightened complement activation. [23, 24] Further, hypoalbuminemia indicates intravascular hypovolemia, which is expected to predispose to AKI. Levels of serum albumin and degree of proteinuria have also been reported to be higher in patients with, compared to those without AKI by other authors [13, 25]. Similarly our study shows patients with low mean serum albumin were more predisposed to develop AKI.

In current study higher serum total cholesterol levels was independently associated with AKI which was in disagreement with other study. The difference could be due to inclusion of both children and adults in previous study [26].

Infections like peritonitis and urinary tract infection predispose to develop AKI. Our study shows patients with UTI are thrice more likely to develop AKI compared to those who have a sterile urine culture. This is in agreement with previous studies. [12, 13, 22, 27] We found that subjects with AKI had an increased duration of hospital stay compared to patients without AKI which is similar to previous reports [8, 12, 13, 15].

#### 5. Conclusion

The study suggested that AKI is common in the present study population with NS. We found that response to steroids, use of nephrotoxic medications, hypertension, urine infection, increased total cholesterol level, and low serum albumin concentration were the main risk factors of AKI.

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