Original Article

Comparative Study of Demographic and Clinico-Biochemical Profile of Pre-Renal and Renal Causes of Acute Kidney Injury in Children

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ABSTRACT

Introduction: *Acute Kidney Injury (AKI) in children is a critical medical condition with diverse etiologies, including pre-renal and renal causes. Understanding the demographic and clinical and laboratorial characteristics associated with these etiologies is crucial for timely diagnosis and management. This comparative study seeks to bridge the knowledge gap in pediatric AKI by elucidating the demographic and clinico-biochemical profiles associated with pre-renal and renal causes.* ***Method and materials:*** *This comparative observational study was conducted in the Department of Paediatric Nephrology, Bangladesh Shishu Hospital and Institute, Bangladesh from January 2020 to December 2021. Children aged between 1 month to 12 years of either sex, diagnosed as AKI stage 2 or 3 due to pre renal and renal causes.* ***Results:*** *In the pre-renal group, the majority (65.4%) of patients were infants, while in the renal group, 51.9% were from the 1-5-year age group. At baseline, oedema was significantly more in the renal group (85.2%) compared to the pre-renal group (34.6%) (p<0.001) and hypertension was exclusively observed in the renal group (77%). Conversely, hypotension was significantly*

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more prevalent in the pre-renal group (65.4%) than in the renal group (18.5%) (p<0.001). In the pre-renal group, sodium was significantly higher than in the renal group (p<0.05). On the other hand, creatinine levels, blood urea, and potassium were significantly higher in the renal group compared to the pre-renal group (p<0.05). ***Conclusion:*** *Pre-renal AKI was observed mainly in infants, whereas older children faced renal AKI and higher rates of hypotension was found in the pre-renal patients in this study.*

Key words: *Acute Kidney Injury, Pediatric, Oedema, Creatinine, Renal, Pre-renal*

INTRODUCTION

Acute Kidney Injury (AKI) is a condition characterized by a sudden and rapid decline in renal function, leading to the accumulation of waste products and electrolyte imbalances in the body [1-3]. Several studies have shown that AKI is associated with short- and long-term adverse outcomes and causes [4-6].

The global burden of AKI stands at 13 million cases annually, with a striking 85% of occurrences recorded in developing countries [7]. In India, AKI incidence ranges from 5% to 9% in inpatient wards and spikes to 25%-36% in Paediatric Intensive Care Units [8]. Bangladesh Shishu Hospital and Institute, reported a prevalence of 14.95% for AKI in the Department of Paediatric Nephrology in 2019, with a concerning 40% mortality rate. Pre-renal causes, notably post-diarrheal hypovolemic AKI, accounted for 63% of cases [9].

The impact of AKI on children is profound, with tragic consequences and far-reaching effects on the economic and social fabric of families in developing countries [10]. The scarcity of dialysis facilities further exacerbates the situation, leading to advanced-stage AKI patients succumbing to the condition [11]. Scientific evidence consistently supports the notion that early detection of AKI, differentiation between renal and prerenal causes, and prompt intervention are crucial for reducing mortality [12]. The causes of AKI in children are multifaceted, encompassing pre-renal factors, which compromise renal blood flow without directly damaging the kidney tissue, and renal factors, involving intrinsic damage to the renal parenchyma [13].

Early detection of AKI, as well as distinguishing between renal and pre-renal causes, is crucial for timely intervention and improved patient outcomes [14]. A study published in the New England Journal of Medicine found that the mortality rate increases significantly with the severity of AKI, emphasizing the need for early identification to prevent progression to more severe stages [15].

Pre-renal AKI is often reversible if the underlying cause, such as dehydration or hypovolemia, is addressed promptly [16]. A study in Critical Care Medicine demonstrated that early fluid resuscitation in patients with pre-renal AKI can lead to a faster recovery of renal function and a reduction in mortality rates [17].

Timely detection of AKI is crucial for managing nephrotoxic drug exposure. Certain medications and contrast agents can contribute to the development of AKI [18]. Identifying AKI early allows healthcare providers to adjust medication regimens, discontinue nephrotoxic drugs, or consider alternative diagnostic approaches to minimize further renal damage [19].

Numerous studies, including a meta-analysis published in the Journal of the American Medical Association, have consistently demonstrated a direct correlation between the time to AKI diagnosis and patient mortality [20-22]. Early detection and intervention significantly decrease the mortality risk associated with AKI.

Identifying patients at high risk for AKI allows for targeted monitoring and intervention. Early recognition of risk factors, such as sepsis or major surgery, enables clinicians to implement preventive measures and closely monitor renal function, reducing the likelihood of AKI development and associated mortality [23-24].

This study aims to conduct a comprehensive comparative analysis of demographic and clinico-biochemical profiles between two distinct pediatric groups: those with pre-renal causes and those with renal causes of AKI.

MATHODS & MATERIALS

After proper approval from the ethical review committee of Bangladesh Shishu Hospital and Institute (BSHI), children with AKI attending the Department of Paediatric Nephrology unit of Bangladesh Shishu Hospital and Institute were assessed for eligibility as the study population from January 2020 to December 2021. Proper informed written consent from the parents or local guardian was taken and for maintaining the confidentiality all information were secured by the investigators. Patients (N=53) were categorized into pre-renal (26) and renal (27) groups based on their clinical history and lab evidence. Demographic details (age, sex and residence), clinical features (pulse, blood pressure, respiratory rate and oedema), and biochemical parameters (hemoglobin, creatinine, urea, pH, bicarbonate, sodium and potassium) were collected and analyzed from medical records and reports of both groups.

This study focuses on the inclusion criteria for participants, encompassing individuals aged between 1 month and 12 years, irrespective of gender. The targeted population comprises those diagnosed with AKI at stage 2 or 3. The causative factors considered for AKI include pre-renal causes like dehydration, hypovolemia due to gastroenteritis, haemorrhage, and sepsis. Additionally, renal causes such as Hemolytic Uremic Syndrome (HUS), Acute Interstitial Nephritis (snake bite, wasp bite, toxin-induced AKI), Post-infectious Glomerulonephritis, Rapidly progressive Glomerulonephritis (RPGN), Henoch-Schonlein Purpura (HSP) nephritis and Lupus Nephritis were included in the renal group.

The exclusion criteria for this study encompass several specific conditions to ensure the clarity and relevance of the research findings. Cases of AKI resulting from obstructive uropathy, as well as those occurring on a backdrop of chronic kidney disease or associated with congenital anomalies of the kidney and urinary tract, are excluded. Additionally, patients who have undergone recent abdominal surgery, are experiencing intestinal obstruction, peritonitis, or have abdominal wall defects are not considered in this study.

Operational definitions

- **Acute Kidney Injury (AKI)** is defined as an increase in serum creatinine by ≥0.3mg/dL from baseline within 48 hours, an increase in serum creatinine to ≥1.5

times baseline within the prior 7 days, or a reduction in urine volume by ≤0.5 mL/kg/hour for 6 hours.

- **Pre-renal AKI** is characterized by decreased renal perfusion and glomerular filtration, with normal tubular function. It is identified by a Blood Urea: Creatinine ratio > 20:1.
- **Renal AKI** is marked by renal parenchymal damage, including sustained hypoperfusion and ischemia. It is associated with a Blood Urea: Creatinine ratio < 20:1

Data was collected using a structured questionnaire containing all the variables (independent- demographic and etiology, dependent- clinical and biochemical). All the data were processed and analyzed by using IBM Statistical Package for Social Science (SPSS 26 version) for Windows software. P value of <0.01 was considered statistically significant and p value of <0.001 was considered highly significant.

RESULTS

In the pre-renal group, 17 (65.4%) patients were from the < 12 months age group, and 6 (23.1%) patients were from 1-5 years age group while in renal group, 4 (14.8%) patients were from < 12 months age group and 14 (51.9%) patients were from 1-5 years age group. Fisher Exact test showed that there was significant statistical difference between the groups regarding age (p=0.001). No significant statistical difference was observed between the groups regarding gender and residence ***[Table I]***.

Table I: Comparative socio-demographic characteristics of the study population(n=53)

Socio-demographic characteristics	Pre renal (n=26)	Renal (n=27)	P value
Age			
<12 months	17 (65.4%)	4 (14.8%)	
1-5 years	6 (23.1%)	14 (51.9%)	0.001*
5-12 years	3 (11.5%)	9 (33.3%)	
Gender			
Male	20 (76.9%)	20 (74.1%)	0.810
Female	6 (23.1%)	7 (25.9%)	
Residence			
Urban	18 (69.2%)	21 (77.8%)	0.480
Rural	8 (30.8%)	6 (22.2%)	

*Data were expressed as frequency (percentage). *p<0.05 = statistically significant. Statistical analysis was done by Chi- square test and Fisher Exact test.*

Among the 26 patients in pre-renal group, 5 (19.2%) had sepsis, 18 (69.3%) had diarrhoea with hypovolemia, 3 (11.5%) had diarrhoea with hypovolemia and sepsis. Among the 21 patients who presented with diarrhoea, 9 (42.86%) of them had a history of taking concentrated oral rehydration solution. On the other

side, among the 27 patients in renal group, 9 (33.33%) had Hemolytic uremic syndrome (HUS), 3 (11.1%) had rapidly progressive glomerulonephritis (RPGN), 7 (25.9%) patients had ATN due to wasp bite, 3 (11.1%) had drug history and 2 (7.4%) had infection ***[Table II]***.

Table II: Comparative Etiology of renal and pre-renal AKI (n=26)

Causes of pre-renal AKI	**Frequency**	**Percentage (%)**
Sepsis	5	19.2
Diarrhoea with hypovolemia	18	69.3
Diarrhoea with hypovolemia and sepsis	3	11.5
Causes of renal AKI	**Frequency**	**Percentage (%)**
Vascular cause		
Hemolytic uremic syndrome (HUS)	9	33.33
Glomerular cause		
RPGN	3	11.1
PSGN	1	3.7
Acute tubulo-interstitial nephritis (ATN)		
Wasp bite	7	25.9
Drug	3	11.1
Infection	2	7.4
Fish bile poisoning	1	3.7
Pigment Nephropathy	1	3.7

Notably, a higher percentage of patients in the pre-renal group exhibited tachycardia (50.0%) compared to the renal group (33.3%), although pulse and respiratory rate did not reach to statistical significance value. Conversely, hypotension was significantly more prevalent in the pre-renal group (65.4%) than the renal group (18.5%) ($p<0.001$). The presence of edema was markedly higher in the renal group (85.2%) compared to the pre-renal group (34.6%), showing a highly significant association ($p<0.001$) ***[Table III]***.

Table III: Comparison of baseline clinical parameters of study patients (n=53)

Clinical Features	**Pre-renal (n=26)**	**Renal (27)**	**P value**
Pulse			
Normal	11 (42.3%)	18 (66.7%)	0.104
Tachycardia	13 (50.0%)	9 (33.3%)	
Bradycardia	2 (7.7%)	0 (0%)	
Blood pressure			

Normotensive	9 (34.6%)	1 (3.7%)	**<0.001****
Hypotension	17 (65.4%)	5 (18.5%)	
Hypertension	0 (0%)	21 (77%)	
Respiratory rate			
Normal	6 (27.3%)	10 (37.0%)	0.268
Tachypnea	20 (76.9%)	17 (73.9%)	
Oedema			
Present	9 (34.6%)	23 (85.2%)	**<0.001****
Absent	17 (65.4%)	4 (14.8%)	

Data were expressed as frequency (percentage). Statistical analysis was done by Chi-square test.
**p<0.05 = statistically significant, **p<0.001 = highly significant*

Biochemical parameters of the patients showed that in pre renal group, sodium was significantly higher compared to renal group. On the other hand, creatinine level, blood urea and potassium were significantly higher in renal group compared to pre renal group ***[Table IV]***.

Table IV: Comparison of baseline laboratory parameters of study patients (n=53)

Biochemical Parameters	Pre renal (n=26)	Renal (n=27)	p value
Hemoglobin	9.9 ±1.5	8.1 ±2.1	0.001*
Creatinine	2.9 ± 1.4	7.2 ± 2.9	<0.001**
Urea	79.8 ± 36.3	103.8 ± 41.9	0.031*
pH	7.2 ± 0.1	7.2 ± 0.1	0.684
Bicarbonate	8.5 ± 4.9	7.7 ± 4.2	0.531
Sodium	159.0 ± 21.9	138.7 ± 9.7	<0.001**
Potassium	4.2 ± 1.2	4.9 ± 1.1	0.023*

*Data were expressed as mean ± SD. Statistical analysis was done by Unpaired t-test.*p<0.05 = statistically significant, **p<0.001 = highly significant*

DISCUSSION

Acute kidney injury (AKI) has emerged as a significant public health problem that affects millions of patients worldwide [23]. In this study, most patients in the pre-renal group were younger than 12 months, while in the renal group, most patients were older than 1 year.

The clinical presentation and predominant causes of paediatric AKI vary in different regions [25]. In the current study, diarrhoea with hypovolemia (69.3%) and sepsis (19.2%) were the major causes of pre-renal AKI. In contrast, Haemolytic uremic syndrome (HUS) and acute tubular necrosis (ATN) due to wasp envenomation were the predominant causes of renal AKI. Moyen et al.reported that out of 253 AKI children, 83% of cases were hypovolemic in their study, out of which 95.8% were due to

acute gastroenteritis [26]. Assounga et al. showed acute gastroenteritis with dehydration was the primary cause of AKI in their study, and there was a higher incidence of HUS reported by Biljon in his study [27, 28]. Afroz et al. showed diarrhoeal complications to be the major cause of pre-renal AKI and Hemolytic uremic syndrome, wasp envenomation, and acute glomerulonephritis to be the common causes of renal AKI [29]. Faraz, Shaikh and Farhan and Mishra et al. also emphasized Hemolytic uremic syndrome and septicemia as the most common causes of AKI in their study [30, 31].

Bangladesh Demographic Health Survey (BDHS) 2014 reported that the incidence of diarrhoeal disease (in 2 weeks before the survey) in 1-6 months and 6-11 months were 6% and 6.7%, respectively. As diarrhoeal diseases are common in infants in Bangladesh, AKI due to diarrhoea with hypovolemia was common in this age group in this study. A retrospective cohort study by Nkoy et al. showed the epidemiology, clinical features, and outcomes of children admitted from January 2018 to January 2019 at the University Hospital of Kinshasa for AKI [24]. A total of 49 children (aged 4 months–15 years) were admitted for AKI, mainly due to severe malaria and sepsis.

Most patients in the pre-renal group were <12 months of age, so they depended on their caregivers for their feeding and water requirements. Faulty thoughts of giving less water during winter to avoid cough and cold is another reason behind it. Improperly prepared ORS often has been reported to cause different degrees of hypernatremia [29]. Hypernatremia was more common in young infants with post diarrheal AKI due to concentrated ORS intake in Bangladesh, which coincides with the findings of this study [32]. Children with post diarrheal AKI were eight times more likely to present with hypernatremia [33].

At baseline, a higher percentage of patients in the pre-renal group exhibited tachycardia (50.0%) compared to the renal group (33.3%), although this difference did not reach statistical significance ($p=0.104$). Blood pressure variations were starkly different, with a significant majority of pre-renal cases presenting with hypotension (65.4%) compared to the renal group (18.5%) ($p<0.001$). Hypertension was exclusively observed in the renal group (77%). Tachypnea was prevalent in both groups without significant differences ($p=0.268$). Oedema, a crucial clinical indicator, was significantly more frequent in the renal group (85.2%) compared to the pre-renal group (34.6%) ($p<0.001$). These findings underscore the importance of considering distinct clinical profiles when evaluating pediatric patients with acute kidney injury, contributing valuable insights for timely diagnosis and targeted interventions. Statistical significance levels are denoted, with $p<0.05$ considered statistically significant and $p<0.001$ highly substantial.

Gunnam and Prasad conducted a retrospective observational study from November 2007 to August 2016, and their findings on children aged one day to 18 with clinical symptoms or abnormal laboratory parameters were similar to our investigation [5]. In this study, baseline creatinine and urea levels were significantly higher in the renal group than in the pre-renal group

($p<0.05$) because the disease severity was higher in the renal group as they presented with oedema, and severe acidosis.

CONCLUSION

In our study, we found that pre-renal cases primarily involved infants. On the other hand, renal cases were more common in the age from 1 to 5 years. Hypertension, and greater rates of oedema were baseline traits that distinguished the two groups apart. Considerable variations in creatinine and sodium levels emphasize the significance of customized care for children with acute renal damage based on etiological variables.

LIMITATION

For classifying as pre renal and renal AKI urinary markers (urine sodium, urine osmolality, fractional sodium excretion, fractional urea excretion, urine/plasma urea, urine/plasma osmolality, and urine/plasma creatinine) were not done.

FUNDING

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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