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Common Risk Factors Responsible for Acute Kidney Injury among Children: Experience at Medical University in Bangladesh

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Abstract

Background: Acute kidney injury can occur among the younger children due to different reasons. **Objective:** The purpose of the present study was to find out the risk factors and primary disease responsible for acute kidney injury among younger children. **Methodology:** This cross-sectional study was conducted in the Department of Paediatric Nephrology with the collaboration of Paediatric Gastroenterology, Paediatric Neurology, Paediatric Neonatology and Microbiology and Immunology at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh from May 2018 to July 2019 for a period of one year. Patients with the age group of 1 month to 17 years who were at risk of AKI, and admitted in the inpatient department of Pediatrics and allied at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh in both sexes were selected as study population. To detect AKI, serum creatinine was measured at 0 h (baseline), 48 h and 5th day respectively. **Result:** A total number of 42 patients, who fulfilled the inclusion criteria were enrolled in this study. The risk factors of AKI was mainly pre renal in 60% (n=9) cases, mostly due to nephrotoxic drugs followed by hypovolemia. Renal causes were in 40% (n=6) cases. Among these 50% cases due to amikacin and 50% cases due to use of radiocontrast agent. Most patients were with renal disease which was 30(58%) cases. Among them 28(93.0%) cases were nephrotic syndrome and 2(7.0%) cases were hydronephrosis. However, 7(13%) cases were cardiac disease presented with congenital heart disease who used radiocontrast agent. **Conclusion:** In conclusion most common risk factors of acute kidney injury among younger children is pre-renal causes which are due to nephrotoxic drugs. *[Journal of National Institute of Neurosciences Bangladesh, January 2021;7(1): 42-46]*

Keywords: : Risk Factors; Acute Kidney Injury; Children

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Introduction

Acute kidney injury (AKI) is a common and potentially catastrophic complication among hospitalized children and especially intensive care unit patients with incidence of 11.0% to 67.0% cases depending on definitions with mortality rate ranges from 20.0% to 47.0% cases[1]. In neonatal intensive care unit (NICU) incidence rate is high ranges from 8.0% to 24.0% cases and the high

mortality rate of this disease 20.0% to 50.0% cases[2]. It has become apparent that children who survive an episode of AKI are at increased risk for chronic kidney disease and warrant long-term follow-up[3]. Early diagnosis is vital for early intervention and prompt implementation of therapeutic measures which can save lives[4].

Creatinine is the most commonly used endogenous marker and become standard in measuring and classifying GFR internationally. A small increase in serum creatinine reflect significant renal damage and associated with poor outcome[5]. Therefore, early detection has a great value, allowing early prompt implementation of therapeutic measures to save lives and prevention of more severe renal damage[6]. However, fallacy of creatinine is, it is influenced by age, sex, height, body mass index, protein intake, dehydration, inflammation and maternal creatinine causing inter and intra-patient variability[7].

Besides glomerular filtration, it is secreted by proximal convoluted tubules, which contributes approximately 20% of total creatinine excretion[6]. On the other hand, the value of serum creatinine does not increase until GFR moderately decreased and GFR is a creatinine blind area[8]. The elevated level of this is not evident until 48 hours of significant renal damage. The purpose of the present study was to find out the risk factors and primary disease responsible for acute kidney injury among younger children.

Methodology

This cross-sectional study was conducted in the Department of Paediatric Nephrology with the collaboration of Paediatric Gastroenterology, Paediatric Neurology, Paediatric Neonatology and Microbiology and Immunology at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh from May 2018 to July 2019 for a period of one year. Patients with the age group of 4 days to 17 years, who were at risk of AKI, and admitted in the inpatient department of Pediatrics and allied at Bangabandhu Sheikh Mujib University, Dhaka, Bangladesh during this study period in both sexes were selected as study population. Patients with nephrotic syndrome at risk of AKI due to hypovolemia or shock, sepsis, use of nephrotoxic drugs for at least 5 days or patients other than nephrotic syndrome with hypovolemia, use of nephrotoxic drugs for at least 5 days and patients with obstructive uropathy and congenital heart disease needed to use radiocontrast agent were included in this study. Patient already diagnosed as AKI, preterm or patients with hypothyroidism and malignancy were excluded from this study. Patients were selected by purposive sampling technique. For exclusion of malignancy and thyroid disorder proper history taking, examination, related investigations (FT_4, TSH) and imaging were done. AKI was defined by any of the two: increase SCr $\geq$ 0.3 mg/dl within a 48 h period or increase SCr $\geq$1.5 times or $\geq$ 50% from baseline within 7 days period. Among nephrotoxic drugs, injectable antibiotics like amikacin, gentamicin, ACE inhibitors. Tab. Indomethacin (1 mg/kg/day) was used in patients with enthesitis related arthritis. Tab. Cyclosporine (3.5-4 mg/kg/d) was used in difficult nephrotic syndrome. Tab. Indomethacin (1 mg/kg/day) was used in patients with enthesitis related arthritis. In case of using cyclosporine and NSAID risk was considered when patient had associated fever / diarrhea / inadequate fluid intake / use of other nephrotoxic drug and pre renal causes was considered as volume correction, drug dose reduction of CsA and withdrawal of NSAID resulted kidney function became normal. Data was collected with appropriate questionnaire containing proper history, clinical examination and findings of laboratory reports of enrolled patients who fulfilled the inclusion criteria after taking informed written consent. All the cases were numbered chronologically. The data were collected and edited manually. The entered data were checked, verified and analyzed by appropriate computer software. Statistical analysis was performed by using SPSS for windows version 22. The data were presented in tubular or diagrammatical form. All qualitative data were expressed as frequency and percentages. All quantitative data were expressed as mean±SD. An analysis plan was developed keeping in view with the objectives of the study. Unpaired t-test and paired t-test were done whenever required. For all statistical test $p<0.05$ was considered statistically significant. Prior to the commencement of this study, the thesis protocol was placed and approved by the Institutional Review Board of BSMMU, Dhaka. For recruitment of study population permission was taken from Pediatrics and allied department. Every ethical issue was discussed with the patient's parents regarding the study. Parents were clearly informed about the nature and purpose of the study, procedures followed, risk associated with it and benefits from the study in easily understandable local language.

Results

A total number of 42 patients, who fulfilled the inclusion criteria were enrolled in this study. Among

them 42 cases were in older age group. In this study the mean age in AKI group was 11.3±3.7 years, statistically significant difference was from non-AKI group (p=0.007). Most patients were male, showed no significant difference between two groups. Male and female ratio was 2:1 in AKI group. The mean baseline serum creatinine value was significantly higher in AKI group ((p=0.007), but no difference had been shown in baseline cystatin C value (Table 1).

Table 1: Demographic and Lab Parameters of the Study Subjects

Parameters	AKI (n=15)	Non AKI (n=27)	P value
Age (year)	11.3 ± 3.7	7.1 ± 4.9	0.007
Gender			
• Male, n (%)	10(66.7)	15(55.6)	0.482
• Female, n (%)	5(33.3)	12(44.4)	0.007
Baseline creatinine (mg/dl)	0.56±0.16	0.41±0.16	0.149
Baseline cystatin C (mg/L)	1.04 ± 0.27	0.94 ± 0.19	

Unpaired t test was done

The risk factors of AKI was mainly pre renal in 60% (N=9), mostly due to nephrotoxic drugs followed by hypovolemia. Renal causes were in 40% (N=6). Among these 50% due to amikacin and 50% due to use of radiocontrast agent (Table 2).

Table 2: Risk Factors in Study Subjects with AKI in Older Age Group (n = 15)

Risk factors	Frequency	Percent
Pre renal	9	60.0
Nephrotic syndrome with		
• Hypovolemia	4	44.5
• CsA	3	33.3
• ACE-I	1	11.1
Other than NS		
• NSAID	1	11.1
Renal	6	40.0
Drug induced	3	50.0
Aminoglycoside		
• Amikacin	3	100.0
• Gentamicin	0	0.0
Radiocontrast agent	3	50.0
Post renal	0	0.0

CsA: Cyclosporine; ACE-I: Angiotensin converting enzyme inhibitor; NSAID: Non-steroidal anti-inflammatory drug; Results were expressed in frequency (N) and percentage (%)

Most patients were with renal disease 30 (58%). Among them 28 (93%) were nephrotic syndrome and 2 (7%) were hydronephrosis, used radiocontrast agent. Ten were neonatal diseases, 7 (13%) were cardiac disease presented with congenital heart disease (undergone cardiac catheterization), who used radiocontrast agent. Three patients presented with rheumatological disease used NSAID followed by GIT and neurological diseases used radiocontrast agent (Figure I).

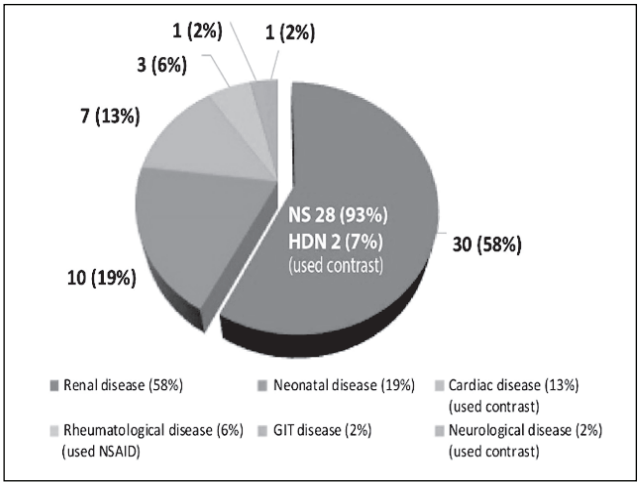

Figure I: Distribution of primary diseases in study subjects (n=52)

In this study 70% risk of AKI was due to pre renal and only 30% was due to renal cause in study subjects with AKI (Figure II).

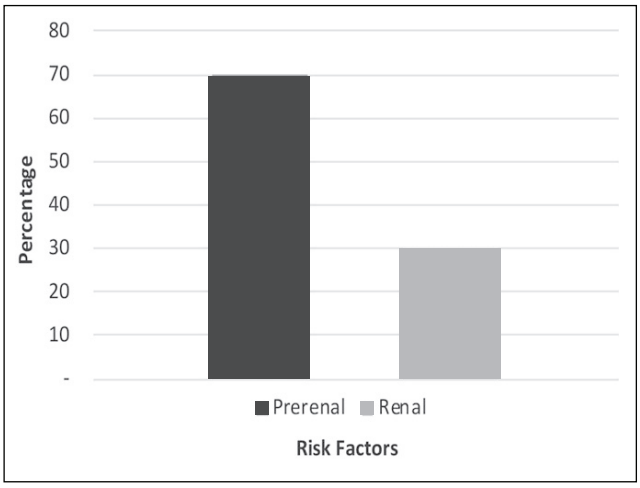

Figure II: Percentage of Pre Renal and Renal Risk Factors in Study Subjects with AKI (n=20)

Discussion

An incidence of AKI of 38% had been demonstrated in patients between 4 days to 17 years of age admitted to BSMMU in different departments during study period. Almost similar finding was found by Sutherland et al[9] where incidence of AKI was of 39% in children. A total 52 children were analyzed in this study. Forty two

patients were in older age group and ten patients in neonatal age group. The mean age in older age group of AKI was 11.3±3.7 years, is similar to Haque et al[10]. They found the incidence was higher in older patients.

In this study the male and female ratio is 2:1 in older age group which is almost matched with Afroz et al[11] where it is 1.9:1. The baseline creatinine has shown significant difference with non-AKI group, is similar to Safdar et al[4].

The present study revealed pre renal risk factors (70.0%) were higher in percentage than renal (30.0%). This finding showed almost similarity with Afroz et al[11] where pre renal causes were 66.0% and renal causes were 32.0%. If we consider the risk factor of AKI in neonate separately, we found that all risk factors were pre renal. Most neonatal AKI was pre renal, accounting for 85.0% cases[12]. Nephrotoxic drug use was the foremost cause followed by hypovolemia. These finding showed dissimilarity with Haque et al[10] where hypovolemia was of higher percentage than nephrotoxic drugs.

In this group, hypovolemia was the risk factor of 44.5% AKI due to presence of acute gastroenteritis (AGE). However, Yaseen et al[13] showed that AGE was the risk factor of 13.4% AKI and drug toxicity was the risk factor of 43.7% patient with nephrotic syndrome. The current study revealed 44.4% patients with nephrotic syndrome developed drug induced AKI. This is similar to Yaseen et al[13]. Among them cyclosporine was mainly responsible followed by ACE inhibitor. Yaseen et al[13] also found almost similar proportion of patient developed cyclosporine induced AKI, which causes renal vasoconstriction due to sympathetic over activity as well as concomitant activation of plasma renin resulting in decreased renal plasma flow. It has been reported that the renal impairment with doses of ≤5 mg/kg/d is low[11]. In this study the possible cause of CsA induced AKI with low dose was the presence of associated risk factors like taking furosemide and presence of anasarca. The present study had relatively higher percentage of AKI due to use of ACE inhibitor in this study. Yaseen et al[13] found only 2.5% patient developed AKI due to ACE-I. Another study showed among antihypertensive ACE inhibitors were the main cause of acute kidney injury[10].

Faught et al[14] observed that the incidence of NSAID induced AKI is of 2.7% in hospitalized children and adolescents. Changes of hemodynamics is account for 78.0% cases resulting in decrease renal blood flow causes low GFR. There is no similarity with present study possibly due to patients with different disease pattern were included in this study. Another study revealed that seven patients developed NSAID induced AKI with recommended dose of drug 1 to 4 days after taking. They had vomiting or inadequate fluid intake after taking of drug as symptoms. Indomethacin is thought to be the most likely to impair renal function[14]. In this study patients with indomethacin induced AKI had inadequate fluid intake after taking this drug. Credible data are lacking regarding role of indomethacin in causing AKI in Bangladesh. Akima et al[15] reported that indomethacin induced renal impairment occurred on day 2 following administration.

Among renal causes nephrotoxic drug was the most important cause of AKI in this study. Afroz et al[11] found among renal causes 12.5% was drug induced. This showed no similarity with the finding of current study possibly due to different methodology. Aminoglycoside suggested to cause AKI mainly due to incurring tubular damage. Mantan et al[16], however, reported much higher incidence (46.0%) and most of them for amikacin. The present study also showed similar finding.

The current study revealed that hypovolemia (60%) was a prominent pre renal risk factor of AKI in neonate due to dehydration following persistent vomiting, heart failure and surgical intervention. The other risk factors were sepsis and asphyxia. Momtaz et al[2] found that sepsis was the most (77.5%) common cause of neonatal AKI followed by hypovolemia (46.9%) and asphyxia (4%). In this study asphyxiated newborn developed cardiogenic shock due to hypoxia. Ghobrial et al[17] found 78.12% asphyxiated neonate developed pre renal AKI, among them 88.0% were in HIE stage II and developed AKI within 72 to 96 h after birth. Though this is not consistent with present study, the risk factor was also pre renal in current study due to poor renal perfusion and developed AKI within 96 to 120 h. Sepsis was present in 20.0% cases in this study. This difference of incidence is possibly due to small sample size.

Conclusion

In conclusion most common risk factors of acute kidney injury among younger children is pre-renal causes which are due to nephrotoxic drugs. The most common nephrotoxic drugs are aminoglycoside especially amikacin. However, NSAID is also the one of the risk factors of acute kidney injury. In these study population mostly are suffering with acute kidney injury due to renal disease especially nephrotic syndrome and hydronephrosis. Therefore, the risk factors among the neonated should be excluded very carefully.

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