Electrolyte abnormalities in acute kidney injury in children admitted in pediatric intensive care unit

Harsha Sangolgikar and Gonesh N Mevundi

DOI: https://doi.org/10.33545/26643685.2021.v4.i1a.127

Abstract
Background: Acute kidney injury (AKI) is defined as rapid deterioration of renal function resulting in retention of nitrogenous wastes and inability of kidney to regulate fluid and electrolyte homeostasis. Objective: To determine the electrolyte abnormalities in Acute Kidney Injury in children admitted in PICU. Setting: This study was conducted in all patients within the age group of 1 month to 18 years admitted in the PICU (Pediatric Intensive Care Unit) at Basaveshwar teaching and General hospital and Sangameshwar hospital attached to Mahadevappa R Ramappa medical college during a period from December 2015 to May 2017. Result: There were 40(38.0%) male AKI cases and 29(42.0%) female AKI cases in the study. The sex ratio of total study cases of Male to Female was 1.4:1. The sex ratio of AKI cases of Male to Female was 1.38:1. Statistically very highly significant difference of Anuria, Gross hematuria and Encephalopathy among AKI and Non-AKI groups (P<0.001) and there were statistically significant differences of Vomiting, Loose motion among AKI and Non-AKI groups (P<0.05). The symptoms of Anuria, Gross hematuria, Encephalopathy, Vomiting and Loose motion were significantly less in the non-AKI cases as compared to AKI cases. There were no statistical significant difference of Oliguria, Fever, Seizures, Breathlessness and Gl. Hemorrhage among AKI and Non-AKI groups (P>0.05).

Conclusion: It was concluded that AKI was associated with increased mortality (p<0.000).mortality rate was 34.8% compared to non AKI. In the present study, mortality was 9.1% in Stage 1 and 28.5% in Stage 2. Stage 3 it is 43.3%. Mortality was high in stage 3. In the present study, the median duration of PICU and Hospital stay was 9.98±7.27 in AKI group compared to7.41±5.62 days in Non AKI group (p<0.001).

Keywords: acute kidney injury, children, clinical profile, outcome, pediatric intensive care unit, ventilation

Introduction
Acute kidney injury (AKI) has become increasingly prevalent in both developed and developing countries, and is associated with severe morbidity and mortality, especially in children. In developed countries, AKI occurs predominantly in urban intensive care units and is associated with multi organ failure and sepsis, high mortality, and occurrence in older populations. While cases of AKI in urban areas of the developing world have similar characteristics to those in the developed world, AKI in rural regions commonly develops in response to a single disease and specific conditions (e.g. gastroenteritis) or infections (e.g. severe malaria, leptospirosis, or hemolytic-uremic syndrome) and in younger otherwise healthy individuals. Many causes of AKI in rural settings, such as diarrhea, poisoning, malaria, or septic abortion, can be prevented by interventions at the individual, community, and regional levels [1]. The etiology of AKI differs in different geographical areas according to the prevalent disease pattern and available health care facilities. For several years (1976-1993) HUS was a leading cause of AKI at most referral centers, but its incidence has declined. Acute GN and ATN are the most common conditions associated with ARF. In coastal regions of south India and Orissa and in rural areas, snakebite is an important cause. In some parts of Kerala leptospirosis is frequently encountered. Hantavirus infections are important in Korea and China [2]. Acute kidney injury is common after pediatric cardiac surgery and is associated with prolonged mechanical ventilation and increased hospital stay. Cardiopulmonary bypass time and age were independently associated with acute kidney injury risk.
Cardiopulmonary bypass time may be a marker for case complexity [3]. Various studies have attempted to identify the risk factors for development of AKI in critically ill children. Mehta et al. found that younger age, shock, sepsis, and need for mechanical ventilation where independent risk factors were AKI in their cohort [3]. Nephrotic drugs account for about 16% of all AKIs most commonly associated with AKI in older children and adolescents. Nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, amphotericin B, antiviral agents, angiotensin-converting enzyme (ACE) inhibitors, calcineurin inhibitors, radiocontrast media, are the most important drugs to indicate AKI as significant risk factor in children [3]. Hence, present study is conducted to determine the electrolyte abnormalities in Acute Kidney Injury in children admitted in PICU.

Materials and Methods: This was a prospective, observational study, in which 1000 patients were screened, all patients within the age group of 1 month to 18 years admitted in the PICU (Pediatric Intensive Care Unit) at Basaveshwar teaching and General hospital and Sangameshwar hospital attached to Mahadevappa Ramipple medical college during a period from December 2015 to Aug 2017.

Methods of collection of data: Following an informed parental consent, clinical history and examination will be done, comorbidities will be noted, and relevant data regarding investigations will be collected for all children admitted to PICU. Serum levels of creatinine estimated at admission and at daily intervals in PICU patients till discharge from PICU. Urine output measured and recorded as ml/kg/hour. Diagnosis and staging of AKI will be based on Acute Kidney Injury Network (AKIN) definition & classification.

Sample size: The minimum sample size required to study the fact based on data in literature [6] with 5% level of significance. The sample size taken will be 300. Using simple random sampling method.

Inclusion criteria: Patients aged 1 month to 18 years, admitted to pediatric intensive care unit (PICU) (Basaveshwar Teaching and General Hospital and Sangameshwar Hospital, Kalaburagi)

Exclusion criteria: Patients with known kidney disease such as congenital polycystic kidney disease and children who were diagnosed with chronic kidney disease on first visit.

Investigations to be done: Serum creatinine will be done on all patients admitted to PICU from day of admission till discharge from PICU. Serum creatinine of patients with AKI will be done at the time of discharge from hospital. If necessary CBC, urine routine, blood urea, serum electrolytes and USG abdomen will be done.

Statistical Analysis: Descriptive statistical characteristics and variables of the patients will be described. The biochemical and other numerical parameters will be compared using t test, Z test, and chi-square or Fischer exact test and other applicable methods. P-value < 0.05 was considered as the level of significance.

Result: Most of the cases 380(38.0%) belongs to the age group of 1-5 years, followed by 5-10years 267(26.7%) and minimum number of cases 13(1.3%) belongs to the age group of 15-18years. The mean and SD of age of boys and girls were 4.56 ± 3.84 and 4.49 ± 4.01 respectively. There was no statistical significant difference of age among males and females (P>0.05). There were 584(58.4%) males and 416(41.6%) females in the study. The sex ratio of Male to Female was 1.4:1. Table 1 There were 40(58.0%) male AKI cases and 29(42.0%) female AKI cases in the study. The sex ratio of total study cases of Male to Female was 1.4:1 The sex ratio of AKI cases of Male to Female was 1.38:1 this is almost same of the total cases There was no statistical significant difference of sex among AKI and Non-AKI groups (P>0.05). Table1

| Age in years | AKI cases | Non AKI cases | Total |
|--------------|-----------|---------------|-------|
|              | No.       | %             | No.   | %     | No. | %    |
| Males        | 40        | 58.0          | 544   | 58.4  | 584 | 58.4 |
| Females      | 29        | 42.0          | 387   | 41.6  | 416 | 41.6 |
| Total %      | 69 (6.9%) | 100.0         | 931 (93.1%) | 100.0 | 1000 (100.0%) | 100.0 |

X²-test value & P-Value, sig

X²= 0.0053
P>0.05, Not significant

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

Table 1: Sex wise distribution of AKI cases and non-AKI cases

Statistically very highly significant difference of Anuria, Gross hematuria and Encephalopathy among AKI and Non-AKI groups (P<0.001) and there were statistically significant differences of Vomiting, Loose motion among AKI and Non-AKI groups (P<0.05). The symptoms of Anuria, Gross hematuria, Encephalopathy, Vomiting and Loose motion were significantly less in the non-AKI cases as compared to AKI cases. There were no statistical significant difference of Oliguria, Fever, Seizures, Breathlessness and GI. Hemorrhage among AKI and Non-AKI groups (P>0.05). Table 2
Table 2: Comparison of symptoms among AKI and Non-AKI cases

| Symptoms       | AKI cases (n=69) | Non-AKI cases (n=931) | χ²-test values | P-value & significance |
|----------------|------------------|-----------------------|----------------|------------------------|
| Oliguria       | 3 (4.3%)         | 39 (4.2%)             | χ²=0.0072      | P>0.05, NS             |
| Fever          | 53 (76.8%)       | 737 (79.2%)           | χ²=0.051       | P>0.05, NS             |
| Vomiting       | 35 (50.7%)       | 344 (36.9%)           | χ²=5.09        | P<0.05, S              |
| Loose motion   | 16 (23.2%)       | 154 (16.5%)           | χ²=5.31        | P<0.05, S              |
| Anuria         | 5 (7.2%)         | 0 (0.0%)              | χ²=37.8        | P<0.001, VHS           |
| Seizures       | 12 (17.4%)       | 176 (18.9%)           | χ²=0.73        | P>0.05, NS             |
| Breathlessness | 28 (40.6%)       | 298 (32.0%)           | χ²=1.87        | P>0.05, NS             |
| Gross hematuria| 5 (7.2%)         | 1 (0.1%)              | χ²=31.82       | P<0.001, VHS           |
| Gl. Hemorrhage | 1 (1.4%)         | 0 (0.0%)              | χ²=0.431       | P>0.05, NS             |
| Encephalopathy | 8 (11.6%)        | 5 (0.5%)              | χ²=33.74       | P<0.001, VHS           |

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

The mean and SD age of AKI cases of hospital stay was 9.98 ± 7.27 and non AKI cases was 7.41 ± 5.62 overall mean and SD of all the cases was 7.62 ± 5.73. Highly statistical significant difference of duration of hospital stay among AKI and Non-AKI groups (P<0.01). Duration of hospital stay was longer in the AKI cases as compared to Non-AKI cases. Fig 1

Study reveal that, maximum number of cases were observed 44(63.8%) in 3rd stage, followed by the 2nd stage 14(20.3%) and minimum number of cases 11(15.9%) were seen 1st stage. Table 3

Table 3: Staging wise distribution of AKI cases

| Staging    | AKI cases |
|------------|-----------|
| No.        | %         |
| 1st Stage  | 11        | 15.9 |
| 2nd Stage  | 14        | 20.3 |
| 3rd Stage  | 44        | 63.8 |
| Total      | 69        | 100.0 |

There was statistically very highly significant difference of outcome in AKI and Non-AKI cases (P<0.001). The case fatality rate of Non-AKI was 1.0%. whereas the case fatality rate of AKI was 34.8%. Overall death rate was 3.3%

Fig 2: Multiple bar diagram represents percentage of outcome in AKI and Non AKI cases
Discussion
Studies have shown AKI is independently associated with poor outcome. Published data about AKI in Indian children are limited. Most data are available from developed countries. Very few Indian studies provide incidence of AKI in pediatric ICU. In the present study, the incidence of AKI in PICU was 6.9%. Compared to other Indian studies by Krishnamurthy et al. [6], however, the incidence rate is lower. Heterogeneity of patient population, diverse regional differences, and sample sizes study designs can explain varying incidence of AKI. In the present study, median age was 4.56% among boys and girls constituted 4.49%, 58% were boys among AKI patients which is comparable to Krishnamurthy et al. [6] study.

In the present study, the mean and standard deviation of serum creatinine value in AKI patients was 2.29 mg/dL, while in Krishnamurthy et al. [6]. Study, it was 1.1 mg/dL. In the present study, AKI Stage 1, 2, 3 was diagnosed in 11 (15.9%), 14 (20.3%) and 44(63.8%) of AKI patients. Maximum numbers of AKI patients were in Stage 3. Similar to Krishnamurthy et al. [6] where the maximum numbers of AKI patients were in Stage 3.

| Table 4: AKI staging among different studies |
|---------------------------------------------|
| Stages | Present | Krishnamurthy et al. [6] | Ts Prabhakar et al. [7] | Mehta et al. [8] |
|--------|---------|--------------------------|------------------------|-----------------|
| Stage 1| 15.9%   | 35.2%                    | 85.7%                  | 65.8%           |
| Stage 2| 20.3%   | 25.9%                    | 11.4%                  | 17.8%           |
| Stage 3| 63.8%   | 38.9%                    | 2.9%                   | 16.4%           |

In the present study, the most common condition associated with AKI was sepsis, followed by encephalitis, cardiac causes, DKA, dengue, and gastroenteritis in decreasing order of occurrence. In Krishnamurthy et al. [6]. and Mehta et al. studies, pneumonia was the most common disease associated with AKI. The mortality in present study, mortality was 34.8%, which is comparable to Mehta et al. [8] study. In the present study, mortality was 9.1% in Stage 1 and 28.5% in Stage 2. Stage 3 it is 43.3%. Mortality was high in stage 3. According to the present study as the staging increases mortality also increases which is comparable to Mehta et al. [8] study.

In the present study, the median duration of PICU and hospital stay was 9.98±7.27 in AKI group compared to 7.41 ± 5.62 days in Non AKI group (p<0.001). This is comparable to Mehta et al. study, where the mean duration of hospital stay was 9 days and 7 days in AKI and Non AKI group. Both the studies support the fact that in the presence of AKI, the PICU and Hospital stay increases.

Conclusion
In the present study, the most common condition associated with AKI was sepsis, encephalitis. In the present study, pre-renal causes accounted for (54) 78.3% of AKI. In the present study, AKI Stage 1, 2, 3 was diagnosed in 11 (15.9%), 14 (20.3%) and 44(63.8%) of AKI patients. Maximum number of AKI patients were in Stage 3 (p<0.001). 63.8%. AKI was associated with increased mortality (p<0.000). Mortality rate was 34.8% compared to non AKI. In the present study, mortality was 9.1% in Stage 1 and 28.5% in Stage 2. Stage 3 it is 43.3%. Mortality was high in stage 3. In the present study, the median duration of PICU and Hospital stay was 9.98±7.27 in AKI group compared to 7.41 ± 5.62 days in Non AKI group (p<0.001).

Acknowledgement
I would like to express my profound gratitude to all the participants for their co-operation and for their immense faith they reposed in me.

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