ACUTE KIDNEY INJURY IN CHILDREN BELOW 7 YEARS OF AGE

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Abstract

Background

Acute Kidney Injury (AKI) is considered as one of the clinical syndromes where the kidneys' capability for maintaining electrolyte hemostasis and fluid is impaired due to an unexpected deterioration in acute renal function. AKI is a disease with bad sequelae that requires immediate attention. Objective: To assess the causes of acute kidney injury in children less than 7 years of age, regarding etiology, presentation, laboratory findings and management.

Methods and patients: A study of patients under the age of 7 who have been admitted to the Central Teaching Hospital with AKI and followed up in the pediatric Nephrology Consultation clinic between June 1, 2016 and February 1, 2017.

Result: The study included 100 patients, 66 male and 34 female children. Male / female ratio has been 1.5:1. Prerenal causes constituted (65%). Most common presentation was decreased urine output and acidotic breathing in all age groups of acute kidney injury.

Conclusion: About 61.2% of causes needed peritoneal dialysis while 38.8% of cases responded to medical management. 15% of cases died in this study.

Keyword: Acute kidney injury, children, peritoneal dialysis.

Introduction:

AKI can be defined as one of the clinical syndromes where the kidneys' capability for maintaining electrolyte homeostasis and fluid is impaired due to a sudden
deterioration in renal function (1). Since precise measurements regarding GFR in the emergency settings are difficult, clinical criteria of AKI depending on changes in indirect measures of GFR, such as BUN, serum creatinine, and urine output, are routinely utilized (1,2). The function of the kidney is determined by the integrity of the renal parenchyma, kidney's blood supply, and the urinary tract's patency. As a result, the well-established classification related to AKI as renal, prerenal, or postrenal is still used (2,3).

**Pathogenesis**

**Prerenal causes**

Reduced effective circulating arterial volume, which results in a lower glomerular filtration rate (GRF) and insufficient renal perfusion, characterizes prerenal causes. Renal function returns to normal in the case when underlying causes of the renal hypoperfusion is treated quickly. If the hypoperfusion continues, intrinsic renal parenchymal damage could occur (2).

**Renal causes**

Renal causes of AKI include rapidly progressive from of several type of glomerulonephritis, that are common causes of AKI in older children. Activation of coagulation system within the kidneys resulting in small vessel thrombosis may lead to AKI.

In toddlers, the most prevalent causes of AKI are hemolytic-uremic syndrome and acute dehydration (2,4).

The term acute tubular necrosis originally described a syndrome of AKI in the absence of arterial or glomerular lesions. The proposed mechanism of renal failure was necrosis of tubular cells (2).
Acute interstitial nephritis is becoming a more common AKI cause, and it is mainly caused by a hypersensitive reaction to a therapeutic agent (1).

Tumors may produce AKI by infiltration of the Kindly or by associated with AKI, inability to conserve Na and H₂O is common in patients having these disorders but losses are usually compensated by increased oral intake, if oral intake is compromised (vomiting or external salt and water loss develops i.e., diarrhea), then these in conjunction volume contraction and renal failure (5,6).

**Post – renal causes:**

Post-renal AKI causes include obstruction of the urinary tract with the two-functioning kidney, ureteric obstruction must be bilateral to produce renal failure. We found almost all patients (100%) developed decrease urine output during the hospitalization. It is important to recognize that dilatation of the upper collecting system may not occur several days after acute ureteric obstruction (4,6,7).

**Clinical manifestations**

The precipitating disease might dominate or modify the presenting symptoms and signs.

Clinical findings associated with renal failure:

- Decreased urine output.
- Pallor (anemia).
- Hypertension.
- Edema (water and salt overload).
- Acidotic breathing.
• Lethargy and Vomiting (in infants).
• Dehydration \(^{(2,3)}\).

Complication of AKI

May include:

1- Volume overload with the pulmonary edema and heart failure
2- Arrhythmia.
3- Gastrointestinal bleeding due to stress ulcers or gastritis.
4- Seizures and coma \(^{(2,3)}\).

Physical examination should include a search for the following signs:

• Eye: Iritis, keratitis, dry conjunctiva, uveitis, autoimmune vasculitis \(^{(8)}\).
• Pulmonary: rales, good pasture syndrome.
  - Hemoptysis – Wegener granulomatosis \(^{(1)}\).
• Skin: Livedo reticularis: butterfly rash palpable purpura systemic vasculitis, digital ischemia, maculopapular rash allergic interstitial nephritis \(^{(3)}\).
• Ears: Aminoglycoside toxicity, hearing loss (Alport syndrome), Wegener granulomatosis, mucosal or cartilage ulceration \(^{(9)}\).
• Cardiac:
  - Atheroemboli, Irregular rhythm
  - Rales, increase Jugular vein distention, S3 CHF \(^{(8)}\)
  - Endocarditis, Murmur.
• Abdomen:
  - Costovertebral angle tenderness – papillary necrosis, nephrolithiasis.
  - Pelvic m rectal mass, urinary obstruction, distended bladder.
  - Pulsatile mass (i.e., aneurysm) – Atheroemboli.
  - Edema, limb ischemia, rhabdomyolysis (7,10).

**Laboratory Findings**

• Metabolic acidosis.
• Hypocalcemia and hyponatremia.
• Anemia (typically dilutional or hemolytic as in HUS, SLE, renal vein thrombosis)
• Increased serum concentration of blood urea nitrogen creatinine, potassium, phosphate, and uric acid.
• Thrombocytopenia (HUS, SLE, renal vein thrombosis).
• Leucopenia (SLE).
• C3 levels might be decreased.

The existence of proteinuria, hematuria, and red blood cell or granular urinary casts suggested the intrinsic AKI (2).

Tubule interstitial disease is indicated by the existence of WBCs and WBC casts, as well as low-grade hematuria and proteinuria.

• Chest radiography could reveal the cardiomegaly as well as pulmonary congestion.
Renal ultrasonography may reveal hydronephrosis and or hydroureter that are suggestive of urinary tract obstruction (2,3).

Aim of the study: For assessing the cause of acute renal failure in children who are younger than 7 years of age regarding:

Methods and patients

A cross-sectional study was conducted on 100 patients under the age of seven (including neonatal period) who were hospitalized to a child central teaching hospital with AKI between June 1, 2016 and February 1, 2017. All participants enrolled in the study had a thorough medical history recorded and a full physical assessment. Serum creatinine, blood urea, serum electrolytes (sodium, potassium, and calcium), GUE, GBR, abdominal ultrasound, and other tests were performed as needed. Based on the physical examination, history, and laboratory data, the causes of renal failure were categorized into three categories: renal, prerenal, and postrenal.

Abnormal renal function was considered if:

1- Blood urea level greater than 50 mg/dl indicating impairment of GFR independent of hydration status.

2- Oliguria considered when urine output <400ml/m2/day or <0.5 ml/kg/hr in children and < 1ml/kg/hr in infant (11).

Indication for dialysis in the AKI included:

- Persistent hyperkalemia.

- Volume overload with the hypertension and / or pulmonary edema refractory to the diuretic therapy.
• Neurologic symptoms (changed mental status, seizures).

• Extreme metabolic acidosis unresponsive to medical treatment.

• Blood urea nitrogen > 100mg/dl-150mg/dl (or lower in the case of the rapid rising).

• Calcium / Phosphorus imbalance, with the hypocalcemic tetany (2).

Results

Among 100 patients included in the study with acute kidney injury There have been 66 males and 34 females with M/F ratio (1.5:1)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Male</th>
<th>Female</th>
<th>M:F</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1day - 6 months</td>
<td>40</td>
<td>20</td>
<td>2:1</td>
<td>60</td>
<td>60.0</td>
</tr>
<tr>
<td>&gt; 6 months - 12 months</td>
<td>18</td>
<td>10</td>
<td>1.8:1</td>
<td>28</td>
<td>28.0</td>
</tr>
<tr>
<td>&gt; 12 months – 24 months</td>
<td>4</td>
<td>2</td>
<td>2:1</td>
<td>6</td>
<td>6.0</td>
</tr>
<tr>
<td>&gt; 24 months - 84 months</td>
<td>4</td>
<td>2</td>
<td>2:1</td>
<td>6</td>
<td>6.0</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>34</td>
<td>1.9:1</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Prerenal causes accounted for 65% of cases (female 20%, male 45%), renal causes 24% (female 7.5%, male 15%), and postrenal causes for 11% (female 5%, male 6%) in this work, as indicated in Table2.

Table (2): Causes of the AKI in relation with sex
Causes | Male | Female | Total | %
---|---|---|---|---
Prerenal | 45 | 20 | 65 | 65.0
Renal | 15 | 9 | 24 | 24.0
Postrenal | 6 | 5 | 11 | 11.0
Total | 66 | 34 | 100 | 100.0

Prerenal causes of AKI

Hypovolemia caused by gastrointestinal fluid loss (moderate to severe dehydration) was the most common cause (approximately 67%), whereas the other causes were less common (see table 3).

Table (3): prerenal causes of AKI

| Cause | NO. | %
---|---|---
Gastroenteritis | 44 | 67.7
Septicemia | 20 | 30.7
Disseminated intravascular coagulopathy | 1 | 1.6
Total | 65 | 100

Renal causes of AKI

In this study hemolytic uremic syndrome was most common renal cause (80%) followed by shock and developmental anomalies as shown in table (4).
Table (4): Renal causes of AKI

<table>
<thead>
<tr>
<th>Cause</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic Uremic Syndrome</td>
<td>16</td>
<td>80.0</td>
</tr>
<tr>
<td>Shock (ATN)</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>Developmental anomalies</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Postrenal causes of AKI

The most common was ureteropelvic junction obstruction (60%) as shown in table (5).

Table (5): post – renal causes of AKI on admission

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ureteropelvic junction obstruction</td>
<td>9</td>
<td>60.0</td>
</tr>
<tr>
<td>Urethral Valve</td>
<td>5</td>
<td>33.3</td>
</tr>
<tr>
<td>Vesicoureteric reflux</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Clinical presentation of AKI admission

The most common clinical presentation was decreased urine output (52%) as shown in table (6).
Table (6) clinical presentations of AKI on admission

<table>
<thead>
<tr>
<th>Clinical presentations</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased urine output</td>
<td>52</td>
<td>52.0</td>
</tr>
<tr>
<td>Acidotic breathing</td>
<td>21</td>
<td>21.0</td>
</tr>
<tr>
<td>Dehydration</td>
<td>10</td>
<td>10.0</td>
</tr>
<tr>
<td>Lethargy and vomiting</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>Edema</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>Pallor</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>Coma</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>GIT bleeding</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Complications of AKI

The number of patients who had an AKI-related complication was rather low (30). Gastrointestinal bleeding (33.3%) and seizures (46.7%) were the most prevalent complications, as seen in the table (7).

Table (7): AKI complications

<table>
<thead>
<tr>
<th>Cause</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure</td>
<td>14</td>
<td>46.7</td>
</tr>
<tr>
<td>GIT bleeding</td>
<td>10</td>
<td>33.3</td>
</tr>
</tbody>
</table>
Melena, hematemesis (stress ulcer), or profuse bleeding DIC were all present in patients experiencing GIT bleeding. Two of the comatose patients were admitted with a coma and have been diagnosed with uremic encephalopathy, whereas the third had nervous system bleeding.

**Investigations:**

High levels of serum creatinine and blood urea were linked to postrenal and renal causes of AKI in the presented work. Despite gastrointestinal loss, the levels of serum potassium were high in 22% of patients, including prerenal causes. Furthermore, the levels of serum calcium levels dropped in 30% of the instances, and 10 of them had developed tetany.

**Table (8): Biochemistry findings in this study group**

<table>
<thead>
<tr>
<th>Patient`s value</th>
<th>No.0f cases</th>
<th>%</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. urea 85-150mg/di</td>
<td>75</td>
<td>75.0</td>
<td>20 – 45mg/di</td>
</tr>
<tr>
<td>More than 150mg/di</td>
<td>25</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>S. creatinine 0.3-4.5mg/di</td>
<td>80</td>
<td>80.0</td>
<td>0.2-0.3 mg/di</td>
</tr>
<tr>
<td>More than 4.5 mg/di</td>
<td>20</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>S. potassium 5-6mmol/L</td>
<td>78</td>
<td>78.0</td>
<td>3.0 – 5.3 mmol/L</td>
</tr>
</tbody>
</table>
Extremely high S.k $^{22}$22 $^{22}$22.0

S. sodium 125-135 mmol/L 58 58.0 136 – 145 mmol/L

More than 135 mmol/L 42 42.0

S. calcium 8-11 mg/dL 70 70.0 8 – 11 mg / dL

Less than 8 mg/dL 30 30.0

S. phosphorous 1-2 mmol/L 88 88.0 0.8 – 1.8 mmol/L

More than 2 mmol/L 12 12.0

**Discussion:**

The male to female ratio in the presented work, which included 100 patients, was 1.5:1. It is higher compared to the ratio (1:1) in research conducted by Richard Sinert $^{(3)}$ and (1,7:1) in research by Dr. Bushra Jalil Salih in Iraq $^{(12)}$, yet it is consistent with studies by Wejdan A. Sabty (2,3:1) in Iraq $^{(13)}$ and Jamal A. et al $^{(14)}$ and lower than the ratio 3.5:1 in research by Srivastava RN $^{(15)}$. In terms of AKI’s etiology, 65% of cases have been because of the prerenal causes in the presented work, which is lower than 71.6% in a study by Wejdan A. Sabty’s research $^{(13)}$, yet higher than 60% in research by R. Sinert $^{(3)}$ in England. Which could be explained by a fact that Iraq has been considered as one of the developing countries, and the majority of cases identified in daily work are cases of sepsis and gastroenteritis, which are considered prerenal. GIT fluid loss (67.7%) is the most frequent cause, according to research by Mark R. Benfield $^{(1)}$, Wejdan A. Sabty (66.7%) and Bushra Jalil Salih (54%) $^{(24)}$.$^{(25)}$
Renal causes were determined to be responsible for (24%) of patients with decreased urine output (20%) in the presented work, which is considered to be greater than (13.6%) in the work of Wejdan A. Sabty (13) and (16%) in the work of Richard Sinert (3).

In the presented research, only 52% of patients had decreased urine output, compared to 85% in a work by John M. Flack (16). Lethargy and vomiting were seen in 5% of cases, compared to 20% in research by Wejdan A. Sabty (13) and 30% in prior research by Richard Sinert (3), yet the result is consistent with the study of Srivastava RN (15). Seizures were the most frequent complication in this work, with 16 cases (46.7%), which is lower than (55%) in a work by Wejdan A. Sabty (13) and greater than 30% in previous research by Morrell Michael Arram (7). Other major consequence bleeding (10 cases) (33.3%), which is comparable to S.P. Mc Donald and JC Craig's (30%) and Wejdan A. Sabty (31%) (13). In this investigation, 3 cases (10%) suffered heart failure, whereas in research by S.P. Mc Donald and Craig, 25% developed heart failure (17).

**Regarding investigations:**

This research found a significantly high serum potassium levels of in 22 cases (22%), compared to 91.60% in research by Wejdan A. Sabty (13). These patients, who had high levels of serum potassium initially or within some hours of renal function deterioration, experienced an increase in levels of serum potassium, despite the fact that majority of them had gastrointestinal potassium loss. Hypocalcemia was identified in 30 patients (30%) in the presented work, which is significantly fewer than (66%) in research by (Pascal and Thadhani R) (18) and (75%) in research by Wejdan A. Sabty (13) and (45%) in research by Bushra Jalil Salih.
Regarding hematological findings, most of the patient in this study (48.2%) were not anemic which is in agreement with previous study (83.5%) done by Goldfonb (26) but higher then (58.4%) in wejdan Sabty study (25). In the anemic group (12 cases), 12 cases had normochromic normocytic anemia while 7 cases reported in this study with hypochromic microcytic anemia. Leukocytosis and thrombocytopenia were found in septicemic patients and in patients with HUS.

With regard to treatment, the results of the presented work indicated that 28% of patients responded to medical management which is not more than 40.3% in research by Wejdan A. Sabty (25) and not more than 60% in Richard sinet study (4), and this could be because of either delay referrals (so the patient deteriorated) or early referral as soon as the study had shown high blood urea prior to the suitable correction of the dehydration and so patients referred with some degree of dehydration which increased during the way down to the hospital and in both cases patients reached our hospital with renal failure and needed urgent dialysis.

Most cases responded to medical treatment were due to prerenal causes of AKI.

In the presented work, 32 causes with prerenal AKI required peritoneal dialysis (25 of them had a delayed rehydration history), indicating that they had acute tubular necrosis. The total number of people who don't respond to medical treatment (47 cases) (47%) is larger than the 30% found in research by Pascial and Thadhani R (22) and is attributable to the same reasons discussed above (timing of referral). In the presented work, 15% of cases died, compared to 4% in a previous work by Pascial and Thadhani R (22). This could be explained by either patients' age that is one of the important risk factors for the mortality, with the youngest patients having a higher rate if mortality, or the underlying disease in some of the patients (such as meningitis, malignancy, and severe developmental anomalies) complicating renal failure.
Conclusion

1- Acute kidney injury was more common in male than female children below 7 years of age.

2- Most common AKI causes are prerenal causes and most common cause of the prerenal was hypovolemia particularly due to gastrointestinal loss.

3- The most prominent complication was seizure and the least in frequency gastrointestinal bleeding.

4- Renal function was worse with renal and postrenal causes of acute renal failure.

No conflicts of interest

Source of funding: self

Ethical clearance: was approved by Iraqi Ministry of health- scientific committee

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