Acute renal failure in neonatal septicemia

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Abstract

Objective: To find out the prevalence, associate factors and outcome of acute kidney injury in neonatal sepsis.

Methods: An observational hospital based prospective study was conducted at outborn NICU, Bal Chikitsalya, RNT Medical College, Udaipur (Raj.) India from August 2015 to January 2016. We enrolled total 107 outborn neonates with sepsis, were evaluated for presence of ARF or not. Sepsis was diagnosed on the basis of either a positive sepsis screen (immature: total (I:T) neutrophil ratio > 0.2, μ -ESR > age in days + 2 mm or >15 mm, CRP > 1mg/dl, TLC<5000 cells/mm^3 or >15000/ mm^3; 2 or more positive) or a positive blood culture in symptomatic neonates. ARF was defined as creatinine >1.5 mg/dl irrespective of day of life. Oliguria was defined as urine output <1ml/Kg/hr.

Results: 34 out of 107 (21.49%) neonates with sepsis had ARF; only 20.58% of ARF was oliguric. The mean gestation of neonates with ARF was similar to those without ARF (34.73±2.88wks vs. 34.52±3.17wk). The association of shock was also significantly higher in neonates with ARF (70.59% vs 29.41%, p<0.001). Mortality in neonates who developed ARF was significantly higher (56.52% vs 25%, p<0.001).

Conclusion: Renal failure occurred in 21.49% neonates with sepsis. Although ARF in neonates has been reported to be predominantly oliguric, it was observed that ARF secondary to neonatal sepsis was predominantly non oliguric. Very Low birth weight was an important risk factor for the development of ARF.

Keywords: Acute kidney injury; Neonatal sepsis.

1. Introduction

The Acute kidney injury (AKI) is a common problem in the neonatal intensive care units (NICUs) and has been shown to occur in 24% of neonates admitted to NICUs. More recent studies have reported an incidence of AKI of 3–8% of all NICU admissions [40]. The most common form of AKI in neonates is prerenal failure due to renal hypo-perfusion or ischemia [41]. Pre-renal failure may result in intrinsic kidney failure if it is not treated promptly.

The kidneys of neonates are particularly susceptible to hypo-perfusion because of the physiologic characteristics of neonatal kidneys, including high renal vascular resistance, high plasma renin activity, low glomerular filtration, decreased intra-cortical perfusion rate and decreased re-absorption of sodium in the proximal tubules in the first days of a neonate [43]. Thus, newborn infants are vulnerable to acute tubular necrosis or cortical necrosis. Acute renal failure (ARF) is commonly present among sick neonates.[1,2] While asphyxia, Respiratory distress syndrome (RDS) and urogenital anomalies are commonly reported causes of ARF in the West[3,9,39] sepsis is the leading cause of ARF in the preliminary reports from India.[9,39] earlier studies have focused on perinatal asphyxia as the cause of ARF. Criteria for ARF in neonates usually include a high Blood urea nitrogen (BUN), but in this study creatinine >1.5mg/dl was taken to label AKI in newborn.

The present study was undertaken with the objective of evaluating occurrence of AKI in neonatal sepsis, associated risk factors and outcome.

2. Materials and methods

The study was conducted in the outborn nursery of BalChikitsalya, RNT Medical College, Udaipur (Raj.) India. Medical records of 107 cases of neonatal sepsis admitted from August 2015 to January 2016 were studied. Neonatal sepsis was diagnosed on the basis of either a positive sepsis screen or a positive blood culture in symptomatic neonates. The screen was positive if 2 or more of the following were present – CRP > 1 mg/dl, micro- ESR > age in days+ 2mm or >15 mm fall in first hour, Total leucocyte count <5000/ mm^3 or >15000/mm^3, immature: total neutrophil ratio > 0.2. Acute renal failure (ARF) was defined as creatinine >1.5 mg/dl irrespective of day of life. Oliguria was defined as urine output < 1 ml/Kg/hr.[5,7,10,11] A thorough clinical examination to see for urethral, meatal abnormalities, palpable bladder and kidneys was done. None of the neonates...
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in the study had any gross congenital anomaly of the kidney or urinary tract on clinical examination.

A retrospective case control study design was used. Risk factors evaluated for occurrence of ARF included gestational age, weight, age on onset of sepsis, culture positivity, meningitis, necrotising enterocolitis (NEC), and shock.

Risk factors evaluated for fatality in sepsis associated ARF included gestational age, weight, early onset, culture positivity, associated meningitis, asphyxia, shock and presence of oliguria. Statistical analysis was done by student’s t-test, Chi square test and Mann Whitney test.

3. Results

For the study, total 107 newborns were enrolled who had probable or proven sepsis. In our study, there was male sex predominance and the male–female ratio was 3.45:1. In this study, regarding the gestational age, 28.04% were term out of which 29.41% had AKI. 71.96% neonates were preterm out of which 31.11% had AKI. 74.77% baby were low birth weight, 31.25% baby had AKI. 25.23% baby were normal birth weight (2.5-4 kg), and 9(33.33%) baby had AKI. 33(30.84%) neonates had early onset septicaemia, out of which 18.18% neonates expired. 22 (66.66%) neonates did not have AKI, out of which 18.18% neonates expired. 33.33% neonates had meningitis, whereas 38.36% neonates had meningitis in without AKI group. Blood cultures were positive in 27% neonates, 32.35% positive in neonates of AKI and 21.92% neonates also had blood culture positive in without AKI group. 39.25% neonates had shock, 70.59% had shock in AKI and 24.66% neonates had shock in without AKI group. 66.66% neonates developed necrotizing enterocolitis, 26.47% neonates of AKI had NEC, whereas 36.99% neonate developed NEC in non AKI group [p=0.28]. Incidence of AKI did not differ with or without NEC. 78.50% were discharged, 25% baby had AKI. 21.50% neonates expired out of which 56.52% had AKI. In this study incidence of AKI 31.77%, out of which oliguric AKI 20.58% and 79.42% of nonoliguric AKI in neonatal sepsis. In Our study out of 107, 21(23%) neonates expired, 84(78.50%) were discharged 25% had AKI (p=0.004). Mortality in AKI group 3 times to the non AKI group.

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<table>
<thead>
<tr>
<th></th>
<th>Total number of neonates with sepsis</th>
<th>107</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean gestational age (weeks ± s.d.)</td>
<td>34.59 ± 3.07</td>
<td></td>
</tr>
<tr>
<td>Preterm</td>
<td>77(71.96%)</td>
<td></td>
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<tr>
<td>Mean weight at presentation (gms ± SD)</td>
<td>2.14 ± 0.57</td>
<td></td>
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<tr>
<td>Mean age at presentation (days ± SD)</td>
<td>9.43 ± 7.39</td>
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</table>

Table 2: Comparison of Septic Neonates with and Without ARF

<table>
<thead>
<tr>
<th></th>
<th>With ARF</th>
<th>Without ARF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Subjects</td>
<td>34</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Mean gest. Age (wks)</td>
<td>34.73±2.88</td>
<td>34.52±3.17</td>
<td>p=0.67</td>
</tr>
<tr>
<td>Term ≥ 37 wk</td>
<td>10(33.33%)</td>
<td>20(66.66%)</td>
<td>p=0.82</td>
</tr>
<tr>
<td>Preterm &lt; 37 wk</td>
<td>24(31.11%)</td>
<td>53(68.83%)</td>
<td></td>
</tr>
<tr>
<td>Mean weight (gms) Wt&lt; 2500 g</td>
<td>25(31.25%)</td>
<td>55.00(68.75%)</td>
<td>p=0.8</td>
</tr>
<tr>
<td>Mean age at presentation (days)</td>
<td>7.88±5.41</td>
<td>10.17±8.09</td>
<td>p=0.78</td>
</tr>
<tr>
<td>Sepsis Early</td>
<td>11(33.33%)</td>
<td>22(66.66%)</td>
<td>P=0.577</td>
</tr>
<tr>
<td>Late onset septicaemia</td>
<td>22(66.66%)</td>
<td>22(66.66%)</td>
<td></td>
</tr>
<tr>
<td>Culture positive sepsis</td>
<td>11(32.35%)</td>
<td>16 (21.92%)</td>
<td>p=0.24</td>
</tr>
<tr>
<td>Meningitis</td>
<td>15(44.12%)</td>
<td>45(61.64%)</td>
<td>P=0.08</td>
</tr>
<tr>
<td>Shock</td>
<td>24(70.59%)</td>
<td>18(24.66%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>13(56.52%)</td>
<td>10.00(43.47%)</td>
<td>P=0.004</td>
</tr>
</tbody>
</table>

Table 3: Prognostic factor in neonatal acute kidney injury

<table>
<thead>
<tr>
<th></th>
<th>Survived (n=21)</th>
<th>Death (n=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Gestational Age In week±1SD</td>
<td>34.90±2.76</td>
<td>34.46±3.18</td>
<td>0.68</td>
</tr>
<tr>
<td>Mean Weight at birth ± 1SD in kg</td>
<td>2.21±0.57</td>
<td>2.11±0.56</td>
<td>0.61</td>
</tr>
<tr>
<td>Shock</td>
<td>13(61.90%)</td>
<td>11(84.61%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Blood culture</td>
<td>8 (3.80%)</td>
<td>3 (23.07%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Meningitis</td>
<td>10 (47.61%)</td>
<td>9 (69.23%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Early Onset Septicaemia</td>
<td>9 (42.85%)</td>
<td>2 (15.38%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Oliguria</td>
<td>2 (9.52%)</td>
<td>5 (38.46%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>
4. Discussion

The neonatal kidney is particularly vulnerable to the effects of hypoperfusion since the renal vascular resistance and plasma renin activity are high. Consequently, renal blood flow is proportionately more reduced in neonates. Acute tubular necrosis (ATN) has many parallels with the physiologic characteristics of neonatal kidney- the low glomerular filtration rate (GFR), decreased intercortical perfusion, decreased proximal reabsorption of sodium and increased plasma renin activity.[13]

In our study, there was male sex predominance and the male–female ratio was 3.45:1 because of more number of male neonates seeks medical treatment as compared to females due to the gender bias persisting in our society.

In the present study, 31.77% of all neonates with sepsis had AKI. This is higher than the reported incidence. Jayashree et al.[35] reported 15% of neonates with sepsis had ARF. Airede et al.[22] reported 3.9% Agras et al reported(3.4%) lower incidence of acute kidney injury. Whereas Mathur et al.[42] reported 26% of neonates with sepsis had ARF[Table.2].

In this study, regarding the gestational age, 28.04% were term out of which 29.41% had AKI. 71.96% neonates were preterm out of which 31.11% had AKI. This agrees to Mathur et al.[42] who reported that the incidence of AKI in term and preterm almost equal and Mathur et al.[42] who reported that the incidence of AKI in term and preterm almost equal. Mortazavi et al.[36], who reported that pre-term cases were less frequently accompanied by AKI (25.2%) than those who were full-term (70.2%). Our study revealed that less than 1.5 kg were 14.95% neonates, 57.15% expired out of which 42.85% with AKI and 47.13% without AKI. Mortality high in very low birth weight baby [Table.2].

74(30.84%) neonates had late onset sepsicaemia and 22(29.73%) had AKI, and 52(70.27%) without AKI. In late onset sepsicaemia 50% neonates expired those who had AKI, and 11.54% expired in the group of without AKI (p<0.001). Mortality in late onset sepsicaemia with acute kidney injury high due to other associate factor e.g. dehydration due to inadequate breast feeding and lactational failure [Table.2].

70.59% neonates had shock in AKI and 24.66% neonates had shock in without AKI group [p<0.001]. Mathur et al.[42] reported 71.2% neonates had shock in AKI group and 27% neonates had shock in non AKI group. It appears that shock and is the main mechanisms through which sepsis causes ARF in neonates. Jayashree et al.[35] reported 66.6% neonates of AKI had shock, incidence of AKI in patient significantly higher [Table.2].

66.66% neonates developed necrotizing enterocolitis, 26.47% neonates of AKI had NEC, whereas 36.99% neonate developed NEC in non AKI group. Incidence of AKI did not differ with or without NEC (p=0.28%). It Supports the Mathur et al.[42] who reported that NEC is not a risk factor for AKI. This study contradict Gupta et al.[25]. Study which revealed that NEC is a risk factor for developing AKI. Ayman et al.[26] reported, incidence of AKI higher in NEC group.

In asphyxiated neonates the main pathogenesis of developing NEC and AKI are similar hypoxia, ischemia whereas in neonatal sepsis, main pathogenesis is infection, but in AKI due to decrease perfusion. That’s why in asphyxiated neonates of AKI had higher number of NEC but in neonatal sepsis this association was not observed [Table.2].

In our study, incidence of oliguria in neonatal sepsis was only 20.58%. This study contradicts the general perception that ARF in neonates is commonly oliguric. Previous studies done by Jayashree et al.[35] on birth asphyxia patients found 69.2% of ARF to be oliguric. In a study by Pereira et al.[7] on 20 cases of ARF (out of which 18 had sepsis), the incidence of oliguria was 80%. Gupta et al. stated that oliguric renal failure predominant in asphyxiated neonates. This study supports Ayman et al.[26] who reported that incidence of oliguric renal failure in critically ill patient were 22%. Mathur et al.[42] study revealed 15.38% had oliguric renal failure. Doronjski et al.[23], reported, non-oliguric ARF was diagnosed in 62% of newborns with ARF, while the rest had the oliguric type (38%). Pathophysiologically non-oliguric renal failure appears to occur because of less severe reduction in GFR and apparent better preservation of tubular function. Periera et al.[39] clearly revealed that the outcome in ARF amongst neonates does not depend on the underlying basic disease alone but is also influenced by the severity of the renal failure and presence of sepsis. No single prognostic variable accurately predicts the final outcome. Even the absence of the oliguria did not significantly alter the prognosis [Table.2].

In this study out of 107, 21(23%) neonates expired, 56.52% had AKI whereas 84(78.50%) were discharged 25% had AKI (p=0.004). Mortality in AKI group 3 times to the non AKI group. This finding comparable to other study Mathur et al.[42] reported, 2.5 times higher mortality in neonatal sepsis with AKI to the sepsis without AKI. Jayashree et al.[35], the mortality rate of ARF in asphyxiated patient was 61.5%. In this study AKI perhaps does not increase the mortality in an already asphyxiated patient because asphyxia itself is profound insult to the neonate and AKI additionally does not increase the stress on asphyxiated patient. Kapil Kapoor et al.[27] revealed the mortality rate of neonates with AKI was 44.4% [Table.2].

Airede et al.[22] reported that the mortality rate of neonates admitted to the NICU with AKI was 35.4%. Agras et al.[24] reported a mortality rate of 24.4% in neonates with AKI in the NICU. Twenty-five percent of premature neonates with ARF died in contrast to 10% of premature neonates without ARF. 78.50% were discharged, 25% baby had AKI. 21.50% neonates expired out of which 56.52% had AKI. Difference was statistically significant. Mortality high in neonates of AKI (P=0.004). ARF in neonates has been
5. Conclusion

We have analyzed the prognostic factors in neonatal acute kidney injury. The present study observations clearly reveal that ARF is a very common entity among septic neonates. The latent period for the development of ARF in neonatal sepsis is short. Coexisting shock was significantly associated with ARF and appears to be the main operating mechanisms causing ARF. The high mortality among septic neonates with ARF stresses the need for septic neonates to be screened for renal failure. We can conclude that early recognition of risk factors for developing AKI may reduce the risk of its occurrence. Shock and oliguria were identified as poor prognostic indicator.

References


Gaurav Jagrawal et al / Acute renal failure in neonatal sepsis reported to be predominantly oliguric, incidence of oliguria varying from 46%-93%.[8] [Table 3]


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