Gaurav Jagrawal et al / International Journal of Biomedical Research 2016; 7(5): 260-264.

260

Original Research Article

Acute renal failure in neonatal septicemia

Gaurav Jagrawal*, Vivek Arora, Maheshwar Gunawat and Pankaj Malik

Department of Pediatrics, R.N.T Medical College, Udaipur, Rajashthan, India

*Correspondence Info:
Dr. Gaurav Jagrawal
Department of Pediatrics,
R.N.T Medical College, Udaipur, Rajashthan, India
E-mail: dr.gaurav077@gmail.com

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 107outborne 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 > 15mm fall in first hour, Total leucocyte count <5000/ mm 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 < 1ml/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

included 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 at 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 whereas.74(69.16%) had late onset septicaemia out of which 22.97% neonates expired. In early onset septicaemia, 33.33% neonates had AKI and out of which 18.18% neonates expired. 22 (66.66%) neonates did not have AKI, out of which 18.18% neonates expired.43.93% neonates had meningitis. 55.88% neonates of AKI 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, 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.

Table 1: Clinical Profile of Study Population

Total number of neonates with sepsis	107
Mean gestational age (weeks ± s.d.)	34.59 ± 3.07
Preterm	77(71.96%)
Mean weight at presentation (gms ± SD)	2.14 ± 0.57
Mean age at presentation (days ± SD)	9.43 ± 7.39
Early onset septicaemia	32.35%
Late onset septicaemia	67.65%
Culture positive sepsis	25.23%
Meningitis	43.13%
Survival	78.50%
AKI	34(31.77%)
Oliguric	7(20.58%)
Nonoliguric	27(79.42%)

Table 2: Comparison of Septic Neonates with and Without ARF

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

Table.3: Prognostic factor in neonatal acute kidney injury

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

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 inncidence 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 septicaemia and 22(29.73%) had AKI, and 52(70.27%) without AKI. In late onset septicemia 50% neonates expired those who had AKI, and 11.54% expired in the group of without AKI (p<0.001). Mortality in late onset septicaemia 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[42] al study revealed 15.38 neonates 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

reported to be predominantly oliguric, incidence of oliguria varying from 46%-93%.[8] [Table 3]

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

[1] David Askenazi, Lori B. Smith, Susan Furth, Bradley A. Warady Chapter 85 Avery's Diseases of the newborn, Christine A. Gleason, Sherine U. Devaskar, 9th edition 2012 Elseveir 1205-1215.

[2] Stapleton FB, Jones DP, Green RS. Acute renal failure in neonates: incidence, etiology and outcome. *Pediatr Nephrol*1987; 1:314-320.

[3] Brion L, Fleischman AR, McCarton C. A simple estimate of glomerular filtration rate in low birth weight infants during the first year of life: non invasive assessment of body composition and growth. *J Pediatr*1986; 109:698-707.

[4] Gallini F, Maggio L, Romagnoli C. Progression of renal function in preterm neonates with gestational age < or = 32 weeks. *Pediatr Nephrol* 2000; 15:119-124. 1.

[5] Hentschel R, Lodige B, Bulla M. Renal insufficiency in the neonatal period. *Clin Nephrol*1996; 46: 54-58.

[6] Norman ME, Asadi FK. A prospective study of acute renal failure in the newborn infant. *Pediatrics*1979; 63: 475-479.

[7] Griffin NK, McElena J, Baratt JM. Acute renal failure in early life. *Arch Dis Child*1976; 51: 459-462.

[8] Norman Jones AS, James E, Bland H, Groshong T. Renal failure in the newborn. *Clin Ped* 1979; 18: 286-290.

[9] Unni JC, Date A, Raghupathy P, Shastry JCM. Medical renal disease in South Indian infants. *Acta Pediatr Scand*1986; 75: 1030-1031.

[10] Grylack L, Medani C, Hultzen C, Sivasubramanian K, Davitt MK, Jose P, Scanlon JW. Nonoliguric acute renal failure in the newborn. *Am J Dis Child*1982; 136: 518-520.

[11] Ellis EN, Arnold WC. Use of urinary indices in renal failure in the newborn. *Am J Dis Child*1982; 136: 615-617.

[12] Gladder BE. Bleeding disorders in the newborn infant. In Schaffer's Diseases of the newborn, Avery ME, Taeusch HW eds. 5th Edn, Philadelphia, WB Saunders Co, 1985, pp562.

[13] Spitzer A. Renal physiology and functional development. In Pediatric Kidney Disease, Edelmann CM (ed): Boston, Little Brown, 1978, pp25.

[14] Chantler C. Renal failure in childhood. In Renal disease, Black DAK, Jones NF eds. ed4, Oxford, Blackwell, 1979; 825.

[15] Clarkson AR, MacDonald MK, Fuster V. Glomerular coagulation in acute renal failure. *Q J Med*1970; 39: 585.

[16] John E. Renal physiology and acute renal failure. *Ind J Pediatr* 1981; 48: 313-321.

[17] Chevalier RL, Campbell F, Brenbridge AG. Prognostic Factors in neonatal acute renal failure. *Pediatr*1984; 74: 265-272.

[18] Arnold W, Holliday M. Renal failure in the newborn. Read before the American Society of Pediatric Nephrology, St. Louis, April 1976. 450. Chevalier RL, Campbell F, Brenbridge AG. Prognostic factors in neonatal acute renal failure. *Pediatrics*1984; 74:265-272.451.

[19] Stapleton FB, Jones DP, Green RS. Acute renal failure in neonates: incidence, etiology and outcome. *Pediatr Nephrol*1987; 1:314-320.452. Norman ME, Asadi FK. A prospective study of acute renal failure in the newborn infant. *Pediatrics*1979; 63:475-47.

[20] Lolekha.P.H Jarthunyaluck S.,Srisawasdi P. Deprteinization of serum :Another best approach to eliminate all forms of bilirubin interference on serum creatinine by the kinetic Jaffe reaction. *J Clin Lab Anal* 2001; 15:166-121 doi:10.1002/jcla.1013.

[21] L Catald L, Leone R, Moretti U. Potential risk factors for the development of acute renal failure in preterm newborn infants: a case-control study. *Dis Child Fetal Neonatal Ed* 2005; 90:F514–F519.

[22] Viswanathan S, Manyam B, Azhibekov T, Mhanna MJ Risk factors associated with acute kidney injury in extremely low birth weight (ELBW) infants. *Pediatr Nephrol*. 2012 Feb; 27(2):303-11.

[23] Airede A, Bello M, Weerasinghe HD. Acute renal failure in newborn: Incidence and outcome. *J Pedaitr Child Health* 1997; 33(3):246-9.

[24] Doronjski A, Stojanovic V, Spasojevic S, *et al*. Acute Renal failure in premature neonates. *Vojnosanit Pregl*. 2009;66(11):863–7

[25] Agras PI, Tarcan A, Baskin E, Cengiz N, Gurakan B, Saatci U. Acute renal failure in neonatal period. *Ren Fail* 2004; 26(3):305-9. %).

[26] Gupta BD, Sharma P, Bagla J, *et al*. Renal failure in asphyxiated neonates. Indian Pediatr. 2005; 42(9):928–34

[27] Ayman A.*et al*. Incidence and risk factors of acute kidney injury among the critically-ill neonates. Saudi journal of kidney Diseases and transplantation; manuscrift No.; 112-14.

[28] Kapil Kapoor, Mamta Jajoo, and Vikas Dabas, Predictors of Mortality in Out Born Neonates with Acute Renal Failure; an Experience of a Single Center. *Iran J Pediatr*. 2013 Jun; 23(3): 321–326

[29] Philip A,Hewitt JR. Early diagnosis of neonatal sepsis. *Paediatrics* 1987; 146:147-151.

[30] Philip Alistair GS, Hewitt JR. Early diagnosis of neonatal sepsis pediatrics 1980 ; 65 : 1036-1041

[31] Gerdes JS, Polin RA. Sepsis screen in neonates with evaluation of plasma fibronectin. *Pediatr Infect Dis J* 1987; 6: 443-446.

[32] Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for Neutrophilic cells. J Pediatr 1979; 95:89-98. Schelonka RL, Yoder BA, Desjardins SE, Hall RB, Butler TJ. Peripheral leukocyte count and leukocyte indexes in healthy newborn term infants. *J Pediatr* 1994; 125:603-606.

[33] Schelonka RL, Yoder BA, Desjardins SE, Hall RB, Butler TJ. Peripheral leukocyte count and leukocyte indexes in healthy newborn term infants. *J Pediatr* 1994; 125:603-606.

[34] Mouzinho A, Rosenfeld CR, Sanchez PJ, Risser R. Revised reference ranges for circulating neutrophils in very low-birthweight neonates. *Pediatrics*1994; 94: 76-82.

[35] Polinski C. The value of white blood cell count and differential in the prediction of neonatal sepsis. *Neonatal Netw* 1996; 15: 13-23.

[36] Jayashree G, Dutta AK, Sarna MS, Saili A. Acute renal failure in asphyxiated newborns. *Ind J Pediatr* 1991; 28: 19-23.

[37] Mortazavi F, Hosseinpour Sakha S, Nejati N.Acute Kidney Failure in neonatal period. *Iran J Kidney Dis* 2009; 3:136-40.

[38] Steele BT, Paes B, Towell ME, Hunter DJ.Fetal renal failure associated with intrauterinegrowth retardation. *Am J Obstet Gyneco1* 1988; 159:1200-2.

[39] Mathew OP, Jones AS, James L, Bland H, Groshong T. Neonatal renal failure:usefulness of diagnostic indices. *Pediatrics* 1980, 65:57-60.

[40] Pereira S, Pereira BJG, Bhakoo ON, Narang A, Sakhuja VS, Chugh KS. Peritoneal dialysis in neonates with acute renal failure. *Ind J Pediatr* 1988, 58: 973-978

[41] Andreoli SP. Acute renal failure in thenewborn. *Semin Perinatol* 2004; 28:112-23

[42] Mathur NB, Agarwal HS, Maria A. Acute renal failure in neonatal sepsis. *Indian J Pediatr* 2006; 73:499-502.

[43] Friedlich PS, Evans JR, Tulassay T, *et al*. Acute and chronic renal failure. In: Taeusch HW, Ballard RA, Gleason CA, eds. Avery'