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RESEARCH ARTICLE

NEONATAL SEPSIS AND ACUTE RENAL FAILURE: A TERTIARY CARE CENTRE EXPERIENCE

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ABSTRACT

Background: Acute Renal Failure (ARF) is a common complication observed in critically ill newborns and neonates admitted in NICU. **Methods and Subjects:** This prospective case control study was carried out in the Neonatal Intensive Care Unit of a tertiary level hospital for a period of one year with an objective of determining the incidence of ARF in neonatal sepsis. 113 neonates, who had a positive sepsis screen and/ or a positive blood culture were evaluated for the presence or absence of ARF. Sepsis was identified on the basis of either a positive blood culture or a positive sepsis screen. ARF was defined as Blood Urea Nitrogen (BUN) > 20 mg/dl on two separate occasions at least 24 hrs apart. Oliguria was defined as urine output <1 ml/kg/hr for more than 24 hours. Data was analysed using Student's t test. **Results:** The sepsis screen positivity rate was 89.4% whereas the culture positivity rate was 44.2%. ARF developed in 32 out of 113 neonates giving an incidence of 28.3%. The ARF in neonates was predominantly non oliguric (59%) and it was significantly associated with gestational age (p value 0.001), birth weight (p value 0.013), weight on admission (p value 0.001) and the place of dwelling (p value 0.034). There was high incidence of volume responsive ARF in those neonates with presumptive ARF on day 1 of admission. The overall mortality of the study group was 25.7%; it was 50% in the neonates with ARF and in neonates with sepsis alone it was only 16% (p value <0.001) showing the significant increase in mortality in neonates with sepsis who develop ARF as a complication. **Conclusion:** There is a high prevalence of volume sensitive ARF in neonatal sepsis that can be corrected by proper fluid and electrolyte management.

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INTRODUCTION

Acute renal failure (ARF), also termed as *acute renal insufficiency*, is a clinical syndrome in which a sudden deterioration in renal function results in the inability of kidneys to maintain fluid and electrolyte homeostasis (Rajasree Sreedharan and Ellis, 2011). It is characterized by an increase in the blood concentration of creatinine and nitrogenous waste products, a decrease in the glomerular filtration rate (GFR) and by the inability of the kidneys to appropriately regulate fluid, electrolyte and acid base homeostasis (Jayashree, 1991). ARF occurs at all ages in critically ill or injured patients with clinical conditions often associated with high mortality rates such as septic shock and multi organ dysfunction syndrome (Stewart, 1997). Neonatal sepsis is a disease of infants who are younger than 1 month of age, are clinically ill and have positive blood cultures (F Sessions Cole). The neonatal age group is at a special risk of developing ARF as a result of wide variety of genetic malformations or prenatal, perinatal and postnatal events predispose the neonate to the development of ARF (Jayashree, 1991; Gharebaghi, 2007). Acute renal failure in the newborn infant may be associated with a variety of disorders including perinatal asphyxia, Hyaline Membrane Disease (HMD), sepsis, diarrhoea and dehydration, hemorrhage, shock, renal vein thrombosis and Disseminated Intravascular Coagulation (DIC) and also following cardiac surgery (Anand, 1978). While asphyxia, respiratory distress syndrome (RDS) and urogenital abnormalities are the commonly reported causes of ARF in the West, sepsis is the leading cause of ARF in the preliminary reports from India (Anand, 1978). The incidence of ARF in neonatal sepsis has been reported to be 15% to 33% in various studies (Gharebaghi, 2007; Agras, 2004; Airede, 1997; Al-Idreesy, 1991). Most of the studies done till now have focussed on the bacteriological spectrum and profile of neonatal sepsis. This study was aimed at determining the incidence of acute renal failure in neonatal sepsis and to correlate the demographic parameters in septicemic neonates with the development of ARF and overall outcome.

SUBJECTS AND METHODS

This study was carried out in the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics, of a tertiary level teaching hospital of North India.

The study design was prospective and non-randomized. The study period was of one year extending from 1st September 2008 to 31st August 2009. The study population included neonates up to one month of age admitted in the Neonatal Intensive Care Unit (NICU) with a positive sepsis screen and/or a positive blood culture.

Sepsis screen was defined as positive if 2 or more of the following listed parameters were met.

- Total leukocyte count < 5000/mm^3
- Immature: Total (I:T) Neutrophil ratio > 0.2
- Micro Erythrocyte Sedimentation Rate (μESR)
  Age in days + 2 mm, or
  15 mm 1st hour, irrespective of age.
- C Reactive Protein (CRP) > 60 mg/ L.

Blood Urea Nitrogen (BUN) analysis was made on the 1st day of admission and then repeated on the 3rd day. Those neonates who had blood urea nitrogen (BUN) of more than or equal to 20 mg/dl measured on these two occasions were labelled as having Acute Renal Failure (ARF). Urine collection of approximately 24 hours was made by spontaneous micturition into clean but unsterile urine bags. Oliguria was defined as urine output less than 1 ml/ kg body weight/hr for more than 24 hours. Cases were defined as all neonates less than 1 month of age with a positive sepsis screen and/ or a positive blood culture with ARF (determined on the basis of BUN levels). All other neonates included in the study with a positive sepsis screen and/or positive blood culture with no evidence of ARF served as controls. Those children who had any congenital or acquired abnormality or co morbidity including perinatal asphyxia, Respiratory Distress Syndrome (RDS), meconium aspiration, any skeletal, renal (structural), cardiac or urinary tract anomalies and perinatal exposure to nephrotoxic medicines, any surgical intervention, polycythemia and twinning were excluded from the study as these could have acted as confounding factors. All the neonates were managed on a uniform routine hospital protocol to avoid any bias. Detailed clinical data was obtained from the attendants of the neonates admitted with clinical suspicion of sepsis and recorded on a pre designed proforma that included a thorough history and a detailed clinical examination.

Exclusion criteria were applied uniformly to all subjects. 4 ml of blood was obtained at the time of admission and aliquots sent for sepsis screen, blood culture, hemogram (Sysmexautoanalyser) and BUN estimation along with other routine investigations as per the hospital protocol. BUN estimation was repeated after more than 24 hrs of admission. 24 hrs' urine was collected and measured using self adhesive plastic urine collecting bags. Immature to Total Neutrophil ratio was obtained manually using Geimsa stained peripheral blood films, depending upon the number of lobes in the neutrophil nucleus. Micro erythrocyte sedimentation rate (μESR) was estimated using 75 mm long calibrated and preheparinized capillary tubes into which blood was drawn by capillary action up to the specified mark and left for standing for 1 hour and results obtained thereafter. C Reactive protein (CRP) was measured by in vitro qualitative and semi quantitative determination in serum using the titration method. Blood urea was measured by DAM (DiacetylMonoxime) Method. Serum creatinine was estimated using the Modified Jaffe's Kinetic method. Ultrasonography was performed in all septic neonates to rule out any congenital structural renal and urogenital anomaly. Statistical analysis was done by Student's t test.

RESULTS

During the study period a total of 3156 neonatal admissions were made in the hospital out of which 1161 (36.8%) had clinical features of sepsis. Amongst these neonates 345 (29.7%) were admitted in the NICU, 113 (32.8%) of which had either a positive sepsis screen or positive blood culture or both and were included in our study. Out of the total neonates included in the study, 60 were male (53.1%) and 53 were females (46.9%) ; 18 were preterm (15.9%) and 95 were term (84.1%) ; 82 were born by vaginal route (72.6%) and 31 were delivered by LSCS (27.4%). The place of delivery was home for 39 (34.5%) and hospital for 74 (65.5%). The mean birth weight of the neonates included in the study (as recorded from the hospital data/ delivery records/ baby notes) in grams was 2432.3 ± 510.1 (Minimum 1300, Maximum 3500). 43 were LBW (38.1%) and 70 were of normal birth weight (61.9%). Eighty three (73.5%) were from a rural background whereas 30 (26.5%) were from urban background. The mean age of presentation of the studied group was 10.3 ± 7.5 days (min 1 day, max 27 days).

The number of neonates admitted with early onset sepsis was 38 (33.6%) whereas the number of neonates admitted with late onset sepsis was 75 (66.4%). The mean WBC count of the study population was 10500.9 ± 5757.4 (min 2500, max 26000) per/ mm^3. The mean I:T Neutrophil ratio was 0.2 ± 0.1 (min 0.1, max 0.4). Micro ESR was 8.1 ± 3.4 (min 4, max 17) mm 1st hour and CRP levels were 113.1 ± 61.9 (min 30, max 192) mg/L. The sepsis screen was positive in 101 neonates (89.4%) whereas it was negative in 12 neonates (10.6%). Overall the sepsis screen positivity rate was 89.4%. Out of the 113 neonates included in the study 50 (44.2%) had a positive blood culture whereas 63 (55.8%) were blood culture negative. The most common organism isolated was Klebsiella (46.0 %) followed by E coli (40.0%). Staph aureus was isolated in 5 neonates (10.0%) whereas Pseudomonas was isolated in 2 (4.0%) neonates. Amongst the early onset sepsis neonates the relative percentages of Klebsiella, E. Coli, Staph aureus and Pseudomonas were 20.0%, 16.0%, 2.0% and 0.0% respectively whereas in the neonates with late onset sepsis the percentages were 26.0%, 24.0%, 8.0% and 4.0% respectively. In our study 19 (50%) of the neonates with early onset sepsis had a positive blood culture whereas 31 (41.33%) of neonates with late onset sepsis showed a growth on culture.

BUN on day 1 was elevated (≥ 20 mg/ dl) in 53 (46.9 %) neonates whereas the number of neonates with elevated BUN on day 3 was 32 (28.3%).The mean BUN on days 1 and 3 of admission were 23.2 ± 14.2 (min 9, max 85) mg/ dl and 18.3 ± 9.6 (min 9, max 50) mg/ dl respectively. In those who had an elevated BUN on days 1 and 3 and who survived up to 10 days following admission, the mean BUN on day 10 was 12.7 ± 2.5 (min 10, max 18) mg/ dl. The mean serum creatinine on day 1 of admission was 1.1 ± 0.8 (min 0.3, max 5) mg/ dl. Forty six neonates (40.7 %) had serum creatinine ≥ 1 mg/ dl and 67 neonates (59.3 %) had a serum creatinine of less than 1 mg/ dl on day 1.. Amongst the former 28 (60.8 %) developed ARF whereas 18 (39.2 %) did not. The mean urine output in the study population was 70.7 ± 30.9 (min 0, max 110) ml/ day. Oliguria was present in 17 (15.0%) neonates.

Table 1. Acute Renal Failure across Demographic Factors

Parameter		Present		Absent		p value
		n	%	n	%	
Gestation Age	Preterm	11	61.1	7	38.9	0.001 (S)
	Term	21	22.1	74	77.9	
Type of Delivery	LSCS	9	29.0	22	71.0	0.918 (NS)
	Vaginal	23	28.0	59	72.0	
Place of Delivery	Home	9	23.1	30	76.9	0.371 (NS)
	Hospital	23	31.1	51	68.9	
Birth Weight	Low	18	41.9	25	58.1	0.013 (S)
	Normal	14	20.0	56	80.0	
Wt on admission	< 2500 grams	23	50.0	23	50.0	0.001 (S)
	≥2500 grams	9	13.4	58	86.6	
Type of Sepsis	Early Onset	14	36.8	24	63.2	0.154 (S)
	Late Onset	18	24.0	57	76.0	
Gender	Male	15	25.0	45	75.0	0.407 (NS)
	Female	17	32.1	36	67.9	
Dwelling	Rural	28	33.7	55	66.3	0.034 (S)
	Urban	4	13.3	26	86.7	

Table 2. Outcome in relation with Demographic and Screening Parameters

Parameter		Recovered		Expired		p value
		n	%	n	%	
Birth Weight	Low	27	62.8	16	37.2	0.028 (S)
	Normal	57	81.4	13	18.6	
Gestation Age	Preterm	7	38.9	11	61.1	0.000 (S)
	Term	77	81.1	18	18.9	
Sepsis Screen	Positive	78	77.2	23	22.8	0.042 (S)
	Negative	6	50.0	6	50	
Blood Culture	Positive	32	64.0	18	36	0.026 (S)
	Negative	52	82.5	11	17.5	
Oliguria	Present	3	17.6	14	82.4	0.000 (S)
	Absent	81	84.4	15	15.6	
Gender	Male	47	78.3	13	21.7	0.303 (NS)
	Female	37	69.8	16	30.2	
Type of Delivery	LSCS	22	71.0	9	29	0.616 (NS)
	Vaginal	62	75.6	20	24.4	
Place of Delivery	Home	33	84.6	6	15.4	0.071 (NS)
	Hospital	51	68.9	23	31.1	
Dwelling	Urban	25	86.2	4	13.8	<0.001 (S)
	Rural	59	70.2	25	29.8	
Weight on admission	<2500 Gms	30	65.2	16	34.8	<0.001 (S)
	>2500 Gms	54	79.4	13	20.6	
ARF	Present	16	50.0	16	50	<0.001 (S)
	Absent	68	84.0	13	16	

S: Significant,NS: Not Significant

Acute renal failure on day 3 of admission was present in 32 (28.3%) neonates. The presence or absence of ARF in the study group across demographic parameters is given in Table 1.In the oliguric group (Total 17 neonates), 13 neonates (76.5%) had ARF as compared to only 4 (23.5%) who did not have ARF. The observation points out that oliguria is significantly associated with development of acute renal failure in neonates (p value < 0.001). The incidence of ARF in neonates (study group) was significantly associated with the gestational age (p value 0.001), birth weight (p value 0.013), weight on admission (p value 0.001) and place of dwelling (p value 0.034). The final outcome in the study population in terms of mortality in the study population comparing the neonates with sepsis and ARF vis a vis those with sepsis alone was statistically significant in our study (p < 0.001). The mean duration of hospital stay was 1.2 ± 0.4 (min 1, max 2) weeks. The overall morbidity in terms of hospital stay and mortality in cases was quite high as compared to the control group. This observation is statistically significant (p value < 0.001). Birth weight, gestational age, wt on admission, place of dwelling, oliguria and presence of acute renal failure were quite significantly associated with the outcome as determined by the respective p values.

Sepsis screen and blood culture positivity were also correlated significantly with the outcome but to a lesser extent. Gender, type of delivery and place of delivery were not significantly associated with the outcome (p value > 0.05) (Table 2)

DISCUSSION

Systemic infection in the newborn is the commonest cause of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries (Bang, 1999; Stoll, 1997). According to data from National Neonatal Perinatal Database (NNPD) 2000, the incidence of neonatal sepsis has been reported to be 38 per 1000 intramural live births in tertiary care institutions (National Neonatology forum, 2000). Acute Renal failure is one of the significant complications accompanying neonatal sepsis. Sepsis can operate through a variety of mechanisms in producing renal failure. It can cause renal failure by shock, Disseminated Intravascular Coagulation (DIC), haemorrhage, cardiac failure and through ATN. The neonatal kidney is particularly vulnerable to the effects of hypoperfusion since the renal vascular resistance and plasma renin activity are high. The neonatal kidney has been described as 'halfway to acute renal

failure'. While sepsis has been said to be one of the important predisposing causes of ARF, the actual incidence of renal failure in all sepsis cases is not documented. In the present study, 28.3% of all neonates with sepsis had ARF. Our study was a hospital based prospective study correlating neonatal sepsis with acute renal failure in newborn infants less than one month of age. There is a paucity of literature on this subject and very few studies have been conducted so far especially in the developing countries. Our endeavour was to find a correlation between the two in our setup where neonatal sepsis continues to be a major cause of morbidity and mortality in the pediatric population. In our study the incidence of ARF as determined by elevated BUN levels on two occasions more than 24 hrs apart was 28.3% and the overall mortality in cases was 50%. A significantly higher number of neonates who developed ARF were less than 2500 grams on admission as compared to those without ARF (65.6% Vs 34.4%, p value <0.001). Out of 32 cases of ARF 13 neonates had oliguria (<1 ml/kg/hr) as documented by 24 hrs urine collection, an incidence of 40.6%.

In earlier studies, the incidence of oliguria was significantly higher (46% to 93%) (Griffin, 1976; Grylack, 1982), but studies conducted in developing countries have shown a much lower incidence of oliguria (Mathur, 2006; Jayashree, 1991). In studies evaluating ARF due to variable causes, perinatal asphyxia may be responsible for a higher incidence of oliguria. ARF was present on onset in significantly higher percentage of neonates reinforcing the fact that neonatal kidneys are very fragile and that the latent period for the onset of renal failure may be very short in neonates with sepsis. Another reason could be a delay in seeking medical attention for the neonates, especially for females in our province. ARF was significantly more common in preterm neonates as compared to term neonates (61.1% vs. 22.1%, p value 0.001). Weight was another important predictor of ARF in septic neonates. A significantly higher number of neonates who developed ARF were less than 2500 grams as compared to those without ARF (65.6% vs. 34.4%, p value <0.001). Another important factor that predicted ARF in septic newborns was the dwelling, whether urban or rural. A significantly higher number of neonates with ARF belonged to a rural background than those with an urban background (33.7% vs 13.3%, p value 0.034). The reason for this may be a delay in seeking treatment in cases of sepsis from rural areas due to lack of proper healthcare facilities. Also the incidence of sepsis is higher in rural setting as compared to an urban setting because of poor hygiene and lack of proper newborn care. Our study revealed no significant association between ARF and the type of delivery, place of delivery, type of sepsis whether early onset or late onset and gender (p value >0.05). Amongst the neonates studied, 101 (89.4%) neonates had a positive sepsis screen.

The blood culture positivity rate was 44.2%. The percentage of early onset sepsis was 33.6% (38 neonates) and that of late onset sepsis was 66.4% (75 neonates). The predominant organisms isolated in culture positive patients in our study was Klebsiella pneumonia (46%) followed by Escherichia coli (44.2%), Staphylococcus aureus (10%) and Pseudomonas (4%) which is consistent with the National Neonatal Perinatal Database (NNPD) 2000. The most common organism isolated in both early onset sepsis as well as late onset sepsis was Klebsiella (55.5% and 41.9 % respectively). There was no significant association between ARF and type of organism isolated from culture.

This observation points towards the fact that systemic factors associated with sepsis are responsible for the development of ARF in sepsis. Mathur et al has pointed out that the most important factors responsible for development in ARF are predominantly shock and DIC (Mathur, 2006). Another remarkable observation was the number of volume responsive presumptive ARF in neonates. The number of neonates with an elevated BUN on day 1 of admission was 53 (46.9%) and those with normal BUN levels were 60 (53.1%). Out of these only 32 (28.3%) had elevated BUN on day 3 also. Twenty one neonates (39.6%) had normal BUN levels on Day 3. This observation points towards the fact that ARF in neonates starts as pre renal azotemia that can be corrected by volume expansion. This finding is consistent with the observations of Norman *et al.* who observed only 28% of neonates with presumptive ARF on presentation had intrinsic renal failure. In our study the duration of hospital stay was more in patients with sepsis and ARF as compared to those with sepsis alone. 77.7% of neonates with ARF had a hospital stay of more than 10 days as compared to only 12.3% of those without ARF (p value 0.00). The mean duration of hospital stay was 1.2 ± 0.4 weeks. The overall mortality observed in our study was 25.7 % with the neonates with ARF having a 50% mortality as compared to only 16% in those with sepsis alone (p value <0.001). The mortality in oliguric neonates was also significantly more than that in non oliguric neonates (82.4% Vs 15.6%, p value <0.001). Besides ARF, the weight on admission (p value <0.001), place of residence, whether rural or urban (p value <0.001), birth weight (p value 0.028), gestational age, whether term or preterm (p value 0.000), sepsis screen positivity (p value 0.042) and culture positivity (p value 0.026) were also significantly associated with high mortality. Out of the oliguric neonates the mortality rate was 82.4% as compared to the non oliguric group where the mortality was only 15.6% (p value 0.000). Oliguria, in particular had a strong and statistically significant association with the final outcome in terms of mortality. The significance of oliguria in predicting fatality has been reported to range from significant to insignificant. Chevalier *et al.* and Loza *et al.* have positively correlated oliguria with increased mortality in neonates. Though Mathur *et al.,* has not found any significant correlation between oliguria and outcome in terms of mortality.

Conclusion

This study concludes that the incidence of Acute Renal Failure in neonatal sepsis is 28.3% in our centre. The factors associated with increased occurrence of ARF in neonates with sepsis include prematurity, weight less than 2500 grams and rural background. The frequency of volume responsive ARF is significant. The mortality is high in neonates with sepsis and ARF (50%) as compared to those with sepsis alone (16%). These observations highlight the importance of monitoring of renal function in neonates with sepsis and volume expansion in neonates with a presumptive diagnosis of ARF. The high mortality of neonates with sepsis and ARF vis a vis those with sepsis alone underscore the need to vigorously manage these neonates with proper antibiotics and supportive care.

REFERENCES

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

Airede A., Bello M., Weersinghe HD. 1997. Acute renal failure in the newborn; incidence and outcome. *J Pediatr Child Health.,* 33(3):246-9.

Al-Idreesy, Abdel Basit OB., Haque KN., Abdurrehman MB. 1991. Acute renal failure in neonates; a prospective study. *Ann Saudi Med.,* 11(3):297-301.

Anand SK., Northway JD., Crussi FG. 1978. Acute renal failure in newborn infants. *J Pediatr.,* 92(6): 985-8.

Bang AT., Bang RA., Bactule SB., Reddy HM., Deshmukh MD. 1999. Effect of home based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. Lancet., 354:1955-61.

Chevaliar RL., Campbell F., Brenbridge AN. 1984. Prognostic factors in neonatal acute renal failure. *Pediatrics.,* 74(2); 265-72.

Gharebaghi MM., Periovifar A. MD. 2007. Evaluating causes of acute renal failure in newborn infants. *Pak J. Med Sci.,* 23(6):877-80.

Griffin, Mc Elnea J, Barrett TM. 1976. Acute renal failure in early life. *Arch Dis Child.,* 51:459-462

Grylack L. MD, Charles Medani MD., Christopher Hultzen MD, KolinjavadiSivasubramanium MD, Mary K Davitt MD, Pedro Jose MD, John W Scanlon MD. 1982. Nonoliguric Acute Renal Failure in the Newborn, A prospective evaluation of Diagnostic Indexes. *Am J Dis Child.,* 136:518-20.

Jayashree G., Dutta AK., Sarna MS., Saili A. 1991. Acute renal failure in asphyxiated newborns. *Indian Pediatr.,* 28(1):19-23.

Jayashree G., Saili A., Sarna MS., Dutta AK. 1991. Renal dysfunction in septicemic newborns. *Indian Pediatr.,* 28(1):25-9.

Loza R., Estremadoyro L., Loza C., Cieza J. 2006. Factors associated with mortality in acute renal failure(ARF) in children. *Ped Nephrol.,* 21(1):106-9.

Mathur NB., Agarwal HS., Maria A. 2006. Acute renal failure in neonatal sepsis. *Indian J Pediatr.,* 73(6): 499-502.

Norman ME., Asadi FK. 1979. A Prospective study of Acute Renal Failure in the Newborn Infant. *Pediatrics.,* 63(3):475-79.

Rajasree Sreedharan and Ellis D. 2011. Avner. Acute Renal Failure. In: Kliegman RM, editor. Nelson Textbook of Pediatrics, 19th ed. Philadelphia: Saunders;. p. 1818-822.

Report of the National Neonatal Perinatal Database (National Neonatology Forum) 2000.

Sessions Cole. F. Bacterial infections of the newborn; Septicemia. In: Taeusch HW, editor. Avery's Diseases of the Newborn, 7th ed. Philadelphia: Saunders; 492.

Stewart CL, Barnett R. Acute renal failure in infants, children and adults. Crit Care Clin 1997; 13(3): 575-90.

Stoll B. 1997. The global impact of neonatal infection. *Clin Perinatol.,* 24:1

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