RENAL DYSFUNCTION IN SEPTICEMIC NEWBORNS

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ABSTRACT

The study was undertaken to assess the association and incidence of acute renal failure (ARF) in septicemic neonates. Thirty neonates with septicemia formed the subject matter. Neonates with renal dysfunction were labelled as ARF patients after non responsiveness to a fluid and a diuretic challenge. Renal function tests were also evaluated. Nearly 15% neonates with septicemia developed ARF which was predominantly oliguric in type. The mortality rate in the septicemic neonates with ARF was significantly high. Further the mortality in neonates with oliguric ARF was significantly higher than those with non-oliguric ARF.

Key words: *Septicemia, Acute renal failure.*

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Acute renal failure (ARF) in the newborn is increasingly attracting the attention of Pediatric nephrologists the world over. In a full term neonate, the kidney functions are not fully mature and functional maturation continues in the postnatal age. Normally a full term neonate is able to cope with most of the rapidly changing functional demands of the body. Under normal circumstances the kidneys adapt to various endogenous and exogenous stresses. However, in sick neonates and in stressful conditions like septicemia, the adaptive capacities of the kidney may be overcome leading to renal dysfunction. This study was undertaken to detect the association and incidence of acute renal failure in septicemic neonates, as well as the incidence of physiological oliguria in normal newborns.

Material and Methods

The study was carried out in the Neonatal Division of Kalawati Saran Children's Hospital over a period of 8 months commencing July, 1987. The study group consisted of 30 term neonates clinically suspected to be septicemic confirmed later by positive blood culture. The control group comprised of 30 term neonates delivered by elective cesarean section. In both groups the cases were selected by the random sampling method. The babies were well matched for gestational age and weight. Only male babies were included in the study due to difficulty in urine collection in female babies.

Detailed clinical examination of the baby was done to exclude any congenital anomaly especially of the urinary tract. The neonates underwent renal function tests at admission, then at 72 hours and after 1 week which included blood urea, serum creatinine and 24 hours urine output. Neo-

nates who appeared to have a renal dysfunction (oliguria-urine output <0.5 ml/kg/h; blood urea >40 mg/dl and serum creatinine >1mg/dl) were subjected to an intravenous fluid challenge of 20 ml/kg N/4 saline with 5% dextrose over 1-2 hours. This was followed by intravenous furosemide 2 mg/kg body weight if oliguria persisted with the first regime. If despite of furosemide challenge, oliguria persisted or renal functions were deranged, then the infant was labelled as a case of ARF. These infants were further subjected to a 24 hours urine collection through a condom, urine analysis and microscopic examination, blood gas analysis and serum electrolytes.

Serum creatinine was measured by modified method of Jaffe while blood urea was estimated by modified method of diacetyl monoxime (Wybenga). The results were tabulated and subjected to standard statistical analysis using t-test and Chi-square tests. All babies who developed renal failure were managed conservatively. All the babies had received 2 potentially nephrotoxic antibiotics, *i.e.,* aminoglycosides and cephalosporins whose doses were adjusted when babies developed renal failure.

Results

The mean urinary output, blood urea and serum creatinine values for control group are depicted in *Table I.* Neither the gradual increase in urinary output from day 1 to day 7 nor the gradual decrease in serum creatinine values was statistically significant ($p > 0.05$). The urinary output for formula fed healthy term neonates from the first day of life ranged between 0.3-1.8 ml/kg/h.

Twenty per cent neonates (6/30) in the study group developed ARF. In contrast none in the control group had biochemical

TABLE I —*Mean Blood Urea and Creatinine Level (Control)*

Day	Blood urea (mg/dl)	Serum creatinine (mg/dl)	Urine output (ml/kg/h)
1	25.2 ± 6.7	0.9 ± 0.2	1.0 ± 2.8
3	25.7 ± 8.0	0.9 ± 0.2	1.4 ± 2.0
7	25.1 ± 6.9	0.9 ± 0.2	1.6 ± 1.8

parameters of renal failure despite 16.6% of the babies having physiological oliguria on the first day. The peak blood urea and serum creatinine in septicemic newborns developing ARF ranged between 72-96 mg/dl and 1.2-2.2. mg/dl, respectively. Four patients were acidotic, while none of these patients suffered from hyponatremia or hyperkalemia.

It was further observed that the renal failure in these babies was predominantly non-oliguric. Out of 6 cases of ARF, only one (16.6%) was oliguric while the other 5 (83.3%) were non-oliguric (*Table II*).

TABLE II – *Type of Acute Renal Failure in Septicemia*

Septicemia (n=30)	Acute renal failure (n=6) (20%)	Oliguric 1/6 (16.6%)
		Nonoliguric 5/6 (83.4%)
Control (n=30)	Nil	

Three babies with septicemia developed shock and all of them developed ARF. On the other hand, out of the 27 babies who did not develop shock, only 3 babies had ARF (11%). The values were statistically significant ($p < 0.001$).

The predominant organism cultured in

the blood septicemic neonates was *E. Coli* (66.6%). Seven neonates (23.3%) had Klebsiella while alpha hemolytic streptococci was found in 2 (16.6%).

The mortality was 50% in the septicemic neonates who developed ARF while the mortality was only 25% in the neonates who did not develop ARF. The development of ARF in septicemic babies definitely increased the mortality. The single patient in the oliguric renal failure died while in the non oliguric renal failure 2 patients out of the 5 (40%) died (*Table III*).

TABLE III—*Mortality Pattern in ARF*

	Death	p value
(*A*) *Septicemia (n=30)*		
(*a*) ARF (n=6)	3/6 (50%)	
(*b*) Non ARF (n=24)	6/24 (25%)	<0.01
(*B*) *Septicemia with ARF* (n=6)		
(*a*) Oliguric (n=1)	1/1 (100%)	
(*b*) Non oliguric (n=5)	2/5 (40%)	<0.01

Discussion

Septicemia in the newborns is a common condition in the developing countries like India(1). Severe septicemia caused by Gram negative organisms results in a shock like state (endotoxic shock). Griffin *et al.* studied 25 newborns with septicemia, of which 4 infants with *E. coli* septicemia had acute renal failure. Renal functions improved rapidly when septicemia was treated with appropriate antibiotics and supportive measures(2).

Sherry and Kramer demonstrated that 23% newborns pass urine within the first 24 hours while 99.4% within the first 48 hours delivery. Renal pathology is suspected if the neonate does not pass urine by 48 hours(3).

Jones(4) demonstrated a urine output of 0.5-5 ml/kg/h body weight in 10% of patients and physiological oliguria was present in 7% of newborns(3). In this study the corresponding values on the first day of life were 1.02 ml/h/kg body weight and physiological oliguria in 16.6% of the control neonates.

In the present study ARF was present in 20% of septicemic neonates while no patient had ARF in the control group. This figure is comparable with Griffin *et al.* who showed that 16% septicemic neonates suffered from ARF(2).

The possible mechanisms of sepsis causing renal failure are as follows: (*i*) Shock like state due to Gram negative septicemia(5,6); (*ii*) Direct damage to blood vessels leading to disseminated intravascular coagulation causing renal ischemia and tubular destruction(7); (*iii*) Possible role of myoglobinuria following renal damage by Gram negative bacteria(8); and (*iv*) Septicemia causing transient acute pyelonephritis(9).

The ARF in the present study was predominantly non-oliguric in type which was in contrast with Griffin *et al.*s serves where all the babies who developed ARF were oliguric(2).

Although oliguria has been considered as a cardinal feature of renal failure, ARF in neonates can occur even with a normal amount of urine output, *i.e.,* azotemia can be present with a normal urine flow. The first prospective study of non oliguric renal failure was done by Grylack where the babies with azotemia without oliguria were studied(10). Uncontrolled studies have shown that renal vasodilator drugs, potent diuretics, volume expansion can convert

oliguric into non-oliguric failure, provided, they are administered early in the course of disease(11).

A high incidence of non-oliguric renal failure could perhaps be due to the kidneys being studied in the diuretic phase of acute tubular necrosis where the oliguric phase being short might have gone unnoticed.

It was further observed that all the septicemic neonates who went into shock also developed ARF. A significant association was noted between septicemic shock and ARF. This suggests that an initial episodes of shock due to sepsis causes renal anoxia and ischemia which triggers renal failure. Renal ischemia is caused by a decreased renal blood flow associated with the shock state.

The prognosis and outcome of ARF patients depends on the early diagnosis of the condition, the underlying pathology and the type of renal failure whether oliguric or non oliguric. The mortality in this study was 50% and was in contrast with the study of Griffin *et al.* where the rate was 25%(2).

The mortality was significantly higher in ARF patients as compared to non-ARF patients ($p < 0.001$). It is inferred that ARF in a septicemic baby is an additional insult to the *milieu* of the infant (*Table III*). Oliguria, if present is the cardinal feature of ARF. But severe oliguria lasting for days or anuria carries a poor prognosis(12). In the present study the only patient who was oliguric, died. A high mortality in oliguric patients has also been reported by others(12,13).

Postmortem renal biopsy done on the ARF patients showed features of acute tubular necrosis(ATN) in all the 3 cases. There was swollen pale, tubular cells with loss of nuclei along with pale cortex and interstitial edema. The microscopic lesion in intrinsic ARF depends on the severity of the ischemia. Severe injury produces acute tubular necrosis. If prolonged and profound ischemia occurs, then cortical and medullary necrosis occurs. ATN has relatively better prognosis than cortical or medullary necrosis.

In the present study all the babies were being treated with 2 potentially nephrotoxic drugs, *viz.*, aminoglycosides and cephalosporins. Cowan *et al.* in their study on neonatal puppies concluded that neonates are relatively resistant to the effects of aminoglycosides. They found no significant changes in the renal functions when the drug was given for 7 days(14). In this study ARF was detected in the first 7 days of life in all the cases; therefore, the problem of nephrotoxicity leading to impairment of renal functions presumably did not play a role in the causation of ARF. However this needs further research as no human studies have been done so far.

It is concluded that 16.6% normal neonates have physiological oliguria, while the mean urine output on the first day of life in a normal neonate was 1.02 ml/kg/h. Almost 15% neonates with septicemia suffered from ARF which was predominantly non-oliguric in nature. Further ARF severely affects the mortality rate in septicemic neonates. Patients with oliguric ARF have a poorer prognosis than those with non-oliguric ARF. Since oliguria may not be noticed in many cases, relevant renal function tests like blood urea and serum creatinine must be carried out in all septicemic neonates, so that an early detection of acute tubular necrosis can be made and necessary management ensued.

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