AN OUTBREAK OF MULTIDRUG RESISTANT *Salmonella typhimurium* IN A NURSERY

Ashok Kumar
Gopal Nath
B.D. Bhatia
V. Bhargava
V. Loiwal

ABSTRACT

A nursery epidemic caused by multidrug resistant Salmonella typhimurium is reported. In total, 21 infants developed symptomatic illness; of these, 17 had septicemia (7 blood culture positive) and 4 had diarrhea alone. Asymptomatic carrier state was identified in 13 infants. Male sex and birth asphyxia increased the risk for symptomatic illness. Fever, lethargy, and diarrhea were the most common clinical features. Amongst the septicemic infants there was no difference in clinical profile whether the blood culture was positive or negative for S. typhimurium. In the symptomatic group, S. *typhimurium was isolated from feces in 19 cases and from blood in 7 cases. In both symptomatic and asymtomatic infants, all isolates of* S. *typhimurium, whether obtained from feces and/or from blood, were resistant to ampicillin, chloramphenicol, and trimeihoprim, and a significant number (almost one-fifth) of them also showed resistance to third generation cephalosporins. More than 90% of isolates were sensitive to aminoglycosides and ciprofloxacin. On a combination of third generation cephalosporin (cefotaxime or ceftriaxone) and amikacin, 17 (81%) infants recovered, 2 succumbed to their illness, and 2 failed to improve and required ciprofloxacin. The origin of epidemic was traced to a carrier staff nurse working in nursery.*

Keywords: *Salmonella typhimurium, Neonate, Septicemia, Diarrhea.*

Salmonella infections in newborns are associated with higher morbidity and mortality due to immaturity of their host defense mechanisms. *Salmonella typhimurium* is one of the most common serotypes responsible for nursery epidemics. The emergence of multidrug resistant S. *typhimurium* is of grave significance as it may be associated with frequent therapeutic failures. Moreover, neonates infected with multidrug resistant organisms pose a great epidemiologic hazard to the family and community because of prolonged carrier state that is typical of this age group(l,2). In this communication we report an epidemic of multidrug resistant S. *typhimurium* in a nursery.

Material and Methods

Thirty-four neonates with *S. typhimurium* infection born between April and July**,** 1993, in the University Hospital, Banaras Hindu University, Varanasi, constituted the study material. Twenty-one infants were symptomatic while 13 were asyptomatic carriers. Complete sepsis work-up (hemogram, examination and/or culture of stool, blood, urine, and CSF, and chest X-ray) was done in every symptomatic case. *In-vitro* antibiotic sensitivity was put up using the Baur and Kirby method(3). Stool cultures were also obtained from healthy infants who stayed in maternity wards

From the Departments of Pediatrics and Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005.

Reprint requests: Dr. Ashok Kumar, B 31/83 R, Bhogabir, Lanka, Varanasi 221 005.

Received for publication: July 26,1994;
Accepted: November 11,1994

for more than 2 days, from nursery staff, and from the mothers of infants admitted in nursery. A detailed bacteriological investigation of the nursery, maternity wards, and labor room was undertaken. *'Z'* test was applied to test the significance of risk factors for symptomatic illness.

Results

In this series, 21 infants developed symptomatic illness; of these, 7 had culture positive septicemia, 10 clinically suspected septicemia, and 4 presented with diarrhea alone. Five infants of culture positive septicemia and 4 infants of clinically suspected septicemia also had diarrhea as a part of their illness. Fever, / lethargy, and diarrhea were the most common manifestations of the illness *(Table I).* Male infants (Z=2.185, p <0.05) and those who suffered birth asphyxia (Z = 2.175, p <0.05) were at greater risk of developing symptomatic illness. There was no difference in clinical features of culture positive and culture negative septicemic infants. Symptoms appeared between 3 and 7 days of life in all infants. Diarrheal stools were watery, yellow-green to green in color, and often contained mucus but not visible blood. *Table II* shows the laboratory data of symptomatic cases. In the symptomatic group, 19 infants grew *S. typhimurium* in their feces, and 7 in their blood. Two cases had meningitis as revealed by abnormal CSF. In 13 out of 174 healthy neonates who stayed in hospital for more than 48 hours, stool culture yielded *S. typhimurium.*

The proportion of stool isolates showing sensitivity to various drugs were as follows: streptomycin (94.2%),

TABLE I– *Clinical Data of Symptomatic and Asymptomatic Neonates*

Parameters	Symptomatic (n=21)	Asymptomatic (n=13)
Males	14	4
Females	7	9
Preterm	8	3
Term	13	10
Birth weight (g)		
< 2500	11	5
≥ 2500	10	8
Meconium stained liquor (thick)	3	1
Leaking per vagina (>24 h)	2	-
Birth asphyxia	10	2
*Clinical manifestations**		
Fever	15	-
Lethargy	14	-
Diarrhea	13	-
Hyperbilirubinemia	6	-
Respiratory distress	5	-
Renal failure	3	-
Apneic spells	3	-
Paralytic ileus	2	-
DIC	2	-
Sclerema	1	-
Outcome		
Improved	19	-
Expired	2	-

* Most of the symptomatic cases had more than one symptom.

TABLE II– *Laboratory Data of Symptomatic Neonates (n=21)*

Parameter	No.
Leucopenia (<5000/mm^3)	7
Leucocytosis (>25000/mm^3)	2
Elevated ESR (>15 mm/h)	2
Stool pus cells (>5/hpf)	9
Stool RBCs (>5/hpf)	6
Elevated blood urea (>40 mg/dl)	3
Abnormal CSF	2
Abnormal chest X-ray (pneumonia)	2
Positive cultures	
Stool	14
Stool + blood	4
Stool + blood + urine	1
Blood	2
CSF	-

gentamicin (89.4%), amikacin (100%), netromycin (89.4%), ciprofloxacin (94.2%), cefotaxime (84.2%), ceftriaxone (78.9%), furazolidone (47.3%), and nalidixic acid (21.1%). All the strains were resistant to ampicillin, trimethoprim, and chloramphenicol. No difference was found in the drug sensitivity pattern of stool isolates obtained from symptomatic or asymptomatic cases. Likewise, in blood culture positive cases, isolates obtained from blood and from feces exhibited similar pattern of drug sensitivity.

All symptomatic cases were treated with antibiotics, given intravenously, for 10-14 days except in a case of meningitis where the duration of treatment was 21 days. Sixteen infants received cefotaxime and amikacin; of these, 13 recovered, 1 failed to respond and required ciprofloxacin to improve whereas 2 died within 2 days of starting antibiotics because of fulminant illness. The organisms in both the cases were sensitive to cefotaxime and amikacin. Four of the 5 infants treated with ceftriaxone and amikacin recovered while one did not respond to this combination and required ciprofloxacin.

The detailed bacteriological investigation of the nursery, maternity wards, and labor room did not reveal contamination of environment by the organism. One staff nurse in nursery grew S. *typhimurium* in her feces and was transferred out of the nursery. Four of the 10 symptomatic cases who came for subsequent follow-up demonstrated positive stool culture after 2 to 4 months period.

Discussion

Clinically salmonellosis in newborns manifests like any other illness caused by Gram-negative organisms. Similar to other Indian studies(4,5) we also found a much higher incidence of septicemia (81%) in this series. This is in contrast to an incidence of 5% reported in western literature(6). However, recent studies report a great variability (3.3%-41%) in rates of positive blood cultures in *Salmonella* gastroenteritis(7,8). In this study certain factors like male sex, and birth asphyxia were more frequently associated with symptomatic illness than with asymptomatic carrier state. Males are well known to have higher incidence of sepsis(9). Besides this, 9 of 14 males with symptomatic illness also had birth asphyxia as additional risk factor. Birth asphyxia may impair host defense mechanisms through hypoxia and acidosis and

thus may predispose to sepsis(10). Thirteen infants had asymptomatic carrier state as revealed by positive stool culture.

In this study most isolates of *S. typhimurium* showed a widespread resistance to multiple drugs. All isolates were resistant to ampicillin, chloramphenicol, and trimethoprim. More than 90% of isolates were' sensitive to aminoglycosides and ciprofloxacin. A significant number of isolates also exhibited resistance to third generation cephalosporins (cefotaxime-16%, ceftriaxone 21%). This is of concern because the emergence of large scale resistance to these newer antibiotics may limit their usefulness in treating *Salmonella* infections.

The therapy of *Salmonella* infections remains controversial. In past, many authors had recommended against the use of antibiotics in *Salmonella* gastroenteritis since they prolonged the carrier 81816(11,12). This is true for infants older than 3 months with normal immune status where the risk of dissemination of infection is minimal. For infants below 3 months who are at high risk for developing systemic and focal complications of the disease, the use of antibiotics is justified(7,13). Antibiotics are not needed for asymptomatic carrier state(13). Similarly, the administration of antibiotics to healthy infants in an attempt to interrupt the spread of *Salmonella* infection during a nursery outbreak is of no value(l). Such practice, may, in fact predispose to disease by altering the enteric flora.

Infection with multidrug resistant *S. typhimurium* is associated with high mortality ranging from 77.7%(5) to 100%(4). Compared to this we lost only 2 (9.5%) neonates; one of these was a preterm infant with paralytic ileus and sclerema and the other, a term infant with meningitis and DIC. It is possible that the outcome was influenced to some extent by the lower proportion of preterm infants in this series compared with previous two studies where preterm infants comprised more than two-thirds of total cases. But even when the data is analyzed separately for preterm and term infants the difference in mortality is striking. The incidence of complications was comparable to previous studies. In our opinion the main reason for improved outcome was the use of amikacin with either cefotaxime or ceftriaxone. On this regimen, 17 (81%) infants recovered, 2 died, and 2 failed to respond and required ciprofloxacin to control their infection. Thus, we would recommend a combination of third generation cephalosporin (preferably cefotaxime) and amikacin as the first-line antibiotics for treating *S. typhimurium* infection in neonates.

The present study also highlights the role of carriers in the initiation of nursery epidemics. Since the end of epidemic no new case of infection by this organisms has occurred over a period of last one year. Stool cultures of all nursery personnel should be obtained at the first instance of *Salmonella* outbreak. This will help prevent the spread of infection in nursery.

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