However, we would require at least 550 patients in each group to ascertain a decrease of mortality from 10% to 5%.

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A Nursery Outbreak of Multidrug Resistant *Salmonella typhimurium*

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Salmonella infection in the neonatal period is associated with high morbidity and mortality, with the development of septicemia in 5% of all salmonella infections(l). Amongst the nontyphoidal salmonella sero-types, *S. typhimurium* is the most common organism responsible for nursery outbreaks. The emergence of multidrug resistant salmonella serotypes over the past few years has become a major problem, because

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of frequent therapeutic failures and these strains are globally widespread now(2-5). In this communications we highlight a report on an outbreak of diarrhea caused by S. typhimurium in our nursery at King Fahad Hospital, Gizan (Kingdom of Saudi Arabia), in view of the rare occurrence of drug resistant salmonella infection in this region(6) and also the problems faced by the treating doctors because of therapeutic failures and prolonged carrier state(l,4).

Subjects and Methods

This study is based on an outbreak of diarrhea caused by *S. typhimurium,* which took place in two phases over a period of 6 months, first time in September-October, 1996 and again in January-March, 1997. Positive stool cultures were obtained in 10 and 17 cases, respectively in two phases of the outbreak. Out of these, 23 cases were symptomatic; complete septic screening (including blood, urine, stool and CSF cultures) was performed in all these cases. A detailed microbiological examination of the nursery, labor room, maternity ward and operating room was performed. Stool culture of all asymptomatic occupants of the ward, doctors, nursing staff, mothers and other associated personnel was carried out. The cases were considered negative, once three successive stool cultures were found sterile and then discharged home. However, those with positive stool culture (after becoming asymptomatic) were managed as carriers and regularly followed in outpatient clinic with weekly stool cultures. Proper instructions were given to their parents and their carrier state was mentioned on follow up cards. Regular feed back alongwith necessary guidelines were sent to referral hospitals.

Results

The clinical profile of the symptomatic babies is depicted in *Table I.* Most the babies were preterm [mean gestational age of 33.6 ± 3.0 wks (range 30-38)] and low birth weight [mean weight of 2.3±0.5 kg (range 1.2-3.5)]. Eleven babies were males. Twelve (52.5%) babies were referred from peripheral hospitals including 10(83.3%) cases, who were positive for *S. typhimurium* at the time of admission and all these 10 cases were referred from a single hospital during the second phase of this outbreak. Most of the babies (69.5%) presented in the first month of their life, 21.7% in second month and 8.7% in the third month of life. Almost 90% babies were on formula feeds at the time of developing illness.

All the 27 babies had *S. typhimurium* in

TABLE I–*Clinical Features of Symptomatic Cases*

Clinical features	Number	(%)
Loose motions	23	(100.0)
Mixed with blood	7	(30.4)
Green	14	(60.9)
Yellow	9	(39.1)
Foul smelling	14	(60.9)
Mucoid	20	(86.9)
Fever	12	(52.2)
Pallor	12	(52.2)
Dehydration	8	(34.8)
Pneumonia	2	(8.7)
Jaundice	3	(13.0)
Hepatosplenomegaly	2	(8.7)
Shock	3	(13.0)
Acidosis	3	(13.0)
Paralytic ileus	2	(8.7)
Sclerema	11	(4.3)
Disseminated intravascular coagulation	1	(4.3)
Outcome		
Suvived	21	(91.3)
Expired	2	(8.7)
Carrier state	7	(33.3)

their stools. Four of the symptomatic cases had positive blood culture also, with the same sensitivity pattern as in the stools. The organism was uniformly resistant to ampicillin, cephalosporins, chloramphenicol, co-trimoxazole, amoxiclav, tobramycin, pipracillin and sensitive to ciprofloxacin, amikacin, gentamicin and nalidixic acid. However, none of the cases, who in their first instance received nalidixic acid (47.8%), amikacin/gentamicin (26.1%) responded to any of these drugs *in vivo* and they were subsequently managed with ciprofloxacin, with appreciable results. Severe anemia (with hemoglobin < 8g/dl) was noted in 9 cases and thrombocytopenia (platelets < 50,000 per cu mm) in 4 cases.

Almost all the babies had received multiple antibiotics for different indications before developing salmonella infection. Eighteen (78.3%) had received cefotaxim/ceftriaxone and 19(82.6%) had received aminoglycosides. Other antibiotics like aztreonam, ampicillin, piperacillin and vancomycin were given to 87%, 26.1%, 4.3% and 4.3% cases, respectively.

Two neonates expired. The first baby with suspected septicemia did not respond to ceftriaxone and amikacin combination (before culture senstivity report) and finally succumbed to fulminant septicemia due to *S. typhimurium* (blood culture positive). The other one with extreme prematurity (30 wks) and hyaline membrane disease did not survive, inspite of ciprofloxacin therapy well in time, although blood culture was negative for S. typhimurium.

Microbiological survey of nursery, labour room, maternity ward and operating room did not yield anything positive. Similarly, stool culture of doctors and mothers did not reveal any pathogen. However, during the first phase of this outbreak, stool culture of one staff nurse working in nursery was positive for *S. typhimurium.* Sensitivity pattern was the same as in the babies. The nurse had recently returned from Phillipine. She was isolated from the nursery and managed as an asymptomatic carrier, treated with ciprofloxacin before being allowed to resume her duties. She was kept under follow up with repeated stool cultures for a period of 6 months, considering her as a source of infection in the first phase of this outbreak.

During follow up, 11 babies were found as carriers with positive stool culture (7 amongst symptomatic and 4 amongst asymptomatic cases). Duration of their carrier state lasted from 28-98 days (mean 55.4 ± 24.8 days). The second phase of this outbreak was traced to one of these carriers, who got admitted in one of the peripheral hospitals, unnoticed about the carrier state by the treating doctor and without taking isolation and other necessary measures. All those babies referred to us from this peripheral hospital were managed with strict isolation measures in a separate room with separate nursing staff and thus the outbreak was controlled, both in our hospital and at peripheral level.

Discussion

S. typhimurium among nontyphoidal salmonella is one of the commonest serotypes responsible for nursery outbreaks. The immature immune system, hypochlorhydria and rapid gastric emptying makes infants vulnerable to systemic infections^). We noted bacteremia in 4(17%) cases, higher than in some western studies(7,8) which have reported bacteremia in 1-5% cases. However, our results are far below than some Indian studies, reporting bacteremia in 81% cases(4-9,10). Early use of ciprofloxacin may be related to low incidence of bacteremia in our study.

Multidrug resistant salmonella is a major problem in most of the countries including India(2-4). However, it was rarely reported from KSA(6). The recent upsurge in drug resistant salmonella in KSA may be due to frequent use of antibiotics right from birth as was noted in this study, which provides an ideal *milen* for emergence of drug resistant strains of S. *typhimiirium* (DT 104). People from different parts of the world, working or visiting KSA might be source of these drug resistant strains of *Salmonella(6).*

In contrast to one previous study(4), the drug sensitivity pattern in this outbreak was rather unique, showing drug resistance to most of the antibiotics including the third generation cephalosporins. The isolates demonstrated *in vivo* resistance to nalidaxic acid and aminoglycosides but with introduction of ciprofloxacin, a dramatic improvement in the clinical picture was noted along with the reversal of stool culture within 48-72 h. Dutta *et al.(3)* has also highlighted the importance of ciprofloxacin in multidrug resistant cases of S. typhimurium in children. However, Kumar *et al.,* managed 81% cases with cefotaxime/ceftriaxone and amikacin combination^). Utility of ciprofloxacin in multidrug resistant *S. typhimiurium* in children has been documented earlier. In contrast to other antimicrobials, effectiveness of ciprofloxacin is attributed to high levels of drug within the bowel mucosa and penetration well into the macrophages, a site of salmonella replication(ll).

As per previous recommendations(4,7), children > 3 months age and asymptomatic carriers donot need any antibiotic therapy to avoid prolongation of the carrier state. However, due to fear of developing septicemia, particularly in neonates, use of antibiotics is justified. Asymptomatic carriers need strict vigil, follow up and isolation measures to avoid recurrences as happened in the second phase of this outbreak.

Drug resistant *S. typhimurium* is associated with high mortality ranging from *77.7*-100%(9,10). However, like one previous study(4), we lost only 2 babies (8.7%); one with fulminant septicemia expired before ciprofloxacin therapy and the other one had extreme prematurity and hyaline membrane disease. The main reason for the better outcome was probably introduction of ciprofloxacin, immediately after noting *in vivo* resistance to many other antibiotics and losing first baby (on ceftriaxone).

This study highlights certain measures which can help in preventing and controlling such outbreaks: (z) Use of ciprofloxacin in the first instance after noting *in vivo* resistance to other antibiotics; (zz) Proper handling, washing and isolation measures taken right from beginning both in symptomatic and asymptomatic cases; *(in)* Isolation of staff, suspicious of source of infection; *(iv)* Follow up of carriers and properly labelling their follow up cards; and *(v)* Proper instructions to be given to parents and feed back to referral units. These measures if strictly adhered to, in addition to restriction of antibiotics, will definitely help in preventing such outbreaks in future.

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Status of Receipt of ICDS Package of Services by Under Three Children and Pregnant Mothers in District Agra

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The present study was undertaken with the objective to assess the receipt of package of services under the Integrated Child Development Services (ICDS) scheme by under three children and pregnant mothers in three ICDS projects in district Agra. In the present evaluation services related to immunization, supplementary nutrition, supplementation of specific nutrients (vitamin A and iron and folic acid), health checkup and treatment of minor ailments were included.

Subjects and Methods

The study was conducted during the year 1996 in district Agra, Uttar Pradesh. Three ICDS projects, namely Fatehpursikri, Khandoli and Bichpuri were selected for the study and these have been referred as projects A, B, and C respectively.

All the Anganwadi centers (AWCs) in each project were enlisted. In each project one circle area of supervisor consisting of

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