Enteric Fever—A Changing Sensitivity Pattern, Clinical Profile and Outcome

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With the changing pattern of bacterial infection and their sensitivity trends, pediatricians throughout the world are facing a challenging problem in day to day practice(l). The recent upsurge in multidrug resistant *S. typhi* infection, has made the treatment of enteric fever a difficult and controversial problem(l,2). The second line therapy suggested for drug resistant typhoid fever has also proven ineffective in managing such cases in recent past(2-6). A lot of work has already been done on MDRST infection. However, our study is based on large data of positive cases of *S. typhi* with changing sensitivity patterns.

Material and Methods

Two hundred and forty three culture

proven cases of enteric fever were studied from January, 1987 to December 1992. A detailed clinical history, examination and complications were noted in them. The diagnosis of enteric fever was based on clinical suspicion supported by positive blood culture and Widal agglutination titre of 'O' and 'H' antigen of 1:160 or fourfold rise in titre. Initially all the patients were put on chloramphenicol (75 mg/kg/day), except in complicated cases, in whom ciprofloxacin/ cefotaxime was used as first line therapy from 1990 onwards. The initial drug was continued as such or replaced by an appropriate antibiotic as per the sensitivity report. Daily clinical monitoring was done in all the cases and the patients were followed at least for six months, particularly ciprofloxacin group. The results thus obtained were interpreted by Students 't'-test and Chisquare test.

Results

Of 243 cases of enteric fever diagnosed over the past six years, 53.9% presented during first four years followed by an unanticipated rise during next two years (1991-1992) *(Table I)*. A definite rise in triple drug resistance from 1989 onwards and multidrug resistance from 1991 onwards was observed during this period *(Fig. 1)*. On the basis of sensitivity pattern, cases were divided into three groups, *i.e.,*

Group A : 127 (52.3%) cases were triple drug sensitive like chloramphenicol and/or amoxycillin and cotrimoxazole.

Group B: 11 (31.7%) cases were triple drug resistant (TDR) and were managed with gentamicin/ amikacin and cephalexin combination.

TABLE I-*Yearwise Distribution of Enteric Fever*

Year	Total		Group A		Group B		Group C	
	n	%	n	%	n	%	n	%
1987-88	60 (24.7)		46 (76.7)		14 (23.3)		-	
1989-90	11 (29.2)		46 (64.8)		21 (29.6)		4 (5.6)	
1991-92	112 (46.1)		35 (31.3)		42 (37.5)		35 (31.2)	
Total	243		127 (52.3)		77 (31.7)		39 (16.0)	

* Ciprofloxacin therapy in 30 (77%) and cefolaxime in 9 (23%) cases.
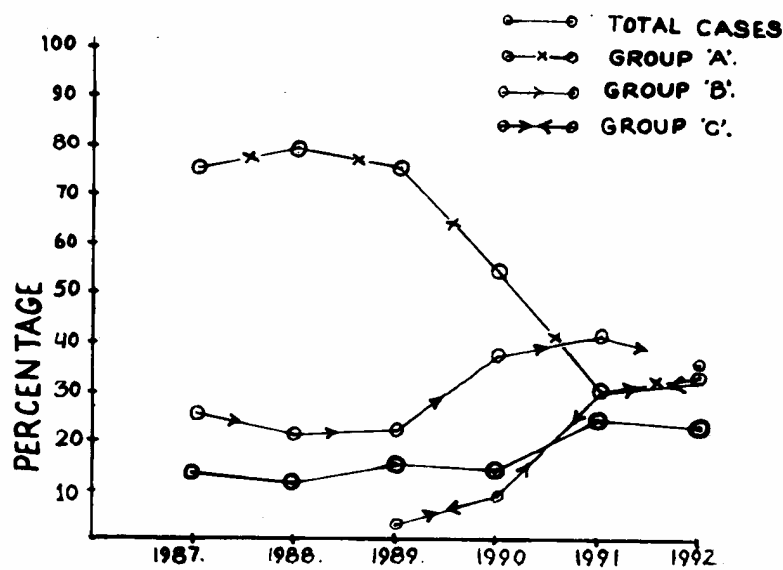

Fig. 1. *Showing yearwise distribution (1987-1992) of enteric fever cases (total), a falling trend of triple drug sensitiveness (Group A) and a rising triple drug resistance (Group B) and multidrug resistance (Group C).*

Group C: 39 (16%) cases were multidrug resistant (MDR) and managed with Ciprofloxacin (15 mg/kg/day) or Cefotaxime.

The clinical features noted in three groups of patients are summarized in *Table II.* A significant number of Group B and C fell in lower age limits compared to Group A cases (p<0.001). Eight of the nine cases below the age of two years were drug resistant and included a 3-month-old child

TABLE II-*Clinical Features of Enteric Fever*

Features	Total		Group A		Group B		Group C		p value
	n	%	n	%	n	%	n	%	
Sex									
Male	139	(57.2)	78	(61.4)	44	(57.1)	17	(43.6)	NS
Female	104	(42.3)	49	(38.6)	33	(42.9)	22	(66.4)	
Age (yr)									
2	9	(3.7)	1	(0.8)	4	(5.2)	4	(10.2)	
2-5	50	(20.6)	11	(8.7)	21	(27.3)	18	(46.2)	
5-9	102	(42.0)	53	(41.7)	38	(49.3)	11	(28.2)	<0.001
10-13	82	(33.7)	62	(48.8)	14	(18.2)	6	(15.4)	
Hepatomegaly	99	(40.8)	34	(26.8)	39	(50.6)	26	(66.7)	
Splenomegaly	146	(60.0)	62	(48.8)	56	(72. 7)	28	(71.8)	
Duration of fever (days)			8.35 ± 4.36		9.49 ± 3.0		12.1 ± 5.5		<0.05
Defervescence of fever (days)			6.45 ± 2.1		6.05 ± 1.0		5.1 ± 2.0		<0.05

with congenital nephrotic syndrome, who presented as MDRST septicemia. The mean time taken for defervescence in Group C was significantly (p<0.05) lower compared to the other two groups. The most serious complications noted were encephalopathy (7.8%), hepatitis (7.0%), shock (3.3%), cholecystitis (2.9%), myocarditis (1.2%) and nephritis (0.8%) and were commonly observed in drug resistant cases. Most of the cases had multiple complications. The overall mortality was 0.8% with one death, each in Groups A and C due to shock and myocarditis, respectively. No serious side effect was noted in 26 cases of ciprofloxacin group during their follow up except in two cases, who complained of self limiting arthragia. Three cases in Group B and 2 in Group C had relapse and were managed

with Ciprofloxacin therapy successfully.

Discussion

A declining trend in conventional triple drug sensitiveness has been observed during the past six years which has declined from 76.7% (1987-88) to 31.3% in recent years. Overall sensitivity to triple drug therapy noticed during the past six years is only 52.3%. An unanticipated 68.7% drug resistance noted during the last two years is comparable with reported figures of 10-83%(2-4). Although only 24.3% cases are below the age of 5 years; however, the incidence in multi drug resistant cases is quite high (56.4%). Earlier studies(7,8) have reported an incidence of 13.5-60% below the age of 5 years. With the emergence of MDRST strains, presence of enteric fever

below the age of 2 years and even in infancy has been reported recently(8,9). In close conformity with these reports, 89% cases below the age of two years in the present study were drug resistant. Early onset of MDRST cases is probably due to frequent occurrence of diarrheal disease in infancy and indiscriminate use of. antibiotics right from birth, which provide an ideal *mileu* for emergence of drug resistant strains of *S. typhi* through plasmid mediated *R' factor.

In close conformity with few earlier re-. ports(2,6,7) a high incidence of complications were observed in MDRST cases: however, contradicting the figures reported by Anand *et al.*(3). The high incidence may be attributed to more virulent genetic strains in MDRST cases, which usually present very late, the duration of fever at the time of presentation being significantly more than in non-resistant cases. Nephritic changes in multidrug resistant typhoid fever, have been reported previously also(10). However, the diagnosis in the present study was based purely on clinical and biochemical parameters and would definitely require histopathological confirmation.

Inspite of serious complications, the low mortality rate in present study may be attributed to early use of Ciprofloxacin/cefatoxime in such cases, before sensitivity reports were available. Although, controversial reports are available regarding the safety of Ciprofloxacin therapy in children; however, its use in life threatening conditions and resistant cases may be justified without any serious side effects(5,7,ll). An alternative group of drugs from 3rd generation cephalosporins have been used in drug resistant cases with successful results(6). Although safe, they cannot be used routinely, because of the prohibitive cost and requiring parcnteral administration and

hospitalization which is beyond the common man's reach. It has therefore, become relevant to restrict newer drugs only for multiresistant and fulminant cases of enteric fever. Multiresistant strains being reported at early age now, the need for an effective and safe vaccination against *S. typhi* in early infancy has become mandatory and an important milestone to be achieved in the near future.

REFERENCES

1. Wang FU, AU Xiau, Zhand mei Fang, Tai TY. Treatment of tyhpid fever with ofoxacin. J Antimicrob Chemother 1989, 23: 785-788.

2. Koul PB, Murali MV, Sharma PP, Ghai OP, Ramchandran VG, Talwar V. Multidrug resistant *Salmonella typhi* infection: Clinical profile and therapy. Indian Pediatr 1991, 28: 357-361.

3. Anand AC, Kataria VK, Singh W, Chatterjee SK. Epidemic of multi resistant enteric fever in Eastern India. Lancet 1990, 1:335-352.' "*

4. Jesudasan MV, Jacob John T. Multi resistant *Salmonella typhi* in India. Lancet 1990, 336: 252.

5. Sen S, Goyal RS, Dev R. Ciprofloxacin in the management of multiple drug resistant typhoid fever. Indian Pediatr 1991, 28: 417-419.

6. Mishra S, Niranjan S, Kumar H, Sharma D. Ceftriaxone: Use in multidrug resistant typhoid fever. Indian Pediatr 1993, 30: 67-70.

7. Pandey KK, Srinivasan S, Mahadevan S, Nalini P, Sambasiva Rao R. Typhoid fever below five years. Indian Pediatr 1990, 27: 153-156.

8. Mishra S, Patwari AK, Anand VK, *et al.* A clinical profile of multidrug resistant typhoid fever. Indian Pediatr 1991, 28: 1171-1174.

9. Garg RA, Krashak R. Typhoid fever before 2 years of age. Indian Pediatr 1993, 30: 805-808.

10. Dhawan A, Marwaha RK. Acute glomerulonephritis in multidrug resistant *Salmonella typhpi* infection. Indian Pediatr 1992, 29: 1039-1041.

11. Adam D. Use of quinolones in pediatric patients. Rev Infect Dis 1989, 11 (Suppl 5):S1113-S1116.

Drug Availability and its Utilization in Anganwadis

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Primary health care strategy had set the goal of providing low cost, effective and efficient health services by involving para-professionals(l). Anganwadi Workers (AWWs) of the Integrated Child Development Scheme have been given the responsibility to provide treatment for common illnesses to pre-school children along with

other preventive and promotive services. A medicine kit is provided to them every 6 month *(Appendix)(2).* However, non-availability of drugs is often reported by AWWs, and concern has also been expressed about the possibility of improper drug use by them(3). This study was planned with the objective to find out the availability of drugs in Anganwadis, the knowledge of AWWs about drug usage, and common ailments management by them.

Material and Methods

Out ofihe 168 anganwadis, 20 were randomly selected for this survey from Raipur Rani Community Health Centre Area, Haryana. The information on drug availability and usage was collected on a pre-tested proforma in the months of July and August, 1990. Medicine kit was checked on the day of the visit to record the number of available drugs. Anganwadi workers were interviewed to find out their knowledge about the drug prescriptions for common diseases and to record the illnesses managed by the in previous 7 days.

Results

Out of the 20 AWWs interviewed, 10 had told that supply of drugs was adequate. On the day of interview paracetamol and co-trimoxazole were available in 12, mebendazole in 11, oral rehydration salts in 8, sulphacetamide and benzyl benzoate in 7,