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## Clinical profile of culture proven enteric fever in children at university teaching hospital, Nepal

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### ABSTRACT

**Introduction:** Enteric fever is one of the major public health issues in Nepal. The present study was designed to analyze the clinical profile and antibiotic sensitivity pattern in the cases of culture positive typhoid fever.

**Methods:** This is a cross sectional study done by reviewing the hospital record files of children admitted in paediatric ward of Patan Hospital with culture positive enteric fever over a period of seven years from January 2007 to December 2013. The mode of presentation, sensitivity pattern of isolates from blood culture, response to therapy and the complications were recorded and analyzed.

**Results:** There were total of 119 culture positive enteric fever admitted to children ward during this period, 64 (53.7%) males and 55 (46.3%) females. Common symptoms were fever (100%), vomiting 37 (31.09%), diarrhea 27 (22.68%), abdominal pain 31 (26%) cough 24 (20%), and constipation six (5%). Common clinical signs were hepatomegaly 41 (34.4%), splenomegaly 25 (21%), and chest signs 10 (8.4%). Sensitivity to ceftriaxone was 96.6% in this study. Ninety four percent of salmonella typhi in 2013 were resistant to quinolones.

**Conclusions:** Apart from fever, diarrhea, vomiting, abdominal pain and cough were major manifestations and encephalopathy was common complication of enteric fever in this study. Resistance to many of the drugs are emerging. An appropriate antibiotic has to be initiated only after culture sensitivity in typhoid fever.

**Keywords:** clinical profile, enteric fever, *salmonella typhi*

### Plain Language Summary

This study was conducted to see the clinical presentation of Enteric fever and sensitivity to antibiotics being used. Presenting symptoms were fever, vomiting, diarrhea, abdominal pain, cough and constipation. During this study Ceftriaxone was found to be highly sensitive.

## INTRODUCTIONS

Enteric Fever (EF) is an important cause of illness and death in the overcrowded and unsanitary areas and is the leading cause of morbidity during summer season in Kathmandu.<sup>1</sup> Peak incidence is in May to August and is one of the leading cause of fever in most of the hospitals in Nepal.<sup>2</sup>

Children above 5 years of age have more complications<sup>3,4</sup> (diarrhea, vomiting, jaundice, febrile convulsions, nephritis, or typhoid meningitis<sup>5</sup>) than adults. Currently, decreased susceptibility has also been reported to fluoroquinolones and third-generation cephalosporins.<sup>6</sup>

With this background in mind, it becomes imperative to assess the extent of drug resistance before treatment is administered. Therefore, we conducted a study to look at the clinical profile of culture proven enteric fever in children admitted in our hospital.

## METHODS

This was a cross sectional hospital based chart review of children at paediatric ward of Patan Hospital, Patan Academy of Health Sciences (PAHS), Nepal from January 2007 to December 2013. All children with culture positive enteric fever (EF) admitted over the seven-year period were included in the study. Patient record files were reviewed for descriptive analysis of mode of presentation, sensitivity pattern of blood culture isolates and response to therapy and complications.

## RESULTS

A total of 16531 patients were admitted in children ward of Patan hospital from January 2007 to December 2013. Among which 1073 (6.49%) cases were diagnosed and treated as EF. Out of these 1073 cases, 119 (11.09%) were culture proven. Of 119 study patients 64 (53.78%) were male and 55 (46.21%) female with the male to female ratio of 1.16:1.

**Table 1. Age & Sex wise distribution of culture proven enteric fever in children (n=119)**

Age group (years)	Male	Female	Total
< 2	8	6	14
2 - 5	17	14	31
5 - 10	21	23	44
>10	18	12	30
<b>Total</b>	<b>64</b>	<b>55</b>	<b>119</b>

None of the children in the study group were immunized with typhoid vaccine. Fever was seen in all cases, and other symptoms and signs were less common.

**Table 2. Common clinical features of culture proven enteric fever in children (n=119)**

Symptoms	Number of Patients	Percentage
Fever	119	100%
Vomiting	37	31.09%
Abdominal pain	31	26.05%
Diarrhea	27	22.68%
Cough	24	20.16%
Headache	12	10.08%
Seizure	7	5.88%
Signs	Number of Patients	Percentage
Hepatomegaly	41	34.45%
Splenomegaly	25	21%
Chest signs (Crackles)	10	8.4%
Toxic look	9	7.56%

Complication were seen in total of 31 (2.8%) patients. Encephalopathy eight (6.72%), pneumonia seven (5.88%), hepatitis six (5.04%), pleural effusion four (3.36%), septic shock four (3.36%) meningitis one (0.84%) and myocarditis one (0.84%) were some of the serious complications observed at the time of admission or during hospitalization.

Of 119 positive blood culture, 104 (87.39%) were *Salmonella typhi* and 15 (12.6%) were *Salmonella Paratyphi A*. Sensitivity to ceftriaxone was 96.6% in this study. Ninety four percent of salmonella typhi in 2013 were resistant to quinolones.

**Table 3. Antibiotic sensitivity pattern in culture proven enteric fever in children (n=119)**

Drugs	2007-2009 (n=52)		2010-2012 (n=50)		2013 (n=17)		
	S	R	S	R	S	R	I
Amoxicillin	49	3	48	2	16	1	0
Chloramphenicol	50	2	47	3	16	1	0
Cotrimoxazole	46	6	46	4	16	1	
Ciprofloxacin	46	6	42	8	0	16	1
Ofloxacin	49	3	46	4	0	16	
Gentamicin	48	4	50	0	16	1	0
Ceftriaxone	52	0	49	1	14	3	
Nalidixic acid	24	28	9	38	0	16	1

Regarding other investigation, we found 77% patient had normal total leukocyte count 15.1% had leukocytosis and 20.1% had leukopenia. Among the 56 children who had chest X-ray, 45 (80.3%) had normal findings and 11 (19.65%) had infiltrations or pneumonia or effusion.

Among various antibiotic used in EF, Ceftriaxone was most common in 41% and in combination therapy, ofloxacin followed by ceftriaxone was used most common in 19.3%.

**Table 4. Antibiotics used in culture proven enteric fever children (n=119) in the study of**

Antibiotics	No. of patients	%
Ofloxacin	20	16.8
Ceftriaxone	49	41.1
Chloramphenicol	4	3.36
Amoxicillin	4	3.36
Ofloxacin followed by Ceftriaxone	23	19.3
Chloramphenicol followed by Ceftriaxone	8	6.7
Ceftriaxone followed by chloramphenicol	6	5.04
Ofloxacin followed by chloramphenicol	4	3.36
Azithromycin followed by chloramphenicol	1	0.84
<b>Total</b>	<b>119</b>	<b>100</b>

Average days of defervescence was 4.6 days (range 2 to 13) and average hospital stay 8.1 days (range 2 to 20).

All children with culture positive enteric fever recovered completely. Sixty four (53.78%) came for follow up.

## DISCUSSIONS

*Salmonella typhi* remains a major problem in developing countries. Poor sanitation, improper sewage disposal, lack of clean water system cause the transmission of typhoid fever. History, physical findings and fever pattern are suggestive but can neither confirm nor exclude typhoid. Blood culture is the gold standard for diagnosis and also gives information about antibiotic sensitivity of the isolate. Culture positivity in our study was 11.09%. Eighty seven percent of the isolates were *Salmonella Typhi* while 13% were *Salmonella Paratyphi A*. Whereas culture positivity was 52.6% and 61% of isolates were *Salmonella Typhi* while 39% were *Salmonella Paratyphi* reported by Jog et al.<sup>7</sup> There was considerable variability in the time period reported across studies, with some studies reporting data for several year periods and others reporting data from discrete seasons or shorter periods of time. In our patients, males (54%) were commonly affected as compared to females (46%). Females 52.3% and males 47.7% were reported by Chowta et al.<sup>8</sup> Majority of our cases (63%) were between (2-10) years of age and as many as 11.7% were below the age of two years which is consistent with that reported by Sharma et al<sup>9</sup> where 88.4% of patients were in school going age (3-12 yrs) with male preponderance (1.46:1). The youngest children were 9 and 10 months, respectively.<sup>9</sup> Data indicate a high infection ratio in this urban population, which is highest among preschool children. These ratios are comparable to recent regional reports and indicate that typhoid fever in preschool children may be underappreciated.<sup>10</sup>

Fever, vomiting, abdominal pain, diarrhea and cough were the most common clinical manifestations of enteric fever in children seen in our study similar to that reported by Patankar et al<sup>11</sup> where as fever, vomiting, diarrhea, abdominal pain and constipation were present in 100%, 20.4%, 20.4%, 11.3% and 9.09% patients respectively according to study done by Chowta et al.<sup>8</sup> Although diarrhea is a common finding of typhoid fever, it is not regarded as a diagnostically useful clinical criterion. The incidence of diarrhea in children with culture proven typhoid fever was 78 percent in one series from Australia<sup>12</sup> and 50% in a report from Vietnam.<sup>13</sup>

In our study, cough was present in approximately 20% of individual. Headache was seen only in 10.08% patients in our study probably because of younger children do not complain about headache where as KC et al<sup>2</sup> has observed very high incidence of headache (90%) in their study which includes adult population.

Hepatomegaly (34.45%) and splenomegaly (21%) were observed less frequently in our study compared to a study by Patankar et al<sup>11</sup> who found very high incidence of hepatomegaly (81.8%) and splenomegaly (48.5%) in their study. But splenomegaly (36%) and hepatomegaly (17%) were seen in study done by KC et al.<sup>2</sup> Briedis et al, reported that 30% of patients with typhoid fever had splenomegaly.<sup>14</sup> Relative bradycardia and constipation considered to be salient features of enteric fever in adult were very infrequently seen in our study. Few other studies have also found these to be inconsistent features of enteric fever.<sup>8</sup>

Twenty six percent of the patients developed complications in our study where as 10 to 15 percent of patients developed complications in the study done by KC et al.<sup>2</sup> Some of serious complications like encephalopathy, meningitis, pneumonia/effusion, septic shock, myocarditis and common complication like hepatitis were observed in our study which is consistent with the study done by Raghu Raman et al.<sup>15</sup> Typhoid encephalopathy (12.8%), hepatitis (5.1%), bronchopneumonia (5.1%) and pleural effusion (2.6%) were some of serious complications were observed by Mishra et al.<sup>10</sup>

Antimicrobial resistance to *Salmonella* is emerging global challenge, especially in developing countries where there is an increased misuse of antimicrobial agents. Significant decrease in vitro sensitivity to ceftriaxone in the year 2013 was observed in our study as shown by the study done by Ranju et al.<sup>16</sup> Sensitivity of *Salmonella Typhi* to ofloxacin was 79.83% and ciprofloxacin 73.94% in our study. Ninety four percent of salmonella typhi in 2013 were resistant to

quinolones. Nalidixic acid showed resistance in 68.9% of cases. Nalidixic acid resistant isolates of salmonella is quite prevalent in our setting. Since fluoroquinolones are widely used, sensitivity of Nalidixic acid should be routinely asked for used for deciding treatment with fluoroquinolones as the isolates that are Nalidixic acid resistant may not show response in VIVO with fluoroquinolones even though the strain is sensitive to it in VITRO.<sup>17</sup>

## CONCLUSIONS

Young children of 2 to 10 years were commonly effected with enteric fever. Cough, diarrhea, vomiting and abdominal pain were major symptoms and hepatomegaly, splenomegaly and chest signs (crackles) were major signs of enteric fever in our study. Hepatitis was common complication. *Salmonella Typhi* was common cause and ceftraixone was most sensitive antibiotic.

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