

Enteric Fever in Children at Dhulikhel Hospital

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Abstract

Introduction: Typhoid fever is one of the most common public health problems in Nepal. It occurs in all parts of the world where water supplies and sanitation are sub-standard. In Dhulikhel hospital, this is one of the top acute febrile illnesses in inpatient department. The objectives of this study were to evaluate the clinical and laboratory parameters including culture and sensitivity, the response to therapy, and complications of enteric fever among child cases at Dhulikhel Hospital. **Materials and Methods:** This retrospective study was conducted at Dhulikhel Hospital, Kathmandu University Teaching Hospital from January 2009 to June 2011. Statistical analysis was done with SPSS. **Results:** There were total of 138 cases of enteric fever admitted. There were 73 (53%) male and 65 (47%) female. Eighty-one percent were above five years of age. The most common clinical presentation was fever (100%) followed by headache and GI symptoms. Hepatomegaly was the most common sign seen among the cases and was seen in 110 cases (79.71%). Most of the patients had normal WBC count 100 (72.46%) Widal test was positive in 70 (50.72%) cases and blood culture was positive in 52 (37.68%) cases. Nalidixic acid was found to be resistant in 26 (50%) cases. Complications were seen in only 7 (5%) enteric fever cases. **Conclusion:** Typhoid fever is predominant in school going children in Nepal with slight male predominance. Fever lasting over 3 days followed by headache and GI symptoms are the major presenting symptoms. In making the diagnosis, the isolation of bacteria from blood is the "gold standard". Nalidixic acid resistant *Salmonella typhi* is on the increasing trend. Pneumonia was found to be the most common complication among all other complications seen in enteric cases. In Dhulikhel Hospital this is one of the top acute febrile illnesses in inpatient department.

Key words: Antibiogram, Hepatomegaly, *S. typhi*, Splenomegaly, Typhoid fever

Introduction

Typhoid or enteric fever is an ancient disease, which has afflicted mankind since human populations grew large enough to contaminate their water and food supplies. It is a waterborne and food borne disease caused by *Salmonella enterica serovar Typhi* (*S.typhi*) and *Salmonella enterica serovar Paratyphi* (*S.paratyphi*).

The WHO conservatively estimates the annual global incidence of typhoid fever at 21 million cases, of which 1-4% end fatally. An estimated 90% of these deaths occur in Asia¹. A recent epidemiologic study showed that south-east and south central Asia are the regions most endemic in the world with rates greater than 100/100,000 cases per year. The rest of Asia, Africa, Latin America, the Caribbean, and Oceania (except Australia and New Zealand) are the next highest with incidence

rates between 10-100/100,000 cases/year. Europe, North America, and the rest of the developed world have low rates of disease less than 10/100,000 cases/year².

Enteric fever (locally known as *Bisham Jworo* or *Myade Jworo*) is endemic in Nepal and constitutes a major cause of morbidity and mortality^{3,4}. The disease is predominantly a disease of school age children and young adults and is reported to be milder in infants and young children^{3,5}. According to the WHO case definition, a probable case of typhoid fever is a patient with fever 38° C and above that lasted for at least 3 days with a positive serodiagnosis or antigen detection test but without *S.typhi* isolation. Typhoid fever confirmed case definition, laboratory confirmed positive culture must be present⁶.

The primary sources of infection are feces and urine of cases or carriers; secondary sources include contaminated water, food, fingers, and flies. The disease may be acute non-complicated (characterized by prolonged fever, disturbance in bowel functions, headache, malaise, and anorexia) and complicated (intestinal bleeding, malena, intestinal perforation, and peritonitis)⁶.

The importance of enteric fever has increased once again due to the emergence of drug resistant strains. The spread of multidrug resistant *S.typhi* has reduced the number of effective treatment options, increased treatment costs, and resulted in higher rates of serious complication and deaths¹. This emergence of multidrug resistant typhoid in the 1990s lead to widespread use of fluoroquinolones as the treatment of choice of suspected typhoid, especially in South Asia and Southeast Asia where the disease was endemic⁷. In recent years, however, the emergence of resistance to quinolones has placed tremendous pressure on public health system in developing countries as treatment options are limited⁸.

Materials and Methods

This retrospective study was conducted at Dhulikhel Hospital, Kathmandu University Teaching Hospital from January 2009 to June 2011. The study was approved by the Kathmandu University School of Health Science Institutional review board.

A total of 138 cases of suspected typhoid fever admitted in the paediatric ward were studied. The diagnostic criteria of typhoid fever were based on clinical and laboratory findings. The clinical findings were high grade fever over three days with headache, myalgia, cough, GI symptoms, hepatomegaly, and splenomegaly. The laboratory findings included in this study were total WBC counts, blood culture positive for salmonella and Widal test with a cut off titer of 1:160. In all clinically suspected cases of Enteric fever, total and differential counts and blood cultures were sent. If child presented in the second week with features of Enteric fever, Widal test was sent. For culture and sensitivity tests, at least 5 ml blood was used to collect and followed up to 7th day of collection. Febrile illnesses of other causes were excluded with necessary investigation. If Widal test and blood cultures were both negative but patients with strong clinical suspicions and low counts were still considered as Enteric fever cases. Demographic data, clinical parameters, laboratory findings, antimicrobial use and their response, and complications were analyzed. The statistical analysis was done with Statistics software version 17.0.

Results

There were a total of 138 cases over the two and a half year period. There were 73 (53%) males and 65 (47%) females included in this study.

Their mean age was 8.5 years. The enteric cases were seen most frequently in children between 6-10 years followed by 11-15 years, and least frequently in children below 5 years of age. Among the study population, 81% (n=112) were school going children.

Table1: Showing the clinical feature and lab reports

Parameter	Total no (n=103)	Percentage (%)
Symptoms:		
Fever	138	100
Headache	100	72.4
Anorexia	66	48
Cough	54	39
Abdominal pain	46	33.3
Nausea	38	27.5
Myalgia	28	20.2
Loose motion	19	13.7
Signs:		
Hepatomegaly	110	79.7
Splenomegaly	20	14.4
Lab parameters:		
Total count		
Leukopenia	16	12
Normal count	100	72.4
Leukocytosis	22	15.9
Widal test positive	70	50.7
Blood culture positive	52	37.6

The clinical features and lab finding of enteric fever are shown in Table1. The most common symptom was fever, which was the presenting symptom of all cases 100% (n=138). Other symptoms were headache 72.4% (n=100), anorexia 48% (n=66), cough 39% (n=54), abdominal pain 33.3% (n=46), nausea 27% (n=38), myalgia 20% (n=28), and loose motion 13.7% (n=19). Among the signs, hepatomegaly 79.7% (n=110) was more common than splenomegaly 14.4% (n=20). In the paediatric age group, the liver may be palpable about 2 centimeters from the right costal margin as normal variant. Hepatomegaly in these cases may be a normal variant or as the result of enteric fever. Hepatomegaly was commonly seen between the ages of 5 to 10 years. In all cases total and differential count, widal and blood culture was done according to duration of illness. Most of the patients had normal blood counts 72% (n=100), while 16% (n=12) had leukocytosis and only 12% (n=16) cases had leucopenia.

Widal test was positive in 50.7% (n=70) of cases while only 18% (n=19) had significant rise (i.e. four fold rise in titer). Among 138 cases, only 52 (38.6%) had a positive blood culture when blood culture was follow up to seven days.

Table 2: Showing the antibiogram of culture positive cases (n=52)

Drug	Sensitive	Partially sensitive	Resistant
Chloramphenicol	42	0	10
Gentamycin	49	0	0
Ciprofloxacin	48	0	4
Cotrimoxazole	43	6	2
Ampicillin	11	7	34
Ceftriaxone	50	1	0
Azithromycin	50	2	0
Cefixime	13	0	0
Nalidixic acid	8	19	26
Amoxycillin	3	0	0
Cefuroxime	1	0	0

Antimicrobial resistance was observed with ampicillin 65% (n=34), nalidixic acid 50% (n=26), chloramphenicol 19% (n=10), ciprofloxacin 8% (n=4) and cotrimoxazole 4%(n=2).

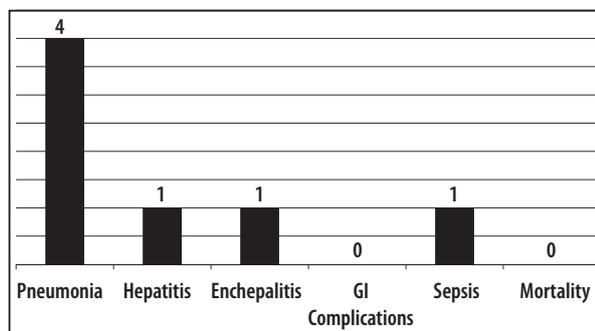


Fig 1: Showing various complications due to typhoid in among 138 cases.

Among the 138 cases, all were completely cured, but only 7 had complications as shown in Figure 1. The complications included 4 cases of pneumonia, 1 with enteric hepatitis, 1 with enteric encephalitis, and 1 with sepsis. There was no mortality among 138 observed cases.

During the hospital stay, the most common antimicrobial used was intravenous Ceftriaxone. Few cases were treated with other intravenous or oral medications. (azithromycin, cefixime, and ciprofloxacin)

Discussion

Enteric fever is a major health problem in developing countries attributed to poor sanitary and

hygienic condition including a lack of potable water. Investigation from the US Centers for Disease Control and Prevention estimate that there are 21.6 million typhoid cases annually, with the annual incidence varying from 100 to 1000 cases per 100,000 population². The global mortality estimates from typhoid have also been revised downwards from 600,000 to 200,000, largely on the basis of regional extrapolations².

In the present study, 138 cases of acute febrile illness, with other strong clinical features were analyzed along with supportive lab reports. In this study, 19% (n=26) of patients with typhoid fever were under 5 years, and the most affected group 81% (n=112) were school children, which was close to figures of other studies^{9,10}.

Enteric fever was more common in the male population than in the female population. Similar results were seen in the study done by Malla T et al¹¹ in Manipal Hospital. Male predominance was also seen in another study done by Shakya KN et al⁵ in Kathmandu Medical College in 2008.

Children in the study group commonly presented with fever 100% (n=138), headache 72.4% (n=100) and gastrointestinal symptoms 48% (n=66). In this study diarrhea was more common than constipation, which is in accordance with the results from other studies¹¹. The recent study done in India by Dhree G et al in 2012 also shows that fever with GI symptoms, including diarrhea, are the most common clinical presentation in children with enteric fever¹². Among the study population, hepatomegaly was seen in 79.7% (n=110) and splenomegaly was seen in only 14.4% (n=20) of cases, which was similar to another study in India^{12,13}.

Most of the cases in this study 72.5% (n=100) had normal total leukocyte counts, only 11.5% (n=16) cases had leucopenia, and 16% (n=22) cases had leukocytosis, which was similar to another study done in India¹⁴ where leucopenia was seen in 8% of the cases and leukocytosis in 12% of the cases. Another study done by Sharma N et al³ and his colleague (at Dhulikhel hospital in 2003) also showed that about 62.5% of cases had normal leukocyte count.

Widal test was positive in 50.7% (n=70) of cases similar to earlier study by Sharma N et al³. Unlike this study, positive widal test was higher in another study¹¹ done in Manipal Teaching Hospital, Pokhara where Widal test was positive in 83% of the cases. The growth positive rate for Salmonella Typhi in this study was the 52 (37.6%) which is high in comparison to the 5.4% reported in a study done by P Pokhrel et al¹⁵ from Nepal Medical College and Khanal et al⁴ from a teaching hospital in eastern Nepal reported 5.1%. In another study done by

Amatya et al¹⁶ from Kathmandu, a positive Salmonella culture rate of 23.1% was reported.

The last two decades have seen a change in the pattern of enteric fever with the emergence of multidrug-resistant strains (MDRS). The emergence of antimicrobial resistance during the last two and half years was also observed in this study. 65% were resistant to ampicillin, 50% to nalidixic acid, 19% to chloramphenicol, 8% to ciprofloxacin and 4% to cotrimoxazole. There was no resistance to ceftriaxone, cefuroxime, ofloxacin and gentamycin. Multidrug resistance (resistance to ampicillin, trimethoprim/sulphamethoxazole and chloramphenicol) was also not seen in this study which is in contrast to other studies done in different countries like 63% in Ghana, 7% in India, 22% in Vietnam and 65% in Pakistan^{18,19}. In the present study *S. typhi* was most resistant to ampicillin. Another study done by Amatya NM in Nepal in 2007 showed that all isolates of Salmonella typhi was susceptible to ceftriaxone, which is consistent with the present study²⁰. In the same study, it was also concluded that chloramphenicol was the foremost drug of choice among the tested antibiotics with its sensitivity rate of 98.4%, which is slightly higher than the present study²⁰. In contrast to this study, another study from Nigeria showed that among sero Typhi strains isolated from hospitalized patients in Lagos during 1997-2004, resistance rates reached 87% from ampicillin. Nalidixic acid resistance was found in 50% of patients among the culture positive cases in this present study. In another study done by Ochiai LR et al²¹ in five different countries in Asia, showed a significant increase in nalidixic acid resistance in 59% of isolates from the sites in Pakistan, 57% from those in India, and 44% from those in Vietnam ($p < 0.0001$) from overall heterogeneity of these proportions among the five sites. *S. typhi* was less resistant to cotrimoxazole, ciprofloxacin, and chloramphenicol followed by others. The finding was closer to previous findings from Nepal^{3,23}. There was no resistance to ceftriaxone and ofloxacin and this finding was similar to the previous studies done in Nepal^{3,5,11}.

There was no mortality in this series. Complications of typhoid fever were seen in 5% of children with Enteric fever. A similar result was seen in the study done in Chennai-South India where complications were seen in 4% of children¹⁴. The complications seen in this series were less in comparison to other studies, where complications occurred in 10-15% cases^{14,22}.

Nepal is considered as the Enteric fever endemic county and still known as an enteric fever capital of the world²³ with the significant burden of enteric fever within the local population and in travelers visiting the area. The same study also showed no significant signs of decreasing pattern of enteric fever in the country.

Typhidot M and Diazo test are good screening tests for early diagnosis of typhoid fever. One recent study done by Beig FK et al²⁴ in 2010 showed Typhidot M is superior to Diazo but the latter is more suitable to resource poor settings being economic and easy to perform.

Conclusion

Typhoid fever continues to be a major health problem resulting in significant number of children requiring hospitalization. In Dhulikhel Hospital this is one of the top causes of acute febrile illness in the inpatient department.

Typhoid fever is predominant in school going children with slight male predominance. Fever over 3 days followed by headache and GI symptom are major presenting symptoms. In making the diagnosis, the isolation of bacteria from blood is the "gold standard" but widespread uncontrolled use of antimicrobial leads to negative culture results. In this situation, Widal test and white blood cell count play a supportive role in diagnosis of enteric fever. The ceftriaxone, ofloxacin, and gentamycin are found to be 100% sensitive to Salmonella typhi. Nalidixic acid resistant strains Salmonella Typhi are on the increasing trend. Ampicillin resistance was detected in 65% of cases. Early diagnosis and instituting appropriate antibiotic therapy has reduced the complication of disease. Pneumonia was found to be the most common complication among all other complications seen in enteric cases.

This study was undertaken to acquire baseline information regarding typhoid fever in Dhulikhel Hospital. Addressing this issue would require a host of measures, including adequate investment in safe water and sanitation services, community education, control over antimicrobial prescribing, and vaccination strategies among others.

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