

## Study of clinical profile and antibiotic sensitivity pattern in culture positive typhoid fever cases

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### Abstract

**Objectives:** The present study was designed to analyze the clinical profile and antibiotic sensitivity pattern in the cases of culture positive typhoid fever.

**Method:** The study was conducted over a period of 1 year. Total of 46 culture positive cases of Typhoid fever were included in the study. The sensitivity pattern of isolates from blood culture was recorded. The modes of presentation, clinical course, lab investigation reports were also recorded.

**Results:** Out of 46 cases, 33 (71.7%) were males and 13 (28.3%) were females. Average age of presentation was 26.17 years. Fever was present in all patients. Resistance of *S. typhi* to amoxycillin, chloramphenicol and co-trimoxazole were significantly high. Ciprofloxacin showed resistance in 2 (4.3%) cases. Sensitivity to ceftriaxone was 100% in our study.

**Conclusion:** Typhoid fever is one of the most common health problem in Nepal. Various drugs are being used in the treatment of typhoid fever, in the mean time resistance to many of them are emerging. An appropriate antibiotic has to be initiated only after culture sensitivity in typhoid fever.

**Keywords:** Typhoid fever, *S. typhi*, Sensitivity, Drug resistance

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Typhoid fever occurs in all parts of the world where there is substandard water supply and sanitation. WHO estimates the annual global incidence of typhoid fever at 0.3%.<sup>1</sup> The annual incidence is markedly higher in some developing countries of Asia and Africa. An estimated 6,00,000 deaths from enteric fever occurs annually worldwide.<sup>2</sup> In India it is endemic with morbidity ranging from 102 to 2219 per 100,000 population.<sup>3</sup> Improved standards of public health have resulted in a marked decline in the incidence of typhoid fever in developed countries<sup>4</sup>.

Nepal as well as other south Asian countries are among the typhoid endemic regions. Typhoid fever has been reported from almost every part of Nepal from Mountains to Terai belt. It is one of the common cause of febrile illness and is the major reason for seeking health service by general population. Frequent outbreaks of typhoid fever have been reported in Nepal. There have been reports of seasonal typhoid outbreaks with recent one in 2002 in Bharatpur, a town in central Nepal. The multi-drug resistant typhoid epidemic in Bharatpur affected more than 6000 patients in a 4 to 5 weeks period and was from a single source- the municipality water supply.<sup>5,6,7,8</sup>

Chloramphenicol was considered the gold standard anti-microbial for the treatment of typhoid fever after its introduction in 1948.<sup>9</sup> However in the last two decades there has been an increase in the resistance of *S. typhi* to chloramphenicol. It was first reported in Britain in 1950.<sup>10</sup> Due to increasing frequency of antibiotic resistance, the use of chloramphenicol, amoxycillin and co-trimoxazole have become infrequent and quinolones have become the first line of treatment of typhoid fever. Emergence of resistance towards quinolones are also being noticed frequently. Ceftriaxone is the drug of choice in the quinolone resistant cases in our clinical practice. Resistance to multiple drugs has become matter of great health concern in the management of typhoid fever. In one of the study conducted for sensitivity pattern of salmonella serotype in Northern India revealed decreased sensitivity pattern against chloramphenicol, ampicillin, co-trimoxazole and norfloxacin (12% to 35%) while the better sensitivity pattern was shown by aminoglycosides, fluoroquinolones and cephalosporin (70% to 87%) in the year 2001.<sup>11</sup>

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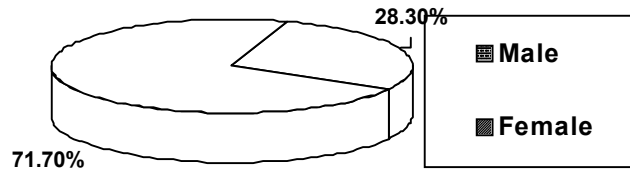
**Materials and Methods**

The study was undertaken in Kathmandu Medical College teaching hospital over the period of 1 year (between 1<sup>st</sup> July, 2004 to 30<sup>th</sup> June, 2005). All the suspected cases of typhoid fever on the basis of clinical features of high grade fever, headache, relative bradycardia, coated tongue, diarrhoea, constipation, vomiting and splenomegaly were investigated. The blood cultures were incubated at 37°C for at least 72 hrs. Only culture positive cases were included in the study. The sensitivity pattern of blood culture, mode of presentation, clinical courses, lab investigation reports and the antibiotic administered were recorded. Antibiotic sensitivities were carried out using Kirby Baur disc diffusion method.

**Results**

A total of 46 cases of culture positive typhoid fever were studied. Out of these, 33 (71.7%) were males and 13(28.3%) were females. Average age of presentation was 26.17 years and the average duration of symptoms before presentation was 5.9 days. Fever was present in all the patients (100%). Headache was present in 82.6% patients and other predominant symptoms were abdominal pain (26.1%), diarrhoea (28.3%), vomiting (21.7%) and constipation (13%). Splenomegaly was present in 28.3% patients [Table 1]. 89.1% of the patients had total leukocyte count in the normal range i.e. 4000-11000/ cu mm [Table 2]

**Pie Chart 1: Male to Female Ratio of Study Group**



**Table 1:** Distribution of Symptoms and Signs in the study population (n=46)

Sign & Symptoms	Number of Patients	Percentage
Fever	46	100
Headache	38	82.6
Diarrhoea	13	28.3
Abdominal pain	12	26.1
Vomiting	10	21.7
Constipation	6	13
Coated tongue	27	58.7
Relative bradycardia	20	43.5
Splenomegaly	13	28.3

**Table 2:** Leukocyte count in the study population (n=46)

<b>Count</b>	<b>Number of Patients</b>	<b>Percentage</b>
Normal (4000-11000/cumm)	41	89.1
Leucocytosis (>11000)	4	8.7
Leucopenia (<4000)	1	2.2

### Antibiotic Sensitivity pattern

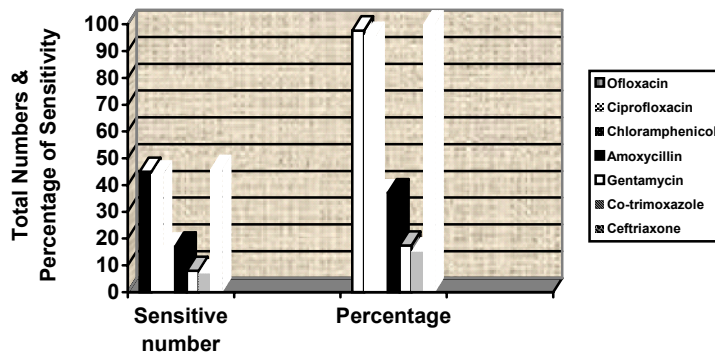
[Table 3] shows that the resistance of *S. typhi* to amoxicillin, chloramphenicol and co-trimoxazole was significantly high. Ciprofloxacin showed

resistance in 2 (4.3%) cases and ofloxacin showed resistance in 1(2.2%) case. Sensitivity to ceftriaxone was 100% in our study.

**Table 3:** Antibiotic Sensitivity Pattern: Antibiotic Sensitivity Pattern

Antibiotics	Sensitive number	Percentage
Ofloxacin	45	97.8
Ciprofloxacin	44	95.7
Chloramphenicol	17	37
Amoxicillin	17	37
Gentamycin	8	17.4
Co-trimoxazole	7	15.2
Ceftriaxone	46	100

**Fig 1:** Bar diagram showing antibiotic sensitivity pattern in culture positive patients (n-46).



### Discussion

Typhoid fever is the systemic infection primarily involving the alimentary tract by the gram negative enterobacteriaceae, the salmonella typhi. This highly adapted human specific pathogen has evolved remarkable mechanisms of persistence in its host that helps to ensure its survival and transmission<sup>12</sup>. Mode of transmission is through faeco-oral route, ingestion of contaminated food and drink is the common mode of infection. After escaping the acid barrier of the stomach, the organism enters the small intestine and adheres on the microvilli of epithelium. The organism breaks the cell membrane and attack the paeayers patches where they multiply. Liberation of endotoxin occurs and the organism travels via the lymphatics to reach the blood. Finally they are taken by reticuloendothelial system. They get reaccess to blood and small intestine through gall bladder. The disease is common in community with low standard of public health. In developing countries millions develop the disease and the mortality is as high as 30%.<sup>13</sup>

Presenting clinical features in our study is comparable to what had been reported earlier in a

study at Dhulikhel hospital Nepal<sup>14</sup> and at Kathmandu Medical College, Nepal<sup>15</sup>. Fever was present in all the 46 patients (100%). Headache was present in 38 patients (82.6%). Other common symptoms were diarrhoea, abdominal pain and vomiting. Adult patients with typhoid fever often have constipation but in young children and in adult with HIV infection diarrhoea is more common<sup>16,17</sup>. In our study, constipation was present only in 6(13%) and diarrhoea in 13(28.3%). On examination coated tongue was present in 27 patients (58.7%). Relative bradycardia and splenomegaly were present in 20 and 13 patients respectively (43.5% and 28.3%). Leucopenia was present in only one patient (2.2%).

Drug resistance in typhoid fever is considered to be an important factor in the morbidity and mortality of the disease. Since its introduction in 1948, chloramphenicol has been the gold standard drug in the treatment of typhoid fever in most parts of the world. However the indiscriminate use of the drug and acquisition of plasmid mediated R factor has led to the development of resistance of *S. typhi* against the drug.<sup>18</sup> Alternative drugs suggested were co-trimoxazole, ampicillin and amoxicillin. During

1990, resistant *S. typhi* not responding to chloramphenicol, ampicillin and co-trimoxazole appeared, in 50 to 52.9%.<sup>19</sup> In South East Asian nations, 5% or more of the strains of the bacteria may already be resistant to several antibiotics.<sup>20</sup> In our study, the incidence of chloramphenicol resistance was found to be 63% with a significant number of patients being resistant to amoxycillin and co-trimoxazole.

The quinolone group of drugs has now emerged as the treatment of choice for typhoid fever. But unfortunately, the same factors of indiscriminate antibiotic use and resistance within the antibiotic group that led to the emergence of chloramphenicol resistant organism are still operative. Resistance to Ciprofloxacin is now reported to be on the rise.<sup>21</sup> In the present study *S. typhi* showed resistance to ciprofloxacin in 4.3% of cases. In our study, sensitivity to ceftriaxone was 100%

### Conclusion

Typhoid is one of the major public health problems in Nepal. Nepal belongs to one of the endemic region and occasional epidemics have also been noticed here. The disease can lead to lethal outcome in the lack of appropriate measures. Various drugs are being used for the treatment of typhoid, at the same time resistance to many of the classical drugs are emerging. Indiscriminate use of drugs for the treatment of suspected cases of typhoid fever should be discouraged. Appropriate antibiotic as indicated by sensitivity test should be employed to prevent the development of resistant strains of *S. typhi*.

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