



Original Article

Antibiotic sensitivity pattern in culture positive typhoid fever cases isolated at Patan hospital

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ABSTRACT

Background: Enteric fever is one of the most common systemic infections of developing countries like Nepal. The changing trend of antibiotic susceptibility and increasing rate of resistance to the commonly used antibiotics has been of great concern in the proper treatment and prevention of this disease. This study aims to investigate the current antibiotic susceptibility pattern of *Salmonella typhi* and paratyphi A and B.

Materials and Methods: This study was carried out at Patan hospital of Lalitpur, Nepal over a period of 3 months. Blood culture sample were collected from suspected patients presenting to different departments of the hospital and tested microbiologically by standard procedure. Antibiotic susceptibility test was performed by Kirby Bauer Disc Diffusion method and results were interpreted by National Committee for Clinical Laboratory (NCCLS) guidelines.

Results: Out of the total sample of 212, 40(18.8%) cases were isolated as *Salmonella* species. Out of these, 29(72.5%) cases were *S typhi* and 11(27.5%) were *S paratyphi*. Isolates were mainly from adult age group. Regarding the antibiotic susceptibility pattern, the sensitivity to chloramphenicol was 95% and to cotrimoxazole 97% whereas the sensitivity to ciprofloxacin was 52.5% and 27.5% for Ofloxacin. Nalidixic Acid Resistance *Salmonella typhi* strain was 60.0 percent. Sensitivity to ceftriaxone, meropenem and colistin was found to be 100 percent.

Conclusion: A high degree of variability is seen in antimicrobial sensitivity pattern with very high degree of sensitivity to the historically used antibiotics like chloramphenicol and cotrimoxazole. Unfortunately, sensitivity to quinolones was seen to be very low, which were used widely in the last two decades. .

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INTRODUCTION

Typhoid fever is one of the commonest systemic infections of public health importance in the developing countries.¹ It is caused by *Salmonella enterica* subspecies enterica serovars typhi (*S typhi*) and paratyphi (*S paratyphi*). The spread of the disease is mainly by the use of substandard water supply, sanitation and contaminated foods. Globally, the annual incidence of typhoid fever is 0.3 percent.² Nepal is regarded as the capital city of typhoid fever and frequent outbreaks have been reported in the past few years.³ After a few days of bacteremia, the bacilli localize mainly in the lymphoid tissue of the small intestine, resulting in typical

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Table 1: Antibiotic sensitivity pattern of culture-positive *Salmonella* (n=40)

Antibiotics	Sensitive number of cases (n)	Percentage (%)
Cotrimoxazole	39	97.5
Chloramphenicol	38	95.0
Gentamycin	36	90.0
Cephalosporin	34	85.0
Ciprofloxacin	21	52.5
Ofloxacin	11	27.5
Colistin	40	100
Meropenem	40	100
Ceftriaxone	40	100
Penicillin	0	0
Amoxicillin	0	0
Erythromycin	0	0
Nalidixic acid	16	40

lesions in Payer's patches and follicles. These lesions swell at first, then ulcerate and usually heal. After clinical recovery, about 5% of the patient's become chronic carriers and pass the bacteria intermittently in stool and rarely in urine.⁴

The clinical presentation, laboratory findings, antibiotic sensitivity pattern of organisms and the clinical response of the illness to the antibiotics differ from one country to another and within the same country in due course of time. The persistence of the organisms in human body in carrier state despite the full course of treatment and its reactivity during the immunodeficiency period is the reason why most of the antibiotic resistance incidence have occurred.⁵ In southern Viet Nam, multidrug resistance in *S. typhi* had become established by late 1992 and early 1993.⁶⁻⁸ These multidrug-resistant *S. typhi* isolates were resistant to the usual first-line antibiotics, chloramphenicol, ampicillin, and co-trimoxazole, but remained fully susceptible to the fluoroquinolones and third-generation cephalosporins.

This is a study of the *Salmonella enterica* species grown in human blood and the resistance pattern of the organisms to the commonly used antibiotics in a tertiary care setting.

MATERIALS AND METHODS

A retrospective, three-month (September 2017 to December 2017), record-based analysis was carried out for all the blood and bone-marrow culture proven typhoid cases from the registry of Patan Hospital, Lalitpur. Due permission was sought from the hospital authorities to access the records. Patients of all the age groups were enrolled during the study. All strains of salmonella were serotyped at the laboratory of Patan hospital. All blood cultures were incubated at 37°C for at least 7 days. *Salmonella* strains were tested for their

sensitivity to 15 anti microbial agents by the disc diffusion method using Mueller Hinton agar according to the Bauer-Kirby method.⁹ The strains were identified as sensitive, intermediate or resistant as per the diameter of zone of inhibition.

RESULTS

There were altogether 212 positive blood cultures in the three-month duration. Culture positive typhoid cases were fourty. Out of these, 24 (60%) were males and 15 (37.5%) were females. Out of the total, there were 29 (72.5%) *Salmonella enterica* subspecies *enterica* serovar *typhi* (*S. typhi*), and 11 (27.5%) were salmonella enterica subspecies *enterica* serovar *paratyphi* (*S. paratyphi A*). Out of the 29 culture-positive *S. typhi* infections, 18 (62.1%) were Nalidixic Acid Resistant *Salmonella typhi* (NARST) strain, whereas 6 out of 11 (54.5%) of *S. paratyphi A* isolates were NARST strain. The sensitivity pattern of the *Salmonella* isolated is shown in the table 1. All the *Salmonella* isolates were found to be resistant to penicillin, amoxicillin and erythromycin.

DISCUSSION

The threat to human health posed by growth of antibiotic-resistant bacterial pathogen is of growing concern in medical practice. Drug resistance in typhoid fever is considered to be important factor in the morbidity and mortality of this disease. The emergence of multidrug-resistant enteric fever led to use of fluoroquinolones as the first-line of therapy. Unfortunately, broad-spectrum antibacterial activity, affordability and easy availability led to their indiscriminate use in human medicine. Furthermore, NARST with reduced susceptibility to ciprofloxacin (MIC 50 of 0.125–1 mg/ml) causing clinical failure emerged worldwide and became endemic in the Indian subcontinent.^{10,11} Chloramphenicol, discovered in 1947, was the first antibiotic successfully used in the treatment of typhoid fever. In view of the bone marrow suppression by this drug in some patients, this drug became less popular and other drugs like amoxicillin and cotrimoxazole were also successfully used to treat typhoid fever. However, indiscriminate use of drugs and acquisition of plasmid mediated R factor led to the development of resistance of *S. typhi* against some of the drugs.¹² However, our study shows quite a surprising result regarding chloramphenicol and cotrimoxazole resistance pattern, the drugs that were used in the early days of typhoid treatment. The sensitivity to the early-days antibiotics, especially chloramphenicol was 95.0% and cotrimoxazole was 97.5% which are in accordance with some other studies.^{13,14} Our findings show a remarkable reversal in the resistance pattern of *Salmonella typhi*. *Salmonella* strains which were almost 100% sensitive to fluoroquinolones a decade or two ago are now seen to have a very low degree of sensitivity to these antibiotics, 52.5% to ciprofloxacin and 27.5% to ofloxacin in this study. NARST strains, which may show

antibiotic susceptibility to fluoroquinolones in vitro are considered to be resistant to fluoroquinolones in vivo.¹⁵ The MIC of nalidixic acid for all NARST isolates was ≤ 32 mg/mL, whereas an MIC of ≤ 8 mg/mL was found for a range of Nalidixic acid sensitive *Salmonella typhi* (NASST) isolates.¹⁵

Out of 40 culture-positive salmonella species 24(60.0%) were NARST strain. Hence, our study shows that there has been increasing trend of resistance to fluoroquinolones, and high degree of sensitivity to early-days antibiotics like chloramphenicol and cotrimoxazole which were less used in the recent past due to their adverse effects or resistance in the past.

CONCLUSION

The prevalence of fluoroquinolone resistance salmonella species is very high, 47.5% are resistant to ciprofloxacin and 89.0% resistant to ofloxacin in our study. Taking into account the NARST strain of 84% in our study it can be deduced that even higher percentage of resistance would be shown by these strains in vivo, because even those strains that are sensitive to fluoroquinolones in vitro would be resistant in vivo when they are resistant to Nalidixic acid.

Conflict of interest: None

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