



### Original Research Article

## Recent trends of drug susceptibility of salmonella isolates in tertiary health care hospital at Patna Bihar

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### Abstract

**Introduction:** Typhoid or enteric fever is a major health problem in India. It is caused by *Salmonella enterica* var *typhi* and it is endemic in India. Its transmission occurs through feco-oral rout; poor hygiene and bad sanitation are main cause of its occurrence. Antibiotics resistance and development of MDR *S.typhi* is a big problem in treatment of typhoid. Chloramphenicol, Fluoroquinolones, Azithromycin and Cephalosporins are the major antibiotics for the treatment of enteric fever. Therefore this study is performed to determine the recent trend of antibiotics susceptibility among *Salmonella typhi* isolates in tertiary health care hospital in Patna, Bihar.

**Material and Methods:** present study is done in the department of Microbiology, Paediatrics, and Medicine at NMCH, Patna. Total 3940 provisionally diagnosed cases of typhoid or enteric fever is included in this study. Venous blood samples were used for the blood culture and blood culture is done on Brain-Heart infusion broth. Further subculture is done on Blood agar, MacConkey agar, and S-S agar media. Antibiotic sensitivity is done through Kirby-Bauer disc diffusion method. Antibiotic discs used are ampicillin, ciprofloxacin, ofloxacin, nalidixic acid, ceftriaxone, imipenem, meropenem etc supplied by Hi-media laboratory, Mumbai.

**Results:** Total no. of 3940 blood samples were collected for blood cultures. From these 228 salmonella isolates were isolated. Out of these 206 (90.3%) were *S. typhi*, 21 (9.21%) isolates were *S.paratyphi* A and 1 isolates (0.44%) was *S.paratyphi* B. Antibiotic susceptibility testing is done for ampicillin, cotrimoxazole, chloramphenicol, ciprofloxacin, ceftriaxone, amikacin, cefixime, meropenem, imipenem, aztreonam etc. Among these antibiotics maximum isolates (188) were resistant against ampicillin and cotrimoxazole and sensitive against azithromycin, meropenem and aztreonam.

**Discussion:** Enteric fever is endemic disease in India. Its incidence and prevalence is high in India due to poor sanitation and unhygienic food and water condition. Among infected persons males were more affected than females. Male female ratio was 1.7:1. Children were more affected than adults; this is due to unhygienic food habit of children and more exposure of males to the external environment than females. Antibiotic resistance and development of MDR *Salmonella enterica* is the major problem in the treatment of enteric fever. However some antibiotics like ceftriaxone, cefixime, azithromycin, meropenem, imipenem, aztreonam and some fluoroquinolones have good sensitivity against *Salmonella* species and are the drug of choice now a days.

## Introduction

Enteric fever is a common health problem among developing country like India<sup>1</sup>. Enteric fever is responsible for high morbidity and mortality in developing country. Enteric fever which is also known as Typhoid fever is caused by *Salmonella enterica* var typhi and Paratyphoid fever which is caused by *Salmonella enterica* var paratyphoid A, B and C<sup>2</sup>. *Salmonella* is gram negative bacilli. Its size is about 1-4 $\mu$  x 0.6  $\mu$  *Salmonella* is motile with peritrichous flagella. *Salmonella* is non capsulated, nonsporing. Enteric fever is endemic in India and affects all ages<sup>3</sup>. Enteric fever is mainly transmitted by faeco-oral route in regions where poor standards of hygiene and sanitation are prevalent. Enteric fever is an acute systemic illness which is manifested by fever, headache, splenomegaly, rose spot rash, constipation (adult), diarrhoea (Children), anorexia, coated tongue, malaise and abdominal discomfort. Antibiotic therapy is now a day's mainstay of management of enteric fever, reducing the mortality from 40% in untreated cases to 4% in patient who are receiving appropriate antibiotic therapy<sup>4</sup>. In India *S.typhi* is predominant serotype of salmonella responsible for enteric fever<sup>5</sup>. Now a day's *S.typhi* has rapidly gained resistance to ampicillin chloramphenicol, co-trimoxazole and ciprofloxacin. Initially sporadic cases of resistance to chloramphenicol in *S.typhi* are reported in 1950 and later in 1965<sup>6</sup>. First major epidemic by multidrug resistant strain is reported in Mexico<sup>7</sup>. In India first multidrug resistant strain (*S.typhi* of Vi phage type D1-N) is reported in Calicut<sup>8</sup>. Since then many cases are reported from India which signifies the broad distribution of chloramphenicol resistant *S.typhi*<sup>9</sup>. Drug resistant strains of *S.typhi* are responsible for treatment failure in typhoid patients. Enteric fever due to MDR *S.typhi* is frequently associated with increased morbidity and mortality. MDR *S.typhi* has been prevalent in India since 1989<sup>10</sup>. During 1990-92 these strains were resistant to three commonly used drugs (antibiotics), Chloramphenicol, ampicillin and co-trimoxazole. During 1993-97 ciprofloxacin a

fluoroquinolone emerges as drug of choice for the treatment of MDR typhoid fever in India. Due to their injudicious use, reports of clinical failure and decreased efficacy of quinolones are reported. Subsequently ciprofloxacin, third generation cephalosporin like ceftriaxone were started to be used for empirical therapy of suspected typhoid fever anticipating resistance to chloramphenicol. WHO guideline 2003 treatment of MDR typhoid depends on quinolone susceptibility pattern, in quinolone sensitive strains, treatment of choice is Fluoroquinolone. For quinolone resistant strains, third generation cephalosporins are recommended. This all prompted us to undertake the present study with the objective to observe any change in sensitivity pattern of *S.typhi* especially to quinolones, cephalosporins and chloramphenicol and some newer drugs in tertiary care hospitals.

## Aims and Objectives

Present study is done to detect the recent trend of antibiotic susceptibility pattern against *Salmonella enterica* in endemic country like India. Rational use of Antibiotics is very important to prevent the development of MDR *Salmonella*. The aim of this study is to prevent the development of MDR enteric fever and to detect the current trend of antibiotic susceptibility against *Salmonella enterica*.

## Material & Methods

Between December 2015 and December 2017, a total of 3940 patients attending outpatient department and wards of Paediatrics and Medicine department of Nalanda Medical College & Hospital provisionally diagnosed as having enteric fever or PUO were included in this study. *Inclusion criteria*- Study included blood cultures of patients suspected of *Salmonella* septicaemia and PUO at Department of Paediatrics and Medicine of NMCH, Patna. Only one isolate per patient was included in study. *Exclusion criteria*:- Patient who had received antibiotics in last 7 days. *Sample*: - Total no. of 3940 venous blood samples was included in this study. *Blood culture*- Blood

samples were collected in brain heart infusion broth with sterile precautions and incubated aerobically at 37<sup>0</sup>C for 48 hours. Subcultures were done on Blood agar, MacConkey agar and S-S (Salmonella-Shigella) agar and incubated aerobically at 37<sup>0</sup>C for 18 to 24 hours. In negative cases, subcultures were done for one week. Presumptive isolates (non-lactose fermenters) were identified biochemically and confirmed by slide agglutination test, first with salmonella polyvalent H and O followed by individual salmonella group antisera. Escherichia coli ATCC 25922 were used as a quality control strain. The antibiotic susceptibility testing was carried out by the Kirby-Bauer disc diffusion method. The antimicrobial agents tested were ampicillin (10microg) ceftriaxone (30microg) cefepime (30microg) imipenem (10microg) meropenem (25microg) and azithromycin (30microg), ciprofloxacin (30microg), ofloxacin (30microg), tigecycline (30microg), nalidixic acid (30microg) supplied by Hi-media laboratories Mumbai.

**Results**

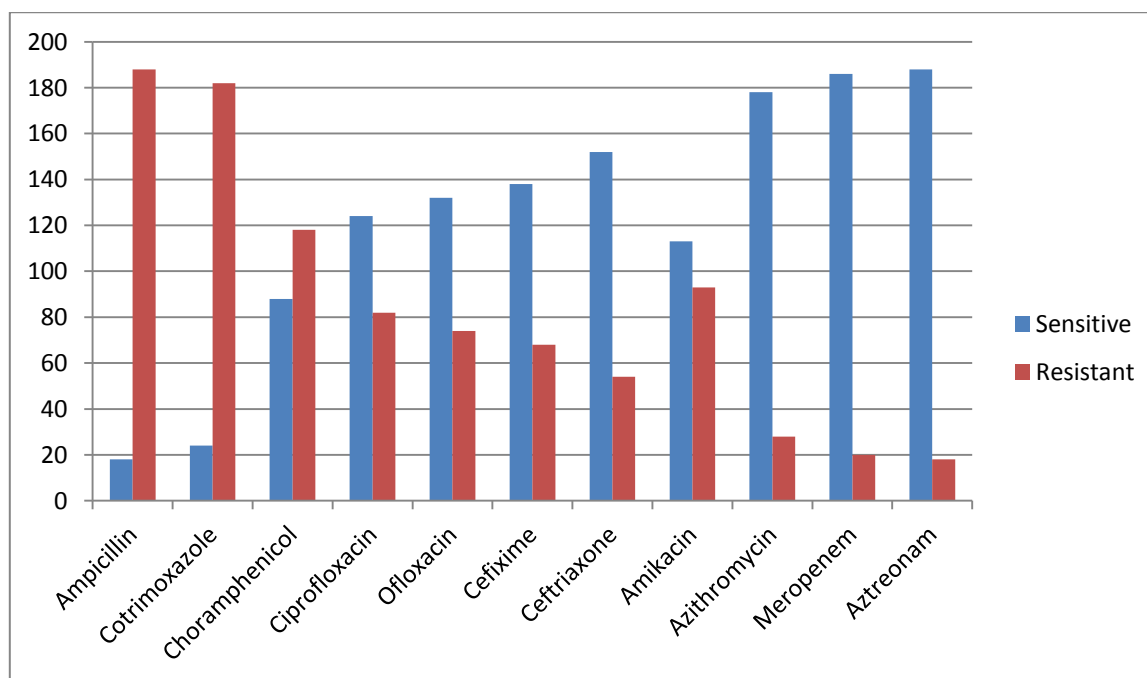
During the study period 3940 blood samples were received at microbiology department in brain heart

infusion broth for blood cultures. From these 228 salmonella isolates were isolated. Out of these 206 (90.3%) were S.typhi, 21 (9.21%) isolates were S.paratyphi A and 1 isolates (0.44%) was S.paratyphi B.

**The antibiotic susceptibility pattern of salmonella typhi is observed in following table**

Antibiotic	Salmonella Typhi (206)	
	S (%)	R (%)
Ampicillin	18 (8.73)	188 (91.26)
Cotrimoxazole	24 (11.6)	182 (88.34)
Chloramphenicol	88 (42.71)	118 (57.28)
Ciprofloxacin	124 (60.2)	82 (39.8)
Ofloxacin	132 (64.07)	74 (35.92)
Cefixime	138 (66.99)	68 (33.01)
Ceftriaxone	152 (73.78)	54 (26.21)
Amikacin	113 (54.85)	93 (45.14)
Azithromycin	178 (86.4)	28 (13.6)
Meropenem	186 (90.29)	20 (9.71)
Aztreonam	188 (91.26)	18 (8.74)

Majority of Isolates recovered were from Paediatric age group. Out of 228, Paediatric age group were 121 (53.07) and adult group 107 (46.93%). Out of 228, Male were 143 (62.71%) and female were 85 (37.28%)



**Fig:** Antimicrobial susceptibility pattern

## Discussion

Enteric fever caused by salmonella enterica is a systemic infection. Enteric fever is associated with high rate of morbidity and mortality. Enteric fever has been a major public health problem in developing country like India due to poor sanitation and overcrowding. In our study total of 218 strains were found over a period of 2 years. Out of which 216 strains belongs to *S. typhi*. Male to female ratio was nearly 1.7:1 in concordance with other reports which may be due to more involvement of males in outdoor activities and also males are more likely to report in hospital<sup>11, 12</sup>. Majority was in age group of 5-20 yrs (Paediatric age group). It may be due to more mobility and high consumption of unhygienic food and water in school or college. Health education may help in bring down this number. These data's are consistent with other studies<sup>13, 14</sup>. Proper treatment with antibiotics can reduce the mortality from 40% to 0.5% but constant rise in antibiotic resistance in *S. enterica* has become a therapeutic concern for clinician in endemic regions for patients and travellers who visit these regions and are not vaccinated<sup>15,16</sup>. In 1948 Chloramphenicol was introduced for treatment of typhoid fever, which reduces the duration of fever from 14-28 days to 3-5 days. Where chloramphenicol could not be used, ampicillin and co-trimoxazole were used as alternative drug but due to its injudicious use chloramphenicol resistant *S.typhi* was emerged in UK within two years of its successful use. In India it was first reported in Kerala in 1972. In 1990 rapid emergence MDR *S. typhi* was reported in many parts of India due to acquisition of R, Plasmid encoding acetyl transferase inactivating chloramphenicol and loss of OMP, Dihydrofolate reductase VI and TEM 1 beta lactamase were found responsible for resistance to ampicillin and co-trimoxazole<sup>17</sup>. In India MDR was first reported in Mumbai in 1990<sup>18</sup>. In our study chloramphenicol was found to be sensitive in 39.8% strain which is consistent with other studies. In our study Ampicillin and Co-

trimoxazole was found to be sensitive in 18% strain and 26% strain respectively. Since 1989 emergence of strains with resistant to ampicillin, chloramphenicol and co-trimoxazole leads to use of fluoroquinolones as ciprofloxacin and ofloxacin. Moderate cost, advantage of oral intake, tolerability, convenient dosage schedule of fluoroquinolones lead to injudicious use and subsequent decrease in sensitivity and clinical efficacy. In our study ciprofloxacin and ofloxacin sensitivity were 60.1% strain and 64.07% strain respectively. However ceftriaxone and cefixime have some good results. Only cefixime can be administered orally while ceftriaxone have parenteral routes of administration. In our study cefixime and ceftriaxone sensitivity are 66.99 % strain and 73.78% strain respectively. Treatment options are becoming limited with increasing resistance for third and fourth generation cephalosporin. Azithromycin can be drug of choice<sup>19</sup>. In our study 86.4% strains were sensitive, similar to other reports. It has negligible relapse rate and favourable outcome. Non availability of breakpoint concentration of azithromycin for salmonella in most standard antibiotic guideline makes the laboratory interpretation difficult. Carbapenem (Meropenem) and aztreonam can be given and found effective<sup>20</sup>. In our study meropenem and aztreonam sensitivity were 90.29% strain and 91.26% strains, where other studies have reported sensitivity of approx. 100%.

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