

# Clinical Spectrum, Bacterological Profile and Antibigram of Culture Proven Enteric Fever in a Private Sector Hospital in Lahore

Bacterological  
Profile and  
Antibiogram of  
Culture Proven  
Enteric Fever

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## ABSTRACT

**Objective:** To determine the Clinical spectrum, frequency of different salmonella strains and their trends of antibiotic susceptibility of culture isolates in patients of culture proven enteric fever in children over one year period.

**Study Design:** Retrospective cross-sectional study

**Place and Duration of Study:** This study was conducted at the Fatima Memorial Hospital Lahore from January, 2020 to December, 2020 for a period of one-year.

**Materials and Methods:** The case record of all patients of both sex diagnosed with enteric fever on blood culture is being reviewed. All patients in the age group of one year to 15 years with a discharge diagnosis of enteric fever for admitted inpatient or from outpatient Department (OPD) were included in the study.

**Results:** Mean age was around five year (61 months) and slight female preponderance (55%) was observed. Mean duration of fever before presentation was eight days and anorexia (82%) was the most common symptom after fever. S. Typhi was found in 76.4% of positive blood cultures and 23.6% of positive culture found S. Paratyphi A, B, C. 5 % cases of enteric fever were multi sensitive with 93% of isolates were either multidrug resistant (41%) or Extended drug resistant (52%).

**Conclusion:** Salmonella typhi is the predominantly isolated organism in cases of enteric fever. Only 5% of isolates are multi sensitive, Extended drug resistance (XDR typhoid) is the most commonly isolated organism with 52% of cases and 41% isolates were resistant to 1st line antibiotics (MDR typhoid). Study recommends azithromycin for OPD patients (sensitivity 98%) or intravenous meropenem (sensitivity 100%) for sick children in hospitals waiting for final culture and sensitivity reports to come.

**Key Words:** Clinical Spectrum, Bacterological Profile, Antibigram of Culture, Enteric Fever

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## INTRODUCTION

Enteric fever is a systemic infection that is caused by Salmonella Typhi, usually through ingestion of contaminated food or water. Children usually have high grade fever with variety of associated features like, myalgia, anorexia, vomiting, diarrhea, abdominal pain, cough and hepatosplenomegaly.

A similar but often less severe disease, paratyphoid fever, is caused by Salmonella Paratyphi A and B or

uncommonly Paratyphi C<sup>1</sup>. Enteric fever continues to be a major public health problem and it is endemic in Pakistan. According to the most recent estimates, between 11 and 21 million cases and 128 000 to 161 000 typhoid-related deaths occur annually worldwide<sup>2</sup>. In most developed countries incidence is <15/100,000 population while estimates in developing countries is 100-1,000/100,000 population<sup>2</sup>. Ochiai LR et al<sup>3</sup>, in their review of disease burden due to enteric fever from five Asian countries reported a higher incidence of typhoid fever from India, Indonesia and Pakistan.

Clinical presentation of enteric fever vary, so clinical diagnosis is difficult<sup>4,5</sup>. Blood culture is regarded as a gold standard for the diagnosis and gives information about antibiotic sensitivity of the isolate<sup>6</sup>. Although, the cost of investigations, lack of laboratory facilities, administration of prior antibiotics and poor awareness amongst health care professionals are obstacles to the diagnosis. We know that almost 30 years back by 1990, salmonella developed resistance simultaneously to all first line drugs like chloramphenicol, cotrimoxazole and ampicillin<sup>5</sup>. Now in the current epidemic in Pakistan we have to face the extremely drug resistant cases of

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enteric fever where the pathogen is resistant to the second line drugs that is quinolones and ceftriaxone <sup>7</sup>.

With the recent out-break of multidrug (MDR) and Extended drug resistant(XDR) typhoid fever, in Pakistan <sup>8,9,10</sup> and Globally <sup>11,12</sup>, we have found a clear trend of very high number of XDR salmonella isolates in culture proven enteric fever at our hospital and that was the main stimulus to explore and determine the antibiogram profile of Salmonella isolates discovered in blood cultures of suspected typhoid cases in children presenting in OPD and admitted in inpatient at Fatima memorial hospital(FMH) Lahore, So that it can be helpful in choice of antibiotics at the time of presentation to treat the patient appropriately especially if they are sick admitted in hospital and can't wait for culture to come.

We studied all cases of Blood culture Proven enteric fever seen by Physician in OPD or Inpatient over a period span of 1 year to describe the clinical and laboratory parameters in children with culture positive typhoid fever, and the trends of antibiotic susceptibility of culture isolates.

## MATERIALS AND METHODS

This was a retrospective cross-sectional study, conducted in the Department of Paediatrics, at Fatima memorial hospital, shadman Lahore, Pakistan over a one year period (January 2020 to December 2020). The medical files of patients diagnosed with enteric fever on blood culture is being reviewed. All patients in the age group of one year to 15 years with a discharge diagnosis of enteric fever for admitted in patient or from Outpatient Department (OPD) were included in the study.

All the data was recorded in a pre-designed proforma. Information on the socio-demographic profile, duration of symptoms and, presenting symptoms, duration of illness, Clinical examination like coated tongue, pallor, hepatosplenomegaly(Liver >2 cm below costal margin and spleen clinically palpable) were included in recorded data. All patients had complete blood counts (CBC), blood culture and sensitivity pattern, hepatic enzymes like ALT (normal<40 IU/L) and CRP (normal<5) done. Cases were diagnosed as a culture positive enteric fever if the blood culture was positive for S. Typhi or S. Paratyphi A,B,C and antibiogram profile was recorded in 110 cases.

**Statistical Analysis:** Data analysis was done by using IBM SPSS statistics (v. 23 IBM SPSS) and cross tabulation formulated to determine the mean (SD) and percentages of clinical and laboratory parameters. Antibiotics sensitivity for culture positive cases and significance of different values was obtained by chi-square test at 5% level of significance or by fishers's exact test.

Permission from the hospital ethical board was taken for using the data of the patients in the research.

## RESULTS

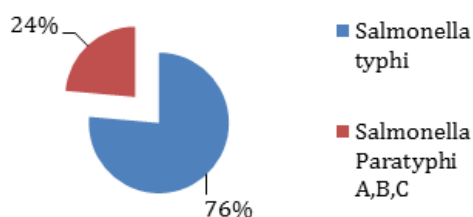
A total of 110 children diagnosed with enteric fever on blood culture. Majority of the patients were in the age range of two to nine years old with mean age of presentation was five year (60 months) and slight female preponderance (55%) was observed. Mean duration of fever before presentation was eight days and anorexia (89%) was the most common symptom after fever, followed by coated tongue (75%) and vomiting with abdominal pain (66%). More than half of the cases has shown fever with chills, rigors and sweating pattern [Table 1].Hepatomegaly and splenomegaly were seen in 37% and 48.5% patients respectively. Splenomegaly was observed in 72% of patients with Salmonella paratyphi infections and P value was found to be significant (0.001).

Mean Haemoglobin and Platelets were 8,185 respectively with 21 % of enteric fever cases showing leukocytosis pattern (WBC>12000/micro L). Mean C-reactive protein (normal CRP<5) found to be 29± 5 and Liver transaminases (SGPT) was elevated in majority of patients with mean of 74 (normal <40)

**Table No.1: Clinical and Laboratory Parameters of Culture Proven Enteric Fever (N=110)**

Parameter	Salmonella typhi (N=84)	S.Paratyphi A,B,C (N=26)	Overall Mean OR %	P value
Age in months*	55(± 23)	63(± 26)	60	.45
Female Sex	56	54	55	.469
Fever duration*	8(4)	8(4)	8	.398
Loose motions	56.3	83.3	70	.095
Vomiting	66.3	66.7	66	.53
Abdominal pain	63.8	61.1	62	.43
Anorexia	86.3	94.4	89	.314
Cough	35	27	31	.72
Chills and rigors	52.5	72.2	62	.31
Sweating	63	50	56	.54
Pallor	20	44	32	.037
Coated tongue	68.8	83.3	75	.44
Hepatomegaly	36	38	37	.92
Splenomegaly	25	72	48.5	.001
Haemoglobin*	8(2)	8(2)	8	.12
Leukocytosis	12	30	21	0.035
Platelets*	168(135)	202(122)	185	3.5
CRP*	30(5)	29(5)	29.5	1.6
ALT*	66(34)	83(54)	74	.98
Blood culture	76.4%	23.6%		.23

\* Mean (SD) without \* % Percentage

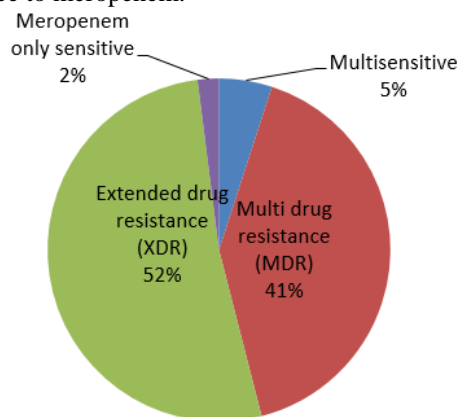


**Figure No.1: Salmonella Isolates**

S. Typhi and S.Paratyphi A,B,C were found in 76.4%(84), 23.6%(26) respectively of positive blood culture. (Figure 1).

The antibiotic susceptibility of Salmonella Typhi and Paratyphi for Ampicillin, Cotrimoxazole, Chloramphenicol (first line antibiotics) Fluoroquinolone, Ceftriaxone, Cefixime (2nd line antibiotics) Imipenem, meropenem, and Azithromycin, is presented in (Figure 2).

Majority of Salmonella Typhi and Paratyphi A,B,C showed resistance to first line antibiotics (Ampicillin, Cotrimoxazole, Chloramphenicol). Only 5% cases of enteric fever were multisensitive with 93% of isolates were either multi drug resistant(41%) or Extended drug resistant (52%).Three isolate of S. Paratyphi A was resistant to azithromycin as well and only sensitive to meropenem.in our study, we did not found any resistance to meropenem.



**Figure No.2: Antibiotics sensitivity of Enteric fever in Children**

Isolate is multisensitive if sensitive to first line antibiotics (Ampicillin, Cotrimoxazole, Chloramphenicol), labeled as a multidrug resistant (MDR) if sensitive to 2nd line antibiotics (Fluoroquinolone, Ceftriaxone, Cefixime) but resistant to first line and called as an Extended Drug resistance (XDR) if sensitive only to Carbapenems and macrolides (Azithromycin).

## DISCUSSION

In this study of children with blood culture proven enteric fever, we have observed that majority of the patients were in the age range of two to nine years

old with mean age of presentation was five year (60 months) and slight female preponderance (55%) was observed. This data set is similar to those reported in the previous literature, with confirmed enteric fever cases in children except Azmatullah A et al. reported slight male predominancy.<sup>1,8,9</sup> Mean duration of fever before presentation was eight days and anorexia (89%) was the most common symptom after fever, followed by coated tongue (75%) and vomiting with Abdominal pain (66%), similar to those reported in the previous studies done by Ochiai RL et al, and Jeeyani et al.<sup>3,4</sup>, although duration of fever before presentation was little prolong in our study, partly explained by consulting health services late in our community by general public.

With the recent outbreak of multidrug (MDR) and Extended drug resistant (XDR) typhoid fever, in Pakistan<sup>8,9,10</sup> and Globally<sup>11,12</sup>, we have documented very high number of XDR salmonella isolates in culture proven enteric fever at our hospital also which has coined the idea of this retrospective study to determine the resistance of Salmonella isolates especially the XDR typhoid fever. Salmonella enteric a ssp. serovar Typhi, haplotype H58 is a common cause of MDR typhoid fever across Asian and African countries and the strain causing the outbreak has coined an extended spectrum beta-lactamase (CTX-M15), the root cause of resistance to third-generation cephalosporins, as well as a mutation that causes resistance to fluoroquinolones as well. The H58 haplotype has also been known to harbor resistance to azithromycin on occasion.<sup>11,12</sup>

In our recorded data overall, 52% of isolates has shown Extended drug resistance pattern(XDR typhoid), quite higher than to others studies documented locally<sup>7,8,9</sup> and globally<sup>12</sup>, most likely explained well by multiple outbreak of XDR typhoid in different parts of Pakistan as reported by Saeed M et al. and Akram J et al. in their studies recently<sup>8,9</sup> and also mentioned very high incidence of XDR typhoid in their report published by Federal Disease Surveillance and Response Unit Field Epidemiology & Disease Surveillance Division, National Institute of Health (NIH) Islamabad.<sup>13</sup>

In our findings, we have also found 21 % of enteric fever cases showing leukocytosis pattern (WBC> 12000/micro L) and among leukocytosis Group strikingly, 89% of patients (16 out of 18) has shown Extended drug resistant pattern with P value of <0.001, which is quite significant finding. Although historically leucopenia is commonly associated with enteric fever<sup>14,15</sup>, but Jeeyani et al.<sup>4</sup> also has documented similar findings of leukocytosis especially in younger children especially less than 5 years old like our study age group cohort and may be explained with a change in sensitivity and virulence pattern of salmonella isolates especially with recent widespread outbreak of Extended drug resistance pattern in Pakistan only

sensitive to carbapenems or Macrolides, predominantly with high CRP and high hospital admission rates for intravenous treatment and globally as well<sup>16-19</sup>. In our data, S. Typhi was found in 76.4% of positive blood cultures and 23.6% of positive culture found S. Paratyphi A, B, C, and this trend was consistent with the current literature<sup>1,4,5,20</sup>. Both S. Typhi and S. Paratyphi had similar susceptibility pattern to third generation cephalosporins, carbapenems and azithromycin. Very high resistance to first line drugs like Amoxycillin, Chloramphenicol and cotrimoxazole, was observed (only 5% isolates were sensitive to first line drugs) which was also evident in similar studies in the region<sup>7,8,9,13,20</sup>. In our patients, 41% of isolates were multi drug resistant which was slightly high as compared to regional similar data<sup>7,8,9,13,20</sup> but is consistent with the trend recently and reflecting judicious use of these drugs by General Practitioners (GPs) and using these drugs in the past for typhoid fever, as a first line antibiotics, without doing blood culture in resource limited countries like Pakistan. The main limitation of this study is nature of data was hospital-based, which may not reflect the actual situation in the community. The retrospective nature of data and small sample size were other potential drawbacks.

## CONCLUSION

We conclude that there is a very high incidence of XDR typhoid, which needs to be validated by more locally well designed studies having said that emergence of XDR typhoid is no more regional concern, rather it's a global Emergency in public health. Pediatric culture proven enteric fever has a highest sensitivity to Carbapenems (100%) or to Azithromycin (98%).

### Author's Contribution:

Concept & Design of Study: Abid Rafiq Chaudhry  
 Drafting: Abid Rafiq Chaudhry  
 Data Analysis: Abid Rafiq Chaudhry  
 Revisiting Critically: Abid Rafiq Chaudhry  
 Final Approval of version: Abid Rafiq Chaudhry

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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