



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.2567500>Available online at: <http://www.iajps.com>

Research Article

**A CROSS-SECTIONAL STUDY TO OUTLINE RESISTANCE
AND SENSITIVITY OF ANTIBIOTIC MEDICINES IN
SALMONELLA TYPHI ISOLATES OF ENTERIC FEVER****¹Dr. Iqra Javed, ²Dr. Kinza Rehman, ³Dr. Muhammad Ahsan Shafiq**
^{1,2,3}District Headquarters Hospital, Rawalpindi.**Abstract:**

Objective: The aim of our study was to outline resistance and sensitivity of antibiotic medicines amongst *Salmonella typhi* isolates of enteric fever in kids.

Study Design: Cross-Sectional Study.

Place and Duration: This study was carried out for a time period of one year starting from January, 2018 to December, 2018 in Pediatric Medicine Department of District Headquarters Hospital, Rawalpindi.

Methodology: Those children who were having enteric fever were selected for the study and in a total quantity of 161. Blood samples 3ml to 5ml were taken from all subjects and instantly sent to the Microbiology laboratory for blood sensitivity and culture tests. Modified Kirby baur disc diffusion on *Salmonella* isolates on Mueller Hinton agar plates method was used for calculating zone's width of reserve of certain medicine, Which afterwards, used for defining the antibiotic drug resistance. Clinically examined the pain abdomen, anorexia and coated tongue. SPSS-20 was used for analysis of all collected data.

Results: Male and female distribution among 161 selected children were as 91 (56.5%) and 70 (43.5%) respectively. With minimum and maximum age as 2 years and 12 years accordingly, in this study the mean age of patients was 5.79 ± 2.451 years. In 93 (57.8%) cases of our study found usage history of antibiotics before 02 days of the sensitivity and culture test. Most patients of current study were having enteric fever along with abdominal pain 40.37% (65), headache 17.39% (28) and diarrhea 17.39% (28). Sensitivity of Ciprofloxacin found in 54.66% (88), Amoxicillin found in 22.36% (36), Gentamycin found in 17.39% (28), Ofloxacin found in 62.73% (101), Chloramphenicol found in 24.84% (40), Ampicillin found in 12.42% (20), Co-trimoxazole found in 12.42% (20).

Conclusion: According to the findings of our study it was found that *Salmonella-typhi* isolates of enteric-fever presented antibiotic medicine resistance at greater degree. Multidrug resistant strains were found extra predominant in this study that indicates to well-focused efforts of our health plan's makers to implement positive strategies about usage of antibiotic medicines in population of Pakistan.

Keywords: Children, Enteric Fever, Drug Resistance, Antibiotic.

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Please cite this article in press Iqra Javed et al., A Cross-Sectional Study To Outline Resistance And Sensitivity Of Antibiotic Medicines In *Salmonella Typhi* Isolates Of Enteric Fever., Indo Am. J. P. Sci, 2019; 06(02).

INTRODUCTION:

Severe systemic diseases which appear with abdominal pain and high fever are very common in typhoid fever [1]. *S. typhi* which is currently known as *Salmonella enteric* serotype Typhi, might be the main contributory organisms causing this systemic sickness. On the basis of clinical observations, it is very difficult to guess culprit organism because additional *Salmonella typhi*'s serotypes like *S. enterica* serotype para-typhi A, *S. enterica* serotype para-typhi B, or *S. enterica* serotype para-typhi C might similarly initiate same alike syndrome's type [2]. Enteric fever is a collective term used for both paratyphoid fever and typhoid fever. In penurious and over-crowded populations consuming unsafe water and foods, having no or poor hygienic facilities, a most common reason of febrile illnesses is salmonella and it is human limited pathogen which is spread by mean of orofecal way [3].

With mortality rate of 2.17 million per year, approximately 21 million cases enteric fever occur in the whole world [4,5]. Only in Asian countries prevalence is > 90% per year of worldwide cases. Prevalence of enteric fever in Pakistan is 413 per lakh annually which is very high. On the other hand, occurrence of enteric fever in SAARC countries is 110 per lakh yearly. There is no report of non-human vector of *Salmonella typhi* and its inoculum very short as one lakh causative agents may become reason for illness in approximately 50% of healthy persons. About 412 cases of enteric fever per one lakh people occur annually in Pakistan as intimated by WHO [6,7].

Formerly Chloramphenicol was exercised for treatment of this illness but its use was restricted in 1980 due to emergence of resistance and hence treatment of enter fever become difficult due to subsequent resistance to antibiotics in areas of satisfaction and the prepared obtainability of over the counter antibiotics. Occurrence of collective resistance to cotrimoxazole, chloramphenicol and ampicillin was at first noticed from Pakistan, Middle East, India and then from remaining world [6]. The reason behind rise of decreased sensitivity to the fluoroquinolones is extensive usage of fluoroquinolones [8]. According to the findings of a study carried out on children affected by enteric fever of shanty town zones of Karachi Ofloxacin, Ciprofloxacin and Ceftriaxone were found fully sensitive whereas, Cotrimoxazole, Ampicillin and Chloramphenicol were found 48%, 67% and 56% resistive respectively [9].

Amoxicillin, Co-trimoxazole, chloramphenicol and Gentamycin were found resistive as 63%, 85%, 63% and 82% respectively as per findings of a study held in

Nepal [10]. Resistance among *Salmonella typhi* separated by samples of children's blood who were affected by enteric fever observed in a study held in India was as Ofloxacin 7.2%, Ciprofloxacin 26%, Gentamycin 9.7%, Co-trimoxazole 69.01%, Ampicillin 74.21%, Chloramphenicol 67% and Amoxicillin 71.01% [10]. Therefore, the present study was carried out to observe the outline of antimicrobial medicine resistance in enteric fever's *Salmonella typhi* isolates.

MATERIAL AND METHODS:

Children who were having enteric fever were selected for the study and in a total quantity of 161. The age of the patients was from 2 years to 12 years. This cross-sectional research study was carried out for a time period of one year starting from January, 2018 to December, 2018 in Pediatric Medicine Department of District Headquarters Hospital, Rawalpindi. With predicting 7.20% medicine resistance of *Salmonella typhi* against Ofloxacin at 95.0% assertion interval used WHO sample size calculator for selection of these children. Included all those patients in our study whom Typhi Dot IgM test result was +ve and having fever as $\geq 101^{\circ}\text{F}$ in addition with headache, anorexia, hepatomegaly, diarrhea, constipation, abdominal pain, coated tongue and splenomegaly. Excluded all those patients with Typhi Dot positive from the study who were having poor oral intake, congenital or acquired immunodeficiency, seizures or shock, with perforations and already taking antibiotics within 48 hours. Noted all previous history of patients such as coated tongue, Splenomegaly, demographics, Hepatomegaly, Pain abdomen, Anorexia, Diarrhea, Constipation, fever and headache.

Blood samples 3ml to 5ml were taken from all subjects and instantly sent to the Microbiology laboratory for blood sensitivity and culture tests. Through applying a Mueller Hinton agar plates in modified Kirby baur disc diffusion technique about medicine resistance/sensitivity test, after 24 hours whichever progress found was recorded. Modified Kirby baur disc diffusion method was used for calculating span of inhibition's zone of particular medicine on *Salmonella* isolates on Mueller Hinton agar plates. Clinically examined the headache, anorexia, pain abdomen and coated tongue. Measured the fever by using thermometer (as $\geq 101^{\circ}\text{F}$). Three watery stools within 24Hrs were subjected to categorize diarrhea. Clinically assessed the splenomegaly and hepatomegaly. SPSS-20 was used for analysis of all collected data.

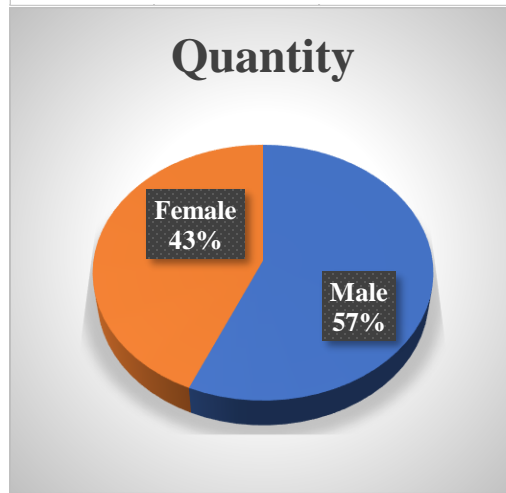
Patient's mean age and standard deviation for age of was calculated by applying descriptive statistics. Rate and quantitative variables were calculated as per category such as antibiotic drugs like Gentamycin, Ofloxacin, Ciprofloxacin, Amoxicillin, Chloramphenicol, Ampicillin, Co-trimoxazole and category of observed complaints like splenomegaly, coated tongue, anorexia, hepatomegaly, pain abdomen, fever, headache, constipation and diarrhea.

RESULTS:

Selected all those children who were diagnosed of enteric fever with +ve isolates of *S.typhi* and fulfilling exclusion and inclusion standards of our research. Total number of selected patients was 161. Among these male and female distribution was as 91 (56.50%) and 70 (43.50%) respectively.

Table No 01: Gender Distribution

Gender	Quantity	Percentage
Male	91	56.50
Female	70	43.50

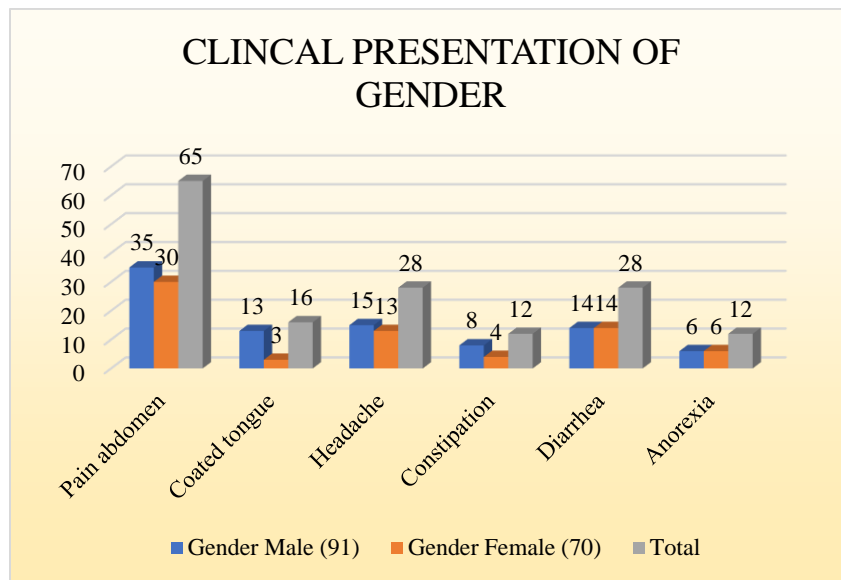


With minimum age of 02 years and maximum age as 12 years, the median age of patients of current research was 5.79 ± 2.450 years. With P-value equal to 0.062, mean age of females was 6.20 ± 2.75 years and median age of males was 5.48 ± 2.140 years. Majority of the

patients were in the age range of 2 year to 7 years as 64.60% (104). Most patients of this research were facing enteric fever along with abdominal pain 40.37% (65), headache 17.39% (28) and diarrhea 17.39% (28).

Table No 02: Distribution of gender with regards to clinical presentation

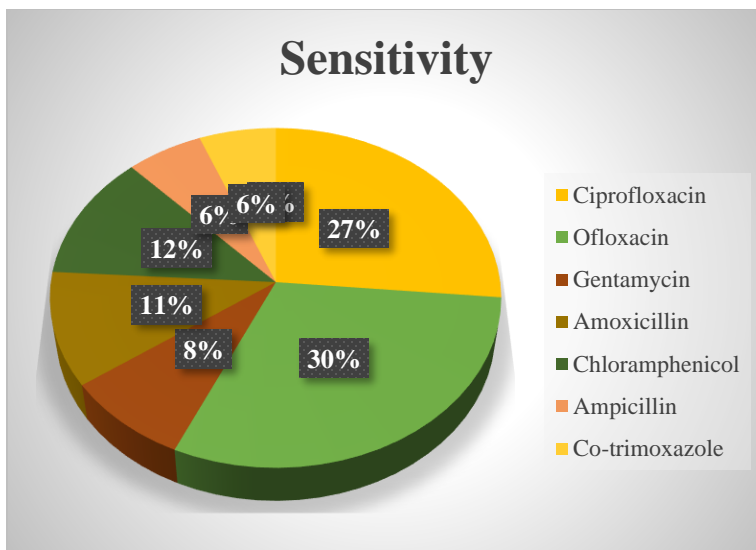
Clinical presentation	Gender		Total	P-Value
	Male (91)	Female (70)		
Pain abdomen	35	30	65	0.062
Coated tongue	13	3	16	
Headache	15	13	28	
Constipation	8	4	12	
Diarrhea	14	14	28	
Anorexia	6	6	12	
Total	161			



Sensitivity of Ciprofloxacin found in 54.66% (88), Amoxicillin found in 22.36% (36), Gentamycin found in 17.39% (28), Ofloxacin found in 62.73% (101), Chloramphenicol found in 24.84% (40), Ampicillin found in 12.42% (20), Co-trimoxazole found in 12.42% (20).

Table No 03: Results of blood culture and sensitivity test among all cases

Antibiotics	Sensitivity	
	Quantity of cases	Percentage
Ciprofloxacin	88	54.7 %
Ofloxacin	101	62.7 %
Gentamycin	28	17.4 %
Amoxicillin	36	22.4 %
Chloramphenicol	40	24.8 %
Ampicillin	20	12.4 %
Co-trimoxazole	20	12.4 %



DISCUSSION:

In under developing countries enteric fever is a main public health issue. In tropical regions including Pakistan it is one of the main health issues. Antibiotic medicines present very operative curing choices in enteric fever but current rise of antibiotic resistance among *Salmonella typhi* has provided increase to a few significant anxieties in our populace [11,12]. Drugs which were effective against *Salmonella* are compounded in the emergence of resistance due to unreasonable usage of these medicines and swiftly obtainability deprived of recommendation of doctor. Male gender prevalence in children with enteric fever was noticed in different studies. Similarity was found among results of our study and findings of these studies. Prevalence of males was found 62% in the study of Hussain et al very close to our study [13]. In another study held by Iqbal et al it was noticed as 63% males [14] and in two more studies by Fazil et al [16] and Lakhany et al carried out in Karachi female to male ratio was 1:2 [15] very close to the calculations of our study.

The medianage of patients of this research paper was 05.80 ± 2.450 years, with minimum age of 02 years and maximum age as 12 years. With P-value equal to 0.062, mean age of females was 6.20 ± 2.75 years and medianage of males was 5.47 ± 2.140 years. Majority of the patients were in the age range of 2 year to 7 years as 64.60% (104). Similar results were observed in the studies of Khurshid et al, Fazil et al, Lakhany et al and Iqbal et al [14,15,16,17]. Most patients of this research were facing enteric fever along with abdominal pain 40.37% (65), headache 17.39% (28) and diarrhea

17.39% (28). Rasaily et al reported similar results in his study as abdominal pain 19.81%, cough 18.01%, vomiting 23.82%, anorexia 26.23%, diarrhea 37.20%, chill and rigor 23.21% and headache 36.01% [18].

Most commonly used drug for the treatment of enteric fever is Chloramphenicol since 1948. An alternative therapy against *S. Typhi* is use of ampicillin and cotrimoxazole but serious concerns are raised in the treatment of these infections, especially in South Asian countries, against these drugs due to the emergence of multidrug resistant *S. typhi*. Chloramphenicol was resistant in 77(47.82%) of isolates and was sensitive in 40 (24.84%) of isolates. In a study by Khan et al [9] stated Chloramphenicol 56.0% resistant, Mathura et al in his study stated 63.0% resistance with this medicine [10] and Imran et al stated same alike results in his study [19] which are close to findings our study. We found 100 (62.11%) cases of ampicillin resistant and 20 (12.42%) sensitive cases of the salmonella isolates in our study. Whereas, Javed et al in his study stated sensitivity to ampicillin as 23% [20]. According to our results a decrease in sensitivity is observed which means that in our people trends of drug resistance is increasing. On the other hand, Kumar et al stated 75.0% resistance [5] with this medicine and Khan et al reported 67% resistance [9], these results are same alike to findings of our research.

There was 109 (67.70%) cases resistive to Co-trimoxazole and 20 (12.42%) sensitive cases as per findings of our study whereas, Khan et al study [9] showed 48% resistant of isolates which indicates growing trends of drug resistance in our people. On the other hand, Mathura et al found 85% resistance to this

drug which is close to results of our study. There was 28 (17.39 %) of the isolates resistive to Ciprofloxacin and 88 (54.67%) sensitive cases according to findings of our study whereas, Khan et al stated ciprofloxacin as 100% sensitive in kids affected by enteric fever [9] whereas, Javed et al described 86.0% sensitivity [20] which indicates rising tendencies of medicine resistance in our people. Close to outcomes of our study were found in a study held in India showing resistance in 26% children with enteric fever [5].

According to the findings of our study, Ofloxacin was resistant in 44 (27.33%) and sensitive in 101 (62.73%) of the isolates whereas, from India, Kumar et al stated 7.20% medicine resistance [5] which indicates resistant strains in our populace. According to the findings of our study, Gentamycin was resistant in 117 (72.67%) and sensitive in 28 (17.39%) cases whereas, Javed et al described sensitivity as in 20.90% [20] that is much greater than current research results. In a study by Mathura et al sensitivity of the Gentamycin reported as 82% [10]. We found 93 (57.76%) cases of Amoxicillin resistant and 36(22.4 %) sensitive cases of the isolates in our study. Kumar et al narrated 71.0% resistance with Amoxicillin [5] which is near enough with results of this study. Mathura et al stated 63.0% resistance in Amoxicillin [10] which is nearby to our conclusions whereas, Javed et al reported Amoxicillin as completely sensitive [20].

CONCLUSION:

In our study, after observations found only ciprofloxacin and ofloxacin to be effective. According to results of our study found greater degree of antibiotic medicine resistance in enteric fever's S.typhi isolates. Multidrug resistant strains were found extra predominant in this study which indicates to focused hard work of our makers of health plans to implement positive strategies concerning usage of antibiotic medicines in population of Pakistan. Drugs which were effective against Salmonella are compounded in the emergence of resistance due to unreasonable usage of these drugs and readily obtain ability without doctor's prescription which might be eliminated through producing awareness in general public of the country.

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