

Prescribing Practices of Doctors Regarding Treatment Options of Typhoid Fever in Pakistan

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Abstract: Objective: To evaluate the prescribing practices of doctors regarding treatment options of Typhoid fever in Pakistan.

Methods: A cross-sectional survey was conducted from November 4, 2015 to December 31, 2015. Structured questionnaire was used as data collection tool. Non probability sampling technique was applied. After explaining the questionnaire, approximately 500 doctors were asked to filled questionnaire across Pakistan. All ethical considerations were observed in collection of data.

Results: A total of 454 doctors participated in the study. Ciprofloxacin came out as the first drug of choice of majority of the doctors while treating typhoid fever patient whereas Cefixime, Ceftriaxone and Ofloxacin were other drug of choice. However, most of the doctors (45%) reported ciprofloxacin as the cause of treatment failure in adult typhoid patient due to growing bacterial resistance. According to majority (74%) of the doctors, reason for bacterial resistance was sub optimal doses in antibiotic use for typhoid fever patients. In most of the cases (61.2%), treatment options for adult typhoid fever did not base on culture sensitivity test.

Conclusion: Resistance to ciprofloxacin has now reached significant level as majority of the doctors reported treatment failure due to bacterial resistance, therefore its use for treatment of adult's patients with typhoid fever should have considerate about emerging resistance.

Keywords: Prescribing practices, Doctors, Treatment options, Typhoid fever, Pakistan.

1. INTRODUCTION

Enteric fever, also known as typhoid fever, is an acute and often life-threatening febrile illness and creating an important global public health problem. It is one of the major causes of morbidity in the developing world. Without effective treatment, the fatality rate of typhoid fever is 10–30%. This number is reduced to 1–4% in those, who are receiving appropriate therapy.¹

In the condition of treatment failure, some patients may die after a progressive clinical worsening who are not responding to the treatment with antibiotics against *Salmonella enterica* subsp. *enterica* serovar Typhi (*S.Typhi*).²

Selecting an appropriate antibiotic for the treatment of enteric fever and its complications requires knowledge of the susceptibility of locally isolated strains and resistance pattern of these bacteria.³ Therefore, it is extremely necessary to constantly monitor the pattern of antibiotic usage and local resistance pattern to preclude the causes of treatment failure in enteric fever patients. For the same reason, this survey was designed to determine the current treatment practices of typhoid fever in adult patients in an endemic country like Pakistan.

2. METHODS

This cross-sectional survey was conducted from November 4, 2015 to December 31, 2015. Structured questionnaire was used as data collection tool. Non probability sampling technique was applied.

For the purpose of sample selection, the study established inclusion and exclusion criteria. Inclusion criterion included (Doctors willing to participate in this survey, Medical specialists, GP's, RMO's and PG's. Whereas, all doctors who were unable to read & write English (Language barrier) that would compromise their ability to fill questionnaire or who are not willing to participate in the survey were excluded.

After explaining the questionnaire, approximately 500 doctors were asked to filled questionnaire across Pakistan. (Annex – Questionnaire)

Analysis was performed by third party statistician on SPSS version 20. For continuous variables, summary statistics included n (number of observations), mean, standard deviation, as well as frequencies and percentages for categorical variables presented. Appropriate statistical test applied. P-value <0.05 was taken as significant.

3. RESULTS

Demographics:

Total of 454 doctors were contacted from all over Pakistan (132 cities/town) and were requested to participate in the survey. The majority of the participants were belonged to major cities of Pakistan is about 32.9% and rest of participants belong to other cities/town (67.1%) of Pakistan. Province wise participation was observed as Punjab (42%), followed by Sindh (33%), KPK (18%) and AJK (8%) whereas no participation from Baluchistan. Qualification of most of the doctors was MBBS only (68%) while medical professionals with additional postgraduate qualification were 32%.

Prescribing Patterns for Typhoid Fever:

Frequency of typhoid fever and current treatment practices are shown in table 1. Majority (90%) of the doctors were seeing typhoid fever cases in their OPDs (Hospital OPD 31.9% & Private Clinic 57.3%). During season (May-Aug), majority of the doctors (48%) were seeing more than 20 patients in a month while during off season (September-April), majority of the doctors (33%) were seeing less than 5 patients in a month. Mean percentage of the typhoid fever patients belongs to adult age group was 57.5 ± 25.63 years. Criteria/rationale considered for prescribing antibiotic treatment while treating adult typhoid fever patient was efficacy in majority (76%), patient compliance (52%), bacterial resistance (51%), economic factor (49%) and safety (41%) with considerable overlap of these factors. Only less than 5% of the doctors came across treatment failure due to bacterial resistance of a particular antibiotic treatment in adult typhoid fever patient. However comparison of three drugs was assessed on the basis of doctor's subjective observations based on his/her experience. In most of the cases (61.2%), treatment options for adult typhoid fever did not base on culture sensitivity test.

In addition, most of the doctors (45%) also reported ciprofloxacin as the cause of treatment failure in adult typhoid patient due to bacterial resistance (Figure 1). Majority of the doctors (74%) considered sub optimal doses as a reason for bacterial resistance in antibiotic use for typhoid fever patients.

Ciprofloxacin was the first drug of choice of majority 195 (43%) of the doctors while treating typhoid fever patient followed by Cefixime 86 (18.9%), Ofloxacin 48 (10.6%) and others 125 (27.5%) (Table 2).

4. DISCUSSION

In this survey, most of the doctors' considered ciprofloxacin on top of the list of antibiotics showing resistance in treatment of typhoid fever. This finding was found constant when compared with respect to provinces (Sindh, Punjab, KPK and AJK) and with setting (private clinic, consulting, chamber, hospital OPD) as well. Ciprofloxacin was reported to be the first drug of choice since 1980s and was safe, effective, and less expensive with a very high sensitivity pattern^{4,5} but misuse of ciprofloxacin has caused development of high resistance resulting in potential treatment failure. These findings are supported by several studies that reported an increased resistance of *S. Typhi* strains to ciprofloxacin.^{6-8,9} A prospective study done in Delhi by Kumar et al. at intervals of three years (1999, 2002 and 2005) found that the incidence of multidrug-resistant typhoid fever (MDRTF) consecutively increased from thirty four percent in 1999 to sixty percent in 2005.⁹ Also, there was a gradual development of resistance to fluoroquinolones over these seven years. These observations of increasing resistance to ciprofloxacin and early evidence of resistance to ceftriaxone matched with several studies worldwide.^{10, 11, 12}

In our survey, treatment options among majority of the doctors did not base on culture sensitivity report. In addition, suboptimal dosing was also found to be a reason for bacterial resistance in antibiotic used for typhoid fever patients. In previous studies, various risk factors has been reported for the development of resistance in *S. Typhi* which include overuse, misuse, and inappropriate antibiotic prescribing practices.^{13,14} Factors such as patient and time pressures and diagnostic uncertainties are some of the main forces behind irrational prescription of antimicrobial combinations.^{15,16}

Thus, in the light of current survey findings and reported literature, it can be concluded that less usage of antibiotic resulted in less resistance. Factors such as misuse of antibiotic and switching of therapies to other antibiotics resulted in increased resistance and treatment failure.

This survey is of great importance as it signifies prescribing pattern of antibiotics in enteric fever by different tiers of doctors in diverse setting. Secondly, to our knowledge, this is the first study which investigated the treatment practices and sensitivity pattern of typhoid fever patients in adults from all provinces of the Pakistan.

However, there were few limitations of the study, which are worth to be reported. First, we used a cross sectional design for this study, which is not the best design to investigate any causal relationships and the emerging resistance trends are reported solely on the subjective assessment of doctors. No culture sensitivity test was performed.

5. CONCLUSION

Resistance to ciprofloxacin is developing to significant level as many of the doctors reported treatment failure due to bacterial resistance, therefore its use for treatment of adult's patients with typhoid fever should be judicious.

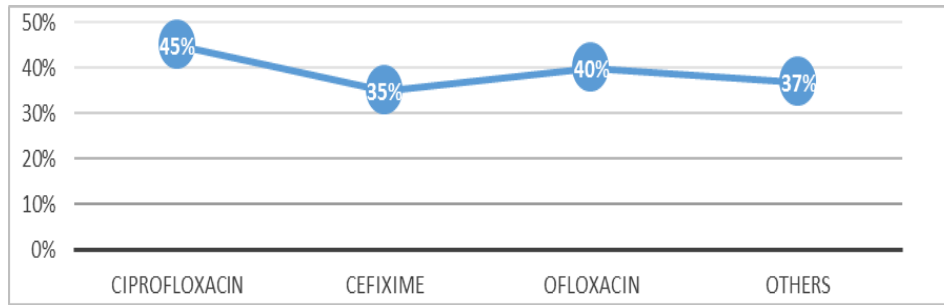
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Table.1: Frequency of typhoid fever and current treatment practices (N=454)		
	N	%
Do you see typhoid patients in your OPD? (n=453)		
Yes	452	99
No	1	0.1
How many typhoid fever patients you see in a month during season? (n=450)		
<5	66	15
6 to 10	54	12
11 to 15	52	11
16 to 20	61	13
>20	217	48
How many typhoid fever patients you see in a month during off season? (n=447)		
<5	146	33
6 to 10	99	21
11 to 15	49	11
16 to 20	24	5
>20	129	29
What percentage of your typhoid fever patients belongs to adult age group? (n=440) (mean with standard deviation)		57.5 ±25.63
What is your criteria/rationale for prescribing antibiotic treatment while treating adult typhoid fever patient? (Prioritize)		
Bacterial Resistance (n=448)	228	51
Economic Factor (n=446)	219	49
Patient Compliance (n=454)	235	52
Efficacy (n=448)	341	76
Safety (n=447)	183	41
How often you come across treatment failure due to bacterial resistance of a particular antibiotic treatment in adult typhoid fever patient? (n=446)		
None	62	14
<5%	212	48
<10%	118	26
<20%	44	10
<30%	10	2
Are your treatment options for adult typhoid fever patient based on culture sensitivity test?		
Yes	106	23.3
No	278	61.2
Don't Know	6	1.3
Do you consider sub optimal dosing as a reason for bacterial resistance in antibiotic used for typhoid fever patient? (n=439)		
Yes	327	74
No	100	23
Don't Know	12	3

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Others include Co-Trimaxazole, Levofloxacin, Azithromycin

Figure.1: Which antibiotic do you consider resulting in treatment failure in adult typhoid patient due to bacterial resistance?

	First drug of choice	In addition to first drug of choice (1)	In addition to first drug of choice (2)
	n (%)	n (%)	n (%)
Cefixime	86 (18.9)	109 (24)	76 (16.7)
Ciprofloxacin	195 (43)	112 (24.7)	47 (10.4)
Ofloxacin	48 (10.6)	63 (13.9)	55 (12.1)
Others	125 (27.5)	170 (30.4)	276 (60.8)

n: number