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FREQUENCY OF ANTIBIOTIC SUSCEPTIBILITY IN CULTURE-POSITIVE SALMONELLA TYPHI AT TERTIARY CARE HOSPITAL HYDERABAD

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Abstract

OBJECTIVE

To determine the antibiotic susceptibility profile among patients with culture positive Salmonella Typhi presenting to a tertiary care hospital in Hyderabad.

METHODOLOGY

A cross-sectional survey was carried out in the Department of Medicine, LUMHS Hyderabad on 144 adult participants aged between 18 to 60 years whose culture is confirmed Salmonella Typhi. They selected the sample by consecutive sampling and evaluated them using clinical and laboratory criteria, such as blood culture and antibiotic sensitivity. Demographic and clinical data were gathered and their association with patterns of antibiotic sensitivity analysed at 5% level of significance.

RESULTS

Out of 144 culture-positive Salmonella Typhi patients, the average age was found to be as 39.92 ± 12.12 years, comprising of 54.9% females and 45.1% males. There was no statistically significant difference in antibiotic susceptibility between genders or age groups ($p > 0.05$ in all comparisons). The sensitivity rates were 42-63% in the commonly tested antibiotics, meropenem and azithromycin also showed a similar response pattern across all demographic categories.

CONCLUSION

The findings of the study indicates that the patterns of antimicrobial susceptibility in the culture-confirmed Salmonella Typhi are insignificantly associated with age and gender, and the resistances to fluoroquinolones are consistently high. The third-generation cephalosporins and meropenem/azithromycin are highly sensitive to resistant strains and averagely sensitive, respectively. These results indicate that the sustained local monitoring and antibiotic stewardship should be sustained in order to inform effective empirical treatment and curtail the transmission of resistant strains.

INTRODUCTION

Typhoid fever is still a significant public health issue in low- to middle-income nations and especially in the South Asian region whereby the water sources, poor sanitation, and population density are all contributing factors to the continued transmission of Salmonella Typhi. As reported through long term

studies in Nepal and India, the burden of enteric fever and its evolving epidemiology has been experienced in the area [1,2]. Throughout the years, antimicrobial resistance has become a significant issue, and initial investigations have shown the decreased susceptibility to commonly used first line agents, such as chloramphenicol, ampicillin, and trimethoprim sulfamethoxazole [3,4].

Recent hospital-based statistics further indicate a high rate of morbidity caused by typhoid fever in Pakistan which explains why the use of effective anti-microbial therapy is still needed [5,6]. There is also growing apprehension concerning azithromycin minimum inhibitory concentration creep that poses a threat to the efficacy of one of the limited available oral therapeutic agents [7]. The same trends have been found in Bangladesh and Nepal where resistance trends have been observed to be on a case of evolving patterns that have been recorded over the last two decades by long term analysis [8,9,10]. In more recent studies Pakistan has reported increased levels of multidrug resistant and extensively drug-resistant Salmonella Typhi isolates, especially in tertiary care hospitals, highlighting why there is an urgent demand to revise susceptibility data to support the decision-making regarding therapy [11,3]. These data demonstrate that there are significant regional differences in antimicrobial resistance within South Asia, and this concept substantiates the need to conduct ongoing local monitoring to guide empirical treatment decisions.

Since the steady increase in the antimicrobial resistance and the limited access to recent susceptibility data of Hyderabad, this study was done to present the current evidence on antibiotic sensitivity and resistance pattern on the culture positive Salmonella Typhi of a tertiary care hospital. Such data are essential for guiding rational antimicrobial therapy and strengthening stewardship efforts

METHODOLOGY

This cross-sectional study was conducted in the Department of Medicine at LUMHS in Hyderabad. A total of 144 participants were included, based on the lowest reported proportion of chloramphenicol sensitivity of 16.1% in culture positive Salmonella Typhi with a precision of 6% as described by Ahmad and colleagues. A consecutive sampling approach was used to recruit adults between 18 and 60 years of age, of either gender, who presented with a clinical diagnosis of enteric fever. Enteric fever was defined as a temperature of 38°C or higher lasting at least 3 days along with gastrointestinal symptoms such as nausea, vomiting, diarrhoea, or constipation. Only patients with culture positive Salmonella Typhi, defined as growth of Salmonella Typhi in blood or stool culture with 1 or more colonies obtained within a maximum of 7 days of incubation, were enrolled. Patients were excluded if they had a confirmed diagnosis of dengue or malaria, were taking corticosteroids or other immunosuppressive medicines, were pregnant or breastfeeding, or had taken antibiotics in the previous 7 days. The findings of physical examination, medical history and available records in the hospital or consultants were keenly examined to exclude proper use of exclusion criteria. Data collection was preceded by informing all the eligible individuals about the purpose of the study and getting written consent. A 10 mL venous blood specimen was taken in aseptic conditions and forwarded to the laboratory of microbiology at the hospital to have it cultured and tested on antimicrobial sensitivity. Antibiotic susceptibility was established as a laboratory outcome of sensitivity and resistance where sensitivity was used as the antibiotics that could eradicate Salmonella Typhi and resistance was the antibiotics that could not eradicate the infection. All the samples were analysed by a senior pathologist that had experience of over five years of laboratory work. Demographic and clinical data such as age, sex, residence, marital status, education, and comorbid conditions such as diabetes mellitus, hypertension, obesity, anaemia, low platelet count and vitamin D deficiency were gathered by using a structured proforma. Data were analysed using SPSS version 26. Descriptive statistics were generated for clinical and demographic variables, and associations with antibiotic susceptibility were evaluated using the Chi square test with significance set at 0.05.

RESULTS

A total of 144 patients with laboratory-confirmed *Salmonella* Typhi infection were enrolled in the study. The average age of the participants was 39.92 years ± 12.12 years. The average BMI was 24.69±4.29 kg/m^2, with most of them falling on normal to slightly overweight. The average time of the illness was 7.58±4.65 years among the participants with diabetes mellitus. Among the entire population, 79 (54.9%) were females and 65 (45.1%) were males. Most of the participants lived in urban regions (121; 84.0%), and 23 (16.0%), lived in the rural areas. Regarding marital status, 84 (58.3%) were married, 51 (35.4%) were single, 6 (4.2%) were widowed or separated and 3 (2.1%) were divorced.

Regarding educational attainment, 40 (27.8%) had completed middle school, 31 (21.5%) primary education, 29 (20.1%) higher education, 23 (16.0%) secondary education, and 21 (14.6%) were illiterate. Comorbidities were common: 30 (20.8%) had hypertension, 35 (24.3%) were obese, and 32 (22.2%) reported a history of smoking. Anaemia was detected in 47 (32.6%) participants, while 50 (34.7%) had vitamin D deficiency. A low platelet count was found in 18 (12.5%) patients, and only 27 (18.8%) had received prior typhoid vaccination ***(Table I)***.

When susceptibility patterns were compared by age, no statistically significant differences were identified between patients aged <45 years (n=86) and those aged ≥45 years (n = 58) for any antibiotic ($p > 0.05$ for all). Ampicillin sensitivity was 57.9% in younger vs. 42.1% in older patients (p=0.789), while chloramphenicol sensitivity was 47.8% vs. 52.2% (p=0.204). Similar findings were noted for cefixime (60.5% vs. 39.5%, p=0.906) and ceftriaxone (63.3% vs. 36.7%, p=0.534). Sensitivity to trimethoprim-sulfamethoxazole (62.5% vs. 37.5%, p=0.673) and amoxicillin (60.4% vs. 39.6%, p=0.801) showed no significant variation. Although ciprofloxacin sensitivity was higher among younger patients (68.8% vs. 31.3%), the difference was not statistically significant ($p = 0.118$). Sensitivity to azithromycin and meropenem was comparable between age groups ($p = 0.804$ and $p = 0.083$, respectively) ***(Table II)***.

Comparison of antibiotic susceptibility patterns between male and female participants showed no statistically significant differences for any antibiotic tested ($p > 0.05$ for all). Sensitivity to ampicillin was 42.1% in males vs. 57.9% in females (p=0.661), and chloramphenicol sensitivity was similar (47.8% vs. 52.2%, p=0.778). Sensitivity to cefixime and ceftriaxone was 48.8% vs. 51.2% ($p = 0.561$) and 46.9% vs. 53.1% (p=0.755), respectively. Comparable patterns were observed for trimethoprim-sulfamethoxazole (42.5% vs. 57.5%, $p = 0.693$) and amoxicillin (41.6% vs. 58.4%, p=0.189). Ciprofloxacin exhibited identical sensitivity proportions (50.0% each, p=0.407). Azithromycin showed slightly higher sensitivity in females (56.0%) than males (44.0%), but the difference was not significant (p=0.054). Meropenem remained highly effective in both groups (45.1% vs. 54.9%, p=0.889) ***(Table III)***.

DISCUSSION

The present study provides an updated assessment of antimicrobial susceptibility patterns among patients with culture confirmed Salmonella Typhi and evaluates potential demographic influences on resistance behaviour. The demographic characteristics of the study population showed a predominance of middle-aged adults and a higher representation of female patients, with a substantial burden of comorbidities including hypertension, obesity, anaemia, and vitamin D deficiency. These results are like the past results in Pakistan where metabolic and nutritional comorbidities have also been reported to affect the severity and presentations of enteric fever [5]. A comparison of antibiotic susceptibility in demographic groups revealed that there were no statistically significant differences. All the comparisons resulted in the $p > 0.05$, which means that both gender and age did not affect the resistance pattern of Salmonella Typhi in this cohort. These findings are congruent to the findings of Ahmad and colleagues who were also able to show that there is no statistically significant difference in susceptibility between male and female patients [2]. Gupta also reported similar patterns of susceptibility of the population to different demographic groups upholding the argument that population features do not significantly change resistance behaviour [9]. Even though Jabin and co-authors found a very minor increase in ampicillin resistance in males, it was not statistically significant [16] ($p > 0.05$).

Similarly, Rosso and colleagues also implied the possible effect of age-associated cumulative antibiotic exposure, but their studies also demonstrated no significant correlation between age and antimicrobial resistance ($p > 0.05$) in their studies [17]. All these are consistent with the current study, where the patients aged below 45 years and those aged 45 years and above showed almost equal susceptibility trend with all antimicrobial agents tested.

In terms of overall susceptibility, the results of the current study revealed the high sensitivity to meropenem and third generation cephalosporins. This is in line with long term surveillance data reported by Tanmoy in Bangladesh that reported maintained activity of carbapenems and cephalosporins in dealing with Salmonella Typhi in 24 years [7]. The same has been observed in Pakistan whereby Khan and others reported a high level of sensitivity, more than 80 percent, to ceftriaxone and meropenem in different regions [11]. The fact that these agents remain useful in the treatment of multidrug resistant and extensively drug-resistant strains that are prevalent in South Asia further testifies to the significance of these agents in treatment. Conversely, intermediate sensitivity to azithromycin was recorded which indicates the current trend of azithromycin minimum inhibitory concentration creep incidence in various regional reports. Khan reported this increasing trend and expressed the apprehension about the future usefulness of azithromycin as an oral treatment modality [6]. The results of the surveillance conducted by Ching in Lahore also support these findings as a continuous decrease in the sensitivity to azithromycin was observed [19]. The present research hence augments the rising literature that indicates the possibility of azithromycin becoming less effective against typhoid fever in the South Asian population over time.

The present study has demonstrated that fluoroquinolone resistance was still very high and had no demographic differences. Such an observation is quite consistent with that of the region, in which the ciprofloxacin resistance has remained above 80 percent. Ching had recorded a resistance of more than 80 percent in Lahore and Ahmad in Khyber Pakhtunkhwa had recorded similar resistance in their cohort [19,4]. These two high resistance levels reiterate previous suggestions that fluoroquinolones are no longer suitable empirical treatment of possible typhoid fever. Another interesting observation was that the sensitivity to trimethoprim sulfamethoxazole was rather high. This observation is similar to those of Mayahi in iraq where sensitivity was more than 90% in isolates of Salmonella Typhi [18]. Other locations have also reported a similar resurrection of vulnerability to older first line agents and such a trend can be explained by the lack of use over time that may have decreased the level of selective pressure, thereby permitting the vulnerability to reoccur. However, these agents will have to undergo careful validation by use of multicentric research before they can be reintroduced into the normal empirical therapy.

In general, the statistical comparisons in this study are in accordance with general trends at a regional level. The lack of effect of the demographic factor on the susceptibility, the prevalence of resistance to fluoroquinolones, the moderate yet decreasing sensitivity to azithromycin, and the persistence of carbapenems and cephalosporins are reflective in several South Asian findings [1,4,7,11]. These findings underscore the necessity to continue with local surveillance efforts, antimicrobial stewardship, and use of evidence-based prescribing practice to ensure that limited available treatment alternatives of typhoid fever remain effective. To reduce the burden of multidrug resistant and extensively drug-resistant Salmonella typhi the capacity to perform laboratory diagnostic and monitor resistance trends on the regional level will be necessary.

CONCLUSION

The findings of the study indicates that the patterns of antimicrobial susceptibility in the culture-confirmed Salmonella Typhi are insignificantly associated with age and gender, and the resistancesto fluoroquinolones are consistently high. The third-generation cephalosporins and meropenem/azithromycin are highly sensitive to resistant strains and averagely sensitive, respectively. These results indicate that the sustained local

monitoring and antibiotic stewardship should be sustained in order to inform effective empirical treatment and curtail the transmission of resistant strains

Table I: Baseline Demographic and Clinical Characteristics of Patients (n=144)		
Mean ± Standard Deviation		**95% Confidence Interval**
Age in years = **39.92 ± 12.12**		37.92–41.91
BMI kg/m² = **24.69 ± 4.29**		23.99–25.40
Duration of Diabetes Mellitus = **7.58 ± 4.65**		6.82–8.35
Frequency (%)		
Gender	Male	65 (45.1)
	Female	79 (54.9)
Residential Status	Urban	121 (84.0)
	Rural	23 (16.0)
Marital Status	Single	51 (35.4)
	Married	84 (58.3)
	Normal	6 (4.2)
	Divorced	3 (2.1)
Education Status	Illiterate	21 (14.6)
	Primary	31 (21.5)
	Middle	40 (27.8)
	Secondary	23 (16.0)
	Higher	29 (20.1)
Hypertension		30 (20.8)
Smoking		32 (22.2)
Obesity		35 (24.3)
Low Platelet		18 (12.5)
Anaemia		47 (32.6)
Vitamin D Deficiency		50 (34.7)

Vaccinated	27 (18.8)

Table II: Comparison of Antibiotic Susceptibility Patterns by Age Group among Patients with Culture-Positive Salmonella Typhi (n=144)

Outcomes	Age Group		95% Confidence Interval	P-Value
	18–45	≥ 45		
Ampicillin	22 (57.9)	16 (42.1)	0.522–2.352	0.789
Chloramphenicol	11 (47.8)	12 (52.2)	0.726–4.360	0.204
Cefixime	26 (60.5)	17 (39.5)	0.462–1.984	0.906
Ceftriaxone	31 (63.3)	18 (36.7)	0.393–1.623	0.534
Trimethoprim / Sulfamethoxazole	25 (62.5)	15 (37.5)	0.402–1.801	0.673
Amoxicillin	61 (60.4)	40 (39.6)	0.441–1.881	0.801
Ciprofloxacin	33 (68.8)	15 (31.3)	0.270–1.164	0.118
Azithromycin	84 (59.6)	57 (40.4)	0.120–15.322	0.804
Meropenem	84 (60.6)	56 (39.4)	2.068–3.109	0.083

Table III: Comparison of Antibiotic Susceptibility Patterns by Gender among Patients with Culture-Positive Salmonella Typhi (n=144)

Outcomes	Gender		95% Confidence Interval	P-Value
	Male (n=65)	Female (n=79)		
Ampicillin	16 (42.1)	22 (57.9)	0.559–2.499	0.661
Chloramphenicol	11 (47.8)	12 (52.2)	0.360–2.148	0.778
Cefixime	21 (48.8)	22 (51.2)	0.395–1.654	0.561
Ceftriaxone	23 (46.9)	26 (53.1)	0.448–1.789	0.755
Trimethoprim / Sulfamethoxazole	17 (42.5)	23 (57.5)	0.556–2.421	0.693
Amoxicillin	42 (41.6)	59 (58.4)	0.788–3.313	0.189
Ciprofloxacin	24 (50.0)	24 (50.0)	0.372–1.494	0.407
Azithromycin	62 (44.0)	79 (56.0)	1.888–2.740	0.054
Meropenem	64 (45.1)	78 (54.9)	0.075–19.871	0.889

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