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Impact of Antibiotic Misuse on Typhoid Fever Resistance Patterns

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ABSTRACT

The overuse of antibiotics is a big reason why *Salmonella Typhi*, which causes typhoid fever, is becoming resistant to drugs. This resistance to common medicines is making it harder to treat typhoid around the world, but we don't know how bad the problem is in some places. This research looks at how resistant *S. Typhi* is to antibiotics and if there is any link between resistance and antibiotics misuse. We checked how antibiotics are misused and how this affects typhoid resistance by surveying healthcare professionals and patients at Govt. Naseerullah Khan Babar Memorial Hospital in Peshawar. The results showed many people (about 36 %) had previously diagnosed clinically with typhoid & now they have same clinical features. The majority of positive history patients were male (maybe due to exposure to the outside environment & street foods). The results show that there is still practice of

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using antibiotics without gold standard tests (culture) and patients with clinical features either self-medicated or treatment hasn't been completed. This information shows we urgently need better control of antibiotic use, better testing, and campaigns to teach the public about the problem. People need awareness sessions specially on health issues & problems. That way we can reduce resistance and treat typhoid better.

Keywords: Typhoid fever, *Salmonella Typhi*, Antibiotic resistance

INTRODUCTION

Typhoid fever, which is caused by the bacterium *Salmonella enterica serovar Typhi (S. Typhi)*, is still a major health problem, especially in poorer countries that lack good sanitation and clean water (Stanaway et al., 2019). The World Health Organization (WHO) figures that there are about 11–21 million cases and 128,000–161,000 deaths each year, with the most cases happening in South Asia and sub-Saharan Africa (WHO, 2023). It spreads usually through unclean food or water, making it common in areas without proper hygiene systems (Andrews et al., 2020). In the past, typhoid fever could be treated with antibiotics like chloramphenicol, ampicillin, and co-trimoxazole. But, more and more *S. Typhi* strains are becoming resistant to multiple drugs, which has made treatment harder. This means doctors have to use pricier and harder-to-get drugs like fluoroquinolones and third-generation cephalosporins (Klemm et al., 2022). The increase in extremely drug-resistant typhoid, especially in Pakistan and nearby areas, shows that we really need to manage antibiotic use better and find other ways to prevent it, like vaccines (Qamar et al., 2022).

Antibiotic Treatment and Historical Efficacy

Before antibiotics, typhoid fever was deadly, killing 10–20% of those who got it. Then chloramphenicol came along in 1948, and the death rate dropped a lot (Parry et al., 2020). But, because antibiotics were used too much, the bacteria became resistant, and then treatments stopped working. By the 1970s, a type of typhoid called MDR *S. Typhi* appeared, which didn't respond to chloramphenicol, ampicillin, or co-trimoxazole. So, doctors started using fluoroquinolones like ciprofloxacin (Britto et al., 2021). At first, fluoroquinolones worked well. However, the bacteria quickly became resistant to them too, because they were used so much in people and

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animals (Hendriksen et al., 2021). Azithromycin became another choice for simple cases, and ceftriaxone was saved for really bad infections. Still, recent reports say that there's now XDR typhoid, which doesn't respond to ceftriaxone, fluoroquinolones, or azithromycin. This shows a big problem coming up (Yousafzai et al., 2023).

Emergence of Antibiotic Resistance

The improper use of antibiotics in people, farming, and animal care has made *S. Typhi* bacteria resistant to drugs faster (Laxminarayan et al., 2022). Some main reasons are: Prescribing antibiotics without proper diagnosis: Using antibiotics without making sure they're needed (e.g in viral, fungal infections) (Dutta et al., 2021).Self-medication (Treating yourself) : Getting antibiotics without a prescription in places where the disease is common (Sulis et al., 2020). * Not finishing medicine: Not taking all of the antibiotics, which can make the bacteria stronger (Bhattacharya et al., 2023). Traveling: Resistant bacteria moving to other countries (Connor et al., 2022). DNA research shows that resistant *S. Typhi* bacteria usually get plasmids with resistance genes (like *blaCTX-M-15* that resists ceftriaxone). These genes can spread fast in and between groups of bacteria (Wong et al., 2023). Even with global efforts to fight AMR, antibiotic overuse keeps making *S. Typhi* more resistant. This means fewer treatment choices and a higher chance of death. In many places where it's common, weak rules, not enough testing places, and people treating themselves make things even worse. The recent spread of XDR typhoid really shows how important it is to stop/control antibiotic overuse so we can keep the treatments that still work.

Methodology

The study was conducted at Govt. Naseerullah Khan Babar Memorial Hospital Peshawar, utilizing a descriptive cross-sectional research design to analyze the target variables. To ensure the research met all professional and moral standards, ethical approval was formally obtained from the Ethical Committee of Sarhad University of Science and Information Technology as well as the host hospital's ethical board. Participants were recruited from the Medical OPD and Medical Ward using a purposive sampling technique, specifically targeting individuals who met the pre-defined inclusion criteria. The sample size was determined using Cochran's

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Formula with a 95% confidence level ($Z = 1.96$), an estimated proportion (p) of 0.50, and a 5% margin of error (e). Although the population size (N) was noted at 100, the final sample size was established at 385 to maintain statistical power.Data collection was carried out by the researcher through a structured questionnaire served to those who met the eligibility requirements. The inclusion criteria focused on adults aged 18 and older who displayed signs and symptoms of typhoid fever and were willing to participate; in instances where a patient was not physically present, data was retrieved from hospital records. Conversely, any individual under the age of 18 or those who declined to participate were excluded from the study. The process began only after obtaining informed written consent from each participant, ensuring they were fully aware of the study's purpose. Following this ethical protocol, the researcher personally handed over the data collection tools to the participants to gather the necessary information for the project.

Data was gathered from Govt. Naseerullah Khan Babar Memorial Hospital Peshawar, Khyber Pakhtunkhwa, for the study in the form of questionnaire from about 385 participants of different age group & gender. The findings showed a significant frequency of positive instances. The gender distribution gave important information about demographic differences among the study group by highlighting the percentage of male and female participants impacted.

DISTRIBUTION ON THE BASE OF PREVIOUS HISTORY

The survey results distribution for a participant of (385) from Govt. Naseerullah Khan Babar Memorial Hospital Peshawar, Khyber Pakhtunkhwa, is depicted in the chart. As 36 % of the participants have positive history, indicating a high prevalence of the illness being studied in the study community. On the other hand, 40 % of participant had negative history, suggesting that a sizable fraction of the community was free of the illness. Participants who were not sure or they really don't, know is questionable because there is limited diagnostic facilities available in their areas, made up a small percentage (24 %). This distribution highlights the prevalence of Typhoid in the population under the study, which could have significant ramifications for hospital-specific disease management plans and public health initiatives.

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Table 4.1: ***Distribution on the basis of previous history***

Result	Frequency	Percent	Valid Percent
Positive History	140	36	36.36
Negative History	154	40	40
Don't know	91	24	23.63
Total	385	100	100

AGE BASE DISTRIBUTION OF PARTICIPANTS

The age distribution of participants among four group, 18-25, 25-35, 35-45, and 45+ years old is depicted in the graphic. The age group that is most represented in the study is the 25-35 age group, which accounts for 38 % of all participants. Following with 25%, the 18-23 age groups makes up a sizable share of the sample. Old age people are less represented in the 45+ age range, which makes up 14 % of the total. There aren't many senior participants in the survey, as seen by the lowest percentage (14 %) in the 45+ age range. With fewer individuals from older group, this distribution implies that the majority of the research's participants are adults in their late 20s and early 30s. The prevalence of the 25-35 age range may emphasize pertinent it is to the study setting or how easily accessible it is for data collecting.

TABLE 4.2: Age base distribution of participant

Age	Frequency	Percent	Valid Percent
18-23	96	25	24.93
25-35	146	38	37.92
35-45	88	23	22.85
45+	55	14	14.2
Total	385	100	100

GENDER BASE PARTICIPANTS

This chart displays the participant's gender distribution, with 57 % of the participants being male and 43 being female. This suggests that there were more male research participants than male participants. Trends in possible gender-based variation in the incidence of Typhoid and associated symptom must be analyzed in light of the gender distribution.

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Table 4.3: Gender base distribution of participant

Gender	Frequency	Percent	Valid Percent
Male	220	57	57.143
Female	165	43	42.86
Total	385	100	100

4.4 Gender base distribution of positive history

Higher percentage of positive history with total 97 (44%) is far greater than of females which is only 43 (26%). Males with higher positive percentage is due to their exposure to outdoor activities
(food, contaminated water).

Table 4.4: Gender base distribution of Positive Typhoid history

Gender	Total	Positive	Percentage
Male	220	97	44
Female	165	43	26

4.5 Gender base awareness level

During questionnaire/survey the awareness level of both genders was observed, in whom female awareness level was high. Female was total 43 (67 %) among aware people while male was just 25 (33%). According to them the awareness level in female was high due to community sessions by lady health workers & their frequent visits to healthcare practitioner & health facilities for child h health & treatment.

Table 4.5: *Gender Base Awareness Level*

Gender	Total	Aware	Percent
Male	220	62	28
Female	165	66	40

4.6 History of Treatment

History of treatment shows that a large number of participants 37 (26 %) with previous past positive history are self-medicated, which is a major threat and here a question is raise that why antibiotics are available over the counter in Pakistan.

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Table 4.6: History of treatment

Treatment	Number of positive patients	Percent	Valid percent
Self-medication	37	26	26.4
Hospitals	103	74	73.6
Total	140	100	100

Discussion

The incidence of Typhoid in District Peshawar is one of the study key findings. In this study, data from total 385 Participants were collected in the form of questionnaire in Govt. Naseerullah Khan Babar Memorial Hospital Peshawar. Among the participants, 140 (36 %) were have past history of Typhoid, 154 (40 %) were negative, and 91 (24 %) were not sure & lack any information about their previous illness. There may be errors & miscalculations. Because the data is not evidence base (Positive Typhidot, Widal, Culture) but only the questionnaire of patients participated in the survey. Regional healthcare availability, study methods, and sample sizes may all have an impact on these discrepancies. Furthermore, dietary practices and socioeconomic level may be important factors in these variations in prevalence.

This study found that the prevalence was higher in males 97 (44 %) than in females 43 (26 %) when looking at gender base positive history distribution. Different studies in Peshawar shows that the prevalence was higher in men than in women. Study by Khan et al. (2017) in Tertiary care hospitals in Peshawar finds Males 58% of diagnosed typhoid cases while Females were 42% of total cases. The reason is due to higher exposure of males to outdoor activities (e.g., contaminated food/water).

Possible Explanations for Gender Disparity:

- Behavioral Factors: Men more likely to eat street food/work outdoors.
- Healthcare Access: Women may be underdiagnosed due to fewer hospital visits.

Males show slightly higher typhoid rates (55-58%) in Peshawar.

Limitations: Data is hospital-based; community surveys might differ.

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Regarding of age distribution, the study found that the most affected age group was 25-35-year-old age group (38%). Next in line were (25 %)of those aged 18-25-45-year-old and (23 %) of those aged 35-45-year-old among those aged 45+, the prevalence was the lowest, at 13.6 %. However other studies show that higher risk group is under 15 whom were not include in the questionnaire/survey. According to a Study by Ullah et al. (2019) in Peshawar hospitals (1,000+ typhoid cases analyzed) found 5–15 years 48% of cases (with highest prevalence) 16–30 years 32% & 30 years 20%. The Reasons Are Poor hygiene habits, school exposure, immature immunity. Reference: Ullah, A., et al. (2019). Pediatric Typhoid Burden in Khyber Pakhtunkhwa. Pakistan Journal of Medical Sciences, 35(2), 345-349.

Another study from Khyber Teaching Hospital Data (2021) results Under 15years 52% of typhoid admissions. Adults (16–45)38% while Elderly (>45) were 10%. Source: Infectious Disease Ward Report (2021), KTH Peshawar.

Conclusion

Typhoid fever remains a major public health challenge in Peshawar & Pakistan, with school-aged children and young adults being the most affected group, constituting nearly 50% of cases. The disease exhibits a slight male predominance (55-58%), likely due to higher exposure to contaminated food and water sources.

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