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Comparative analysis of risk factors of typhoid fever occurrence in different villages of Astore valley, Gilgit Baltistan Pakistan

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ABSTRACT

Background: *Salmonella enterica* serotype Typhi and, to a lesser extent, serotypes *Paratyphi A*, B, and C, cause typhoid fever. Higher prevalence of typhoid is a concern, particularly with remote areas in Astore valley. This study was conducted to investigate the risk factors, vulnerable segments of population, and the efficacy of antibiotics against typhoid pathogen.

Methods: Study was conducted in District Astore from October 2022-august 2023, which encompasses a population exceeding 70,000 individuals residing across more than a hundred communities. Choungrah, Eidgah, Gorikot, Louse, and Harcho were selected as research sites from five distinct villages. This study utilized modern statistical tools to investigate the risk factors associated with typhoid incidence in multiple villages. The research involved both diagnostic and community-based surveys. Microbiological analysis of water samples was conducted using the pour plate technique, while antibiotic susceptibility tests on bacterial colonies were initially performed using disc diffusion methods.

Results: In Choungrah tap water, the bacterial load was 180.10 cfu/ml, while Gorikot tap water had the lowest load 61.33 cfu/ml. Gorikot pipe water had the highest Salmonella species concentration at 11.33 × 10^5 cfu/ml, with Eidgah tap water at 2.33 × 10^5 cfu/ml being the lowest. Ciprofloxacin was most effective antibiotic, while cefixime showed the least efficacy, indicating increased bacterial resistance. Regarding water sources, 70.66% preferred tap water, 16.68% spring water, and 12.66% bottled water. Drainage systems and waste collection techniques were reported insufficient by the majority. Three-quarters consumed street food, with only 5% practicing hand washing before and after meals. 30.33% of males (56.66%) and 18% of females (43.33%) had experienced typhoid fever, while 62% of respondents were aware of illness.

Conclusion: The study reveals a significant prevalence of typhoid fever in the Astore valley, underscoring multiple risk factors including contaminated water sources, poor hygiene practices, and inadequate sanitation.

Keywords: Microbiology, Salmonella Infections, Salmonella, Sanitation, Typhoid Fever

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Introduction

A multi-systemic infection, typhoid fever is usually caused by *Salmonella Typhi* and *Salmonella Paratyphi A* infection. Specially, it is common in regions with poor water quality and inadequate sanitation systems. Typhoid is transmitted solely among humans with no animal reservoir. Asymptomatic carriers complicate transmission by serving as bacterial reservoirs Major sign and symptoms of the sickness include malaise, fever, constipation, profuse diarrhea, hepatomegaly, and splenomegaly (1).

Left untreated, it can lead to serious complications such as internal bleeding and perforation, with a fatality rate of 10 to 30 percent (2, 3). The primary challenge lies in the current diagnostic methods for both acute infection and chronic carriage (4).

Typhoid fever is prevalent in many low- and middle-income nations. In Southeast Asia, it ranked as the thirteenth most common cause of years of life lost in 2010, contrasting with its much lower rank in Western Europe and North America. Enteric fever is a common term for these infections. While *S. typhi* historically caused most cases, recent reports suggest an emergence of enteric fever caused by S. *Para typhi A*, particularly in Asia. (5,6,7). In 2017, a global study estimated 10.9 million typhoid fever cases, with about 116,800 deaths, and 12.1% of cases occurring in sub-Saharan Africa (7). Significant morbidity and mortality is caused by enteric fever especially in developing countries where it displays widespread antibiotic resistance (9). Research suggests that humans are the natural host for the bacteria, thriving at 37°C, the human body temperature (WHO, 2018). Approximately 212 million cases, leading to 129,000 deaths annually worldwide, with children and young adults particularly vulnerable in tropical regions (10).

Typhoid fever is a major health concern in Pakistan. It reflects the socio-economic status, especially in rural areas with inadequate access to safe drinking water, hygiene, and food sanitation (11). Pakistan, India, Egypt, Mexico, Indonesia, Peru, and Nepal are global hotspots for typhoid fever. Risk factors, influenced by changes in health behaviors and hygiene conditions, contribute to untreated cases, causing about one third of cases and 75% of deaths, with a 10% fatality rate without proper treatment (11).

Gilgit Baltistan (GB), formerly known as the Northern Areas, is renowned for its unique economic, socio-political, traditional, and geographical features (13). The Gilgit-Baltistan EPA reported all nine water samples from Gilgit city's Bermas and Jutial areas as unsuitable for human consumption due to high contamination levels. This contaminated water is contributing to typhoid spread in Gilgit town. Director Shehzad Hasan's EPA report revealed significant microorganism concentrations responsible for waterborne diseases. (14). In Skardu district, Baltistan, a study found 98 typhoid cases; with 66% being females aged 21-30. Infections were linked to household cohabitation and drinking water from storage tanks. Additionally, six water samples were deemed unsafe (15). Despite the presence of COVID-19, typhoid cases persist in the Astore valley district of GB, prompting research on risk factors.

This study is conducted to assess the threat elements of typhoid fever incidence, association of typhoid fever with drinking water sources and to find out the efficacy of antibiotics against typhoid pathogen in distinct villages. This will enhance understanding of the risk factors influencing the spread of typhoid fever in prominent villages.

Methods

The study was conducted in District Astore, which encompasses a population exceeding 70,000 individuals residing across more than a hundred communities. Choungrah, Eidgah, Gorikot, Louse, and Harcho were selected as research sites from five distinct villages in the Astor valley. The study was approved by institutional review board of Karakoram International University (KIU) Gilgit Baltistan in Oct 2022. The targeted respondents ranged in age from 18 to 27, 28 to 37, 38 to 47, and over 47 years old.

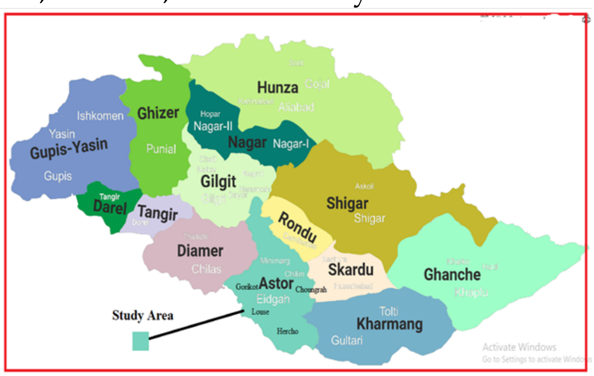


Figure 1: Map of Study area

Data was gathered randomly from 150 individuals. A structured questionnaire was developed to assess the risk of typhoid fever occurrence. Primary information was centered around demographic details and factors contributing to the risk of typhoid fever, including water supply, hygiene practices, sanitation, and instances of typhoid disease. Secondary data primarily consisted of analyses of water samples and the effectiveness of antibiotics against pathogens. The study relied on descriptive statistics to determine bacterial load and antibiotic susceptibility towards the typhoid pathogen. Frequency distribution was utilized to identify the impact of various risk factors on the incidence of typhoid disease.

A total number of 15 water samples were collected under aseptic conditions from taps, pipes, and rivers across different study locations. Each sample, approximately 500 ml in volume, was transported to the Microbiology Laboratory at the Agriculture Department of KIU Gilgit .Bacterial content in the samples was determined using both pour plate and membrane filtration methods (16).Four types of media were used to detect salmonella: MacConkey agar, Nutrient agar, and Salmonella-Shigella agar. (17).

After 24 hours pure Bacterial isolates were processed for identification by the usage of trendy biochemical test (18).The isolated salmonella species were subjected to antibiotic susceptibility testing, using the modified Kirby Bauer method. The susceptibility of different bacterial isolates was made against various antimicrobials using the standard disk diffusion method commonly known as the Kirby Bauer method, requires Muller Hinton agar for its execution. Salmonella isolates were tested for susceptibility against six antibiotics (OXOID, England) - Amoxicillin (15 µg, 25 µg, 30 µg), Tetracycline (15 µg, 25 µg, 30 µg), Ampicillin (15 µg, 25 µg, 30 µg), ceftriaxone (15 µg, 25 µg, 30 µg), Augmentin (15 µg, 25 µg, 30 µg), Ciprofloxacin (15 µg, 25 µg, 30 µg), and Cefixime (15 µg, 25 µg, 30 µg) using the disk diffusion method outlined by the CLSI (2016). After 24 hours, the isolates showed varying susceptibility patterns, and the diameters of inhibition zones were recorded to the nearest mm (19), categorized as resistant, intermediate, or susceptible following CLSI guidelines (2016).

Data processing was conducted using Microsoft Excel and Strata 8.1 software. Descriptive statistics were employed to summarize the results of water samples and antibiotic susceptibility testing against pathogens. Mean and standard deviation were calculated for the obtained data. Tables, graphs, pie charts, and bar graphs were utilized to present the processed data.

Results

The study found that the majority of respondents in Choungrah, Harcho, and Gorikot were aged 18-27, while in Eidgah and Louse, most fell between 28-37 years. Overall, 54.66% were aged 18-37, and 45.12% were 38 years or older. In Gorikot village, the majority were male (63.33%) and female (36.66%) respondents. Choungrah had an equal distribution of 50% male and female respondents. Similar gender proportions were observed in Louse, Eidgah, and Harcho, with 56.66% male and 43.33% female respondents. Overall, the study found that 56.66% of respondents were male, while 43.33% were female.

Educational levels among respondents varied: Gorikot had 33.33% primary, 40% secondary, 10% intermediate, and 3.33% non-formal education. Choungrah had 20% primary, 30% secondary, 33.33% intermediate, and 16.66% non-formal education. Eidgah had 23.33% primary and secondary, 46.665% intermediate, and 10% non-formal education. Louse had 20% primary, 33.33% secondary, 40% intermediate, and 10% non-formal education. Harcho had 33.33% primary, 26.66% secondary and intermediate, and 13.33% non-formal education. Overall, respondents showed 26.66% primary, 33.33% secondary, 31.33% intermediate, and 9.33% non-formal education.

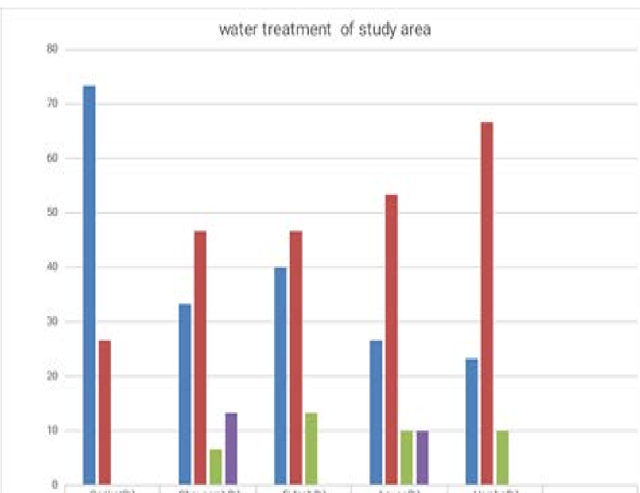
In Gorikot, 23.33% used river water, while 76.66% used tapped water. Choungrah respondents predominantly (70%) used tapped water, with 30% using roof or spring water. In Eidgah, 23.33% used river water, 66.66% used tapped water, and 10% used roof or spring water. Louse respondents had 16.66% using river water, 40% using tapped water, and 43.33% using roof or spring water. Harcho respondents solely relied on tapped water for drinking. Overall, the majority of respondents used tapped water as their primary water source.

There was variations in water supply distance across the study area. In Gorikot village, 66.66% of respondents accessed water within 0-4 km, while 20% obtained it from 5-9 km, 6.66% from 9-14 km, and another 6.66% from distances above 14 km. Similarly, in Choungrah, 30% of participants accessed water within 0-4 km, 16.66% within 5-9 km, 20% within 9-14 km, and 33.33% from distances above 14 km. Eidgah respondents reported 16.66% accessing water within 5-9 km, 20% within 9-14 km, 30% within 0-4 km, and 33.33% from distances above 14 km. In Louse, 6.66% accessed water within 0-4 km, 6.66% within 5-9 km, 40% within 9-14 km, and 26.66% from distances above 14 km. In Harcho, 70% of respondents accessed water within 5-9 km, while 10% accessed it from 9-14 km, and 6.66% from distances above 14 km.

Figure 2 shows water consumption practices varied across villages. Gorikot had 73.33% consuming untreated water and 26.66% using boiled water. In Choungrah, 33.33% consumed untreated water, 46.665% used boiled water, and small percentages used sieve or decanting. Eidgah had 46.66% using boiled water, 40% using untreated water, and 13.33% using sieve water. Louse showed 53.33% using boiled water, 26.66%

consuming untreated water, and 10% using sieve or decanting. Harcho had 66.66% using boiled water, 23.33% consuming untreated water, and 10% using sieve water. Overall, 40% did not treat water, 48% used boiled water, and 12% used sieve or decanting.

In Figure 3, the study found varying awareness levels of diseases across villages. Gorikot had 83.33% aware of typhoid fever, 16.66% knew about malaria, and 3.33% were aware of tuberculosis and bilharziasis. Choungrah had 50% aware of typhoid fever, 36.66% knew about malaria, and 13.33% were aware of tuberculosis and bilharziasis. Similarly, in Eidgah, 43.33% knew about typhoid fever, and 56.66% were aware of malaria. In Harcho, 23.33% were aware of typhoid fever, 83.33% knew about malaria, and 6.66% were aware of bilharziasis. In Louse, 66.66% were aware of typhoid fever, 26.66% knew about malaria, and 3.33% had knowledge about tuberculosis.



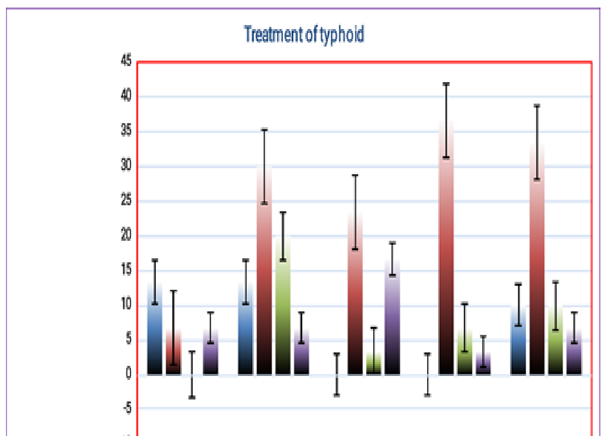
	Gorikot(%)	Choungrah(%)	Eidgah(%)	Louse(%)	Harcho(%)
Don,t treat	73.33	33.33	40	26.66	23.33
Boil	26.66	46.66	46.66	53.33	66.66
Sieve	0	6.66	13.33	10	10
Decating	0	13.33	0	10	0

Figure 2: Frequency distribution of water sources treatment

According to the findings, Gorikot had 20% of respondents reporting few waste collections, with 53.33% expressing dissatisfaction and 26.66% satisfied. Similarly, Choungrah had 56.66% reporting few collections, with 43.33% dissatisfied. In Eidgah, 50% reported few collections, with an equal dissatisfaction rate. Louse had 56.66% reporting few collections, with 33.33% dissatisfied and 10% satisfied. Harcho had 73.33% reporting few collections, with 16.66% dissatisfied and 10% satisfied.

The findings revealed that 60% of respondents practiced hand washing before and after eating, while 40% did not. In Choungrah, 53.33% of respondents reported practicing hand washing, while 46.66% did not. Similarly, in Eidgah, 46.66% practiced hand washing, while 53.33% did not. Among participants from Louse, 56.66% practiced hand washing, while 43.33% did not. In Harcho, 50% of respondents reported practicing hand washing, while 50% did not.

Figure 3 shows Typhoid treatment fascilities of study area



	Gorikot	choungra	Eidgah	Louse	Harcho
Dispensoy	13.33	13.33	0	0	10
Astore district Hospital	6.66	30	23.33	36.66	33.33
Herbal clinic	0	20	3.33	6.66	10
Did not go to the treatmnet	6.66	6.66	16.66	3.33	6.66

Figure.3 Typhoid treatment facilities of study area (%)

Table.1 Typhoid fever cases reported in the study area.

Suffering Typhoid fever	Gorikot (%)	Choungrah (%)	Eidgah (%)	Louse (%)	Harcho (%)
Yes	26.66	66.66	43.33	46.66	60
No	73.33	33.33	56.66	53.33	40

The research study revealed that 1011 typhoid cases were reported at DHQ hospital Astor during 2019.The result also showed that more cases were reported in the month of June and July.(figure: 4)

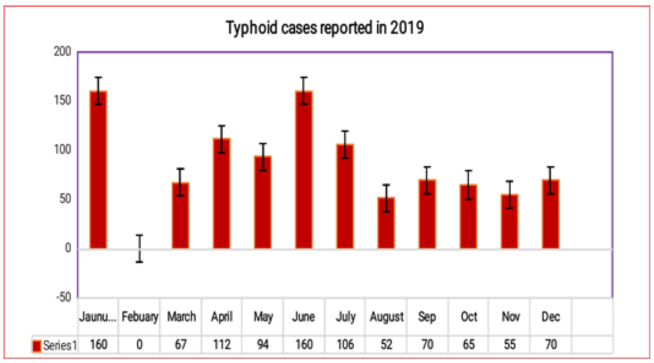


Figure 4 Typhoid cases reported in DHQ Hospital Astore 2019.

Typhoid cases reported during 2020

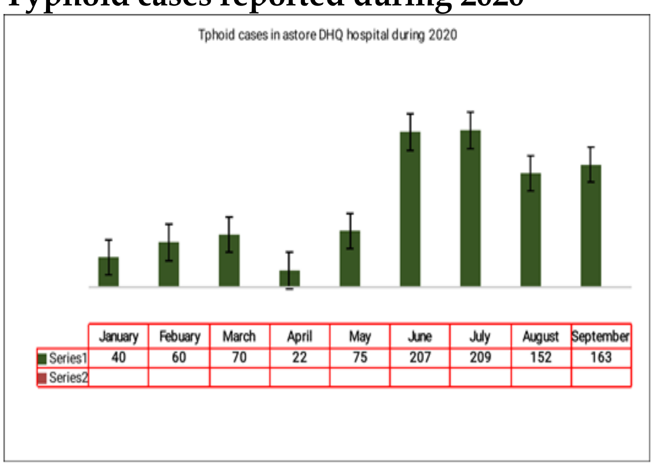


Figure: 5 Typhoid cases reported in DHQ Hospital Astore 2020

Figure 5 revealed that during 2020 research study showed that more cases were reported, because typhoid fever were also co-pandemic to covid-19. Despite corona restrictions typhoid cases were reported during the study of data collection from DHQ hospital Astore. 998 cases were reported in the first nine month till September 2020.The month of July, August and September had more typhoid cases along with pandemic covid-19.

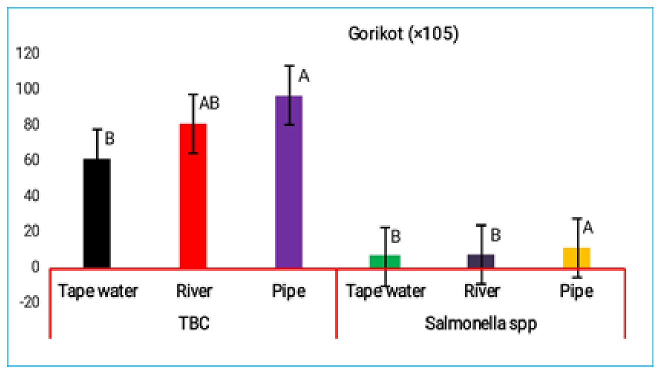


Figure.6: Total bacterial count and Salmonella species colonies of different water sources in Gorikot village

Figure 6 showed water source bacteriology of Gorikot. Tap water source had mean 61.33×10^5 TBC and also showed salmonella species 6.00×105in tap water source. River water indicated 81.0×10^5 TBC mean and 7.66×10^5 salmonella species. Pipe water showed more bacterial colonies as 96.66×10^5 TBC and 11.33×10^5 salmonella species mean. The result of study revealed pipe water source had more total bacterial colonies mean and showed more salmonella species than the other water sources.

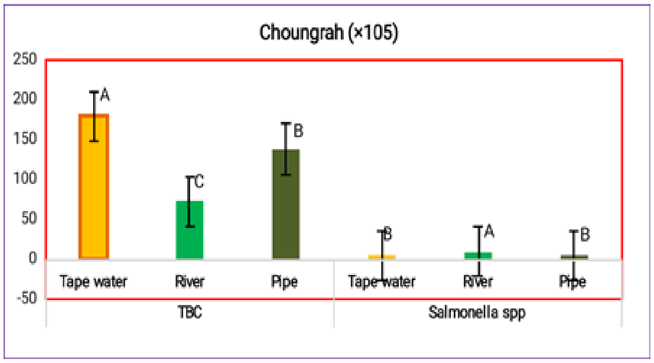


Figure.7: Total bacterial count and Salmonella species colonies of different water sources in Choungrah village

Figure.7 results showed that majority of Choungrah area respondents used tap water. Tap water indicated more contamination and had more total bacterial colonies as 180.00×10^5TBC and showed 5.00×10^5 salmonella species,more than the other sources of water.

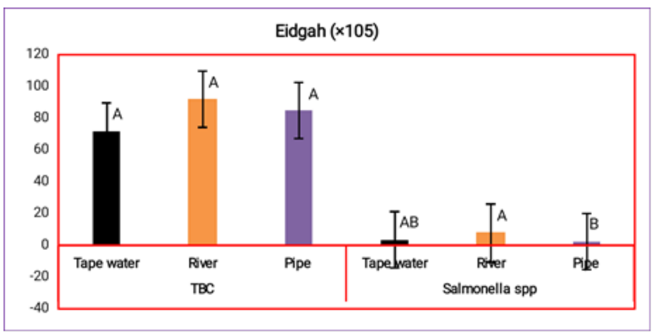


Figure.8 Total bacterial count and Salmonella species colonies water sources in Eidgah village.

Figure.8 showed that the river water confirmed more bacterial infection and salmonella species than other sources of water as 91.66×10^5 TBC and 7.66×10^5 salmonella species.

Figure.9 showed the pipe water supply had greater bacterial colonies as 138.33×10^5 TBC and 5.00×10^5 salmonella species then tap and river water sources in louse respondents.

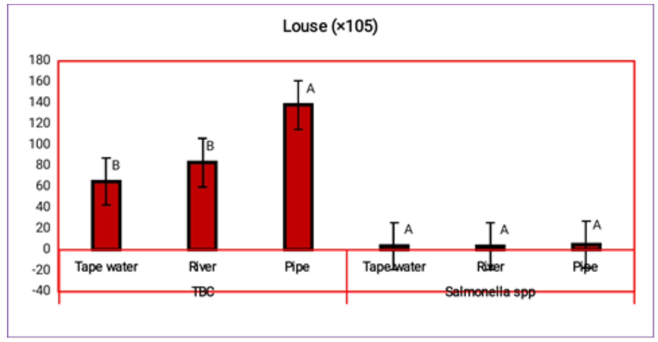


Figure.9 Total bacterial count and Salmonella species colonies water sources in Louse village

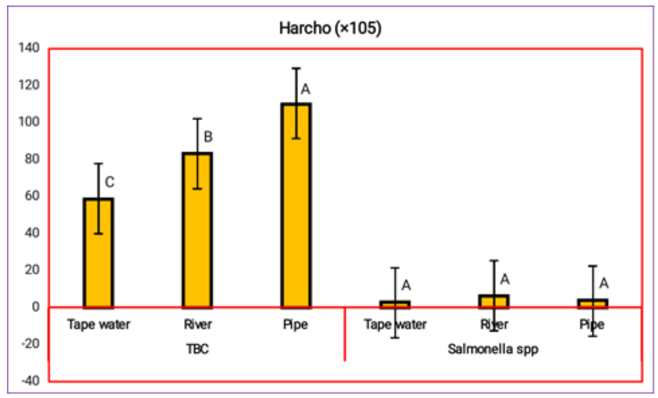


Figure.10 Total bacterial count and Salmonella species colonies water sources in Harcho village

Figure.10 of result revealed that among Harcho respondent's water source, pipe water had 110.00×10^5 salmonella species while the river water confirmed extra salmonella species $6.33\text{x}10^5$.

The statistical analysis showed that Choungrah village had higher contamination levels in their tap water sources, with counts exceeding 180×10^5 bacterial colonies, compared to other areas. Additionally, Gorikot respondents' pipe water sources showed higher total bacterial counts and 11.33×10^5 more Salmonella species compared to other water sources.

The statistical analysis showed significant differences in total bacterial counts between most groups, except for Harcho and Louse River water, which had similar mean values, Similarly, the analysis of Salmonella species revealed significant differences in water sources, except for Eidgah tap water and Louse River water, which demonstrated similar levels, suggesting they are not significantly different from each other.

Table.2 Mean of zone of inhibition, of different antibiotic at different concentration

Antibiotics	Augmentin	Ciprofloxacin	Amoxicillin	oxacillin	Cefixime	Tetracycline
15µg	3.13±0.1^{C}	3.11±0.10^{C}	0.5±0.10^{C}	0±0.00^{B}	0±0.00^{C}	2.66±0.01c
25µg	3.16±0.01^{B}	3.15±0.03^{B}	1.14±0.01^{B}	0±0.00^{B}	0.8±0.01^{B}	3.89±0.01^{B}
30µg	4.6±0.10^{A}	4.8±0.10^{A}	2.24±0.01^{A}	0.12±0.01 A	1.13±0.02 A	4.4±0.01^{A}

Table 2 presents the statistical results of antibiotic efficacy against Salmonella species at concentrations of 15 µg, 25 µg, and 30 µg. Augmentin, Ciprofloxacin, Amoxicillin, Cefixime, and Tetracycline exhibited significantly different mean values at various concentrations, while Oxacillin did not show significant differences between 15 µg and 25 µg concentrations.

Figure 11 and Figure 12 revealed the antibiotic susceptibility of Salmonella at 15µg and 25 µg concentrations respectively. At 15µg concentration, Augmentin, Ciprofloxacin, and Tetracycline were more susceptible, while Amoxicillin showed the least susceptibility. Oxacillin and Cefixime exhibited 100% resistance. Similarly, at 25µg concentration, Augmentin and Ciprofloxacin were more susceptible, while Amoxicillin showed the least susceptibility. Oxacillin and Cefixime showed total resistance against Salmonella.

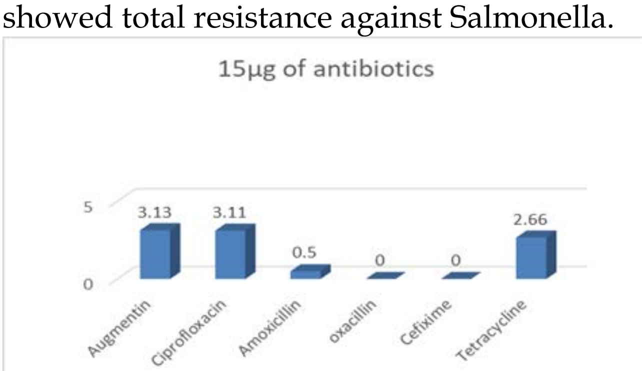


Figure.11 Antibiotic efficacy at 25µg to salmonella pathogen

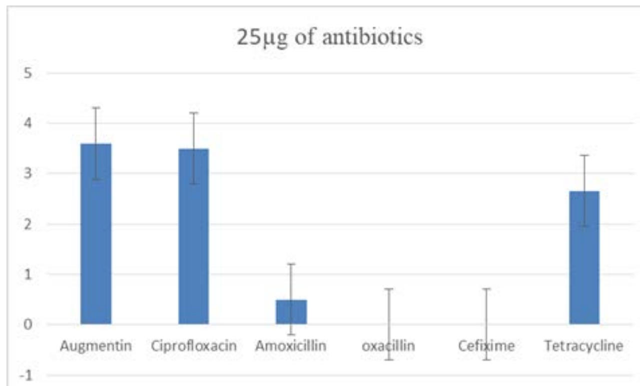


Figure.12 Antibiotic efficacy on salmonella bacteria at 25 µg concentration

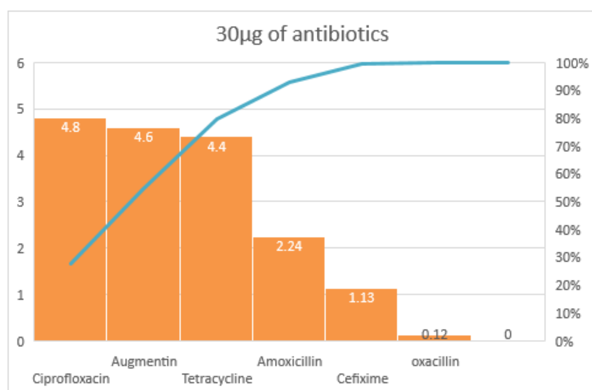


Figure.13 Efficacy of antibiotic on salmonella pathogen at 30 µg

Figure 13 revealed antibiotic susceptibility against Salmonella at 30µg concentration. Ciprofloxacin showed 80% susceptibility, Augmentin 75%, and Tetracycline 72%. Amoxicillin demonstrated 35% susceptibility, Cefixime 20%, and Oxacillin 0.12%. Oxacillin and Cefixime exhibited higher resistance against Salmonella species.

Discussion

Most prevalent form of typhoid fever occurs in impoverished communities characterized by poor living standards, inadequate sanitation, and limited access to clean water (20). Among respondents, 53.33% were knowledgeable about typhoid fever and its prevention, while 46.66% lacked awareness. Hand washing rates improved slightly between December 2015 and the study period, with 37% before eating and 39% after using the latrine. However, understanding about typhoid prevention and management remains inadequate, contributing to the spread of Salmonella typhi. Only 25% received health education during the outbreak, and just 34% knew how the disease was transmitted, despite ongoing hygiene efforts. Less than 40% knew how typhoid fever could be prevented. House-to-house hygiene promotion, primary form of health education, accounted for less than 50% of the information provided, indicating challenges in local organization and participation in hygiene education interventions. (21).

The study found that 48.66% of surveyed individuals had experienced typhoid fever, with 51.33% unaffected.Males (30.33%) reported higher typhoid incidence than females (18%), possibly due to increased outdoor activities and roadside food consumption, which heightens the risk of ingesting contaminated food. A study in Quetta district showed similar trends, with rural males facing a higher infection risk (15.86%) compared to urban areas (13.45%) (20). Females' lower infection rates may stem from indoor activities and better hygiene practices, consistent with previous research.

Water emerged as the primary risk factor for typhoid fever, with 70.66% of respondents relying on tap water, 12.66% on rivers, and 16.66% on springs for drinking water. The study revealed that 40% of respondents did not treat their drinking water, and even among those who did, 54.7% still suffered from typhoid due to inadequate treatment. Globally, over1.2 billion people lack access to filtered water, underscoring the present issue of water accessibility, particularly in developing countries. This strain on safe drinking water provision is a major concern for communities reliant on private water supply systems (23). The increasing human population exacerbates this issue, emphasizing the urgent need for improved water infrastructure in developing nations (24).

Poor environmental sanitation was linked to high childhood disease prevalence and mortality rates. WHO notes that communities lacking adequate sanitation and safe water are most vulnerable to typhoid fever, with water pollution impacting health and economic development, as seen in Nigeria (23). Multivariate analysis identified significant environmental exposures, including cooking and cleaning with river water and using open wells for these tasks. Surprisingly, no specific drinking water sources were associated with typhoid, contrary to previous research (25, 26).

Increased prevalence of typhoid due to waterborne illness, highlights the risks of unequal water access in low-resource countries (27). Inadequate water availability affects sanitation and personal hygiene, further increasing the risk of typhoid (28). Handwashing with soap, especially after defecating, is associated with lower chances of typhoid fever (29).

A recent hospital-based study observed an increase in typhoid cases during July and August 2020 compared to 2019, despite the COVID-19 pandemic. In 2019, there were 1011 cases reported, which slightly decreased to 998 in 2020. The study aimed to address the lack of precise epidemiological data for Islamabad by collecting 1500 medical isolates from suspected typhoid fever cases at the Capital Development Authority (CDA) health center between January and December 2014 (30). Globally, the Global Burden of Diseases 2019 study estimated approximately 10.9 million typhoid cases in 2017 (8). The ongoing typhoid outbreak overwhelmed local hospitals, with over 1500 cases reported in one week. Typhoid remains a significant health concern, causing approximately 220,000 deaths and 21 million cases globally each year (31). Amidst the COVID-19 crisis, Pakistan faced around 20,000 typhoid cases within 10 days in June 2020 alongside COVID-19 cases (WHO, 2018). Diagnosing typhoid alongside COVID-19 presents challenges for doctors due to similar symptoms. In Lahore, Punjab, Pakistan, 8,000 cases were identified out of 20,000 typhoid patients in five major hospitals (News a, 2020). Poor hygiene facilities are identified as a major source of Salmonella Typhi, with contaminated water contributing to enteric fever (25). Annually, over 26 million people are affected by S. Typhi and Paratyphoid (32). The potential transmission of microbial pathogens through drinking water poses a significant health risk worldwide (33).

This research confirms growing concerns about Salmonella resistance. While Ciprofloxacin, Augmentin, and Tetracycline were effective at some concentrations, Amoxicillin, Cefixime, and Oxacillin showed lower effectiveness. This aligns with reports of increasing resistance, highlighting the need for continued research and appropriate antibiotic use (34). Increasing Salmonella resistance to first-line antimicrobial drugs has led to testing alternative antibiotics like streptomycin and tetracycline. However, in many developing countries, multi-drug resistant strains of Salmonella, termed MDR strains, show resistance to these agents as well (35). This resistance contributes to increased mortality and morbidity rates in affected individuals due to ineffectiveness of antibiotic remedy (36). Generally, first-line antibiotics for treating typhoid fever include ampicillin, chloramphenicol, and co-trimoxazole (34). However, Salmonella bacteria are becoming more resistant to antibiotics, particularly nalidixic acid. While common antibiotics like ampicillin, chloramphenicol, and co-trimoxazole still show high effectiveness in some areas, resistance is rising. This problem is worse in some regions, with strains resistant to multiple antibiotics like azithromycin, ciprofloxacin, and ceftriaxone – likely due to antibiotic misuse (37, 38).

Conclusion

The study reveals a significant prevalence of typhoid fever in the Astore valley, underscoring multiple risk factors including contaminated water sources, poor hygiene practices, and inadequate sanitation. Factors such as consumption of street-vended food and improper waste management were identified as contributing to the spread of the disease. Furthermore, a lack of health education and community participation in cleanliness efforts exacerbates the problem. Microbiological analysis confirmed contamination of water sources with bacterial pathogens, particularly in villages like Choungrah and Gorikot. Overall, the study highlights the urgent need for improved water treatment, hygiene promotion, and community engagement to mitigate the risk of typhoid fever in the region.

Conflicts of Interest: None declared.
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