

BioScientific Review (BSR)

Volume 6 Issue 1, 2024

ISSN (P): 2663-4198 ISSN (E): 2663-4201

Homepage: <https://journals.umt.edu.pk/index.php/bsr>



Article QR



Title: Knowledge, Attitude, and Practices (KAPS) of the Inhabitants of Punjab, Pakistan toward XDR Typhoid Outbreak During COVID-19

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DOI: <https://doi.org/10.32350/bsr.61.03>

History: Received: June 5, 2023, Revised: October 19, 2023, Accepted: November 21, 2023,
Published: January 30, 2024

Citation: Khalid A, Janiad S, Munir I, Iqbal A, Yasmeen H, Naeem N. Knowledge, attitude, and practices (KAPS) of the inhabitants of Punjab, Pakistan toward XDR typhoid outbreak During COVID-19. *BioSci Rev.* 2024;6(1):81–94.
<https://doi.org/10.32350/bsr.61.03>

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Conflict of Interest: Author(s) declared no conflict of interest



A publication of

The Department of Life Sciences, School of Science
University of Management and Technology, Lahore, Pakistan

Knowledge, Attitude, and Practices (KAPS) of the Inhabitants of Punjab, Pakistan toward XDR Typhoid Outbreak During COVID-19

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ABSTRACT

Background Typhoid fever, caused by the bacterium *Salmonella typhi*, is the most prevalent in areas that have poor hygienic conditions. The most alarming situation is the development of the resistant strains of *Salmonella typhi*, first reported in 2016 in Hyderabad, Sindh. Later, there was a widespread outbreak of extensively drug-resistant (XDR) typhoid. This survey aims to investigate the risk factors for the spread of XDR typhoid in Pakistan based on the knowledge, attitude, and practices (KAPs) of the affected or at-risk population to help plan preventive actions.

Method For this purpose, a community-based random KAP study was conducted in Punjab, Pakistan. Data was collected online and also by face-to-face interaction from those who had no access to the Internet.

Result More than half of the respondents were aware of the fact that bacteria is the causative agent (60.6%) of XDR. Similarly, with regard to practice, it was found that 67.7% of them washed their hands before eating and 88.8% washed their hands after using the toilet. A common practice in the form of using filtered water for drinking purposes was adhered to by 73.8% of respondents.

Conclusion The study concluded that preventative and control measures are necessary to avoid XDR typhoid pandemic spread.

Keywords: COVID-19, disease correlation, extensively drug-resistant (XDR) typhoid, KAP gap, typhoid

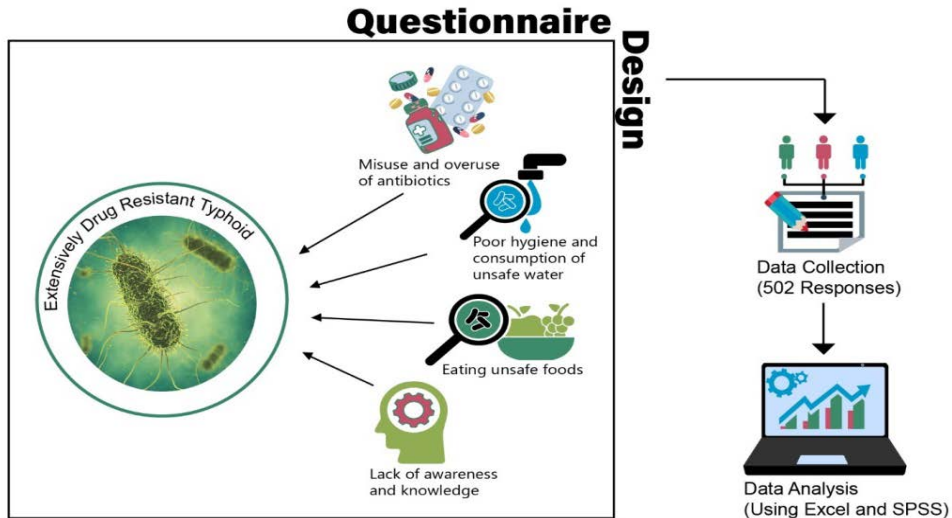
Highlights

- Pakistani population lacks awareness about the XDR typhoid outbreak amidst the challenges of COVID-19.
- Inadequate preventive measures and treatment were practiced during the XDR typhoid outbreak that occurred during the COVID-19 pandemic.

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- The survey highlights misconceptions and negative attitudes towards XDR typhoid prevention and control measures among Pakistani individuals in the era of COVID-19.

GRAPHICAL ABSTRACT



1. INTRODUCTION

Salmonella enterica serovar Typhi is the agent that causes typhoid fever [1]. The bacterium has an incubation period of 3-30 days. Its symptoms include progressive onset of fever, loss of appetite, headache, abdominal discomfort, and constipation followed by malaise, dry cough, diarrhea, rash, and bradycardia [2]. The bacterium is frequently present in poor hygienic and sanitary conditions, marked with a short supply of clean water, poor hand-washing practices, intake of unsafe foods, and close contact with cases or carriers [3]. Infection is transmitted through the fecal-oral route by contaminated water or food; humans are the only identified reservoir [4]. *S. typhi* can only be treated successfully with antibiotics [5].

Currently, the development of a resistant strain of *S. typhi* is a major threat

to efficiently controlling typhoid fever in Pakistan. Multiple drug-resistant (MDR) strains of *S. typhi* show resistance to all of the first line antibiotics suggested by the WHO, namely chloramphenicol, trimethoprim-sulfamethoxazole, and ampicillin. According to a study conducted at Agha Khan University in Karachi, Pakistan between 2001 and 2006, the prevalence of MDR *S. typhi* strains increased from 34.2% to 48.5% during the said period, while quinolone resistance increased from 1.6% to 64.1% [6]. Following the development of a fluoroquinolone-resistant *S. typhi*, 3rd generation cephalosporins, such as ceftriaxone, have become the treatment of choice.

Since November 2016, ceftriaxone-resistant typhoid fever reports have increased in the Sindh province of Pakistan. This type has the potential to change from

MDR to XDR by conjugation. XDR strain of *S. typhi* exhibits resistance to cotrimoxazole, ampicillin, fluoroquinolones, and chloramphenicol, along with 3rd generation cephalosporins [7]. The symptoms of XDR are generally non-specific and indistinguishable from other febrile diseases and even COVID-19 [8].

According to the WHO, *S. typhi* recorded cases are between 11 and 21 million worldwide per annum, out of which 128,000 to 161,000 individuals die. Vulnerable populations and even whole communities lacking scheduled vaccination, adequate sanitation, and safe drinking water are the most susceptible to becoming infected from typhoid. In specific areas of Pakistan where these circumstances have been recorded, the frequency of XDR typhoid has increased from 7/100,000 to 15/100,000 cases [9].

Pakistan, a developing country, has been encountering COVID-19 since February 2020. The outcomes of COVID-19 appear to be highly concerning, with a low level of abidance to lockdown events due to lethargy and socioeconomic dysfunction. The potential overlap of typhoid fever and COVID-19 is particularly concerning but has received little attention thus far [8]. In Pakistan and other middle-income countries, XDR typhoid fever is a serious public health hazard. Not only poor waste management and hygiene conditions but the misuse and overuse of azithromycin has also resulted in chaos [9]. From January to December 2020, 2510 XDR cases of typhoid were stated in Pakistan. With the outbreak of the pandemic, the treatment of COVID-19 with azithromycin has gained ground [8].

Another factor contributing to the overlap between COVID-19 and typhoid fever are the diagnostic limitations in Asian

countries, particularly in Pakistan, due to false-positive Widal testing in COVID-19 patients. Moreover, the lack of diagnostic approaches has not only strengthened the overuse of azithromycin but has also made it difficult to clinically distinguish between malaria, dengue, and COVID-19 [10].

Awareness is essential to attain optimum health. Likewise, increasing community awareness about typhoid fever is an effective way to promote preventive behavior. To adopt adequate preventive and control methods, it is critical to determine community KAPs towards typhoid fever, *S. Typhi* prevalence, and their associated factors [11].

This study aimed to evaluate the knowledge about the causes, treatment, and prevention of typhoid fever, as well as the practices regarding food, water, and hygiene, and attitude towards antibiotics use in the era of COVID-19.

2. METHODOLOGY

2.1. Data Collection

Data was collected from all adult age groups in Punjab, Pakistan through a structured questionnaire from January 2022 to May 2022. The questionnaire was based on previous literature and composed of five sections, namely demographic information, knowledge, attitude, practices, and effects of COVID-19 on XDR [12]. The information regarding gender, age, educational background, and residence in a developed or under developed area were included in demographic information. Knowledge about typhoid causes, treatment, and preventive measures was assessed. Practices of sanitation, hygiene, and safe use of water and food were also monitored. Attitude towards the use of antibiotics was also recorded. Data was generated online as well as through face-to-

face interaction where participants had no access to the Internet. Furthermore, the questionnaire was translated into the native language for proper understanding where needed.

2.2. Data Analysis

SPSS (version 21) was used to code and analyze each response. Descriptive statistics were used to assess the respondents' knowledge, attitude, and practices. The findings were displayed as numbers and percentages. Correlation was determined through Pearson chi-square. For this purpose, the respondents were divided into groups according to their scores. These groups included *Poor Knowledge* - participants who scored <70% for knowledgeable questions, *Good Knowledge* - participants who scored 70% or >70% for knowledgeable questions, *Bad Attitude* - "Yes" answer to attitude based questions, *Good Attitude* - "No" response

to the survey's attitude based questions, *Poor Practice* - participants who keep count <70% for correct practices, and *Good Practice* - participants who keep a record of 70% or >70% for correct practices [13].

3. RESULTS

3.1. Demographic Data

The questionnaire was circulated randomly in different cities of Punjab, Pakistan (Figure 1). A total of 502 responses from different districts were received, the highest from Multan (163, 32.5%) and the lowest from Gujranwala (13, 2.6%). Half of the respondents were female (283, 56.4%) and the prevalent age group was 21-40 years (Table 1). Interestingly, the majority belonged to biological sciences (302, 60.2%) with 16 years of education (227, 45.2%).

Table 1. Demographic Information

Variables	Frequency	Percent
Gender		
Female	283	56.4
Male	215	42.8
Transgender	4	0.8
Age		
1-20	150	29.8
21-40	247	49.2
41-60	75	15
>60	30	6
Educational status		
No formal education	19	3.8
Primary	25	5
Post-primary	27	5.4
Secondary/matric	28	5.6
Higher secondary/intermediate	78	15.5
Graduate	227	45.2
Post-graduate	98	19.5
Educational background		
Biological Sciences	302	60.2
Non-biological Sciences	134	26.7
Other	66	13.1



Figure 1. Map of Punjab Province in Pakistan Showing Response Rate in Different Districts

3.2. Knowledge of Typhoid Fever Causes, Treatment, and Prevention

The majority of respondents (304, 60.6%) were aware of bacteria as a typhoid causative agent because they had an educational background in biological sciences. Three causes of typhoid fever

reported by the respondents were the consumption of unsafe drinking water (341, 68.2%), unsafe food (296, 59.2%), and poor hygiene (251, 50.2%), as enlisted in Table 2. A good aspect was that nearly all (412, 82%) the respondents preferred to go to the hospital or a clinic for its treatment.

Table 2. Knowledge of Causes, Treatment, and Prevention of Typhoid Fever

Variables	Frequency	Percent
Typhoid is a disease		
Bacterial	304	60.6
Don't know	88	17.5
Viral	82	16.3
Fungal	19	3.8
Genetic	9	1.8
Causes of typhoid fever (can be more than one)		
Drinking unsafe water	341	68.2
Consuming unsafe food	296	59.2
Poor hygiene	251	50.2
Unwashed fruits and vegetables	227	45.4
Flies	150	30
Person-to-person spread	114	22.8
People from other tribes	73	14.6
Don't Know	51	10.2
Methods of preventing typhoid fever (can be >1)		
Boil or treat water	336	67.2
Wash hands	276	55.2
Wash vegetables and fruits	234	46.8
Cook food thoroughly	230	46
Clean cooking utensils and vessels	166	33.2
Don't Know	65	13
Cannot be prevented	29	5.8
Treatment of typhoid fever		
Go to the clinic or hospital	412	82
Don't Know	25	5
Go to Homeopathic	22	4.4
Home Remedy	20	4
Go to Hakeem	18	3.6
I do not treat	5	1

3.3. Practices of Water, Food, Sanitation, and Hygiene

It was observed that the majority of the respondents followed good hygiene practices, that is, washing hands after using the toilet (446, 88.8%) and before eating (340, 67.7%). The participants who preferred outdoor dining at street food stalls were 266 (53.2%), mobile food vendors were 167 (33.4%), and diners at restaurants

were 346 (69.2%). Drinking filtered water was commonly practiced (369, 73.8%). A total of 409 (81.5%) respondents used covered sewage systems. It was found that preference regarding the use of household toilets not only depends on personal choices but is also determined by available circumstances, that is, private 250 (49.4%), shared 223 (46.7), and open defecation 29 (3.9%), as mentioned in Table 3.

Table 3. Practices Regarding Water, Food, Sanitation, and Hygiene

Variables	Frequency	Percent
Washing hands after using the toilet?		
Yes, with soap and water	446	88.8
Yes, with only water	54	10.8
No	2	0.4
Do you wash your hands before eating?		
Yes	340	67.7
Rarely	146	29.1
Never	16	3.2
How often do you eat outdoors?		
Daily	11	11.7
At least once a week	114	16.7
At least twice a week	89	15.6
At least once a month	174	47.2
At least twice a month	60	8.9
You eat outdoors at		
Restaurant	346	69.2
Street Food Stall	266	53.2
Mobile Food Vendor	167	33.4
Sources of drinking water (can be more than one)		
Filtered water	369	73.8
Boiled water	181	36.2
Covered container	123	24.6
Taps (household)	119	23.8
Water Supply	109	21.8
Taps (communal distribution)	68	13.6
Chlorinated water	63	12.6
Well	53	10.6
Uncovered container	30	6

3.4. Knowledge and Attitude among People towards Antibiotics Use

The trend among the respondents towards antibiotics use when they encountered typhoid and/or COVID-19 was analyzed (Figure 2). A total of 315 (63%) respondents were aware that

antibiotics are used to treat bacterial infections. Furthermore, 232 (46.2%) knew that amoxicillin and penicillin are antibiotics. Positive responses to the questions regarding the use of antibiotics showed that their overuse and misuse is commonly practiced.

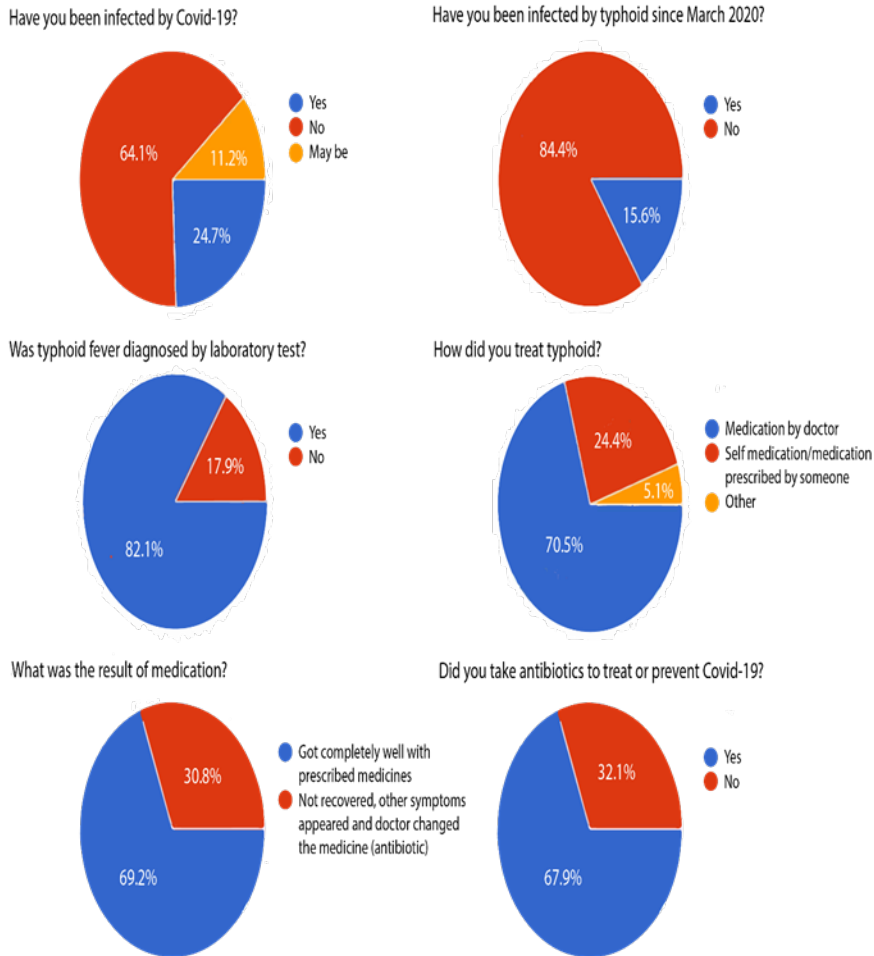


Figure 2. Knowledge and Attitude among People Regarding Use of Antibiotics

Multivariate analysis of data showed that washing hands before eating ($p = 0.05$) and gender ($p = 0.05$) were significantly associated with using antibiotics not prescribed by the doctor. While educational background ($p = 0.000799$) was strongly associated with using antibiotics that were not prescribed. It was also found that the correlation of variables with usually taking antibiotics following a phone contact with

the doctor was not significant ($p > 0.05$) (Table 4A). Multivariate analysis showed that gender ($p = 0.005$) and washing hands before eating ($p = 0.005$) were associated with stop taking antibiotics when start to feel better. Educational background ($p = 0.043$) and washing hands after using toilet ($p = 0.021$) were correlated with using left over antibiotics without consulting a doctor (Table 4B).

Table 4A: Multivariate results based on attitude among people towards antibiotics use

		Do you use antibiotics without a doctor's prescription?			Do you usually take antibiotics without a proper medical examination following a simple phone contact with your doctor?		
		Yes	No	P Value	Yes	No	P Value
Gender	Male	107	108	0.05	117	98	0.091
	Female	101	182		126	157	
	Transgender	1	3		2	2	
Educational Background	Biological	113	189	0.000799	143	159	0.369
	Non-Biological	74	60		72	62	
	Other	22	44		30	36	
Typhoid is a disease	Viral	40	42	0.523	45	37	0.223
	Fungal	7	12		7	12	
	Bacterial	120	184		143	161	
	Genetic	5	4		7	2	
	Don't know	37	51		43	45	

Table 4 B: Multivariate results based on attitude among people towards antibiotics use

		When you begin to feel better, do you normally stop taking antibiotics?			Do you usually use antibiotics that have been left over without consulting a doctor?		
		Yes	No	P Value	Yes	No	P Value
Gender	Male	114	101	0.005	79	136	0.614
	Female	187	96		93	190	
	Transgender	1	3		1	3	
Educational Background	Biological	182	120	0.5	91	211	0.043
	Non-Biological	84	50		55	79	
	Other	36	30		27	39	
Typhoid is a disease	Viral	54	28	0.615	35	47	0.492
	Fungal	9	10		7	12	
	Bacterial	183	121		97	207	
	Genetic	5	4		3	6	
	Don't know	51	37		31	57	

3.5. COVID-19 Insinuations on XDR Typhoid Strain in Pakistan

From a total of 502 respondents, 124 (24.7%) were infected by COVID-19, 56 (11.2%) were not sure whether they were infected or not, and 322 (64.1%)

individuals reported that they were not infected by COVID-19. Similarly, out of the 502 respondents 78 (15.6%) were infected by typhoid, of which 64 (82.1%) cases were diagnosed by a laboratory test, 55 (70.5%) cases were medicated by a

doctor, and 23 (29.5%) were treated by self-medication or other means. A total of 54 (69.2%) cases recovered from fever with prescribed medicines, while for 24 (30.8%) cases prescription was modified after they

failed to recover at first. It was observed that 53 (67.9%) typhoid patients used antibiotics either to prevent or treat COVID-19 (Table 5).

Table 5. Multivariate analysis of COVID-19 Insinuations on XDR typhoid strain in Pakistan

		Have you been infected by Covid-19?			P Value
		Yes	No	May be	
Have you been infected by typhoid since march 2020?	Yes	41	26	11	0.000
	No	83	296	45	
Was typhoid fever diagnosed by laboratory test?	Yes	3	23	8	0.5
	No	8	3	3	
How did you treat typhoid?	Medication by doctor	30	20	5	0.17
	Self medication	10	5	4	
	Other	1	1	2	
What was the result of medication?	Got completely well	29	20	5	0.158
	Need to change antibiotics	12	6	6	
Did you take antibiotics to treat or prevent Covid-19?	Yes	37	9	7	0.000
	No	4	17	4	

The results showed that there is a significant correlation ($p = 0.000$) between typhoid and COVID-19 infected individuals. As such, 41 individuals infected by COVID-19 were also infected by typhoid. Another significant correlation ($p = 0.000$) was between COVID-19 and the use of antibiotics used to treat or prevent COVID-19. Of COVID-19 infected individuals, 37 had used antibiotics to treat the infection. While, among non-infected individuals, 9 had used antibiotics to prevent the infection. Both of these groups remain at the risk to develop resistance against antibiotics used in *S. typhi*. Moreover, data showed no significant correlation ($p = 0.5$) between laboratory test diagnosis and COVID-19.

4. DISCUSSION

The current study's findings are almost in accordance with those of a study conducted in Ethiopia (61.5% females) [12]. In terms of the participants' educational status, 60.2% graduated with a biological sciences background.

Typhoid fever can be prevented by sustaining a safe water supply, proper sanitation, vaccination, food safety, and health education aimed to build public awareness and persuade behavioral changes. This may be achieved after ascertaining gaps of knowledge, attitude, and practices (KAPs) and by acclimatizing it to local situations in the study area. Regarding knowledge about typhoid fever in the current study, only 60.6% of

respondents knew that it is a bacterial disease. This percentage does not fall under the operational definition of 'good knowledge'. Furthermore, 82% of respondents knew that they should go to a clinic or hospital when infected by typhoid and this percentage reflects good knowledge. The mean score of the causes of typhoid fever was 41.5%, which is poor knowledge. The mean score of preventive measures against typhoid was 49.7%, which indicates an overall poor knowledge. This percentage was less than the percentage in the research carried out in the Ethiopian state of Amhara [11].

The study conducted by Nahimana, Ngoc, Olu, Nyamusore, Isiaka, Ndahindwa, Dassanayake, Rusanganwa [14] in a Burundian refugee camp displayed that 38.6% and 34.6% of participants had knowledge about the prevention and spread of typhoid fever, respectively. The study of food handlers at Mettu University, Ethiopia reported 50.6% and 47.2% knowledge regarding the prevention and transmission of typhoid [15].

Concerning the practices of hygiene, it was found that 88.8% of respondents followed the 'good practice' of washing hands with water and soap after using the toilet. On the other hand, only 67.7% washed their hands before eating and it is not a good practice. As shown in the graph, the level of eating outdoors at the restaurants is 69.2% (near 70%), a good practice among Pakistani people because it is somewhat safe to eat at restaurants, rather than to eat at mobile food vendors and street food stalls. Moreover, the respondents maintained good practice towards the safe use of drinking water. The majority treated water by different methods, such as 36.2% used boiling and 73.8% used filtered water. The findings of this study are lesser than

those of the one conducted at Mendida Town, Ethiopia [12].

Numerous studies have shown that individuals with higher levels of education know more about antibiotic resistance than those with lower levels of education. The lack of awareness about diseases that may or may not be treated with antibiotics is an important factor in their misuse. Indeed, this ignorance can result in the emergence of resistance [16-18]. In the current study, 46.2% of people were found to be misusing and overusing antibiotics. Concerning the knowledge regarding antibiotics, 63% knew that these are used to treat bacterial infections, while 46.2% recognized them as antibiotics. Mallah, Orsini, Figueiras, Takkouche [19] reported the meta-analysis of 85 studies from 42 different countries. They determined that medium education (> 9-12 years) is linked to a 20% lower risk of antibiotic misuse than low education (9 years or less), while a high educational background (more than 12 years) is linked to 14% lower risk of the use of antibiotics in high-income countries.

Typhoid fever is an endemic disease that affects developing nations, particularly those in South and Southeast Asia including Vietnam, Pakistan, Bangladesh, India, Nepal, and Indonesia. The false-positive results of the Widal test in COVID-19 infected individuals became a serious public health concern for developing countries during the pandemic [10]. Due to improper diagnosis during the COVID-19 pandemic, irrational pharmacotherapy was adopted by doctors. Broad-spectrum antibiotics were used as medication to treat typhoid and this became a contributing factor towards the XDR strain of typhoid [8]. After medication, if the patient did not recover and the doctor changed the antibiotics, it also indicated emerging resistance to antibiotics in

Salmonella typhi. Furthermore, 67.9% of typhoid patients in the current study used antibiotics to treat or prevent COVID-19, which might have developed resistance in *Salmonella typhi* due to their overuse and misuse. These findings are in agreement with other studies [20].

4.1. Conclusion

KAP studies urge the need of increasing awareness regarding safe eating and drinking and the safe use of antibiotics. In a nutshell, education plays a significant role in disease prevention and control. Furthermore, there is still a need to spread awareness regarding typhoid and its resistant strains. To conclude, it would be sagacious to introduce courses and training programs about antibiotics. In the curriculum of medical colleges and universities, there should be an emphasis on the right prescribing rules.

CONFLICT OF INTEREST

The authors of the manuscript have no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

DATA AVAILABILITY STATEMENT

The data associated with this study will be provided by the corresponding author upon request.

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