Prevalence and antimicrobial resistance profile of Salmonella typhi infection in Iraq, 2019–2021

Kawthar Faris Nassir, PhD[1], Besmah Mohammed Ali, FIBMS[2], Ziyad Hazim Ibrahim, FIBMS[3], Zainab Jumaa Qasim, PhD[4], Sinan Ghazi Mahdi, FIBMS[5], Nabil Mansur Mustafa, FIBMS[6], Ameer A oudah, PhD[7], Aaya Ayad Okab, MBChB[8], Jawad Kadhim Al-Diwan, FIBMS[9]

[1]Iraqi Board Clinical Pharmacy, Therapeutic Drug Monitoring Center, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq, [2]Head of Public Health Department in Ghazi Al-Hariri Hospital for Surgical Specialties, Medical City, Ministry of Health, Baghdad, Iraq, [3]Iraqi Ministry of Health, Baghdad, Iraq, [4]Department of Pharmacy, Baghdad College of Medical Sciences, Baghdad, Iraq, [5]Ministry of Health, Public Health Directorate, Communicable Diseases Control Center, Baghdad, Iraq, [6]Public Health Specialist, Communicable Diseases Control Center, Directorate of Public Health, MoH, Baghdad, Iraq, [7]Iraqi Board in Clinical Pharmacy, Therapeutic Drug Monitoring Center, Bagdad Teaching Hospital, Medical City, Baghdad, Iraq, [8]Department of Medicine, Bagdad Teaching Hospital, Medical City, Baghdad, Iraq, [9]Departments of Family and Community Medicine, College of Medicine, University of Baghdad, Iraq

ABSTRACT

Introduction: *Salmonella typhi* could infect the intestinal tract and the bloodstream or invade body organs and secrete endotoxins. It is endemic in developing countries. It is increasingly evolving antimicrobial resistance to several commonly used antimicrobial agents.

Materials and Methods: A cross-sectional study was done at Iraqi Communicable Disease Control Center, where all confirmed cases of *Salmonella typhi* are reported, for a period 2019–2021. All demographic, epidemiological and clinical characteristics of patients, comorbidities, type of samples, distribution of *S. typhi* by age and gender, time distribution in each year and profile of bacterial resistance and sensitivity to antibiotics were gathered and analysed.

Results: Most samples were taken from blood. The mean age of cases during 2019, 2020 and 2021 was 18.7 ± 6.5, 17.7 ± 14.1 and 17.3 ± 12.8. Males constituted 56.7%, 58.5% and 39.8%, respectively. Some cases had comorbidities. Most cases had headache and fever. Some of them had nausea, diarrhoea, vomiting and epigastric pain. The age and sex were significantly associated with years of reporting. The most months of case reporting were June–July (2019 and 2021), Jan. –Feb. (2020). There was an obvious increase in *S. typhi* resistance to ceftriaxone (92.2%, 86.1%, 88.8%) and ampicillin (77.1%, 76.9%, 81.27%). There was a gradual increase in sensitivity to tetracycline (83.1%, 88.1%, 94%), cotrimoxazole (86.7%, 86.1%, 92.2%), ciprofloxacin (78.3%, 90.1%, 87.8%) and cefixime (77.7%, 72.3%, 72.7%).

Conclusions: There was a sharp rise in resistance rates of the S. typhi in Iraq (during 2019–2021) to ceftriaxone and ampicillin, while there were highest sensitivity rates to imipenem, aztreonam and chloramphenicol. The following recommendations were made: (1) Improvement of general hygiene and food safety measures. (2) Emphasis on vaccination and surveillance of Salmonella infection. (3) Rational use of appropriate antibiotics through implementation of treatment guidelines. (5) Educate communities and travelers about the risks of S. typhi and its preventive measures.

KEYWORDS:
Salmonella; typhoid fever; antimicrobial resistance; S. typhi; resistance profile

INTRODUCTION

Salmonella is a genus of rod-shaped (bacillus) Gram-negative bacteria of the family Enterobacteriaceae. It is comprised of two species: *Salmonella bongori* and *S. enterica*. Salmonella species can be classified according to their ability to develop specific pathologies in humans into two main serotype groups: typhoidal and non-typhoidal.[1] Non-typhoidal serotypes (NTS) are zoonotic and can be transferred from animal-to-human and from human-to-human. They usually invade only the gastrointestinal tract and cause salmonellosis while typhoidal serotypes can only be transferred from human-to-human and can cause food-borne infection and bacterial infection of the intestinal tract and occasionally of the bloodstream (which is called typhoid fever) or in addition spreading throughout the body, invading organs and secreting endotoxins (the septic form).[2,3] This can lead to life-threatening hypovolemic shock and septic shock and requires intensive care including antibiotics.[3] According to the World Health Organization (WHO), Salmonella spp. are among the 31 pathogens displaying the highest capability of triggering intestinal or systemic disease in humans among diarrheal and/or invasive agents (viruses, bacteria, protozoa, helminths and chemicals) and the third leading cause of death among food-transmitted diseases.[4] This pathogen was the second leading causative agent of food-transmitted diseases in the European Union and the United States.[4] Globally, infections with *S. typhi* are responsible for approximately 20 million new cases of typhoid each year, and it is one of the most common infections in developing countries and low- or middle-income countries where typhoidal Salmonella is endemic and that have poor sanitation with lack of access to safe food and

This article was accepted: 07 January 2024
Corresponding Author: Ziyad Hazim Ibrahim
Email: drziyad2005@gmail.com

water.5 Infections with *S. typhi* are serious public health problems in Iraq, especially when the antimicrobial resistance of Salmonella species increasing and growing worldwide.[6] The most commonly prescribed antibiotics that are used in the treatment of *Salmonella typhi* are ampicillin, amoxicillin, trimethoprim-sulfamethoxazole, ceftriaxone, cefixime, chloramphenicol fluoroquinolones (ciprofloxacin, ofloxacin, or fleroxacin), azithromycin, Imipenem, aztreonam and tetracycline.[7] Salmonella species are increasingly evolving antimicrobial resistance to several commonly used antimicrobial agents. Historically, the first-line agents (ampicillin, chloramphenicol and trimethoprim-sulfamethoxazole) were the drug of choice for the management of *Salmonella typhi*.[7] However, due to the emergence of multidrug-resistant (MDR) *S. typhi* in the 1970s, fluoroquinolones became the standard of care for the treatment of *Salmonella typhi*.[8] Since the 2000s, there have been frequent reports of decreased ciprofloxacin sensitivity to *S. typhi* in the endemic regions of South and Southeast Asia.[9] Currently, ceftriaxone, a third-generation cephalosporin (intravenous), and azithromycin, a macrolide (oral), are increasingly being used for complicated and uncomplicated typhoid fevers, respectively.[9] However, the indiscriminate use of antibiotics has encouraged resistance and selection for virulent MDR clades; thus, antibiotic resistance in *Salmonella typhi* is now a clinical and economic challenge.[10] In this context, controlling infections caused by Salmonella spp. is a global concern and monitoring its possible contamination routes to humans is essential. The aim of this study was to determine the prevalence and distribution of *S. typhi* infections and its antimicrobial susceptibility pattern among patients in Iraq.

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted at the Communicable Diseases Control Center in Iraq (CDCI), where all confirmed cases of *Salmonella typhi* infection occurring in all governorates of Iraq are reported, collected, and documented in this center to be as a database for infection with this disease. The strategy of collection and documentation of *Salmonella typhi* infection cases was done by collecting the patient's information, whether the patient is from primary health care center auditors or outpatient in the consulting clinics, or if the patient is inside one of the hospital's halls (inpatient), the attending physician after diagnoses the *Salmonella typhi* infection with clinical symptoms and confirm it with laboratory investigations, writes the diagnosis of *Salmonella typhi* infection in the communicable diseases register then the health care giver who is responsible for the communicable disease registry will entering data on a daily basis by using special programs and sent it to the Communicable Diseases Control Center to be a database for infection with this disease. In this study, cases of *Salmonella typhi* were collected and sorted over a period of three consecutive years, from 2019 to 2021. The total number of samples entered the study was 1471, comprising 1408 (95.71%) blood samples and 63 (4.28%) stool samples. These samples were distributed across three consecutive years (2019, 2020 and 2021) as follows: 817, 152 and 502, respectively. All demographic and clinical characteristics of patients, comorbidity, type of the samples, epidemiologic information, distribution of Salmonella typhi by age and gender, month-wise distribution of cases in each year and profile of Salmonella typhi resistance and sensitivity to antibiotic were gathered and analysed using the Statistical Package for Social Science (SPSS)- version 16. The result values are presented as numbers and percentages to compare values in all parameters and presented as mean ± standard deviation to estimate the age of patients. The results were presented by using tables. p values ≤ 0.05 were considered significant.

Ethical approval

This study was authorised from Arab Board of Health Specialisations Committee. The permission and approval have also been obtained from Center for Communicable Diseases Control, Public Health Department, Iraqi Ministry of Health.

RESULTS

Distribution and Characteristics of Salmonella typhi in Iraq

The distribution of positive Salmonella typhi in the blood and stool samples in this study is shown in Table I, while the demographic characteristics and clinical manifestations of the patients are shown in Table II.

Age and Gender Distribution of Cases of Salmonella typhi

The distribution cases of *Salmonella typhi* in different age groups showed a varying number of cases in each year of the three consecutive years with significant differences (*p* value ≤0.05), but the age distribution in the three consecutive years reveals the highest rate of cases recorded in age group of young adults between (18–35) years followed by (children ≥ 1 year to18 year) and then middle-aged adults between (36–55) years. In 2019, the highest rate was recorded in age group of young adults between18 and 35 years 325 (39.77%) followed by children ≥ 1 year–18 years 234 (28.64%) and then middle-aged adults between 36 and 55 years 110 (13.46%) while the neonates ≤ one month showed less prevalence of Salmonella typhi 7 (0.85%). In 2020, the highest rate was recorded in the age group of young adults (18–35 years) 82 (53.94%) followed by children ≥ 1 year–18 years 37(24.43%) and then middle-aged adults between 36 and 55 years 18 (11.84%) while the neonates ≤ one month showed less prevalence of Salmonella typhi 3 (1.97%). In 2021, the highest rate was recorded in age group of young adults (18–35 years) 302 (60.16%) followed by children ≥ 1 year to18 years 92 (18.32%) and then middle-aged adults between 36 and 55 years 49(9.76%) while the neonates ≤ one month showed less prevalence of Salmonella typhi 7 (1.39%). In contrast, the distribution of Salmonella typhi cases with the gender the highest rate was recorded in male more than female in all 3 years (2019, 2020, 2021) 464 (56.79%), 89 (58.55%), 302 (60.16%), respectively, with significant difference (p = 0.05) in the distribution of Salmonella typhi cases between male and female in all 3 years as illustrated in Table III.

Month-Wise Distribution of Cases of Salmonella typhi

The epidemiology distribution of cases of Salmonella typhi is also affected by seasonal variations. In the year 2019, we notice that the cases begin to gradually increase until they reach their peak and noticeably in July and June followed by May and August 129 (15.78%), 116 (14.19%), 94 (11.50%) and 71 (8.69%) respectively, and then decreasing gradually

Table I: Frequency and percent of the positive Salmonella typhi in the blood and stool samples, Iraq 2019–2022

	2019	2020	2021	Total
Blood	787 (96.33%)	141(92.76%)	480 (95.62%)	1408 (95.71%)
Stool	30 (3.67%)	11 (7.23%)	22 (4.38 %)	63 (4.28%)
Total	817 (100%)	152 (100%)	502 (100%)	1471 (100%)

Table II: Demographic characteristics and clinical manifestation of patients

Parameters	2019	2020	2021
Age (mean ± SD)	18.75 ± 6.55	17.74 ± 14.18	17.35 ± 12.80
Gender n (%)			
Male	464 (56.79%)	89 (58.55%)	302 (39.84%)
Female	353 (43.21%)	63 (41.44%)	200 (60. 16%)
Comorbidity: n (%)			
Lung infection	88 (10.77%)	18 (11.76%)	87 (17.33%)
Upper respiratory tract infection	98 (11.99%)	22 (14.37%)	73 (14.54%)
Sepsis	60 (7.34%)	8 (5.22%)	76 (15.13%)
Urinary tract infection	110 (13.46%)	43 (28.10%)	68 (13.54%)
Hepatitis	46 (5.63%)	11 (7.19%)	43 (8.56%)
Cardiovascular disease	136 (16.64%)	24 (15.68%)	80 (15.93%)
Hypertension	157 (19.21%0	34 (22.22%)	162 (32.27%)
Malnutrition	43 (5.26%)	11 (7.19%)	23 (4.58%)
Immunocompromised	22 (2.69%)	6 (3.92%)	11 (2.19%)
Systemic lupus erythematosus	10 (1.22%)	1 (0.65%)	0 (0.0%)
Diabetes militias	115 (14.07%)	18 (11.76%)	59 (11.75%)
Clinical manifestation (n) %			
Fever (T>37.2 C)	510 (62.42%)	131 (85.62%)	238 (47.42%)
Nausea	563 (68.91%)	109 (71.24%)	210 (41.83%)
Vomiting	479 (58.62%)	81 (52.94%)	239 (47.60%)
Epigastric pain	382 (46.75%)	63 (41.17%)	211 (42.03%)
Reduced appetite	117 (14.32%)	37 (24.18%)	32 (6.37%)
Myalgia	154 (18.84%)	41 (26.79%)	95 (18.92%)
Headache	515 (63.03%)	103 (67.32%)	320 (63.74%)
Diarrhoea	361 (44.18%)	56 (36.60%)	152 (30.27%)
Constipation	44 (5.38%)	4 (2.61%)	20 (3.98%)
Reduced consciousness	22 (2.69%)	59 (38.56%)	6 (1.19%)

Table III: Age and gender distribution of cases of Salmonella typhi

	2019	2020	2021	P value
Age				
Neonates ≤ 1 month	7 (0.85%)	3 (1.97%)	7 (1.39%)	0.000
Children < 1 year	68 (8.32%)	5 (3.28%)	19 (3.78%)	
Children ≥ 1–18 years	234 (28.64%)	37 (24.43%)	92 (18.32%)	
Young adults (18–35)	325 (39.77%)	82 (53.94%)	302 (60.16%)	
Middle age adults (36–55)	110 (13.46%)	18 (11.84%)	49 (9.76%)	
Older adults (≥55)	73 (8.93%)	7 (4.60%)	33 (6.57%)	
Total	817 (100%)	152 (100%)	502 (100%)	
Gender				
Male	464 (56.79%)	89 (58.55%)	302 (60. 16%)	0.05
Female	353 (43.21%)	63 (41.44%)	200 (39.84%)	
Total	817 (100%)	152 (100%)	502 (100%)	

Table IV: Month-wise distribution of cases of Salmonella typhi

Distribution by months in the years	Salmonella typhi n (%)		
Month	2019	2020	2021
January	60 (7.34%)	34 (22.36%)	46 (9.16%)
February	40 (4.89%)	32 (21.05 %)	26 (5.17%)
March	69 (8.44%)	20 (13.15%)	12 (2,39%)
April	68 (8.32%)	8 (5.26 %)	27 (5.37 %)
May	94 (11.50%)	6 (3.94 %)	14 (2.78 %)
June	116 (14.19%)	10 (6.57%)	96 (19.12%)
July	129 (15.78%)	9 (5.92%)	93 (18.52%)
August	71 (8.69%)	7 (4.60%)	54 (10.75%)
September	49 (5.99%)	7 (4.60 %)	40 (7.96%)
October	38 (4.65%)	6 (3.94 %)	26 (5.17%)
November	20 (2.44%)	7 (4.60%)	37 (7.37%)
December	21 (2.57%)	6 (3.94%)	31 (6.17%)
Total	817	152	502

Table V: Year-wise trend in antibiotic sensitivity and resistance rates of Salmonella typhi in three consecutive years (2019, 2020, 2021)

Antibiotic	Antibiotic resistance and sensitivity rates of Salmonella typhi n (%)					
	2019		2020		2021	
	Resistance	Sensitive	Resistance	Sensitive	Resistance	Sensitive
Ampicillin	630 (77.11%)	187 (22.88%)	117 (76.97%)	35 (23.03 %)	408 (81.27 %)	94 (18.72%)
Ceftriaxone	754 (92.28%)	63 (7.71%)	131 (86.18 %)	21 (13.82%)	446 (88.84 %)	56 (11.15%)
Cefixime	182 (22.27%)	635 (77.72%)	42 (27.63 %)	110 (72.37%)	137 (27.29%)	365 (72.70%)
Chloramphenicol	53 (6.48%)	764 (93.51%)	11 (7.24%)	141 (92.76%)	39 (7.76%)	463 (92.23 %)
Ciprofloxacin	177 (21.66%)	640 (78.33%)	15 (9.87%)	137 (90.13 %)	61 (12.15%)	441 (87.84 %)
Imipenem	29 (3.54%)	785 (96.08%)	5 (3.28 %)	147 (96.71 %)	15 (2.99 %)	487 (97.01%)
Aztreonam	48 (5.87%)	769 (94.12%)	8 (5.26 %)	144 (94.74 %)	21 (4.18 %)	481 (95.82%)
Azithromycin	253 (30.96%)	564 (69.03%)	82 (53.95%)	70 (46.05%)	163 (32.47 %)	339 (67.53 %)
Tetracycline	138 (16.89%)	679 (83.10%)	18 (11.84 %)	134 (88.16 %)	30 (5.98 %)	472 (94.04 %)
Co-trimoxazole	108 (13.21%)	709 (86.78%)	21 (13.82%)	131 (86.18 %)	72 (14.34%)	430 (92.23 %)

until it reaches its lowest number in November 20 (2.44%), also in 2021 the cases reach their peak and noticeably in the of June and July followed by August 96 (19.12%), 93 (18.52%) and 54 (10.75%), respectively, reaches its lowest number in march 12 (2,39%) but in 2020, there is a great disparity and difference in monitoring cases, as it reaches its highest in the first two months of the year January 34 (22.36%) and February 32 (21.05 %) and then begins to decrease to record a few numbers over all the months of the year, In general, it is clear from the results that in Iraq, the peak incidence of *Salmonella typhi* occurs between the months of June, July and August (dry season) as illustrated in Table IV .

The Antimicrobial Susceptibility Pattern of Salmonella typhi

As shown by Table V, there was a dramatic increase in the resistance of *S. typhi* to ceftriaxone (92.28%, 86.18%, 88.84%) and ampicillin (77.11%, 76.97%, 81.27%) in the three consecutive years (2019, 2020, 2021). The highest rates of *Salmonella typhi* resistance to ceftriaxone were in 2019, followed by 2021 and 2020, with close proportions. As for ampicillin, it reached the highest level of resistance to *Salmonella typhi* in 2021, followed by 2019 and then 2020 at similar rates of resistance for both years. Whereas, in the three consecutive years (2019, 2020, 2021) the highest sensitivity rates of *Salmonella typhi* was in imipenem (96.08%, 96.71%, 97.01%), followed by aztreonam in a similar proportion (94.12%, 94.74%, 95.82%) respectively, then followed by chloramphenicol (93.51%, 92.76%, 92.23%) As the top three sensitive antibiotics against *Salmonella typhi*. In the three consecutive years (2019, 2020, 2021), there was noticed and gradual increase in sensitivity of Salmonella typhi bacteria to tetracycline (83.10%, 88.16%, 94.04%) and cotrimoxazole (86.78%, 86.18%, 92.23%) with similar antibiotic sensitivity profile of *Salmonella typhi* for both antibiotic, then followed by ciprofloxacin (78.33%, 90.13%, 87.84%) and cefixime (77.72%, 72.37%, 72.70%). As for azithromycin, there is a decrease in the sensitivity profile to Salmonella typhi, especially in 2020, where it reached less than 50% (46.05%), while it was approaching 70% in 2019 and 2021 (69.03%, 67.53%) respectively.

DISCUSSION

The distribution of *Salmonella typhi* infection cases that were occurring in all governorates of Iraq and reported, documented and collected in the Communicable Diseases Control Center in Iraq (CDCI) showed varying numbers of cases in each 1 year of the three consecutive years (817, 152, 502) in 2019, 2020, 2021, respectively. There was a noticeably decrease in *Salmonella typhi* infection cases in 2020 compared to the other 2 years. A potential several reasons for this decreased rate of infection, such as the start of the COVID-19 pandemic and its subsequent repercussions like restrictions for both public and private gatherings including those where food and drinks are normally served and might provide opportunities for large-scale exposure to *Salmonella typhi* infection, such as receptions, parties, festivals, etc. which reduced the exposure to *Salmonella typhi* infection via contaminated food consumed outside the household moreover reduced exposure to infection due to travelling, people were generally discouraged to travel, the travel restrictions and permitted as only for essential purposes.[11] Our results do not exclude the reasons for reporting compliance when the healthcare system was overwhelmed by COVID-19 cases, and they were giving priority only to severe cases Salmonella typhi infection that requires admission to hospital and recorded them as a result of larger than usual number of *Salmonella typhi* cases with only mild to moderate symptoms that could have been unascertained and unreported in primary healthcare center. Moreover, the patients themselves could have refrained from seeking medical attention (to avoid contagion, reduce burden on healthcare, etc. Furthermore, increasing personal and household hygiene and continuous sterilisation to reduce the risk of infection with COVID-19 all of them were factors contributing to the decreased the Salmonella typhi infection incidence 2020.[12] The impact of the COVID-19 pandemic on *Salmonella typhi* infection was confirmed with a previous study (Lapo Mughini-Gras et al)[13] that explains the impact of the COVID-19 pandemic on human salmonellosis in the Netherlands. Regarding the monthly distribution of *Salmonella typhi* cases in each year in 2019, it was noted that the incidence of *Salmonella typhi* infection cases was constant with a small increase in the first quarter of the year (January, February, March, April), which begins to increase gradually in the second quarter of the year (May, June, July, August) with its maximum peak in June and July then gradually decreased in September in the third and fourth quarters of the year and continues to decrease significantly throughout the year 2020 at close rate of infection in each month in the year. In 2021, the incidence of *Salmonella typhi* infection had decreased in the first half of the year, until the months of June, July, and August, when the rate of infections started to increase noticeably with its maximum peak in June and July then returned to decreased in the fourth quarters of the year. It is clear from the results that in Iraq, the peak incidence of *Salmonella typhi* occurs between the months of June, July and August (dry season). Regarding the analysis of the distribution of *Salmonella typhi* cases in age groups and gender, it revealed the clustering of cases was recorded in the age group of young adults (18–35 years), and most cases of *Salmonella typhi* were males in all three consecutive tears. The plausible explanation for this age group predominance is the fact that age groups have more outdoor exposure and are more likely to consume street foods as compared to other age groups. Street food consumption is an important risk factor for *Salmonella typhi* which usually results from eating raw or undercooked meat, poultry, eggs, or egg products or drinking unpasteurised milk. Also, reasonable explanation for the male predominance because of the similar reasons that explain young adults (18–35 years) prevalence. The results of this study are in agreement with the previous studies (Umair et al.[14] that conclude the distribution of most of the cases of *S. typhi* belonged to 18–25 years and males. In the analysis of sensitivity and resistance pattern of *Salmonella typhi* to common antimicrobial agents in three consecutive years (2019, 2020, 2021), there was a sharp rise in resistance rates of the *S. typhi* isolates to ceftriaxone and ampicillin, with the highest sensitivity rates of *Salmonella typhi* that were in imipenem followed by aztreonam then followed by chloramphenicol as the top three sensitive antibiotics against *Salmonella typhi* furthermore gradual increase in sensitivity of *Salmonella typhi* to tetracycline and cotrimoxazole with similar antibiotic sensitivity profile for both antibiotics then followed by ciprofloxacin and cefixime but for azithromycin, there is a decrease in the sensitivity profile to Salmonella typhi, especially in 2020 where it reached less than 50%. Although the emergence of antimicrobial resistance is a natural phenomenon, but overprescribing of antibiotics and misuse in humans and animals is accelerating this resistance. The increase in consumption of antibiotics that are easily available over the counter and not clinically justified owing to the lack of any health regulation across the country specially ceftriaxone and ampicillin which are used as first-line treatment for many infections in hospitals and community and overuse of them lead to increase resistance and an important driver of emerging widespread drug-resistant pathogens including *S. typhi*. The frequency and *S. typhi* profiles and their antibiotic sensitivity pattern vary widely from one geographical region to another as well as from one country to country and even center to center or hospital to another. The results of this study were confirmed with the previous reports studies[15] that reported a significantly ceftriaxone-resistant Salmonella typhi outbreak in Pakistan[16] that showed injudicious use of antimicrobials has resulted in the development of antimicrobial resistance among Salmonella pathogens and Salmonella showed widespread resistant to ampicillin which resulted in the use of alternative antimicrobials like fluoroquinolones. The results of this study also confirmed with some results of studies[17] that conclude Salmonella typhi showed the highest sensitivity to imipenem 100 (n = 39) and less sensitivity with ampicillin (14%) and not confirmed with other result of the same study in sensitivity of azithromycin 95%, ceftriaxone 49.4%, cotrimoxazole 33.3%, chloramphenicol 26% and lowest sensitivity was to ciprofloxacin 3.7%.

Our study had a few limitations. First, the data that were taken was during the COVID-19 pandemic and its subsequent repercussions. This may be due to several reasons, including:

- Healthcare strain: The pandemic may have strained healthcare systems, affecting the ability to collect and report Salmonella data.
- Changes in reporting: Shifting priorities during the pandemic could lead to changes in reporting practices, impacting the accuracy and timeliness of Salmonella data.
- Public behaviour changes: Measures like lockdowns and increased hygiene may influence the spread of Salmonella as people change their behaviours.
- Testing challenges: The focus on COVID-19 testing may affect resources for testing other infections, potentially leading to underreporting or delays in identifying Salmonella cases.
- Data Collection Disruptions: Disruptions in routine healthcare services and research during the pandemic may affect the availability and quality of Salmonella-related data.

Secondly, we did not investigate factors responsible for increased resistance. These factors include recent use of antibiotics, over-the-counter use of drugs and the knowledge, attitude and practice of antibiotic prescription and use among healthcare workers and patients. Furthermore, we did not explore the effect of these factors on the prevalence of the burden of *Salmonella typhi*. Additionally, the role of several socio-economic factors, such as sanitation, hygiene, source of water supply and eating habits, was not established in this study. Thirdly, our study did not examine the role of genetic factors in conferring drug resistance to bacterial strains. We suggest conducting frequent studies in the future to keep pace with changes in the prevalence and antimicrobial resistance profile of Salmonella typhi infection in Iraq. Exploring factors contributing to increasing resistance is recommended. This can be achieved through further molecular studies, including genotype studies to detect multidrug resistance in *S. typhi*.

CONCLUSIONS

According to our findings in three consecutive years (2019, 2020, 2021), there was a sharp rise in resistance rates of the *S. typhi* isolates to ceftriaxone and ampicillin, so these antibiotics cannot be used as a potential option for the treatment due to their resistance. There were the highest sensitivity rates to imipenem followed by aztreonam then followed by chloramphenicol as the top three sensitive antibiotics against Salmonella typhi. Other antibiotic like tetracycline, cotrimoxazole, ciprofloxacin, cefixime and azithromycin can also be used, but their use depends on the sensitivity and resistance profile of *Salmonella typhi*. Controlling the prevalence and antimicrobial resistance of *Salmonella typhi* infection involves a multifaceted approach that combines public health measures, healthcare practices and community education. Some recommendations are as follows: 1) water, sanitation, and hygiene (WASH) Improvement, 2)vaccination to reduce the incidence of infection, 3) surveillance and reporting to monitor the prevalence of *Salmonella typhi* infections and detect outbreaks, 4) infection control in healthcare settings to prevent the spread of infection among patients and healthcare workers, 5) rational use of antibiotics through the development and implementation of guidelines for appropriate antibiotic use in the treatment of typhoid fever, 6) educate communities about the risks of *Salmonella typhi* infection and the importance of preventive measures, 7) traveler education about the risks of typhoid fever in endemic areas and recommend preventive measures, including vaccination, 8) food safety measures to prevent contamination of food and water sources, 9) collaborate with international organisations to share best practices, data and strategies for controlling typhoid fever and antimicrobial resistance, 10) invest in research to develop new diagnostic tools, vaccines and treatment options for typhoid fever and 10) advocate for policies that prioritise public health and antimicrobial resistance prevention.

REFERENCES

1. Jajere SM. A review of Salmonella enterica with particular focus on the pathogenicity and virulence factors, host specificity and antimicrobial resistance including multidrug resistance. Veterin World 2019; 12(4): 504.
2. Bhunia AK. Salmonella enterica. InFoodborne microbial pathogens 2018 (pp. 271–287). Springer, New York, NY.
3. Smith SI, Seriki A, Ajayi A. Typhoidal and non-typhoidal Salmonella infections in Africa. Eur J Clin Microbiol Infect Dis 2016; 35(12): 1913–22.
4. Ferrari RG, Rosario DK, Cunha-Neto A, Mano SB, Figueiredo EE, Conte-Junior CA. Worldwide epidemiology of Salmonella serovars in animal-based foods: a meta-analysis. Appl Environ Microbiol 2019; 85(14): e00591-19.
5. Sánchez-Vargas FM, Abu-El-Haija MA, Gómez-Duarte OG. Salmonella infections: an update on epidemiology, management, and prevention. Travel Med Infect Di 2011; 9(6): 263–77.
6. Watkins LK, Winstead A, Appiah GD, Friedman CR, Medalla F, Hughes MJ, et al. Update on extensively drug-resistant Salmonella serotype Typhi infections among travelers to or from Pakistan and report of ceftriaxone-resistant Salmonella serotype Typhi infections among travelers to Iraq—United States, 2018–2019. Morbid Mortal Week Report 2020; 69(20): 618.
7. Khadka P, Thapaliya J, Thapa S. Susceptibility pattern of Salmonella enterica against commonly prescribed antibiotics, to febrile-pediatric cases, in low-income countries. BMC Pediatr. 2021; 21(1): 1-8.
8. Chuang CH, Su LH, Perera J, Carlos C, Tan BH, Kumarasinghe G, et al. Surveillance of antimicrobial resistance of Salmonella enterica serotype Typhi in seven Asian countries. Epidemiol Infect. 2009; 137(2): 266–9.
9. Britto CD, Wong VK, Dougan G, Pollard AJ. A systematic review of antimicrobial resistance in Salmonella enterica serovar Typhi, the etiological agent of typhoid. PLoS neglected tropical diseases. 2018;12(10): e0006779.
10. Dyson ZA, Klemm EJ, Palmer S, Dougan G. Antibiotic resistance and typhoid. Clin Infect Dis. 2019;68(Supplement_2): S165–70.
11. Banai R. Pandemic and the planning of resilient cities and regions. Cities. 2020; 106: 102929.
12. Martelli F, Lambert M, Butt P, Cheney T, Tatone FA, Callaby R, et al. Evaluation of an enhanced cleaning and disinfection protocol in Salmonella contaminated pig holdings in the United Kingdom. PloS One 2017;12(6): e0178897.
13. Mughini-Gras L, Pinedo LC, Pijnacker R, Van Den Beld M, Wit B, Veldman K, et al. Impact of the COVID-19 pandemic on human salmonellosis in the Netherlands. Epidemiol Infect 2021; 149.
14. Umair M, Siddiqui SA. Antibiotic susceptibility patterns of Salmonella typhi and Salmonella paratyphi in a tertiary care hospital in Islamabad. Cureus. 2020; 12(9): 22-30.
15. Yousafzai MT, Qamar FN, Shakoor S, Saleem K, Lohana H, Karim S, et al. Ceftriaxone-resistant Salmonella typhi outbreak in Hyderabad City of Sindh, Pakistan: high time for the introduction of typhoid conjugate vaccine. Clin Infect Dis 2019;68(Supplement_1): S16–21.
16. KaushiK D, Mohan M, BoraDe DM, Swami OC. Ampicillin: rise fall and resurgence. J Clin Diagn Res 2014; 8(5): ME01.
17. Shah SA, Nadeem M, Syed SA, Abidi ST, Khan N, Bano N. Antimicrobial sensitivity pattern of Salmonella typhi: emergence of resistant strains. Cureus 2020; 12(11): 10-17.