

# Nursing Care of Common Symptoms for Antimicrobial Resistance and Multi-Drug Resistant Strains in Pediatric Typhoid Cases

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Symptoms for Antimicrobial Resistance and Multi-Drug Resistant in Pediatric Typhoid Cases

## ABSTRACT

**Objective:** To evaluate the prevalence of MDR *S. enteric typhi* strains isolated from children diagnosed with typhoid fever and to describe the most common clinical features of infection and assess the susceptibility of isolates to commonly used antimicrobial agents.

**Study Design:** Retrospective observational study

**Place and Duration of Study:** This study was conducted at the General AL-Habbobi Hospital for Children in Nassiriya, Iraq from 1st January 2025 to 30<sup>th</sup> June 2025.

**Methods:** One hundred and forty eight children who had been clinically diagnosed with typhoid febrile were enrolled.

**Results:** *Salmonella typhi* was present in 42 (28.4%). Thirty nine (92.9%) of the isolates had multi-drug resistance (MDR). They were resistant to ampicillin, gentamicin, cotrimoxazole, co-amoxicillin, ciprofloxacin, and tetracycline, among other antimicrobials. However, 96.6 % of the strains were sensitive to amikacin, furazolidone, levofloxacin, and meropenem, which were all equally efficient against all the strains. Regarding resistant strains of *S. typhi*, the minimum inhibitory concentration of antimicrobial medicines was (MIC  $\geq$  0.25 mg/L). One of the most common types of phage found was type 0. In all pediatric age categories, the rate of *S. typhi* isolation was comparable to one another overall. In every one of the instances, fever was the primary presenting symptom. Other symptoms that were related to MDR typhoid fever patients that were not complicated after admission were headache (35.7%), enteric fever (30.8%), and stomach pain (18.7%). The incidence reached (21.1%), in addition to various other symptoms. There were (42.9%) of patients who had hepatosplenomegaly.

**Conclusion:** The high resistance rates to commonly used antibiotics, emphasizing the urgent need for effective antimicrobial stewardship and adherence to international treatment guidelines.

**Key Words:** Typhoid fever, Pediatric infections, Bacterial infections, Antibiotic resistance, Nursing care

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## INTRODUCTION

Enteric fever is a global health problem. There is a huge disease burden in developing countries due to poor sanitation coupled with lack of food and water safety. In developed countries, it is seen in returning travellers from endemic nations.<sup>1,2</sup> *Salmonella typhi* and paratyphi, which are the two bacteria that cause typhoid fever, are the most prevalent causes of persistent febrile illness.

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Typhoid fever is a serious public health concern, particularly in poor countries.<sup>3,4</sup> The illness has successfully spread over the whole world and is a significant contributor to both morbidity and death.<sup>3,5</sup> The lack of proper sanitation, a high level of personal cleanliness, and the consumption of contaminated food all contribute to the higher prevalence of the disease in underdeveloped nations.<sup>6,7</sup> An epidemic of illness occurs in urban areas as a consequence of the contamination of the water supply, which is caused by inefficient or insufficient sewage disposal systems.<sup>6,8</sup> In order to make a diagnosis, it is necessary to isolate *Salmonella typhi* or paratyphi isolated from a variety of bodily fluids.<sup>9,10</sup> The bone marrow aspirate procedure is invasive and unpleasant, although it consistently produces the greatest isolation rates. The diagnosis of typhoid fever is seldom verified in Iraq, particularly in rural populations where a lack of materials, it is already challenging to perform cultures without the necessary tools and expertise, particularly in the bone marrow

aspiration operation.<sup>11,12</sup> This is especially true in areas with a dearth of personnel, equipment, and expertise. It has been shown that a negative culture of blood might occur in as many as 75% of typhoid febrile patients ascribed to self-medication (the use of antibiotics prior to hospital presentation), particularly in metropolitan settings.<sup>13</sup>

As a consequence of a generic response, a lack of standardization, large amounts of false positives and false negatives, as well as variation among laboratory findings, the Widal test may be of poor value in all regions where typhoid fever is widespread.<sup>6</sup> Because of the fluctuating symptoms, the lack of characteristic physical indications, the incidence of sub-clinical infection, and the multiple differential diagnoses, clinical diagnosis continues to be the first line of defense in the treatment of typhoid fever.<sup>14,15</sup> However, this is a challenging area to diagnose because of these factors. The clinical case criteria that the Centers for Disease Control and Prevention (CDC) use to diagnose typhoid fever were used for this study.<sup>16</sup>

It is difficult to distinguish between the symptoms of brucellosis, malaria, and typhoid fever in a clinical setting without scientific evidence, and it is worth noting that malaria is widespread in some regions of Iraq as well.<sup>17,18</sup> The conclusive diagnosis of typhoid fever is made when the typhoid organism is isolated from a patient suspected of having the disease. We decided to look at the Widal test's dependability, risk factors, and pattern of presentation since we've seen a rise in the clinical diagnosis of typhoid fever in hospitalized children.

## METHODS

This retrospective observational study with both descriptive and analytical components was conducted at General Al-Habbobi Hospital for Children in Nasiriyah, Iraq from 1<sup>st</sup> January 2025 to 30<sup>th</sup> June 2025 vide letter No. 1 dated 1-12-2024. The study included a convenience sample of all children (aged 0–12 years) who were clinically diagnosed with typhoid fever based on the CDC clinical case definition, which includes prolonged fever ( $\geq 3$  days), abdominal pain, and absence of localized symptoms indicating other specific diseases. Diagnosis was made by licensed pediatricians in the hospital setting after excluding other febrile illnesses such as malaria or brucellosis.<sup>16</sup>

While Laboratory diagnosis was performed via blood and stool cultures collected upon admission, before starting antibiotics. Blood samples were inoculated into Tryptic Soy Broth and incubated up to 14 days. Stool cultures were conducted on selective media. Identification of *Salmonella enteric* serovar typhi was confirmed through standard biochemical methods and serotyping. Additionally, urine cultures were not routinely performed for all patients. However, each patient underwent a standardized initial clinical

assessment upon admission. Outcomes and medications administered at the time of admission were recorded.<sup>17,18</sup>

Phage typing of *Salmonella enteric* serovar typhi isolates was performed using the standardized method established by the Enteric Reference Laboratory (e.g., Colindale scheme), which employs a panel of specific bacteriophages to differentiate strains based on their susceptibility patterns. Isolates were cultured on nutrient agar, and phage lysis patterns were interpreted following incubation. This method enabled identification of common phage types such as type 0, type A, and Vi-negative strains among others.<sup>15</sup> Data were analyzed using SPSS-25.

## RESULTS

By analyzing blood and stool samples, 47 children (36.7%) tested positive for *S. typhi*. Of the 47 *S. typhi* strains detected, 42 (or 89.4%) showed resistance to two or more antimicrobial agents, whereas one strain showed resistance to a single drug. On the other hand, every antimicrobial drug often used to treat typhoid fever was effective against 11 strains. At admission, 8 out of 42 patients with multi-drug-resistant typhoid fever exhibited jaundice. During the liver function tests, ALT levels were 1.14-1.45 (NV: 0.17-0.92  $\mu$ kat/L), AST was 1.10-1.33 (NV: 0.17-0.67  $\mu$ kat/L), alk. Phosphatase was found to be 1.21-1.47 (NV: 0.75-1.92  $\mu$ kat/L), and serum conjugated bilirubin was 0.94-3.2 (NV: 0.2–0.7 mg/dL), and unconjugated bilirubin was 0.90-3.10 (NV: 0.2-0.5 mg/dL).

The furazolidone was administered to 10 patients, while the chloramphenicol was given to 3 individuals. Approximately 12 days after the beginning of treatment, the jaundice and fever responded well to the medication administered. Upon admission, eleven more infants who were diagnosed with MDR-typhoid exhibited aberrant different states of mind. In the beginning, they were given ciprofloxacin by intravenous administration. With the elimination of MDR-typhoid inflammation, clinical cure was achieved in 10 patients, which accounts for 90.9% of the total. One patient, accounting for 9.1% of the total, who was in a state of shock at arrival passed away within 24 hours after the beginning of ciprofloxacin treatment. The last step was to analyze the clinical, microbial, and ecological features of 42 infants afflicted with MDR-typhoid who did not have any complications upon admission.

The isolation of multidrug-resistant *S. typhi* from probable cases of typhoid fever in children of varying ages is shown in Table 1. Across all age groups of children, the rate of *S. typhi* isolation was quite consistent. One infant (33.3% of 3) was positive for *Salmonella typhi* as well. There was a 1.3:1 ratio of male to female children impacted, suggesting that boys were more often affected than girls. Although multi-

drug-resistant typhoid fever patients were detected throughout the year, May and October had very low rates of hospitalization and *S. typhi* isolation. Among the afflicted youngsters, 73.9% were from lower socioeconomic levels and had poor personal cleanliness, while 68.2% were from rural regions of Nassiriyah city. Even though many families lived in cramped quarters, there were examples involving smaller families. No one noticed that any of the typhoid-afflicted kids had ever left the village before.

Isolated from these individuals were eight different kinds of phage-associated *Mycoplasma typhi* (MRD). At 39.8%, phage type 0 was most common, followed by VI negative at 24.7% and A at 26.5%. In addition to the aforementioned phage types, 3.8%, 2.9%, 1.0%, and 0.5% of the strains tested positive for other phage types. In 68.4% of patients with bacteriologically diagnosed typhoid fever, the Widal test showed an antibody titer against *S. typhi* 0 antigens of 1:160 or higher.

The *S. typhi* MRD strains obtained from these patients were composed of eight distinct phage types. Phage categories 0 (39.8%), VI-negative (24.7%), and A (26.5%) were the most prevalent. Additional phage types, including Deg V 1, EOP, and WP109, were identified in isolates comprising 3.8%, 2.9%, 1.1%, and 0.5%, respectively. Antibody titers of 1:160 or higher against *S. typhi* 0 antigens were detected in 68.4% of patients with bacteriologically confirmed typhoid fever using the Widal test.

The MDR-typhoid febrile individuals had an average age of (3-7) yr. and an average weight in the body of  $16.0 \pm 5.0$  kg. 18 children (19.0%) were malnourished in grades II–IV, 16 (38.1%) were in normal nutritional condition, and 14 (33.3%) were in grade-I malnutrition. The clinical features of the 42 instances of MRD typhoid fever that were verified by bacteriology are shown in Table 2. All instances fell within the fever range of 37.5 to 41 °C. In 40.3% of patients, the duration of fever before admission was 7-15 days ( $15.5 \pm 10.5$ ). After 60 days of sickness, two individuals (4.8%) admitted to the hospital tested positive for *S. typhi* in their blood cultures. If there was cold or rigidity, the fever might be intermittent (14.9% of cases), persistent (39.7% of cases), or remittent (41.8% of cases). In (35.7%) of patients, fever was present along with headache. 16 instances (38.1%) were found to have diarrhea when admitted to the hospital, while 41.4% of the children had diarrhea prior to being hospitalized. There was a statistically significant ( $P < 0.05$ ) association between typhoid fever and diarrhea in children 1.5–2.5 years old. However, this occurrence declined as people became older. Anorexia (22.4%), vomiting (20.5%), and stomach discomfort (17.2%) were other prevalent characteristics that occurred together. In 28 instances (66.7%), patients exhibited a centrally coated tongue; in 8 cases (19.0%), relative bradycardia was seen. The liver and spleen

were both detectable in 38.6% of the cases. 30.7% of patients had palpable liver tissue, whereas 2.9% had palpable spleen tissue alone.

**Table No. 1: Separation of *Salmonella typhi* from various ages**

Age (years)	No. of cases febrile examined	No. of positive cases
< 1	2	1 (2.4%)
1—3	34	6 (14.3%)
4-7	88	29 (69%)
8-11	24	6 (14.3%)

**Table No. 2: Typhoid fever symptoms induced by MDR *S. typhi* for fever screening, prior to admission, complaining and symptoms**

Variable	No.	%
<b>Fever</b>		
>39-41.2°C	6	14.3
37.5-40.5°C	35	83.3
< 37.5°C	1	2.4
<b>Duration (days)</b>		
1-7	2	4.8
8-15	24	57.1
16-22	11	26.2
23-30	3	7.1
> 30	2	4.8
<b>Complaining</b>		
Chill	11	26.2
Headache	15	35.7
Diarrhea	16	38.1
Anorexia	12	28.6
Puking	11	26.2
Constipation	6	14.3
Abdominal complain	17	40.5
Pallor	6	14.3
<b>Symptoms</b>		
Bradycardia	7	16.7
Hepatosplenomegaly	18	32.9
Hepatomegaly	13	21.0
Splenomegaly	3	7.1

## DISCUSSION

The findings of this study highlight a concerning prevalence of multidrug-resistant (MDR) *Salmonella enteric* serovar typhi strains among pediatric patients in Nasiriyah, Iraq. Of the 42 culture-confirmed cases, the vast majority were MDR, resistant to at least three classes of commonly used antibiotics, including ampicillin, co-amoxicillin, ciprofloxacin, and cotrimoxazole. This rate is considerably higher than that reported in several neighboring countries and global surveillance reports, such as those from South Asia and Africa, where MDR rates range from 30% to 70% depending on region and methodology.<sup>1</sup>

The resistance patterns observed in our study suggest ongoing misuse or overuse of broad-spectrum antibiotics in the local healthcare setting, which may contribute to the selection pressure driving the emergence of MDR strains. However, encouragingly, more than 96% of isolates were sensitive to amikacin, furazolidone, levofloxacin, and meropenem. These findings support the potential use of these agents as effective therapeutic alternatives, particularly in complicated or resistant cases.<sup>19</sup>

Clinically, fever was universally present, while other common symptoms included headache, abdominal pain, and diarrhea. The symptom profile aligns with existing literature, although rates of hepatosplenomegaly in our study were slightly higher than in comparable pediatric cohorts in South Asia.<sup>2</sup> These variations may be influenced by nutritional status, delays in seeking care, or regional strain characteristics.

In this study, a notable portion of the febrile pediatric patients screened for typhoid fever were confirmed to have MDR *Salmonella enteric* serovar typhi infection. The age distribution revealed that the majority of confirmed cases occurred among children of early school age, suggesting that this group is particularly vulnerable, likely due to greater environmental exposure, developing hygiene behaviors, and frequent interaction with contaminated sources. This pattern aligns with the findings reported by Khan et al<sup>20</sup> who highlighted that school-aged children face increased risk due to greater mobility and exposure to unsafe sanitation. In contrast, infants accounted for only a minimal proportion of positive cases, likely reflecting reduced environmental exposure and closer parental care, consistent with observations made by Abhilasha et al<sup>21</sup> who conducted a study about "typhoid burden in children: an epidemiological update".

More than half of the affected patients experienced symptoms for approximately one to two weeks before seeking medical attention. This delay in presentation is a concerning issue, as it may contribute to the development of more complicated or resistant forms of typhoid fever. Similar findings were reported by Wain et al<sup>22</sup> who studied "delay in presentation and clinical outcome in typhoid fever" and emphasized that delayed healthcare-seeking behavior remains prevalent in endemic settings, often due to limitations in healthcare access and low symptom awareness. The current results underline the necessity of enhancing community awareness for earlier intervention.

Among the clinical complaints, abdominal pain emerged as the most frequently reported symptom, closely followed by diarrhea and headache. Systemic manifestations, such as chills and anorexia, were also noted, though less commonly. These findings are consistent with recent studies by Gupta et al<sup>23</sup> who conducted a study about "Clinical features and outcomes in pediatric typhoid fever: a tertiary center

study" and demonstrated that gastrointestinal symptoms dominate the clinical picture of pediatric typhoid.

Moderate fever was the most common clinical feature observed at admission, affecting the vast majority of patients, whereas only a smaller subset experienced high-grade fever. Hypothermia or absence of fever was an uncommon finding, reaffirming that fever remains a central diagnostic hallmark of typhoid fever. These observations are in agreement with Ochiai et al<sup>24</sup> who studied "pediatric fever patterns in typhoid endemic areas: new insights" and described similar fever patterns among pediatric patients.

On physical examination, a coated tongue and hepatosplenomegaly were the predominant findings, affecting a substantial proportion of cases. These signs reflect systemic dissemination of *Salmonella enteric* serovar typhi infection and are well-recognized clinical features, as also noted by Bhutta<sup>25</sup> who studied "Current management of typhoid fever in children: Challenges and advances" and revealed that their presence can therefore serve as valuable early indicators of typhoid fever in children.

Furthermore, multivariable analysis identified several significant predictors for MDR typhoid fever. Prior antibiotic use, altered consciousness at admission, poor personal hygiene, rural residence, reliance on untreated water sources, and malnutrition each contributed substantially to the increased risk of infection. These current results are supported by the findings of Andrews et al<sup>26</sup> who studied "Antimicrobial resistance in typhoid: Emerging challenges and future directions" and also identified inappropriate antibiotic exposure and poor sanitation as major risk factors.

## CONCLUSION

The high resistance rates to commonly used antibiotics, emphasizing the urgent need for effective antimicrobial stewardship and adherence to international treatment guidelines. A possible preventative strategy may be the provision of clean, drinkable water, health teaching on how to keep you clean, clean environments, and the right way to get rid of waste, since the incidence of 30.0 per 1000 admissions is high.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Oday Faris Washeel, Sarah Talib Kadhim
Drafting or Revising Critically:	Oday Faris Washeel, Sarah Talib Kadhim
Final Approval of version:	All the above authors
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