

Management of Typhoid Fever in Children: A Literature Review

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Article Info	Abstract
<p>Article History: Received: 20 February 2025 Revised: 25 February 2025 Accepted: 15 Maret 2025</p> <p>Keywords: Antibiotic Therapy; Children; Typhoid Fever; <i>Salmonella enterica</i> Typhi</p> <p>Corresponding Author: Muhammad Assagaf Sayyidusy Mandala Waluya University</p> <p>Email: alafasgaf@gmail.com</p>	<p>Background: Typhoid fever is an infectious disease caused by the bacterium <i>Salmonella enterica</i> serotype Typhi (<i>S. Typhi</i>). It is one of the most common causes of fever, often presenting without distinctive features or specific signs of illness, particularly in areas with limited water sanitation and medical facilities.</p> <p>Purpose: To explore the management of typhoid fever in children.</p> <p>Methods: A systematic literature search was conducted using several databases, including ScienceDirect and Google Scholar. Boolean terms and search restrictions were applied to identify articles that appropriately addressed the research question. Inclusion criteria included full-text articles published between 2022 to 2025.</p> <p>Results: The search yielded 10 articles that met the predefined criteria and keywords.</p> <p>Conclusion: Active involvement of parents plays a crucial role in the management of typhoid fever in children. This role includes supervising treatment adherence, recognizing clinical symptoms, and understanding the importance of completing antibiotic therapy as prescribed by medical professionals.</p>

Background

Typhoid fever is an infectious disease caused by the bacterium *Salmonella Typhi*. It spreads through contaminated food or water, especially in areas with poor sanitation. Common symptoms include high fever, fatigue, abdominal pain, and either constipation or diarrhea (Hadju et al., 2024). If left untreated, typhoid fever can become dangerous and even life-threatening. Vaccination and proper hygiene in food and water consumption are the most effective preventive measures (I. Putu Sudayasa et al., 2022).

According to the World Health Organization (WHO), typhoid fever remains a leading cause of morbidity and mortality in low- and middle-income countries, with an estimated 12.5 to 16.3 million cases and approximately 140,000 deaths globally each year. WHO has recommended the use of the Typhoid Conjugate Vaccine (TCV) in endemic countries as part of routine immunization programs to help reduce the burden of this disease (Islamiah et al., 2019).

WHO also promotes vaccination as a strategy to combat antibiotic resistance, considering it an effective tool to curb the rising challenge of drug-resistant bacteria. In December 2017, WHO prequalified the Typbar-TCV vaccine for use in children aged six months and older (A. M. Andas et al., 2024). The organization also recommends the use of this vaccine in regions experiencing outbreaks or high numbers of drug-resistant typhoid cases (Darmayanti Waluyo et al., 2022). Children under the age of five are noted to be the most vulnerable group. A study

in Southeast Asia reported a typhoid incidence rate of 219.8 cases per 100,000 population, reinforcing the notion that typhoid fever continues to pose a major public health challenge (Purnamasari, Nazaruddin, et al., 2023).

The aim of this literature review is to identify the management strategies of typhoid fever in children, both within the family environment and in clinical settings during hospitalization.

Method

A systematic literature search was conducted through several databases, including ScienceDirect and Google Scholar, using Boolean terms. The articles included were selected based on their relevance to the research question and methodology, which encompassed study samples, sample sizes, research design, results, and levels of evidence. The authors systematically conducted a literature search using the PICO method as follows:

- Patient : Children
- Intervention : Antibiotic
- Comparison : -
- Outcome : Typhoid Fever

Subsequently, the author conducted a literature search on several databases, namely ScienceDirect and Google Scholar, using Boolean terms and limitations to find relevant articles that address the research question. The Boolean terms used were: “children” AND “antibiotic” AND “typhoid fever”, with the limitation criteria being full-text articles and publications from the years 2022–2025.

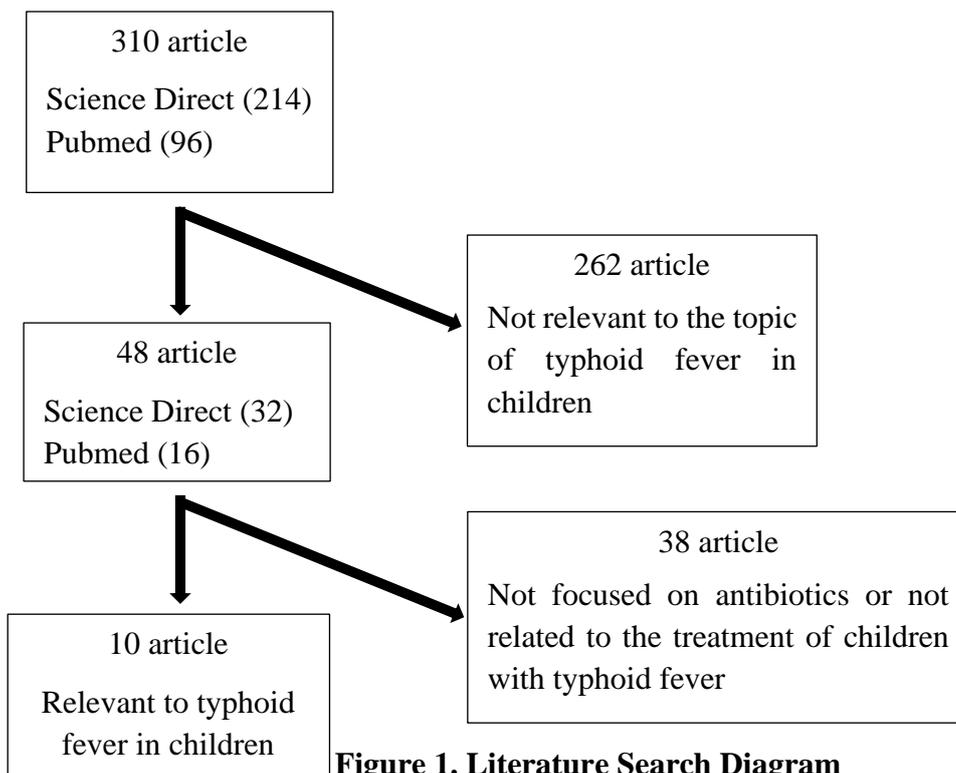


Figure 1. Literature Search Diagram

Results

The first article discusses standard protocols for assessing the performance of in-vitro diagnostic tests for typhoid fever, both in laboratories and in field settings. The analysis of the journal in this article shows that it offers protocols for evaluating in-vitro diagnostic (IVD) performance for typhoid fever, which is crucial for endemic areas such as India and Southeast Asia. Given the limitations of blood cultures and serological tests in diagnosing typhoid, this document provides the first comprehensive guideline for the analytical and clinical evaluation of typhoid IVDs. Additionally, the journal recommends the establishment of national-level biobank resources for typhoid. This protocol is expected to serve as a reference to improve diagnostic accuracy and support the development of high-performing, affordable molecular or antigen-based tests (Viswanathan et al., 2025).

The second article discusses the duration of immune response after a single dose of typhoid conjugate vaccine (TCV) for *Salmonella typhi* in children in Hyderabad, Pakistan. The analysis reveals that after one TCV dose, 95.8% of children seroconverted by week 4–6. The highest response was observed in children aged ≤ 2 years, although this group also experienced the fastest decline in antibodies. Four years after vaccination, 75.6% of children maintained seroconversion. During the follow-up period, ten confirmed typhoid cases were recorded, most without complications. Children who received a second dose showed stronger and more persistent immune responses (Qamar et al., 2024).

The third article on the effectiveness of typhoid conjugate vaccine includes the final analysis of a 4-year phase 3 randomized controlled trial in Malawi, specifically in children. Results show that out of 28,130 vaccinated children, 134 blood culture-confirmed typhoid cases were identified during the study, with TCV efficacy at 78.3% (95% CI: 66.3–86.1%) in the intent-to-treat analysis and 80% (95% CI: 68.3–87.3%) in the per-protocol analysis. Vaccine efficacy remained stable over 4.6 years with a non-significant annual decline of 1.3%. Similar effectiveness was observed across all age and gender groups and study locations. Most *S. Typhi* isolates (99%) were multi-drug resistant, but no extensively drug-resistant (XDR) strains were found. The vaccine was deemed safe, with no serious adverse events reported and only one typhoid-related death occurring in the control (MenA) group (Patel et al., 2024).

The fourth article addresses fever in travelers returning from tropical and subtropical regions: a hospital-based study on factors influencing investigation and diagnosis in both children and adults. Analysis shows that 2,441 patients were involved (90% adults and 10% children), with mean ages of 35 years for adults and 6 years for children. Most travel destinations were in Sub-Saharan Africa (40.7%). The main travel reasons were tourism (62.2%) and visiting friends and relatives (VFR) (24.5%), with children accounting for a higher percentage (34.8%). About 83.8% of participants had no comorbidities, and 13% sought medical help at night (Sondén et al., 2025).

The fifth article discusses parental acceptance of typhoid conjugate vaccine for children aged 6 months to 15 years in an outbreak-affected area in Lyari Town, Karachi, Pakistan. The analysis indicates that 2,325 children were assessed, and 79.9% received TCV, with most vaccinations conducted in schools. Parental willingness to vaccinate their children was high at 92.2%. Factors that increased the likelihood of child vaccination included

knowledge about the campaign (aOR: 4.57), willingness to vaccinate (aOR: 2.54), understanding service hours (aOR: 1.92), and lower vaccine hesitancy (aOR: 1.39–1.49) (Batool et al., 2023).

The sixth article discusses pyogenic vertebral osteomyelitis and iliopsoas muscle abscess caused by non-typhoidal *Salmonella* infection. *Salmonella* infection can be rapidly detected through genetic testing in adolescent males with healthy immune systems and no hemoglobinopathies. The analysis reveals an unusual case of lumbar vertebral osteomyelitis and psoas abscess due to non-typhoidal *Salmonella* (NTS) in an adolescent with Marfan syndrome. Although the initial diagnosis was challenging due to negative culture results, genetic testing enabled rapid pathogen identification and facilitated targeted therapy. Treatment was limited by antibiotic allergies and Marfan syndrome-related risks. This article highlights the need to consider NTS as a cause of lumbar spondylitis in children and the importance of genetic testing to accelerate management. However, there is a lack of evidence on treatment duration, indicating the need for further research (Hirai et al., 2025).

The seventh article discusses the frequency and factors associated with malaria, typhoid, and co-infections in febrile children aged six months to twelve years at Kampala International University Teaching Hospital in western Uganda. This cross-sectional study used a questionnaire covering demographic, clinical, and behavioral information. Blood samples were taken for malaria via peripheral smear and typhoid culture from a total of 108 consecutively consenting participants. Ethical clearance was granted by the KIU-TH Research and Ethics Committee, reference number UG-REC-023/201,834. Multivariate regression analysis was conducted using Stata 14.0 software (StataCorp, 2015) with a 95% confidence interval (Nakisuyi et al., 2023).

The eighth article examines the impact of a mass typhoid conjugate vaccine campaign on antimicrobial prescribing for children in Harare, Zimbabwe: a mixed-methods study. The analysis reveals that among 27,107 children who visited, 66.2% received antimicrobial prescriptions, mainly for respiratory infections and diarrhea. Typhoid cases increased during the rainy season and remained sporadic due to poor sanitation and high population density. The Typbar-TCV vaccination campaign did not significantly reduce antimicrobial use for typhoid, as diagnostic challenges and clinical uncertainty made it difficult for health workers to limit antibiotic prescriptions. Socioeconomic factors, lack of medical personnel, and limited access to diagnostic facilities worsened the trend of overprescription, despite existing guidelines recommending otherwise (Olaru et al., 2023).

The ninth article reports on the incidence of typhoid fever in Burkina Faso, the Democratic Republic of Congo, Ethiopia, Ghana, Madagascar, and Nigeria (Severe Typhoid in Africa program): a population-based study. Analysis shows that the study involved 25 healthcare facilities across six African countries, with 82,491 patients and 27,544 blood cultures, of which 7.7% tested positive for pathogens. *Salmonella Typhi* (STyphi) was identified in 16.2% of positive cases, with the highest incidence among children aged 2–14 years in rural areas such as the DRC, Madagascar, and Burkina Faso. The inpatient mortality rate was 5.9%, with serious complications like intestinal perforation occurring in nearly 29% of cases. Antibiotic resistance was high, especially to ampicillin, cotrimoxazole, and ciprofloxacin, with most multidrug-resistant cases

found in Nigeria, the DRC, and Ghana. These findings highlight the heavy burden of typhoid and the treatment challenges posed by antimicrobial resistance in the study areas (Marks et al., 2024).

The tenth article discusses immune responses to two doses of typhoid conjugate vaccine in children in Nepal. Analysis of this study shows that the Vi-TT vaccine stimulated IgG and IgA antibody responses in infants aged 9 and 12 months after the initial dose, with stronger responses in the 9-month group. A booster dose at 15 months further increased antibody levels, especially in the 9-month group, while the 12-month group had a lower response. The vaccine was deemed safe with minimal side effects. The COVID-19 pandemic led to some unscheduled visits, which may have affected the study outcomes (Bijukchhe et al., 2024).

Table 1. Journal Review

No	Authors	Title	Objective	Method	Results	Conclusion
1	Viswanathan et al., 2025	Standard protocols for performance evaluation of typhoid fever in-vitro diagnostic assays in laboratory and field settings.	To develop and present standardized protocols for the performance evaluation of in-vitro diagnostic (IVD) assays for typhoid fever, both analytically in laboratories and clinically in field settings.	Controlled diagnostic accuracy study for analytical evaluation. Testing included various IVD formats: antibody, antigen, and molecular. Standardized and representative samples were used, including cross-reactive samples. Evaluation covered sensitivity, specificity, and reproducibility.	The developed protocols provide a standardized framework for evaluating various typhoid IVDs. These protocols enable early and accurate detection of <i>S. Typhi</i> infection, help reduce unnecessary antibiotic use, and improve disease control.	This is the first comprehensive guideline in India for typhoid IVD evaluation. The protocol is vital for ensuring test quality, especially in endemic areas, and may be adopted by countries with similar disease burdens. It can also serve as a blueprint for establishing a typhoid sample biobank for future R&D.
2	Qamar et al., 2024	Longevity of immune response after a single dose of typhoid conjugate vaccine against <i>Salmonella Typhi</i> among children in Hyderabad, Pakistan.	To assess the duration of immune response to a single dose of typhoid conjugate vaccine (TCV) among children under 10 years in Hyderabad, Pakistan, during an extensively drug-resistant <i>Salmonella</i>	Prospective cohort study (March 2018 – January 2023). Population: 958 children aged 6 months to 10 years who received one TCV dose. Follow-up at baseline, 4–6 weeks, 6 months, and annually up to 4 years. IgG anti-Vi measured by ELISA. Fever surveillance and blood culture for febrile children.	Initial seroconversion : 95.8% at 4–6 weeks. After 4 years: 75.6% retained antibody above seroconversion threshold. Children ≤ 2 years had faster antibody decline than older children.	A single TCV dose induced a strong immune response lasting up to 4 years, particularly in children over 2 years. Younger children showed faster antibody waning, suggesting the need for booster dose scheduling in high endemic areas.

No	Authors	Title	Objective	Method	Results	Conclusion
			Typhi outbreak.			
3	Patel et al., 2024	Efficacy of typhoid conjugate vaccine: final analysis of a 4-year, phase 3, randomised controlled trial in Malawian children.	To evaluate the long-term efficacy of a single dose of typhoid conjugate vaccine (Vi-TT) in children aged 9 months to 12 years in Malawi over more than 4 years of follow-up.	Phase 3 double-blind randomized controlled trial in Blantyre, Malawi. 28,130 children randomized to receive Vi-TT or MenA control vaccine. Passive surveillance for culture-confirmed typhoid. Analysis by intent-to-treat and per-protocol.	Vi-TT efficacy: 78.3% (95% CI: 66.3–86.1). Age-group efficacy: <2 years: 70.6%, 2–4 years: 79.6%, 5–12 years: 79.3%. Mean follow-up: 4.3 years. No serious vaccine-related adverse events. 163 vaccinations needed to prevent one case.	A single Vi-TT dose provides significant long-term protection for up to 4 years in all age groups, including under 2 years. Supports use in mass immunization campaigns and routine programs in endemic countries like Malawi.
4	Sondén et al., 2025	Fever in travelers returning from tropical and subtropical areas: a hospital-based study of factors affecting investigations and diagnoses in children and adults.	To evaluate the management and disease patterns in children and adults with fever after returning from tropical/subtropical areas, and identify factors affecting etiological investigation and diagnosis.	Retrospective study of febrile travelers and migrants at emergency departments in Karolinska University Hospital and Astrid Lindgren Children's Hospital, Stockholm (2014–2024). Included patients $\geq 38.0^{\circ}\text{C}$ within 2 days and returned from tropical/subtropical areas within 60 days. Clinical, demographic, and microbiological data were collected.	2441 patients included: 2197 adults and 244 children. Etiological diagnosis confirmed in 63.3%. Most common tropical infections: malaria (5.6%), dengue (4.0%), typhoid (0.9%). Higher diagnostic yield in hospitalized and febrile patients. Children had lower diagnostic rates.	Management of febrile returning travelers varies by group. Children, migrants, and VFR travelers often received less thorough investigation, indicating a need for equitable care, especially for vulnerable populations.
5	Batool et al., 2023	Parental acceptance of typhoid conjugate vaccine for children aged 6 months to 15 years in an outbreak setting of Lyari Town	To evaluate parental acceptance of TCV and identify predictors of TCV vaccination status in children	Cross-sectional survey using WHO's rapid vaccine coverage assessment. Random sampling from 11 union councils. One parent or primary caregiver	Of 14 VAS items, 78.0% of parents scored <40 (positive attitude), 22% scored ≥ 40 (negative). Parents with VAS <40 were	Parental awareness of campaigns and positive vaccine attitudes significantly associated with child TCV vaccination. Well-structured

No	Authors	Title	Objective	Method	Results	Conclusion
		Karachi, Pakistan.	during an extensively drug-resistant typhoid outbreak in Karachi.	interviewed. Local validated Vaccine Attitude Scale (VAS) used. Logistic regression identified predictors of TCV vaccination.	more likely to vaccinate (aOR 1.30; 95% CI 1.02–1.66). Awareness of ongoing campaign linked to higher vaccination.	pre-vaccine awareness campaigns targeting parents are needed to improve vaccine acceptance.
6	Hirai et al., 2025	Pyogenic vertebral osteomyelitis and iliopsoas muscle abscess caused by non-typhoidal <i>Salmonella</i> rapidly identified by genetic testing in an immunocompetent teenage boy without hemoglobinopathies.	To report a rare case of lumbar osteomyelitis and iliopsoas abscess caused by non-typhoidal <i>Salmonella</i> in an immunocompetent child with multiple drug allergies.	Diagnostic imaging confirmed lumbar osteomyelitis and iliopsoas abscess. Initial blood cultures and biopsy samples were negative. Genetic testing on vertebral biopsy identified <i>Salmonella</i> with O antigen type 4.	Early identification of the causative organism is critical due to long-term treatment needs and limited options in children. Genetic testing should be considered for identifying the pathogen in osteomyelitis.	Vertebral osteomyelitis due to non-typhoidal <i>Salmonella</i> is very rare in immunocompetent children. Genetic testing is useful for selecting appropriate antimicrobial therapy and avoiding unnecessary drugs.
7	Nakisuyi et al., 2023	Prevalence and factors associated with malaria, typhoid, and co-infection among febrile children aged six months to twelve years at Kampala International University Teaching Hospital in Western Uganda.	To determine the prevalence and associated factors of malaria, typhoid, and co-infection among febrile children at KIU-TH in Western Uganda.	Cross-sectional study using a structured questionnaire. Blood tests: peripheral smear for malaria and culture for typhoid. Multivariate regression analysis with Stata 14.0.	Most participants were male (62%), cared for by mothers (86.1%). Malaria prevalence: 25%, typhoid: 3.7%, malaria-typhoid co-infection: 2.8%. Drinking untreated well water increased co-infection risk; treated tap water reduced it.	Confirmed prevalence of malaria-typhoid co-infection via blood culture is lower than in previous serological studies. Highlights the need for gold-standard diagnostics in epidemiological research. Emphasizes hygiene and clean water.
8	Olaru et al., 2023	The effect of a comprehensive typhoid conjugate vaccine campaign on antimicrobial prescribing in	To examine whether a typhoid conjugate vaccine campaign affected antimicrobial	Mixed methods. Outpatient data from 5 clinics (Jan 2018–Mar 2020). Interrupted time-series analysis compared prescribing	Of 27,107 pediatric consultations, 17,951 (66.2%) received antimicrobials. The campaign	The TCV campaign did not reduce antimicrobial prescribing in children. Contextual factors like

No	Authors	Title	Objective	Method	Results	Conclusion
		children in Harare, Zimbabwe: a mixed methods study.	prescribing in children in Harare, Zimbabwe.	before/after vaccination campaign. Ethnographic data from 14 clinics.	did not reduce overall or typhoid-related antimicrobial prescribing. Inadequate water access and diagnostics contributed to continued prescribing.	unsafe water and inadequate health services must be addressed for vaccines to fully reduce antimicrobial use.
9	Marks et al., 2024	Incidence of typhoid fever in Burkina Faso, DRC, Ethiopia, Ghana, Madagascar, and Nigeria (Severe Typhoid in Africa Programme): a population-based study.	The Severe Typhoid in Africa programme aimed to close regional data gaps on typhoid burden and identify target populations for TCV interventions.	Hybrid design: hospital-based prospective surveillance + population-based health care utilization surveys in 6 sub-Saharan African countries. Fever $\geq 37.5^{\circ}\text{C}$ (axillary) or $\geq 38.0^{\circ}\text{C}$ (tympanic) for ≥ 3 days. Blood cultures and Bayesian mixed model for incidence estimates.	27,866 (33.8%) of 82,491 eligible participants were enrolled; 27,544 (98.8%) had blood cultures. Clinically significant organisms found in 7.7% (n=2136); <i>S. Typhi</i> isolated in 346 (16.2%).	High incidence (>100 per 100,000 person-years) in 4 countries. Prevalence of hospitalization, severe disease, and resistant strains underscore the urgent need for TCV delivery and improvements in water, sanitation, and hygiene.
10	Bijukchhe et al., 2024	Immune responses to typhoid conjugate vaccine in a two dose schedule among Nepalese children.	To evaluate immunogenicity of Vi-TT at 9 and 12 months of age and response to a booster at 15 months.	Infants recruited at Patan Hospital, Kathmandu, received Vi-TT at 9 or 12 months, with booster at 15 months. Blood collected at 4 time points. Antibody titers measured via ELISA. Primary outcome: 4-fold IgG increase after each dose.	50 children per group. 100% seroconversion after the initial dose in both groups. After booster, IgG seroconversion significantly higher in 9-month group (68.42%) vs 12-month group (25.8%), $p < 0.001$.	Vi-TT is highly immunogenic at 9 and 12 months. Stronger booster response in the 9-month group may be due to longer interval between doses.

Discussion

Typhoid fever is an infectious disease caused by the *Salmonella Typhi* bacterium. It can spread through contaminated food or water, particularly in areas with poor water management and sanitation. Symptoms include high fever, weakness, abdominal pain, and digestive issues such as constipation or diarrhea (A. M. Andas et al., 2022). Without proper treatment, typhoid can become dangerous and potentially life-threatening.

Vaccination and maintaining hygiene in food and water preparation are the most effective preventive measures (Wahyuni, S et al., 2022).

According to the World Health Organization (WHO), typhoid fever remains one of the leading causes of health problems and mortality in low- and middle-income countries, with an estimated 12.5 to 16.3 million cases and approximately 140,000 deaths annually worldwide (Purnamasari, Saragih, et al., 2024). WHO has recommended the use of the Typhoid Conjugate Vaccine (TCV) in endemic countries as part of routine immunization programs to address this health challenge (Mokodompit et al., 2025).

WHO advocates for the use of vaccines to combat antibiotic resistance, recognizing vaccines as an effective tool in reducing the burden of resistant bacterial infections. The organization recommends the use of the Typbar-TCV vaccine for this purpose (Islamiah et al., 2024). In December 2017, WHO approved the use of the Typbar-TCV vaccine for children aged six months and older. It is also recommended for use in outbreak settings or in regions with high rates of typhoid cases that are difficult to treat due to bacterial resistance to antibiotics (A. Andas et al., 2024). Children under the age of five are known to be the most vulnerable group to this infection. A study conducted in the Southeast Asia region reported an incidence rate of 219.8 cases per 100,000 population, highlighting that typhoid fever continues to pose a significant public health challenge (Purnamasari, Zoahira, et al., 2023).

This review reveals that antibiotic treatment for children with typhoid fever involves several types of antibiotics, including ampicillin, cotrimoxazole, and ciprofloxacin (Israeli et al., 2024). The article presents significant information regarding the high rates of drug resistance and multi-drug resistance found in isolates from pediatric patients, providing a critical foundation for selecting and managing appropriate antibiotic therapy for typhoid fever in children, as outlined in the ninth journal reviewed (Purnamasari, Wa Ode Aisa Zoahira, et al., 2024).

These findings are consistent with studies that have shown high levels of antibiotic resistance in *Salmonella Typhi* across various African countries, particularly among children aged 2 to 14 years. This underscores the necessity of selecting appropriate antibiotic therapy based on local sensitivity data. Therefore, monitoring resistance patterns and practicing prudent antibiotic use are essential to improving the effectiveness of typhoid fever treatment in children and reducing the risk of serious complications (Mortin Andas et al., 2024).

The literature review also highlights the increasing role of parents in supervising and ensuring adherence to treatment in children with typhoid fever. Parents must be vigilant in recognizing clinical symptoms and understand the importance of completing antibiotic therapy as prescribed to prevent further resistance and serious complications (Wahyuni et al., 2024). Moreover, educating parents about the importance of choosing appropriate healthcare facilities and strictly following medical advice is crucial for successful treatment and recovery. With active parental involvement, the management of typhoid

fever in children can become more efficient, and the risk of antibiotic resistance can be minimized.

Conclusion

Based on the literature review, it can be concluded that active parental involvement plays a crucial role in the management of typhoid fever in children. This role includes supervising treatment adherence, being alert to clinical symptoms, and understanding the importance of completing the full course of antibiotics as prescribed. Educating parents about selecting appropriate healthcare services and complying with medical instructions greatly contributes to the success of therapy and the prevention of antibiotic resistance and severe complications. Thus, increasing awareness and participation of parents is one of the key strategies in ensuring effective and sustainable management of typhoid fever in children.

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