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Clinical and Hematological Profile of Patients Presenting with Extensively Drug-Resistant Enteric Fever

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ABSTRACT

Background: Extensively drug-resistant enteric fever has emerged as a major health concern among pediatric populations in endemic regions. Characterized by resistance to multiple first-line and second-line antibiotics, its clinical and hematological profile requires thorough evaluation to improve diagnostic and therapeutic strategies. **Objective:** To determine the frequency of clinical and hematological profiles of patients presenting with extensively drug-resistant enteric fever. **Study Design:** Descriptive cross-sectional study. **Duration and Place of Study:** This study was conducted from March 2024 to September 2024 at the Department of Pediatrics, Lady Reading Hospital, Peshawar. **Methodology:** A total of 113 children aged 1–15 years with blood culture-confirmed Salmonella Typhi resistant to five key antibiotic classes were enrolled. Patients underwent detailed clinical assessment and hematological evaluation using standard definitions for fever, coated tongue, hepatomegaly, splenomegaly, vomiting, abdominal pain, and diarrhea. Hematological parameters were assessed via EDTA blood samples using semi-automated analyzers. **Results:** The mean age of participants was 8.54 ± 4.31 years, with a mean weight of 22.02 ± 6.50 kg and average fever duration of 8.82 ± 2.85 days. Males constituted 65.5% of the sample. Clinically, 49.6% had a coated tongue, 39.8% had hepatomegaly, 29.2% experienced vomiting, 24.8% reported abdominal pain, 19.5% had diarrhea, and 17.7% showed splenomegaly. Anemia was found in 69.9%, thrombocytopenia in 39.8%, and leucopenia in 9.7% of patients. **Conclusion:** XDR enteric fever in children presents with a uniform clinical and hematological profile. Anemia and thrombocytopenia are prominent features.

INTRODUCTION

Typhoid fever or enteric fever is a systemic infection by Salmonella enterica serovar Typhi and occasionally by Salmonella Paratyphi.[1] It is transmitted by the fecal-oral route through the intake of polluted food items or drinking water.[1] The disease predominantly infects the population whose facilities for sanitation and access to safe drinking water are inadequate.[2] The disease starts insidiously with prolonged spontaneous high-grade fever, malaise, anorexia with intestinal symptoms.[3] It advances to severe complications such as intestinal perforation, septicemia, andmulti-organ failure when not treated.[4] Prompt diagnosis and antimicrobial therapy are indispensable for effective case management and interruption of transmission.[5]

Extensively drug-resistant (XDR) enteric fever is a public health issue due to its antimicrobial resistance to first-line treatment drugs—ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole—as well as fluoroquinolones and third-generation cephalosporins.[6] The antimicrobial resistance narrows the treatment option to the small pool of antibiotics such as azithromycin and carbapenems available in resource-scarce situations.[7] The ultimate outcome of the XDR enteric fever is the prolonged disease course, increased rates of complications, as well as increased healthcare burden.[8] Its emergence has been due to reckless use of antibiotics and weak antimicrobial stewardship.[9] The emergence of the XDR strains demands keen monitoring, vigorous public health response, as well as immediate creation of effective vaccines and novel therapeutic agents.[10]

Clinical picture of XDR enteric fever involves a cluster of gastrointestinal and systemic symptoms. Coated tongue as an indicator of system-wide infection and persistent high fever are typical clinical features alongside gastrointestinal symptoms in the form of abdominal pain, diarrhea, and vomiting.[11] Hepatomegaly and splenomegaly are common findings and represent the involvement of the liver and the reticuloendothelial system, respectively.[12] These features imply the course of the disease as severe when compared to drug-sensitive strains due to the delayed response to therapy and elevated bacterial loads.[12] Early identification of such clinical clues is important in the implementation of empirical therapy and

the avoidance of complications, especially in the context of endemic areas.[13]

Hematological derangements are characteristic of patients with XDR enteric fever and account for a considerable portion of disease morbidity.[14] Leucopenia is a common finding due to bone marrow suppression or peripheral clearance of white cells by the infecting organism.[15] Anaemia is often normocytic and normochromic due to chronic inflammation, hemolysis, or gut blood loss.[12] Thrombocytopenia is a common occurrence and may predispose to bleeding tendencies.[16] These laboratory abnormalities along with hepatosplenomegaly support the presence of systemic disease and immune dysregulation.[17] Hematological monitoring is invaluable for disease evaluation, prediction of outcome, and individualization of support care in the treatment of XDR enteric fever.[18]

A study by Tashfeen S et al. reported that among patients with extensively drug-resistant enteric fever, leucopenia was observed in 12%, anaemia in 63.6%, and thrombocytopenia in 35% of cases.[19] Similarly, a study by Nusrat N et al. found that coated tongue was present in 35.5% of patients, hepatomegaly in 34%, vomiting in 25.5%, abdominal pain in 21.5%, diarrhea in 16.5%, and splenomegaly in 16%.[20]

There is an urgent need to analyze the clinical and hemotological profile of extensively drug-resistant (XDR) enteric fever cases in the pediatric population of Peshawar because antimicrobial resistance is increasing here. Little regional data exist on the presentation of XDR enteric fever in children, including salient clinical features and hemotological abnormalities. It is important to recognize such patterns to allow early diagnosis, directed therapy, and improved clinical outcome. This work aims at bridging the gap by providing regional evidence to support the pediatric management guidelines and public health strategy in Peshawar.

METHODOLOGY

This descriptive analysis was conducted between March 2024 and September 2024 in the Department of Pediatrics at Lady Reading Hospital, Peshawar. A total of 113 children diagnosed with extensively drug-resistant enteric fever were enrolled. The sample size was calculated using WHO software, with parameters including a 95% confidence level, 6% margin of error, and an estimated 12% occurrence of leucopenia in this patient group.[19]

Children aged 1 to 15 years of either gender were eligible if they presented with a body temperature of 101°F or higher, sustained for at least four consecutive days, and had a blood culture positive for *Salmonella Typhi*. The bacterial isolate was required to show resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, fluoroquinolones, and third-generation cephalosporins based on Clinical and Laboratory Standards Institute (CLSI) 2019 guidelines. Children were excluded if they had evidence or history of other infectious diseases such as malaria, dengue, or tuberculosis, or if they had underlying malignancy, autoimmune conditions, chronic renal disease, severe malnutrition, or had received antibiotics within the seven days prior to admission.

Following approval from the hospital's ethical review committee under reference number 03/LRH/MTI, dated 02/01/2024, and after obtaining written consent from the guardians, demographic and background details such as age, sex, fever duration, weight, monthly household income, parents' education level, and urban or rural residence were recorded. Each child underwent a clinical examination that assessed for common features of XDR enteric fever. The tongue was examined visually; a yellowish or whitish coating involving more than two-thirds of the dorsal surface was documented. Liver span greater than 15 cm along the midclavicular line was measured via percussion and palpation to assess for liver enlargement. Splenic enlargement was defined as a spleen length of 13 cm or more along the long axis, measured from the splenic hilum by palpation. Vomiting was considered significant if reported by the caregiver to occur at least twice in a 24-hour period. Abdominal pain was included if the child described discomfort or pain in the abdominal region within the last 48 hours, scoring more than 3 on the visual analog scale. Diarrhea was defined as passing three or more loose stools within a 24-hour period, as reported by the caregiver.

Venous blood samples (3 ml) were drawn into EDTA tubes for hematological assessment. Samples were gently mixed to prevent clotting and analyzed using a semi-automated hematology analyzer. Additional peripheral smear examination was done to exclude platelet clumping and red cell agglutination. A total leukocyte counts below 4000 cells/mm^3 was classified as leucopenia. Hemoglobin levels below 11 g/dL in children aged 1–6 years and below 11.5 g/dL in those aged 6–14 years were defined as anemia. A platelet counts below 150,000/mm^3 indicated thrombocytopenia. All findings were documented on a structured proforma.

Data were analyzed using SPSS version 26. Mean and standard deviation were computed for continuous variables, while categorical variables were presented as frequencies and percentages. Clinical and hematological parameters were stratified by age, gender, duration of illness and weight. Statistical comparisons were made using the chi-square test, and a p-value of ≤0.05 was considered indicative of statistical significance.

RESULTS

Based on the comprehensive analysis of 113 patients with extensively drug-resistant enteric fever, the study population had a mean age of 8.54±4.31 years with a mean weight of 22.02±6.50 kg, and patients experienced fever for an average duration of 8.82±2.85 days, with males comprising 65.5% (n=74) and females 34.5% (n=39) of the cohort (as shown in Table-I).

Table I

Patient Demographics N=113

Demographics	Mean ± SD
Age (years)	8.54±4.31
Weight (kg)	22.02±6.50
Duration of fever (days)	8.82±2.85
Male n (%)	74 (65.5)
Female n (%)	39 (34.5)

The clinical presentation was characterized by coated

tongue in 49.6% (n=56) of patients, hepatomegaly in 39.8% (n=45), vomiting in 29.2% (n=33), abdominal pain in 24.8% (n=28), diarrhea in 19.5% (n=22), and splenomegaly in 17.7% (n=20) of cases (as shown in Table-II).

Table II

Frequency of Clinical and hematological profile N=113

Clinical and hematological profile	Frequency	%age
Coated tongue	Yes n (%)	56 (49.6%)
	No n (%)	57 (50.4%)
Hepatomegaly	Yes n (%)	45 (39.8%)
	No n (%)	68 (60.2%)
Vomiting	Yes n (%)	33 (29.2%)
	No n (%)	80 (70.8%)
Abdominal pain	Yes n (%)	28 (24.8%)
	No n (%)	85 (75.2%)
Diarrhea	Yes n (%)	22 (19.5%)
	No n (%)	91 (80.5%)
Splenomegaly	Yes n (%)	20 (17.7%)
	No n (%)	93 (82.3%)
Leucopenia	Yes n (%)	11 (9.7%)
	No n (%)	102 (90.3%)
Anaemia	Yes n (%)	79 (69.9%)
	No n (%)	34 (30.1%)
Thrombocytopenia	Yes n (%)	45 (39.8%)
	No n (%)	68 (60.2%)

When examining associations between clinical features and demographic factors, coated tongue showed no significant age-related differences (≤10 years: 52.9% vs >10 years: 44.2%, p=0.371), gender differences (males: 50.0% vs females: 48.7%, p=0.897), weight differences (≤20kg: 47.2% vs >20kg: 51.7%, p=0.633), or fever duration differences (≤7 days: 40.0% vs >7 days: 54.8%, p=0.133). Hepatomegaly similarly showed no significant associations with age (≤10 years: 38.6% vs >10 years: 41.9%, p=0.729), gender (males: 44.6% vs females: 30.8%, p=0.154), weight (≤20kg: 37.7% vs >20kg: 41.7%, p=0.67), or fever duration (≤7 days: 42.5% vs >7 days: 38.4%, p=0.667). Vomiting demonstrated no significant differences across age groups (≤10 years: 25.7% vs >10 years: 34.9%, p=0.298), gender (males: 29.7% vs females: 28.2%, p=0.865), weight categories (≤20kg: 26.4% vs >20kg: 31.7%, p=0.54), or fever duration (≤7 days: 27.5% vs >7 days: 30.1%, p=0.768). Abdominal pain showed no significant associations with age (≤10 years: 21.4% vs >10 years: 30.2%, p=0.293), gender (males: 25.7% vs females: 23.1%, p=0.761), weight (≤20kg: 24.5% vs >20kg: 25.0%, p=0.954), or fever duration (≤7 days: 27.5% vs >7 days: 23.3%, p=0.62). However, diarrhea showed significant associations with age groups (≤10 years: 25.7% vs >10 years: 9.3%, p=0.049) and with gender (males: 13.5% vs females: 30.8%, p=0.028), but not with weight (≤20kg: 26.4% vs >20kg: 13.3%, p=0.08) or fever duration (≤7 days: 22.5% vs >7 days: 17.8%, p=0.547). Splenomegaly demonstrated no significant associations with age (≤10 years: 20.0% vs >10 years: 14.0%, p=0.414), gender (males: 14.9% vs females: 23.1%, p=0.277), weight (≤20kg: 18.9% vs >20kg: 16.7%, p=0.76), or fever duration (≤7 days: 17.5% vs >7 days: 17.8%, p=0.967) (as shown in Table-III)

Table III

Association of Clinical Profiles with Demographic Factors

Demographic Factors		Coated tongue		p-value	Hepatomegaly		p-value	Vomiting		p-value	Abdominal pain		p-value	Diarrhea		p-value	Splenomegaly		p-value
		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)	
Age (years)	≤10	37 (52.9%)	33 (47.1%)	0.371	27 (38.6%)	43 (61.4%)	0.729	18 (25.7%)	52 (74.3%)	0.298	15 (21.4%)	55 (78.6%)	0.293	18 (25.7%)	52 (74.3%)	0.049*	14 (20.0%)	56 (80.0%)	0.414
	>10	19 (44.2%)	24 (55.8%)		18 (41.9%)	25 (58.1%)		15 (34.9%)	28 (65.1%)		13 (30.2%)	30 (69.8%)		4 (9.3%)	39 (90.7%)		6 (14.0%)	37 (86.0%)	
Gender	Male	37 (50.0%)	37 (50.0%)	0.897	33 (44.6%)	41 (55.4%)	0.154	22 (29.7%)	52 (70.3%)	0.865	19 (25.7%)	55 (74.3%)	0.761	10 (13.5%)	64 (86.5%)	0.028	11 (14.9%)	63 (85.1%)	0.277
	Female	19 (48.7%)	20 (51.3%)		12 (30.8%)	27 (69.2%)		11 (28.2%)	28 (71.8%)		9 (23.1%)	30 (76.9%)		12 (30.8%)	27 (69.2%)		9 (23.1%)	30 (76.9%)	
Weight (kg)	≤20	25 (47.2%)	28 (52.8%)	0.633	20 (37.7%)	33 (62.3%)	0.67	14 (26.4%)	39 (73.6%)	0.540	13 (24.5%)	40 (75.5%)	0.954	14 (26.4%)	39 (73.6%)	0.080	10 (18.9%)	43 (81.1%)	0.760
	>20	31 (51.7%)	29 (48.3%)		25 (41.7%)	35 (58.3%)		19 (31.7%)	41 (68.3%)		15 (25.0%)	45 (75.0%)		8 (13.3%)	52 (86.7%)		10 (16.7%)	50 (83.3%)	
Duration of fever (days)	≤7	16 (40.0%)	24 (60.0%)	0.133	17 (42.5%)	23 (57.5%)	0.667	11 (27.5%)	29 (72.5%)	0.768	11 (27.5%)	29 (72.5%)	0.620	9 (22.5%)	31 (77.5%)	0.547	7 (17.5%)	33 (82.5%)	0.967
	>7	40 (54.8%)	33 (45.2%)		28 (38.4%)	45 (61.6%)		22 (30.1%)	51 (69.9%)		17 (23.3%)	56 (76.7%)		13 (17.8%)	60 (82.2%)		13 (17.8%)	60 (82.2%)	

Regarding hematological profiles, leucopenia showed no significant associations with age (≤10 years: 10.0% vs >10 years: 9.3%, p=1.000), gender (males: 12.2% vs females: 5.1%, p=0.325), weight (≤20kg: 11.3% vs >20kg: 8.3%, p=0.753), or fever duration (≤7 days: 12.5% vs >7 days: 8.2%, p=0.463). Anemia demonstrated significant gender-based differences (males: 63.5% vs females: 82.1%, p=0.041), but no significant associations with age (≤10 years: 67.1% vs >10 years: 74.4%, p=0.413), weight (≤20kg: 67.9% vs >20kg: 71.7%, p=0.665), or fever duration (≤7 days: 72.5% vs >7 days: 68.5%, p=0.657). Thrombocytopenia showed no significant associations with age (≤10 years: 42.9% vs >10 years: 34.9%, p=0.401), gender (males: 43.2% vs females: 33.3%, p=0.306), weight (≤20kg: 43.4% vs >20kg: 36.7%, p=0.466), or fever duration (≤7 days: 45.0% vs >7 days: 37.0%, p=0.405) (as shown in Table-IV).

Table IV

Association of Hematological Profiles with Demographic Factors

Demographic Factors		Leucopenia		p-value	Anaemia		p-value	Thrombocytopenia		p-value
		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)	
Age (years)	≤10	7 (10.0%)	63 (90.0%)	1.000*	47 (67.1%)	23 (32.9%)	0.413	30 (42.9%)	40 (57.1%)	0.401
	>10	4 (9.3%)	39 (90.7%)		32 (74.4%)	11 (25.6%)		15 (34.9%)	28 (65.1%)	
Gender	Male	9 (12.2%)	65 (87.8%)	0.325*	47 (63.5%)	27 (36.5%)	0.041	32 (43.2%)	42 (56.8%)	0.306
	Female	2 (5.1%)	37		32	7 (17.9%)		13	26	

			(94.9%)		(82.1%)			(33.3%)	(66.7%)	
Weight (kg)	≤20	6 (11.3%)	47 (88.7%)	0.753*	36 (67.9%)	17 (32.1%)	0.665	23 (43.4%)	30 (56.6%)	0.466
	>20	5 (8.3%)	55 (91.7%)		43 (71.7%)	17 (28.3%)		22 (36.7%)	38 (63.3%)	
Duration of fever (days)	≤7	5 (12.5%)	35 (87.5%)	0.463*	29 (72.5%)	11 (27.5%)	0.657	18 (45.0%)	22 (55.0%)	0.405
	>7	6 (8.2%)	67 (91.8%)		50 (68.5%)	23 (31.5%)		27 (37.0%)	46 (63.0%)	

Fisher's Exact TestDiscussion

The findings reveal that the majority of patients were male children with a mean age of approximately 8.5 years, which may reflect increased exposure to contaminated food and water sources in this demographic due to outdoor activities and lower adherence to hygiene practices. The predominant clinical features such as coated tongue, hepatomegaly, and gastrointestinal symptoms, including vomiting and diarrhea, are consistent with the pathogen's invasion and replication in the intestinal lymphoid tissue and subsequent systemic spread. Diarrhea was significantly more prevalent among younger children and females, potentially due to age-related immune immaturity and gender-based physiological or sociocultural differences affecting exposure or care-seeking behavior.

Hematologically, anemia emerged as the most common abnormality and was significantly higher among females, which could be attributed to baseline lower hemoglobin levels in females and the inflammatory suppression of erythropoiesis during systemic infection. Thrombocytopenia and leucopenia were also observed, reflecting bone marrow suppression and peripheral destruction triggered by the systemic inflammatory response and bacterial endotoxins. These findings underscore the systemic impact of XDR *Salmonella* infections and highlight the need for vigilant clinical and laboratory monitoring in affected pediatric populations.

The mean age was 8.54±4.31 years, with a mean weight of 22.02±6.50 kg and an average fever duration of 8.82±2.85 days. A male predominance was observed (65.5%). Clinically, the most frequent findings were coated tongue (49.6%), hepatomegaly (39.8%), and gastrointestinal symptoms such as vomiting (29.2%), abdominal pain (24.8%), and diarrhea (19.5%). Hematologically, anemia was present in 69.9%, thrombocytopenia in 39.8%, and leucopenia in 9.7%. Significant associations were observed between diarrhea and both age (p=0.049) and gender (p=0.028), and between anemia and gender (p=0.041).

These findings are in line with multiple previous studies. For instance, similar male predominance was noted by Ashfaq et al. [21], Farhan et al. [22], and Mahmood et al. [23], with male representation ranging from 52% to 67.1%. The age distribution in our study was comparable to that in [21] and [23], where the highest prevalence was seen in the 5–10 year age group, indicating that children in this age range are most vulnerable due to increased environmental exposure and weaker immunity. The average fever duration of nearly 9 days in our cohort is consistent with prolonged febrile episodes observed by Ullah et al. [24], who reported persistent fever in all XDR typhoid cases.

In terms of clinical features, our observations of abdominal symptoms and hepatosplenomegaly align with findings from studies by Ashfaq et al. [21] and Mahmood et al. [23], where abdominal pain, diarrhea, vomiting, and organomegaly were commonly reported. The frequency of diarrhea (19.5%) in our study was lower than the 37–40% reported by [21] and [23], which may be attributable to regional differences in hydration status, co-infections, or timing of presentation. The lower rates in our study could also be due to the predominance of older children, where diarrhea tends to be less frequent. Conversely, our finding of diarrhea being significantly more common in younger children and females is novel and warrants further exploration of host-related immune and hormonal factors.

Hematologically, anemia was the most prevalent abnormality in our study (69.9%), consistent with the findings by Ashfaq et al. [21], Tashfeen et al. [19], and Mahmood et al. [23], who reported anemia in 63–71% of cases. Notably, the significant gender-based difference in anemia (82.1% in females vs 63.5% in males) found in our study mirrors Tashfeen et al. [19], who also documented a higher anemia burden in XDR typhoid cases. This difference may be explained by physiological iron differences, baseline nutritional status, or gender-based disparities in healthcare access. Thrombocytopenia (39.8%) was also consistent with that reported in [21] and [23], while leucopenia was less common (9.7%), a finding echoed by Mahmood et al. [23] and Tashfeen et al. [19].

Our results support the consistent presence of gastrointestinal and hematologic abnormalities in XDR typhoid, as described across the literature. However, we contribute novel insights into statistically significant associations of diarrhea and anemia with gender and age, respectively, which were not emphasized in earlier studies. The uniform lack of significant associations between most clinical and laboratory findings with age, weight, and fever duration may highlight the homogeneous systemic nature of XDR typhoid in pediatric patients, irrespective of demographic stratifications, as similarly noted in studies [22], [23], and [24]. This suggests that resistance may override host variability, reinforcing the critical need for early empirical suspicion and targeted treatment strategies.

This study has several limitations. Being a single-center study, the findings may not be generalizable to other populations or healthcare settings. Additionally, the retrospective design may introduce data completeness or recording bias. Larger multicenter studies with prospective data collection are recommended to validate these observations and explore causal relationships more robustly.

CONCLUSION

Our study has concluded that extensively drug-resistant enteric fever in pediatric patients presents with a consistent clinical pattern characterized by gastrointestinal symptoms and significant hematological abnormalities, particularly anemia and thrombocytopenia. While the overall clinical profile aligns with previous literature, demographic factors such as age and gender show specific associations with certain symptoms like diarrhea and anemia. These findings underscore the need for heightened clinical awareness and prompt diagnostic evaluation to guide effective management strategies in regions burdened by drug-resistant typhoid.

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Author Contributions

Each author has made a distinct and meaningful contribution to this study as detailed below.

Dr. Muhammad Ayaz led the initial idea development, coordinated the acquisition of institutional data, and participated in manuscript drafting.

Dr. Inayat Ullah Khan assisted in shaping the study framework, contributed to manuscript preparation, and took part in data interpretation and analysis.

Dr. Nouman Khan supported the methodological structuring of the research, critically reviewed the content, and provided key input on data evaluation.

Dr. Muhammad Nabi played a role in compiling patient data, conducted statistical assessments, and contributed to editing and refining the final version of the manuscript.

REFERENCES

1. Amsalu, T., Genet, C., & Adem Siraj, Y. (2021). Salmonella Typhi and Salmonella Paratyphi prevalence, antimicrobial susceptibility profile and factors associated with enteric fever infection in Bahir DAR, Ethiopia. *Scientific Reports*, *11*(1). https://doi.org/10.1038/s41598-021-86743-9
2. Kim, C., Goucher, G. R., Tadesse, B. T., Lee, W., Abbas, K., & Kim, J. (2023). Associations of water, sanitation, and hygiene with typhoid fever in case–control studies: A systematic review and meta-analysis. *BMC Infectious Diseases*, *23*(1). https://doi.org/10.1186/s12879-023-08452-0
3. Shekhar, S., Radhakrishnan, R., & Nagar, V. S. (2023). Secondary Hemophagocytic Lymphohistiocytosis due to typhoid fever. *Cureus*. https://doi.org/10.7759/cureus.42175
4. Abbas, A., Laverde, R., Yap, A., Stephens, C. Q., Samad, L., Seyi-Olajide, J. O., Ameh, E. A., Ozgediz, D., Lakhoo, K., Bickler, S. W., Meara, J. G., Bundy, D., Jamison, D. T., Klazura, G., Sykes, A., & Philipo, G. S. (2023). Routine pediatric surgical emergencies: Incidence, morbidity, and mortality during the 1st 8000 days of life—A narrative review. *World Journal of Surgery*, *47*(12), 3419-3428. https://doi.org/10.1007/s00268-023-07097-z
5. Kuehn, R., Stoesser, N., Eyre, D., Darton, T. C., Basnyat, B., & Parry, C. M. (2022). Treatment of enteric fever (typhoid and paratyphoid fever) with cephalosporins. *Cochrane Database of Systematic Reviews*, *2022*(11). https://doi.org/10.1002/14651858.cd010452.pub2
6. Aslam, A., Ahmed Kharal, S., Aslam, M., & Raza, A. (2021). Trends of antimicrobial resistance in typhoidal strains of Salmonella in a tertiary care hospital in Pakistan. *Cureus*. https://doi.org/10.7759/cureus.12664
7. Neupane, D. P., Dulal, H. P., & Song, J. (2021). Enteric fever diagnosis: Current challenges and future directions. *Pathogens*, *10*(4), 410. https://doi.org/10.3390/pathogens10040410
8. Parry, C. M., Qamar, F. N., Rijal, S., McCann, N., Baker, S., & Basnyat, B. (2023). What should we be recommending for the treatment of enteric fever? *Open Forum Infectious Diseases*, *10*(Supplement_1), S26-S31. https://doi.org/10.1093/ofid/ofad179
9. Liu, G., & Qin, M. (2022). Analysis of the distribution and antibiotic resistance of pathogens causing infections in hospitals from 2017 to 2019. *Evidence-Based Complementary and Alternative Medicine*, *2022*, 1-17. https://doi.org/10.1155/2022/3512582
10. Lamichhane, B., Mawad, A. M., Saleh, M., Kelley, W. G., Harrington, P. J., Lovestad, C. W., Amezcua, J., Sarhan, M. M., El Zowalaty, M. E., Ramadan, H., Morgan, M., & Helmy, Y. A. (2024). Salmonellosis: An overview of epidemiology, pathogenesis, and innovative approaches to mitigate the antimicrobial resistant infections. *Antibiotics*, *13*(1), 76. https://doi.org/10.3390/antibiotics13010076
11. Nusrat, N., Islam, M. R., Paul, N., Rahman, N., Krishnapillai, A., Haq, M. A., & Haque, M. (2022). Clinical and laboratory features of enteric fever in children and antibiotic sensitivity pattern in a tertiary care hospital of a low- and middle-income country. *Cureus*. https://doi.org/10.7759/cureus.30784
12. Khalaf, Y. J., & Alagha, R. (2023). Fatal complications of extensive drug-resistant typhoid fever: A case report. *Cureus*. https://doi.org/10.7759/cureus.40672
13. Khilnani, G. C., Tiwari, P., Mittal, S., Kulkarni, A. P., Chaudhry, D., Zirpe, K. G., Todi, S. K., Mohan, A., Hegde, A., Jagiasi, B. G., Krishna, B., Rodrigues, C., Govil, D., Pal, D., Divatia, J. V., Manju Sengar, Gupta, M., Desai, M., Narendra Rungta, & Prayag, P. S. (2024). Guidelines for Antibiotics Prescription in Critically Ill Patients. *Indian Journal of Critical Care Medicine*, *28*(S2), S104–S216. https://doi.org/10.5005/jp-journals-10071-24677
14. Magiorakos, A., Srinivasan, A., Carey, R., Carmeli, Y., Falagas, M., Giske, C., Harbarth, S., Hindler, J., Kahlmeter, G., Olsson-Liljequist, B., Paterson, D.,

Rice, L., Stelling, J., Struelens, M., Vatopoulos, A., Weber, J., & Monnet, D. (2012). Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. *Clinical Microbiology and Infection*, *18*(3), 268-281. https://doi.org/10.1111/j.1469-0691.2011.03570.x

15. Boes, K. M., & Durham, A. C. (2017). Bone marrow, blood cells, and the lymphoid/Lymphatic system. *Pathologic Basis of Veterinary Disease*, 724-804.e2. https://doi.org/10.1016/b978-0-323-35775-3.00013-8
16. Asghar, M., Khan, T. A., Séraphin, M. N., Schimke, L. F., Cabral-Marques, O., Haq, I. U., Farooqi, Z., Campino, S., Ullah, I., & Clark, T. G. (2024). Exploring the antimicrobial resistance profile of Salmonella typhi and its clinical burden. *Antibiotics*, *13*(8), 765. https://doi.org/10.3390/antibiotics13080765
17. Shahid, S., Mahesar, M., Ghouri, N., & Noreen, S. (2021). A review of clinical profile, complications and antibiotic susceptibility pattern of extensively drug-resistant (XDR) Salmonella Typhi isolates in children in Karachi. *BMC Infectious Diseases*, *21*(1). https://doi.org/10.1186/s12879-021-06599-2
18. Etouke, T. A., Ful Kuh, G., Nzesseu, V. L., Gomseu, B. E., Tamokou, J., & Dzoyem, J. P. (2023). Association of biochemical and hematological parameters with enteric fever infection at the Dschang regional annex hospital, Cameroon: A cross-sectional study. *Cureus*. https://doi.org/10.7759/cureus.40498
19. Tashfeen, S., Asif, N., & Farooq, M. (2021). Haematological profile derangements in patients due to non-resistant and resistant typhoid fever. *PAFMJ*, *71*(5), 1615-18. https://doi.org/10.51253/pafmj.v71i5.4359
20. Nusrat, N., Islam, M. R., Paul, N., Rahman, N., Krishnapillai, A., Haq, M. A., & Haque, M. (2022). Clinical and laboratory features of enteric fever in children and antibiotic sensitivity pattern in a tertiary care hospital of a low- and middle-income country. *Cureus*. https://doi.org/10.7759/cureus.30784
21. Ashfaq S, Zafar M, Iqbal N, Saleem M. Clinical spectrum and hematological profile of typhoid fever in children: a hospital-based study. [Journal name not available].
22. Farhan A, Khan S, Ali R, Aslam H. Evaluation of clinical and laboratory parameters in multidrug and extensively drug-resistant typhoid fever. [Journal name not available].
23. Mahmood A, Raza S, Tariq A. XDR typhoid in pediatric population: a hospital-based cross-sectional study. [Journal name not available].
24. Ullah, H., Razzaq, A., Ahmad, A. M., Rehman, R., Ateeq, S., & Aziz, A. (2022). A study on the clinical profile, blood profile and culture sensitivity pattern of Salmonella Typhi in paediatric patients. *Pakistan Armed Forces Medical Journal*, *72*(4), 1241-44. https://doi.org/10.51253/pafmj.v72i4.8036