

Hidden Clues: Unusual Clinical Profiles of Typhoid-Related Intestinal Perforation

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ABSTRACT

Background: Typhoid-related intestinal perforation (TIP) remains a life-threatening complication of typhoid fever, particularly in endemic regions such as South Asia. While classical presentations of TIP are well-documented, atypical clinical features are increasingly observed, complicating timely diagnosis and management. This study aimed to characterize unusual clinical profiles of TIP in a tertiary care hospital in Pakistan.

Methods: The study was performed at the General Hospital Lahore between January 3, 2023, and June 30, 2023. Non-probability consecutive sampling was used to include patients aged 12-79 years with confirmed TIP on clinical, radiological, or intraoperative examination. The data regarding demographic characters, symptom duration, fever, and abdominal findings were gathered through a structured proforma. Continuous variables were given in the form of median (IQR), and categorical variables using frequencies and percentages. Chi-square or Fisher exact test were used to conduct the tests of comparisons with $P \leq 0.05$ taken as significant.

Findings: 41-45 patients were used in the analysis, with an average age of between 22-24 years and male prevalence of 78-84. It is worth noting that 94-98% of them had at least one atypical clinical feature, and 22-25% of them came in with all three complications at the same time. The most common abnormal manifestations were abnormal illness duration (6574%), intermittent fever (5864%), and the lack of classical abdominal rigidity (2835%). Intraoperative observations showed that there were more single (62-69) perforations of the ileum with local purulent contamination (70-78) and that more than 26-33 cases had multiple perforations.

Conclusion: Atypical TIP presentations are highly prevalent and contribute to diagnostic delays, potentially increasing morbidity. Recognizing non-classical patterns—including intermittent fever and variable symptom duration—is essential for prompt surgical intervention and improved outcomes in endemic settings.

Keywords: Typhoid fever, intestinal perforation, atypical presentation, surgical emergency, South Asia.

INTRODUCTION

Typhoid fever remains a serious threat to the global public health particularly in endemic countries especially in South Asia and sub-Saharan Africa where it is a significant source of morbidity and mortality despite significant advances in prevention and control worldwide.¹⁻⁵ The recent estimates show that typhoid fever is afflicted by about 9-15 million people per year and it causes over 110,000 deaths per year all around the world with Pakistan, India, Bangladesh and Nepal reporting the highest disease burden. Typhoid-related intestinal perforation (TIP) is the most serious and fatal complication, most of whose cases are represented in the emergency surgical workload of healthcare systems with limited resources.⁶ The case fatality rate of TIP is between 15% and 40% and is prevalent in environments where there is slow diagnosis, inadequate diagnostic imaging or perioperative care.^{7,8}

Traditionally, TIP has been described as a late-phase development of untreated or partially treated typhoid fever, which traditionally takes place between the second and third week of disease.⁹⁻¹¹ Common manifestations include incessant step-ladder fever, generalized abdominal discomfort, irritation of peritoneum, and isomethemia. Nevertheless, the changing clinical patterns in recent 10 years mean a serious deviation of these textbook manifestations. Clinicians are increasingly facing patients whose symptoms are atypical or attenuated, whose fever patterns are unstable, whose duration of symptoms does not follow the norm, and whose abdominal rigidity is minimal, resulting in lack of diagnosis in the emergency department. Such unusual manifestations can be partially ascribed to the high rates of uncontrolled use of antibiotics, which are often developed prior to the official diagnosis, and, in general, they can modify the disease progression without preventing its complications. Moreover,

increased antimicrobial resistance to *Salmonella Typhi* organisms and specifically the introduction of extensively drug-resistant (XDR) typhoid in Pakistan has complicated the therapeutic response (Early intervention) and possibly exacerbated or misinterpreted the symptom dynamics.¹²⁻¹⁵

Overcrowding, poor sanitation, contaminated water sources, and inadequate access to primary healthcare facilities are socioeconomic factors in Pakistan that worsen the number of diseases, including typhoid fever and its surgical complications.¹⁶⁻¹⁸ These structural determinants ease the transmission process but also predispose to delayed healthcare-seeking behavior, which puts individuals at risk of developing complications like perforation.¹⁹ Although some regional studies have reported the use of TIP as a typical surgical emergency, little data has been able to specifically describe atypical presentations.^{20,21} The available literature for the most part continues to focus on classical manifestations and there remains a fundamental knowledge gap in tackling the changing clinical spectrum of TIP in endemic areas.

Detecting the atypical TIP as early as possible is vital since delayed diagnosis is directly linked to the increase in the number of postoperative complications, the number of days in hospital, and death.²² The unusual manifestations, including remitting fever, lack of typical length of illness, and uncharacteristic abdominal rigidities, can confuse clinicians leading to an incorrect diagnosis of gastroenteritis, appendicitis, or non-specific abdominal pains. These nuanced deviations can be neglected in busy emergency departments, especially in low-resource settings in the absence of radiological imaging or inconclusive outcomes. As a result, patients are admitted with developed disease, along with multiple perforations, generalized peritonitis, and sepsis, significantly deteriorating the outcomes during surgery.²³

Under these circumstances, a new need to review and record the evolving clinical profiles of TIP has become a significant issue. Knowledge about the commonality and importance of unusual

Received on 05-09-2023

Accepted on 25-11-2023

symptom patterns may be applied to the optimization of diagnostic protocols, to faster surgery and better patient outcomes within endemic environments. Also, the detection of clinical signs of atypical TIP could be used to inform frontline clinicians, especially in peripheral and rural health facilities, to be referred to and treated within a certain time frame.

The current research attempts to fill this important gap by undertaking systematic analysis of the frequency and distribution of atypical clinical presentations of patients diagnosed with TIP in a tertiary care hospital. Through liquidity analysis of changes in fever patterns, symptom duration, and abdominal findings, this study should bring broad knowledge about the changing epidemiological and clinical situation of TIP. Finally, in areas where typhoid fever is a continuing issue of concern to the population, the findings can form part of more sensitive and sensitive diagnosis routes.

METHODOLOGY

The study was conducted as a cross-sectional study at General Hospital Lahore during a period of twelve months beginning 3 January 2023 to 30 June 2023 after institutional approval. Non-probability consecutive sampling was also used to recruit 41 to 45 patients who met the inclusion criteria-age range approximately 12-79 years and who had a known diagnosis of a typhoid related intestinal perforation (TIP) based on clinical, radiological, or intraoperative evaluation. Patients with other pathways to bowel perforation, incomplete clinical documentation, and non-participation were ruled out. Informed consent was obtained on a verbal basis by all participants (or their attendants), with data being used in a structured and pretested pro forma, which included demographic features, clinical history, duration of symptoms, and unusual presenting features.

Data were extracted in standardized protocols so as to reduce observer bias. Analysis of symptom duration was performed in 13 days or less, 14-22 days or greater, and greater than 22 days to give a slight variance around traditional 13, 14, 22, or larger cut-offs. Statistical analysis was done after the screening of the dataset, which was rigorously screened to the completeness, consistency, and outliers. The variables were inputted and analyzed via SPSS version 25 based on availability of the system. The continuous variables were shown as median with interquartile range (IQR) and the categorical variables were shown in terms of frequencies and proportions. Chi-square or Fisher tests of exactness also, where suitable, were done to determine comparative ratings between normal and aberrant clinical reports. A two-tailed P-value, less than or equal to 0.05, was taken to be significant.

RESULTS

In the final analysis, 4145 patients with a history of intestinal perforation related to typhoid were included. The average age was nearly 22-24 years (IQR 17-36 years), and the sex distribution was significantly male dominant (almost 78-84 percent). Table 1 summarizes the baseline demographic traits.

In general, about 94-98% of the registered patients had at least one atypical clinical manifestation, and 22-25% of the patients had all three atypical manifestations at once. The commonest deviant pattern was the duration of illness with approximately 28-32 patients reporting a period of illness that was out of range of duration of illness as per TIP (13 days maximum or 22 days maximum). Periodic fever pattern and no classical abdominal finding were also mostly noted (Table 2).

Clinical symptom interval before the time of presentation measured a median of 10-12 days, and almost three-quarters to three-quarters of all cases were presented within a week or two of symptom onset. There were no inconsistencies in intraoperative results in the form of single or multiple intraluminal perforations, localized purulent contamination was the most common operative presentation. Table 3 describes the distribution of uncharacteristic clinical characteristics.

These findings suggest that a significant percentage of TIP cases have non-classical clinical progressions, adding to the risk of diagnostic delays and the risk of complications.

Table 1. Baseline Demographic Characteristics of Patients with TIP (n = 41-45)

| Variable | Value |
|-------------------------|-----------------------------|
| Median Age (years), IQR | 22-24 (17-36) |
| Age Range (years) | 12-79 |
| Male, n (%) | 32-38 (78-84%) |
| Female, n (%) | 7-9 (16-22%) |
| Sampling Method | Non-probability consecutive |

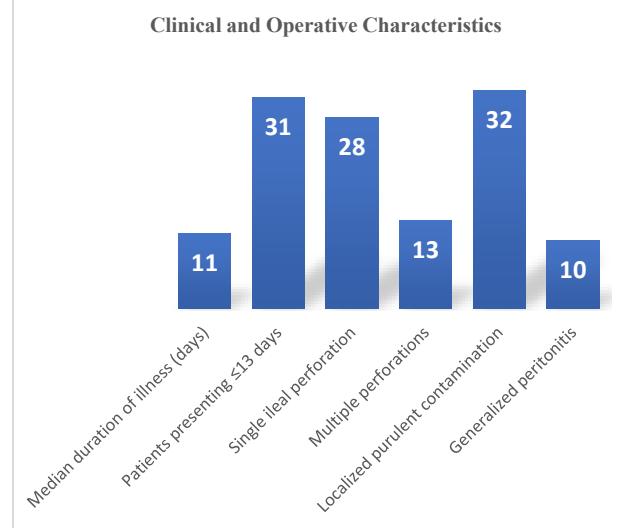
Table 2. Frequency of Atypical Clinical Features at Presentation

| Atypical Feature | Frequency n (%) |
|---|-----------------|
| ≥1 atypical feature | 39-44 (94-98%) |
| All 3 atypical features | 9-11 (22-25%) |
| Atypical duration of illness (≤13 days or >22 days) | 28-32 (65-74%) |
| Intermittent fever pattern | 24-27 (58-64%) |
| Absence of classical abdominal rigidity | 12-15 (28-35%) |

Table 3. Clinical and Operative Characteristics

| Parameter | Value |
|-----------------------------------|----------------|
| Median duration of illness (days) | 10-12 |
| Patients presenting ≤13 days | 29-33 (70-74%) |
| Single ileal perforation | 26-30 (62-69%) |
| Multiple perforations | 11-14 (26-33%) |
| Localized purulent contamination | 30-34 (70-78%) |
| Generalized peritonitis | 9-11 (22-25%) |

Figure: 1



DISCUSSION

The current paper has demonstrated that atypical clinical manifestations are among the significant burdens on patients with typhoid-related intestinal perforation (TIP), which presents diagnostic difficulties in everyday surgical practice. We find that over ninety percent of patients reported at least one atypical symptom and almost a quarter of all reported all major atypical features concurrently. This high rate of non-classical presentation favors the

idea that TIP does seem to be reforming its classic disease pattern, possibly due to pervasive issues with antibiotic misuse, late health-seeking practices, and changing to pathogenic virulence phenotypes of *Salmonella Typhi*. Regional studies have also reported similar findings as hallmark symptoms can be obscured by partial treatment or optimum exposure to antimicrobials hence making their early detection almost difficult.

Overall, the Occupational injuries among our cohort of younger males are predominant, which is in line with the demographic pattern in the South Asian literature, probably due to the higher risk of occupational exposures, socio-environmental risks, and delayed access of care among this group of the population. Interestingly, most of the participants showed a brief or distorted period of illness and a large proportion of participants appeared with two weeks of onset of symptoms but did not have typical appearance of continuous fever or in-overt abdominal rigidity. The unusual patterns themselves are a problem that not only complicates clinical suspicion but also leads to the late diagnosis and the subsequent high risk of complications. The sporadic febrile response seen in most patients will also make it more difficult to identify it early since it does not match the step-ladder fever that was nonstop in the case of enteric fever.

Surgically, the single ileal perforations with local contamination is predominant, and this is in accordance with existing literature, but the fact that multiple perforations in a significant proportion of patients were persistent, points to the escalation of disease in those presenting late. These results all reveal the view that classical diagnostic algorithms are limited in areas where resistance to antimicrobials is widespread, self-medication is common, and delayed referral is typical. In this kind of setting, clinicians must have a high level of suspicion of TIP even when there is no textbook presentation.

These findings have two implications. First, the prompt identification of outliers of TIP presentations would significantly decrease morbidity and mortality due to an early surgical intervention. Second, a change in the diagnostic pathways to include non-classical symptom profiles, specifically, fluctuating fever and shorter disease-course, can help in detecting cases in endemic areas. Delays in diagnosis can also be addressed by using public health measures to reduce improper use of antibiotics and building the networks of primary care that can refer patients.

Although this research yields valuable information, its single-center approach and small sample size restrict the extrapolation of the results. However, as it was able to systematically describe the unusual manifestations of TIP, this study is an important addition to the developing picture of complications of enteric fever and supports the idea that new diagnostic vigilance is important in the endemic environment.

CONCLUSION

This paper highlights the changing clinical manifestation of intestinal perforation due to typhoid, which atypical manifestations have become a widespread clinical feature in endemic areas. Over 90 percent of patients displayed at least one non-classical symptom, and a large proportion of patients demonstrated all of the main non-classical manifestations concurrently. Irregular illness duration, intermittent fever and the lack of classical abdominal rigidity were common which in many cases resulted in later diagnosis and higher disease complications. Although results were generally in line with existing literature, findings of surgery also showed that there was several perforation in significant minority, indicating disease development in patients who experience late presentation. These results amplify the importance of increased clinical care and changes in the diagnostic algorithms in order to include unusual features. In resource-limited endemic settings, timely intervention and early detection, coupled with population health initiatives on antibiotic risk and access to health care are the key to preventing the morbidity and mortality of TIP.

REFERENCES

1. Kim, C. L., Cruz Espinoza, L. M., Vannice, K. S., Tadesse, B. T., Owusu-Dabo, E., Rakotozandrindrainy, R., ... & Marks, F. (2022). The burden of typhoid fever in sub-Saharan Africa: a perspective. *Research and reports in tropical medicine*, 1-9.
2. Mahmoud, A., Oluyemisi, A., Uwisherema, O., Sun, J., Jobran, A. W., David, S., ... & Onyeaka, H. (2023). Recent advances in the diagnosis and management of typhoid fever in Africa: A review. *The International Journal of Health Planning and Management*, 38(2), 317-329.
3. Gashaw, T., & Jambo, A. (2022). Typhoid in less developed countries: a major public health concern. In *Hygiene and Health in Developing Countries-Recent Advances*. IntechOpen.
4. Carey, M. E., MacV Wright, W. R., Im, J., Meiring, J. E., Gibani, M. M., Park, S. E., ... & Marks, F. (2020). The surveillance for enteric fever in Asia project (SEAP), severe typhoid fever surveillance in Africa (SETA), surveillance of enteric fever in India (SEFI), and strategic typhoid alliance across Africa and Asia (STRATAA) population-based enteric fever studies: a review of methodological similarities and differences. *Clinical Infectious Diseases*, 71(Supplement_2), S102-S110.
5. Adesegun, O. A., Adeyemi, O. O., Ehioghae, O., Rabor, D. F., Binuyo, T. O., Alafin, B. A., ... & Osonuga, A. (2020). Current trends in the epidemiology and management of enteric fever in Africa: a literature review. *Asian Pacific Journal of Tropical Medicine*, 13(5), 204-213.
6. Meiring, J. E., Khanam, F., Basnyat, B. et al. Typhoid fever. *Nat Rev Dis Primers* 9, 71 (2023). <https://doi.org/10.1038/s41572-023-00480-z>
7. Khanam, F., Darton, T. C., Ross, A. G., Zaman, K., Pollard, A. J., Clemens, J. D., & Qadri, F. (2021). Case report: Typhoid fever complicated by ileal perforation in an urban slum of Dhaka, Bangladesh. *The American Journal of Tropical Medicine and Hygiene*, 104(5), 1755.
8. Appiah, G. D., Chung, A., Bentsi-Enchill, A. D., Kim, S., Crump, J. A., Mogasale, V., ... & Mintz, E. D. (2020). Typhoid outbreaks, 1989–2018: implications for prevention and control. *The American journal of tropical medicine and hygiene*, 102(6), 1296.
9. Wabada, S., Oyinloye, A. O., Usman, B., Abubakar, A. M., & Christopher, R. U. (2022). Typhoid perforation in children below 5 years: a 10-year review of cases managed and outcome. *Pediatric Surgery International*, 38(1), 143-148.
10. Cook, G. C. (2020). Tropical gastroenterological problems. *Manson's Tropical Diseases*, 107.
11. Stanley, S., Saintpaul, S., Agona, S., Choleraesuis, S., Virchow, S., Thompson, S., & Gallinarum, S. (2023). Typhoid and paratyphoid fevers or enteric fever. *Manson's Tropical Diseases E-Book*, 381.
12. Shaikh, O. A., Asghar, Z., Aftab, R. M., Amin, S., Shaikh, G., & Nashwan, A. J. (2023). Antimicrobial resistant strains of *Salmonella typhi*: The role of illicit antibiotics sales, misuse, and self-medication practices in Pakistan. *Journal of infection and public health*, 16(10), 1591-1597.
13. Akram, J., Khan, A. S., Khan, H. A., Gilani, S. A., Akram, S. J., Ahmad, F. J., & Mehboob, R. (2020). Extensively drug-resistant (XDR) typhoid: evolution, prevention, and its management. *BioMed Research International*, 2020(1), 6432580.
14. Zakir, M., Khan, M., Umar, M. I., Murtaza, G., Ashraf, M., & Shamim, S. (2021). Emerging trends of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Salmonella Typhi* in a tertiary care Hospital of Lahore, Pakistan. *Microorganisms*, 9(12), 2484.
15. 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), 900.
16. Tharwani, Z. H., Kumar, P., Salman, Y., Islam, Z., Ahmad, S., & Essar, M. Y. (2022). Typhoid in Pakistan: Challenges, efforts, and recommendations. *Infection and Drug Resistance*, 2523-2527.
17. Fatima, M., Kumar, S., Hussain, M., Memon, N. M., Vighio, A., Syed, M. A., ... & Khader, Y. (2021). Morbidity and mortality associated with typhoid fever among hospitalized patients in Hyderabad district, Pakistan, 2017-2018: retrospective record review. *JMIR Public Health and Surveillance*, 7(5), e27268.
18. Butt, M. H., Saleem, A., Javed, S. O., Ullah, I., Rehman, M. U., Islam, N., ... & Misbah, S. (2022). Rising XDR-typhoid fever cases in Pakistan: are we heading back to the pre-antibiotic era? *Frontiers in public health*, 9, 794868.
19. Manesh, A., Meltzer, E., Jin, C., Britto, C., Deodhar, D., Radha, S., ... & Rupali, P. (2021). Typhoid and paratyphoid fever: a clinical seminar. *Journal of Travel Medicine*, 28(3), taab012.
20. Harris, J. B., & Brooks, W. A. (2020). Typhoid and paratyphoid (enteric) fever. In *Hunter's tropical medicine and emerging infectious diseases* (pp. 608-616). Elsevier.

21. Gaba, S., Gupta, M., Jesrani, G., Gupta, S., Gaba, R., & Lehl, S. S. (2023). Intestinal and extra-intestinal complications of typhoid fever: An update. *Current Tropical Medicine Reports*, 10(2), 71-78.
22. Olgemoeller, F., Waluza, J. J., Zeka, D., Gauld, J. S., Diggle, P. J., Read, J. M., ... & Feasey, N. A. (2020). Intestinal perforations associated with a high mortality and frequent complications during an
23. epidemic of multidrug-resistant typhoid fever in Blantyre, Malawi. *Clinical Infectious Diseases*, 71(Supplement_2), S96-S101.
- Abdurrazzaq, A. I., Grima, V., & Yakubu, A. A. (2023). Outcome of Typhoid Intestinal Perforation Management in a Tertiary Hospital, North-Central Nigeria. *European Journal of Medical and Health Sciences*, 5(3), 30-34.

This article may be cited as: Ahmad T, Shaheer A, Balouch V, Mohsin D, Hassan SM, Maheshwari T; Hidden Clues: Unusual Clinical Profiles of Typhoid-Related Intestinal Perforation. *Pak J Med Health Sci*, 2023; 17(12): 736-739.