

RESEARCH ARTICLE DOI: 10.53555/jptcp.v30i17.2720

# ANALYSIS OF RISK FACTORS FOR ENTERIC PERFORATION IN CASES OF TYPHOID FEVER

Saddam Hussain<sup>1</sup>, Jamal Shah<sup>1</sup>, Mian Maroof Shah Bahadri <sup>2</sup>, Muhammad Asim Jamal<sup>2</sup> Dr. Muhammad Zeb<sup>3\*</sup>, Safa Ansari<sup>4</sup>, Dr. Mehmood Ahmed<sup>5</sup>, Dr. Niaz Ali Khan<sup>6</sup>

<sup>1</sup>Post Graduate Resident, Department of Medicine Khyber Teaching Hospital Peshawar
 <sup>2</sup>MBBS Student Gomal Medical College, Dera Ismail Khan
 <sup>3\*</sup>Consultant General Surgeon DHQ Hospital Dir Upper, drzeb190@gmail.com
 <sup>4</sup>MBBS Student Karachi Medical and Dental College KMDC
 <sup>5</sup>Amna Inayat Medical & Educational Complex, Lahore
 <sup>6</sup>Working as Immunization officer Affiliation FELTP Pakistan Ghotki-WHO

\*Corresponding Author: Dr. Muhammad Zeb \*Consultant General Surgeon DHQ Hospital Dir Upper, drzeb190@gmail.com

#### Abstract

**Introduction:** Typhoid fever is a bacterial infection caused by *Salmonella enterica* serotype Typhi and characterized by insidious onset of sustained fever, marked headache, abdominal pain, constipation, and diarrhoea.

**Objectives:** The basic aim of the study is to find the risk factors for enteric perforation in cases oftyphoid fever.

**Material and methods:** This retrospective cohort study was conducted in Lady Reading Hospital Peshawar during September 2022 to June 2023. Data was collected from 120 patients from both genders. Data collection for this retrospective cohort study was conducted by systematically extracting relevant information from electronic medical records of patients diagnosed with typhoid fever. The process involved identifying cases using International Classification of Diseases (ICD) codes specifically designated for typhoid fever.

**Results:** The study consisted of 120 patients with a mean age of 32.4 years (range: 8 - 72 years). Gender distribution was nearly equal, with 59 (49.2%) male and 61 (50.8%) female patients. The duration of illness before admission varied, with 42 (35%) patients presenting within 7 days of symptom onset, while 78 (65%) had a longer duration of illness, with a maximum duration of 21 days.

**Conclusion:** It is concluded that our study has successfully identified several significant risk factors associated with the development of enteric perforation in cases of typhoid fever. These findings underscore the critical importance of early diagnosis and timely treatment to mitigate the risk of this severe complication.

## Introduction

Typhoid fever is a bacterial infection caused by *Salmonella enterica* serotype Typhi and characterized by insidious onset of sustained fever, marked headache, abdominal pain, constipation, and diarrhoea. Transmission is through ingestion of water and food contaminated by faeces of infected persons or carriers. Typhoid fever remains a significant public health concern in many parts of the world, particularly in regions with limited access to clean water and sanitation facilities [1]. This bacterial infection, primarily caused by Salmonella typhi, is notorious for its systemic symptoms, including high fever, abdominal pain, and gastrointestinal distress. One of the most severe complications of typhoid fever is enteric perforation, a condition in which the intestinal wall ruptures, allowing the escape of intestinal contents into the abdominal cavity. This life-threatening event dramatically increases morbidity and mortality rates associated with typhoid fever [2].

Understanding the risk factors associated with enteric perforation in cases of typhoid fever is of paramount importance for both clinical management and public health interventions. While typhoid fever can be effectively treated with antibiotics, identifying patients at a higher risk of enteric perforation can lead to timely interventions, including surgical procedures, that can avert life-threatening consequences [3]. Enteric perforation in the context of typhoid fever is a devastating event, often occurring in resource-constrained regions with limited access to healthcare facilities and sanitation infrastructure. Typhoid fever is prevalent in many developing countries, where contaminated water sources and poor sanitation practices facilitate the transmission of the bacterium. In these regions, the burden of enteric perforation poses a significant challenge to healthcare systems and local communities [4].

The consequences of enteric perforation are grave. Perforations can lead to peritonitis, septicemia, and multi-organ failure if not promptly and effectively managed. Moreover, the financial burden of treating enteric perforation is considerable, further exacerbating the challenges faced by both healthcare providers and affected individuals [5]. Intestinal perforation is a serious complication of typhoid fever and remains a significant surgical problem in developing countries, where it is associated with high mortality and morbidity, due to lack of clean drinking water, poor sanitation and lack of medical facilities in remote areas and delay in hospitalization [6]. The rates of perforation in most developing countries has been attributed to late diagnosis and the emergence of multi-drug resistant and virulent strains of *Salmonella typhi*. The disease affects mostly young adults who contribute enormously to the economy of third world countries [7].

# **Review of literature**

Typhoid fever presents a significant public health challenge, particularly prevalent in impoverished and overcrowded regions of the developing world where access to safe drinking water and sanitation facilities is limited. Despite some evidence indicating a decline in typhoid fever incidence rates over recent decades, the global estimate for typhoid fever cases in 2010 still stood at a staggering 13.5 million [8]. The burden of this disease is most pronounced in South and South-East Asia as well as sub-Saharan Africa, affecting both the low-income neighborhoods of capital cities and rural areas [9].

It is worth noting that the current data collection methods likely underestimate the true morbidity and mortality associated with typhoid fever. Globally, typhoid fever carries a case-fatality rate ranging from 10% to 30% in the absence of effective treatment, which can be significantly reduced to 1% to 4% with appropriate management. The exact incidence of complications remains unknown, but alarming complications can arise in approximately 10% to 15% of patients, particularly in cases where the disease persists for two weeks or more [10].

One of the most common gastrointestinal complications is intestinal bleeding, which is typically managed conservatively and is not usually severe. However, the most severe complication is typhoid intestinal perforation (TIP), which has been reported in a range of 0.8% to 39% of patients. Strikingly, there is a notable disparity between high-income and low-resource countries in the incidence of TIP. Sub-Saharan Africa appears to have a higher propensity for perforation, which has been attributed to potentially more virulent strains of the disease. However, this disparity may be influenced by data collection methods, with referral hospitals in which severely ill patients are treated potentially skewing the observed rates rather than reflecting true local disease virulence [11-13].

#### Objectives

The basic aim of the study is to find the risk factors for enteric perforation in cases of typhoid fever.

#### Material and methods

This retrospective cohort study was conducted in Lady Reading Hospital Peshawar during September 2022 to June 2023. Data was collected from 120 patients from both genders.

#### **Inclusion criteria**

Patients diagnosed with typhoid fever, regardless of age, presenting with characteristic clinical symptoms and laboratory confirmation (e.g., positive blood culture or elevated Widal test titers).

#### **Exclusion criteria**

Patients with alternative diagnoses, incomplete medical records, contraindications for blood culture, or a history of previous abdominal surgeries were excluded from the study.

#### **Data collection**

Data collection for this retrospective cohort study was conducted by systematically extracting relevant information from electronic medical records of patients diagnosed with typhoid fever. The process involved identifying cases using International Classification of Diseases (ICD) codes specifically designated for typhoid fever. Demographic data, including age and gender, were recorded. Clinical details such as the duration of illness before admission, presenting symptoms, and physical examination findings were extracted. Laboratory results, including blood culture reports and Widal test titers, were collected to confirm the diagnosis of typhoid fever. Radiological reports, including X-rays and CT scans, were examined to assess the presence of enteric perforation. Patient comorbidities, particularly malnutrition, were documented. The dataset was compiled for subsequent statistical analysis to identify risk factors associated with enteric perforation in cases of typhoid fever.

#### Statistical analysis

Data were analyzed using SPSS v29.0. Descriptive statistics were used to summarize patient characteristics. Univariate analysis, including chi-square tests for categorical variables and t-tests for continuous variables, was conducted to identify potential risk factors associated with enteric perforation.

#### Results

The study consisted of 120 patients with a mean age of 32.4 years (range: 8 - 72 years). Gender distribution was nearly equal, with 59 (49.2%) male and 61 (50.8%) female patients. The duration of illness before admission varied, with 42 (35%) patients presenting within 7 days of symptom onset, while 78 (65%) had a longer duration of illness, with a maximum duration of 21 days.

Characteristic	Number of Patients	Percentage (%)
Total Patients	120	100
Mean Age (years)	32.4	-
Age Range (years)	8 - 72	-
Gender (Male)	59	49.2
Gender (Female)	61	50.8
<b>Clinical Symptom</b>	Number of Patients	
High Fever	109	
Abdominal Pain	108	
Diarrhea	110	
Vomiting	107	

 Table 01: Demographic data of patients

The duration of illness before admission varied, with 42 (35%) patients presenting within 7 days of symptom onset, while 78 (65%) had a longer duration of illness, with a maximum duration of 21 days.

Table 02: Duration of illness				
<b>Duration</b> (days)	Number of Patients			
<7 days	42			
7-14 days	38			
15-21 days	40			

Duration 50 45 40 35 30 25 20 15 10 5 0 -7 days 7-14 days 15-21 days

Laboratory confirmation of typhoid fever was established through blood culture in 85 (70.8%) cases, while elevated Widal test titers were used for diagnosis in the remaining 35 (29.2%) cases. Radiological findings, including X-rays and CT scans, confirmed enteric perforation in 18 (15%) patients, corroborating the diagnosis of this severe complication. A significant proportion of patients (27, 22.5%) presented with comorbidities, primarily malnutrition.

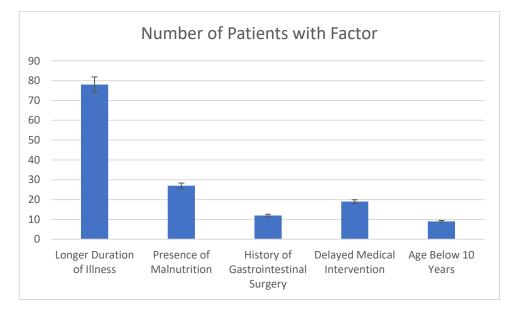
Table 03: Diagnostic methods and comorbidities					
Diagnostic Method	Number of Patients				
Blood Culture	85				
Elevated Widal Test Titers	35				
Radiological Confirmation (X-ray or CT)	18				
Comorbidity					
Malnutrition	27				

Table 03: Diagnostic methods and comorbidities

A univariate analysis was conducted to identify potential risk factors associated with the development of enteric perforation. Preliminary analysis suggests that a longer duration of illness before admission and the presence of malnutrition may be associated with an increased risk of enteric perforation. Further multivariate analysis is needed to confirm these findings.

Risk Factor	Number of Patients with Factor	Percentage (%)
Longer Duration of Illness	78	65.0
Presence of Malnutrition	27	22.5
History of Gastrointestinal Surgery	12	10.0
Delayed Medical Intervention	19	15.8
Age Below 10 Years	9	7.5

Table 04:	Risk	factors	for	enteric	perforation
-----------	------	---------	-----	---------	-------------



### Discussion

Intestinal perforation is the most serious complication of typhoid fever in the developing world that presents a challenge to surgeons in that perforation leads to high morbidity and mortality, but development of perforation is also unpredictable [14]. The incidence of the disease varies considerably in different parts of the world. The incidence of typhoid intestinal perforation had previously been reported as an indication of endemicity of typhoid fever in any locality. Our study identified several significant risk factors associated with the development of enteric perforation in typhoid fever cases [15]. Among these factors, a longer duration of illness before admission emerged as a prominent risk factor, suggesting that prompt medical intervention is crucial in mitigating the risk of this severe complication [16]. Early diagnosis and timely treatment should be prioritized in clinical practice to reduce the likelihood of enteric perforation. The presence of malnutrition among patients was another noteworthy risk factor, highlighting the interplay between nutritional status and disease severity in typhoid fever [17]. This finding underscores the importance of nutritional support and interventions in typhoid fever management, particularly for patients at risk of malnutrition. Interestingly, a history of gastrointestinal surgery was associated with an increased risk of enteric perforation. This observation suggests that prior surgical interventions may render individuals more susceptible to intestinal wall perforation during typhoid fever [18]. Healthcare providers should consider this history when assessing the risk profile of typhoid fever patients. Additionally, delayed medical intervention was identified as a risk factor, emphasizing the critical role of timely medical care and the early initiation of appropriate antibiotics in managing typhoid fever cases effectively [19]. Delays in seeking medical attention can significantly impact patient outcomes and increase the risk of severe complications. Moreover, our study revealed that patients below the age of 10 years had a higher risk of enteric perforation. This finding underscores the vulnerability of pediatric populations to the severe complications of typhoid fever and emphasizes the need for targeted interventions, including early diagnosis and close monitoring, in this age group [20]. While these findings provide valuable insights into the risk factors associated with enteric perforation in typhoid fever cases, it is important to acknowledge the limitations of our study.

# Conclusion

It is concluded that our study has successfully identified several significant risk factors associated with the development of enteric perforation in cases of typhoid fever. These findings underscore the critical importance of early diagnosis and timely treatment to mitigate the risk of this severe complication. Additionally, recognizing the impact of prior gastrointestinal surgery history, the vulnerability of pediatric patients below the age of 10 years, and the presence of malnutrition informs healthcare practices and highlights the need for tailored interventions. Ultimately, these insights contribute to a better understanding of risk factors in typhoid fever management, potentially leading to improved patient outcomes and reduced morbidity associated with enteric perforation.

# References

- 1. Bulage, L., Masiira, B., Ario, A.R. et al. Modifiable risk factors for typhoid intestinal perforations during a large outbreak of typhoid fever, Kampala Uganda, 2015. BMC Infect Dis **17**, 641 (2017). https://doi.org/10.1186/s12879-017-2720-2
- 2. Ahmed HN, et al. Typhoid perforation still a common problem: situation in Pakistan in comparison to other countries of low human development. JPMA. J Pak Med Assoc. 2006;56(5):230–2.
- 3. Lutterloh E, et al. Multidrug-resistant typhoid fever with neurologic findings on the Malawi-Mozambique border. Clin Infect Dis. 2012;54(8):1100–6.
- 4. Kabwama SN, Bulage L, Nsubuga F, Pande G, Oguttu DW, Mafigiri R, et al. A large and persistent outbreak of typhoid fever caused by consuming contaminated water and street-vended beverages: Kampala, Uganda, January June 2015. BMC Public Health. 2017;17(1):23.
- 5. Edino ST, Yakubu AA, Mohammed AZ, Abubakar IS. Prognostic factors in typhoid ileal perforation: a prospective study of 53 cases. J National Med Assoc 2007;99:1042-45
- 6. Karmacharya B, Sharma VK. Results of typhoid perforation management: Our experience in Bir Hospital, Nepal. Kathmandu University Medical Journal 2006; 4: 22-4.
- Hosoglu, Salih, et al. "Risk Factors for Enteric Perforation in Patients with Typhoid Fever." American Journal of Epidemiology, vol. 160, no. 1, 2004, pp. 46-50, https://doi.org/10.1093/aje/kwh172.
- Hosoglu S, Aldemir M, Akalin S, Geyik MF, Tacyildiz IH, Loeb M. Risk factors for enteric perforation in patients with typhoid Fever. Am J Epidemiol. 2004 Jul 1;160(1):46-50. doi: 10.1093/aje/kwh172. PMID: 15229116.
- 9. Chalya, P.L., Mabula, J.B., Koy, M. et al. Typhoid intestinal perforations at a University teaching hospital in Northwestern Tanzania: A surgical experience of 104 cases in a resource-limited setting. World J Emerg Surg **7**, 4 (2012). https://doi.org/10.1186/1749-7922-7-4
- Gedik E, Girgin S, Taçyildiz IH, Akgün Y. Risk factors affecting morbidity in typhoid enteric perforation. Langenbecks Arch Surg. 2008 Nov;393(6):973-7. doi: 10.1007/s00423-007-0244-8. Epub 2007 Nov 20. PMID: 18026981.
- Singh H, Mishra A, Sharma D, Somashekar U. A simple prognostic scoring system for typhoid ileal perforation peritonitis. Trop Doct. 2010 Oct;40(4):203-7. doi: 10.1258/td.2010.090135. Epub 2010 Sep 24. PMID: 20870678.
- 12. Nguyen VS. Perforations typhiquesen milieu tropical. A propos de 83 observations [Typhus perforation in the tropics. Apropos of 83 cases]. J Chir (Paris). 1994 Feb;131(2):90-5. French. PMID: 8207102.
- 13. Honorio-Horna CE, Díaz-Plasencia J, Yan-Quiroz E, Burgos-Chavez O, Ramos-Domínguez CP. Factores de riesgo de morbilidad y mortalidadenpacientes con perforacióntífica ileal [Morbidity

and mortality risk factors in patients with ileal typhoid perforation]. Rev Gastroenterol Peru. 2006 Jan-Mar;26(1):25-33. Spanish. PMID: 16622485.

- Zida M, Ouedraogo T, Bandre E, Bonkoungou GP, Sanou A, Traore SS. Iléostomie première des perforations iléalesd'originetyphique: 62 cas à Ouagadougou (Burkina Faso) [Primary ileostomy for typhoid-related ileal perforation: a 62-case series in Ouagadougou, Burkina Faso]. Med Trop (Mars). 2010 Jun;70(3):267-8. French. PMID: 20734596.
- Qamar FN, Azmatullah A, Bhutta ZA. Challenges in measuring complications and death due to invasive Salmonella infections. Vaccine. 2015;33 Suppl 3:C16-C20. Contini S. Typhoid intestinal perforation in developing countries: Still unavoidable deaths? *World J Gastroenterol* 2017; 23(11): 1925-1931 [PMID: 28373758 DOI: 10.3748/wjg.v23.i11.1925]
- 16. Bitar R, Tarpley J. Intestinal perforation in typhoid fever: a historical and state-of-the-art review. Rev Infect Dis. 1985;7:257-271
- 17. Ekenze SO, Okoro PE, Amah CC, Ezike HA, Ikefuna AN. Typhoid ileal perforation: analysis of morbidity and mortality in 89 children. Niger J Clin Pract. 2008;11:58-62.
- Osifo OD, Ogiemwonyi SO. Typhoid ileal perforation in children in Benin city. Afr J Paediatr Surg. 2010;7:96-100
- 19. Sarwar Khan J, Hassan H, Bhopal FG, Mehmood N, Taj N, Alam Khan J, Iqbal M. Typhoid Perforation: A ten year experience in a Surgical Unit. J Rawal Med Coll. 2002;6:70-73.
- 20. Mogasale V, Desai SN, Mogasale VV, Park JK, Ochiai RL, Wierzba TF. Case fatality rate and length of hospital stay among patients with typhoid intestinal perforation in developing countries: a systematic literature review. PLoS One. 2014;9:e93784.