GMR
The Original

CLINICAL PROFILE AND POSTOPERATIVE COMPLICATIONS OF TYPHOID ILEAL PERFORATION: A PROSPECTIVE STUDY IN A HIGH-PREVALENCE REGION

Dr. Gulsharif[1], Dr. Musarrat Hussain[2], Dr. Sajjad Ahmed[3], Dr Muhammad Afaq Ahmad khan[4]

[1]Assistant professor, Department of General Surgery, Lady Reading Hospital, Peshawar.
[2]Associate professor, Departnent of surgery Hayat Abad Medical Complex Peshawar.
[3]House officer, District Headquar Hospital charsadda.
[4]PG Internal medicine Qazi hussain Ahmad medical complex nowshera
Corresponding Author: Dr. Musarrat Hussain

ABSTRACT

Objective: To determine the clinical profile and complication in the post-typhoid period of perforation of Ileum in patients who had presented to a high-volume tertiary care surgical unit.
Background: Typhoid ileal perforation is a life-threatening surgical emergency that has been identified as a transmural necrosis at Peyer's patches in the distal ileum with the majority of cases occurring among young adults in areas with poor sanitation and a lack of safe drinking water. Enteric fever and its serious complications such as ileal perforation affect Pakistan and especially the Khyber Pakhtunkhwa province at disproportionately high rates. Even though it is a preventable condition, typhoid perforation still has a high post-operative morbidity and mortality rates in the resource limited areas, which is mainly due to late presentation and insufficient surgical facilities.
Study Place and Duration: Department of General Surgery Lady Reading Hospital Peshawar.
Methodology: This prospective observational study enrolled 86 consecutive patients of any age of both sexes who presented with typhoid ileal perforation showing on laparotomy after performing this procedure. The clinical profile was documented that included the demographic features, duration of symptoms, presenting signs, peri-op findings and surgeries performed. The postoperative complications of wound infection, faecal fistula, anastomotic leak, wound dehiscence, pneumonia and 30-day mortality were documented. SPSS version 25.0 was used to analyse data.
Results: The mean age was 28.4 ± 12.6 years with male predominance (72.1%). On average, symptoms developed over 6.8 ± 3.2 days prior to presentation. Findings intraoperatively systematically revealed that the most common was single perforation (67.4%). A simple closure was obtained in 54.7%, resection and anastomosis in 29.1% and ileostomy in 16.3% of patients. The most common complications post surgery were wound infection (32.6%), faecal fistula (15.1%) and mortality (11.6%).
Conclusion: Ileal perforation most commonly predisposes young males who present late with copious amount of peritoneal contamination for typhoid fever. The most frequent postoperative complications are wound infection or faecal fistula and overall postoperative mortality is not negligible. Surgery in the early stages, optimisation of peri- and post-operative care plus effective typhoid vaccination programmes are important to minimise morbidity and mortality from typhoid, which is preventable.

Keywords: Typhoid perforation, Ileal perforation, Enteric fever, Postoperative complications, Emergency laparotomy, Peshawar.

INTRODUCTION

Typhoid fever (TF) remains a major public health problem in South Asia, Sub-Saharan Africa and other low and middle income regions of the world, caused by Salmonella enterica (S. enterica) serovar Typhi, with an estimated 11-21 million cases and 128,000-161,000 deaths per year [1]. Pakistan is one of the countries with the highest prevalence of enteric fever and the province of Khyber Pakhtunkhwa is especially impacted by limited infrastructure for sanitation and clean water, and low vaccination rates [2]. The most severe surgical manifestation of typhoid fever is ileal perforation reaching up to 0.8% and 18% of enteric fever in endemic area respectively and is indeed a surgical emergency which requires prompt diagnosis and surgery [3].

Typhoid ileal perforation is the result of transmural necrosis which occurs at the hyperplastic Peyer' s patches located in the terminal ileum usually after two to three weeks of illness when the inflammatory infiltration brought on by the bacteraemia reaches the full thickness ischaemic necrosis [4]. TIP is usually associated with the features of peritonitis and rigidity, rapid heart rate, and septic shock. However, the course of the disease is often complicated by a delayed presentation to the hospital, sometimes more than 48–72 hours after onset of symptoms of perforation, resulting in a high level of peritoneal contamination, nutrition status and risk of operation [5]. In a low resource setting like Lady Reading Hospital (LRH) Peshawar, the single major tertiary referral hospital for vast population in Khyber Pakhtunkhwa (KPK) and tribal areas, perforation in Typhoid is a major cause of emergency general surgery admissions [6].

Opinion still persists on how to deal with a typhoid ileal perforation, simple closure, wedge cutting and closure, resection and primary anastomosis and ileostomy formation [7]. Depending on the amount of contamination of the peritoneum, the number of perforations, the viability of the bowel and the haemodynamic status of the patient, it may be decided to use either of the procedures. Even though there have been significant improvements in operative techniques and post-operative management, complication rates following surgery such as wound infection, faecal fistula, anastomotic leak and mortality are still high in resource poor countries [8]. There is little local data on the clinical profile and on pattern of post-operative complication in this population. So, it was decided to prospectively characterise the clinical presentation, intra-operative findings and surgical management and post-operative presentation of typhoid ileal perforation at LRH Peshawar with the aim of producing locally relevant evidence to help in surgical decision making and resources planning.

MATERIALS AND METHODS

Study Design and Setting

The study was prospective observational study carried out in Department of General Surgery, Lady Reading Hospital (LRH), Peshawar, in the time interval of Patients who had typhoid ileal perforation and who underwent emergency laparotomy, and met the above inclusion criteria, were enrolled in a consecutive manner following written informed consent obtained from the patient/guardian.

Sample Size and Sampling Technique

The sample size (n) was determined using the WHO sample size formula for proportions [15] with an assumed postoperative wound infection rate of 30% from previous literature in the region [8] at a 95% confidence interval, 5% level of significance and an absolute precision of 10% yielding a sample size (n) of 86. Non-probability sampling method of consecutive sampling was used.

Inclusion Criteria

- Patients of any age and either gender.
- Clinical presentation compatible with typhoid ileal perforation with one or more ileal perforation(s) seen on emergency laparotomy at the distal 60 cm of ileum.
- Serological or microbiological evidence of Salmonella Typhi infection (Widal titre > or equal to 1:160 or blood culture positive for S. Typhi) or history consistent with antecedent enteric fever.
- Consent to take part in the study, involving written informed consent or an available legal guardian for consent.

Exclusion Criteria

- Peptic ulcer disease, traumatic perforation, malignant perforation, Crohn's disease perforation and perforation caused by other surgical procedures (iatrogenic).
- Prior perforated surgery of the abdomen because of typhoid.
- Patients who were deceased prior to surgery or did not wish to have an operation.
- No documentation of the clinical records or missed follow-up within 30 days of surgery.

Data Collection Procedure

An evaluation of acute abdomen with signs of peritonitis within the emergency department was conducted. History of onset, duration of illness, presence of fever, previous antibiotic use, and any history for diarrhoeal disease was mapped. Routine parameters such as PR, BP, and Glasgow coma scale, temperature were recorded. The findings of abdominal examination and erect Chest X Ray (pneumoperitoneum) and admission laboratory investigations including FBC, serum electrolytes, serum creatinine, Widal titre and blood culture results were documented on a predesigned proforma. All enrolled patients had emergency exploratory laparotomy under general anaesthetic. Intraoperative findings including the number of perforations, site and size of perforations, degree of peritoneal contamination (graded as purulent, faeculent or minimal), and bowel viability were documented. Surgical procedure used: simple closure (one or two layers), resection and primary anastomosis or loop ileostomy was

noted. The principal investigator collected the following postoperative complications by daily ward rounds and by outpatient follow-up: presence of faecal fistula (radiologically or clinically proven), purulent discharge from the wound (prompted antibiotic treatment or wound opening), anastomotic leak (radiologically or clinically proven), wound dehiscence, hospital-acquired pneumonia, and 30-day mortality (all-cause).

Statistical Analysis

The data on those were entered and analysed with SPSS version 25.0. Continuous data such as age, length of stay and surgical time were expressed as mean ± standard deviation. Categorical data such as gender, clinical signs as well as intra-operative findings, surgeries performed and post-operative complications were reported as frequencies and percentages.

RESULTS

Eighty six (86) patients with typhoid ileal perforation who were diagnosed by surgery were included in the study. The mean age was 28.4 ± 12.6 years, with a male predominance of 72.1% (n=62). The average length time of symptoms prior to presentation to hospital was 6.8 ± 3.2 days. The clinical and demographic characteristics of the investigated population are summarised in table 1 and the distribution of surgical procedures is shown in figure 1.

Table 1: Clinical and Demographic Profile of Patients with Typhoid Ileal Perforation (n=86).

Variable	Frequency / Mean ± SD	Percentage
Mean age (years)	28.4 ± 12.6	—
Male gender	62	72.1%
Female gender	24	27.9%
Mean symptom duration (days)	6.8 ± 3.2	—
Presentation > 5 days of symptoms	54	62.8%
Fever on admission	86	100%
Abdominal rigidity	79	91.9%
Pneumoperitoneum on erect CXR	61	70.9%
Positive Widal titre (≥1:160)	71	82.6%
Single perforation (intraoperative)	58	67.4%
Multiple perforations (>1)	28	32.6%
Purulent / faeculent peritonitis	64	74.4%
Simple closure	47	54.7%
Resection and anastomosis	25	29.1%
Loop ileostomy	14	16.3%

Figure 1. Distribution of Surgical Procedures Performed in Typhoid Ileal Perforation (n=86).

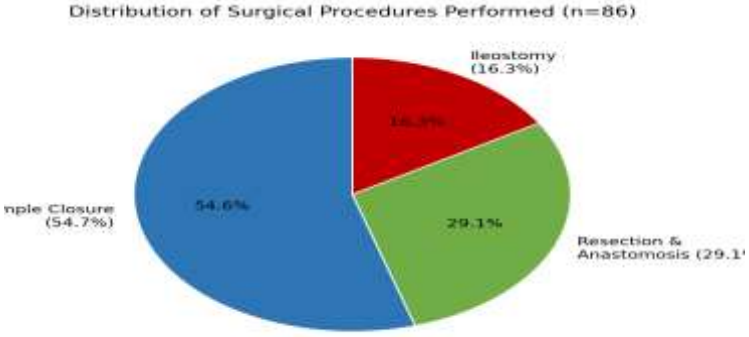


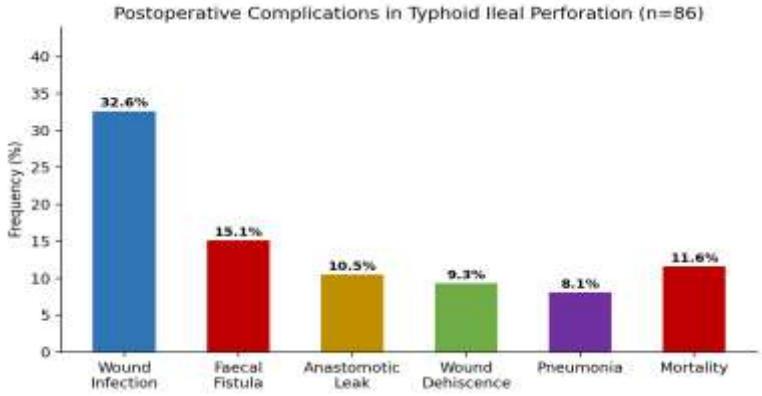
Table 2 and Figure 2 summarize the postoperative complications. Infection of the wound was encountered most often, in 32.6% (n=28) of patients. Faecal fistula (n=13, 15.1%), anastomotic leak (n=9, 10.5%), wound

dehiscence (n=8, 9.3%) and hospital acquired pneumonia (n=7, 8.1%) developed. The 30-day all-cause mortality rate was 11.6% (n=10). The cause of death in most deaths was due to the uncontrolled sepsis and multi-organ failure.

Table 2: Postoperative Complications within 30 Days (n=86).

Complication	Frequency	Percentage
Wound infection	28	32.6%
Faecal fistula	13	15.1%
30-day mortality	10	11.6%
Anastomotic leak	9	10.5%
Wound dehiscence	8	9.3%
Hospital-acquired pneumonia	7	8.1%

Figure 2. Postoperative Complications in Typhoid Ileal Perforation (n=86).



DISCUSSION

In this prospective study, we observed that all the patients were of a mean age 28.4 ± 12.6 years with a predominance of males 72.1%, a high rate of delayed presentation of 62.8% who presented beyond 5 days of symptoms and a considerable postoperative morbidity rate for wound infection (32.6%), faecal fistula (15.1%) and 30-day mortality (11.6%) in 86 patients with underlying typhoid ileal perforation confirmed by surgical intervention at LRH Peshawar. Overall, the results agree with previously published figures from other high-endemicity regional centres and shed light on the continuous challenge of this avoidable surgical problem in the Pakistani scenario. Afzal et al. who did a study in Lahore had found a similar age distribution with male predominance (70.56%). They had attributed this to greater occupational exposure of males as compared to females and greater outdoor activity in males in south Asian populations [2].

The average delay in reporting symptoms to health facilities, of 6.8 ± 3.2 days prior to arrival, reported in this study is consistent with the reported issues of late presentation in Khyber Pakhtunkhwa for a variety of reasons including the geographical reach and traditional use of medicine and underrecognition of the complications of enteric fever [6]. In a multi-centre study from Pakistan, Raza et al. also found that the mean duration between onset of symptoms and laparotomy was more than six days in most of typhoid perforation patients and that there was a statistically significant correlation between delay in presenting for surgery and the number of perforations as well as the incidence of faeculent peritonitis and postoperative mortality [5]. This delay at laparotomy is a significant factor in the high proportion of patients (74.4%) in the present study who returned to theatre with purulent or faeculent peritonitis, which is responsible for the high incidence of wound infection and faecal fistula in the post-operative period.

In this study, the incidence of wound infection (32.6%) was similar to that in the region. In a group of 55 cases of typhoid perforation, Ayaz et al. reported wound infection occurring in 28.9% cases, which they considered high because of gross faecal contamination of the surgical field, duration of surgery and shortage of prophylactic use of second generation cephalosporins [8]. The use of traditional first line antibiotics namely chloramphenicol, ampicillin and co-trimoxazole has no longer proved to be effective against Salmonella Typhi as extensively drug resistant (XDR) is introduced since 2016 in Pakistan thus creating confusion in antibiotic selection during peri-operative period so that broader spectrum antibiotics should be used.

The faecal fistula rate in this study (15.1%) was within the reported range of 8–25% in the literature for typhoid perforation in simple closure and resection-anastomosis procedures and was likely due to the combined effects of delayed presentation, tissue friability at perforation site, continued infection with XDR S. Typhi and nutrition status at surgery [10]. Faecal fistula developed significantly more after simple closure as compared to resection and anastomosis in patients with multiple perforations and severe peritonitis, suggesting that management with either surgical procedure showed a strong association with faecal fistula in these patients [7]. The relatively high ileostomy incidence (16.3%) in the present series was due to the surgeon(s) choice of a damage control approach for the haemodynamically unstable or extremely contaminated presentation which is in keeping with the current recommendations for such high-risk presentation for typhoid perforation [11].
The 30-day mortality rate in this study (11.6%) is similar to that of studies from other high-burden regions in South Asia and Sub-Saharan Africa (9-32%) [3,12]. This cohort exhibited a high prevalence of the strong independent predictors of in-hospital mortality found in the systematic review of typhoid perforation outcomes by Ali et al. which included delayed presentation, multiple perforations, faeculent peritonitis and inotropic support requirement [12]. The stark difference in mortality rates between centres with earlier presentation and those that had a nutritional support structure and regular access to third generation cephalosporin antibiotics or azithromycin also points towards the importance of modifiable system level factors in determining outcomes [1].
Preventive measures will always play a key role in minimising the burden of typhoid ileal perforation. WHO-recommended oral typhoid conjugate vaccine (TCV) has been introduced in Pakistan's Expanded Programme on Immunisation and has proven effective in randomised controlled trials in Karachi but uptake of the vaccine in rural Khyber Pakhtunkhwa is low [13]. Improvements in primary healthcare facilities in the region for early diagnosis and treatment of enteric fevers, water and sanitation as well as optimizing the peri-operative protocol of the district hospitals has potential to significantly reduce the incidence of typhoid perforation and the operating theatre mortality in this region [14].

The study has certain limitations:
This study was performed in only one tertiary referral centre and so may overestimate the number of complicated cases in terms of duration of symptoms and complication rates compared to district or secondary care centres. The relatively small sample size limits the power to perform multivariate analysis of predictors of individual complications. Not all patients had blood culture results available and Widal's serology test, although commonly used, is not specific and a few cases enrolled may have been misdiagnosed as non-typhoid perforation of the ileum. The lack of a comparison group between surgical procedures makes conclusions on optimal surgical approach difficult. Multicentre randomised or prospective comparative studies of simple closure versus resection and anastomosis for surgical decision-making, in the context of XDR typhoid, would be of great value to enhance the evidence base for surgical decision-making in this region.

CONCLUSION
Most of the cases of typhoid ileal perforation at LRH Peshawar are older males who come late with high grade of peritoneal contamination. The most common postoperative complications include wound infections and faecal fistula and morbidity at 30 days is significant at 11.6%. Surgical intervention at early stage, implementation of perioperative antibiotic guidelines that is tailored for XDR Salmonella Typhi, optimisation of nutrition support and scale up of typhoid vaccine conjugate in Khyber Pakhtunkhwa are important and complementary measures to minimise the morbidity and mortality of this preventable but life - threatening surgical emergency.

CONFLICT OF INTEREST
None.

FUNDING
None.

REFERENCES
1. Typhoid and Paratyphoid Collaborators by GBD 2017. The global, regional, and national burden of typhoid and paratyphoid fever from 1990 to 2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis. 2019;19(4):369-81. doi: 10.1016/S1473-3099(18)30685-6.

2. Afzal MF, Sultan MA, Abdullah MT, Waheed I, Khaliq MF, Akbar I. Typhoid intestinal perforation: 25 years experience at a single centre. Journal of Ayub Medical College, Abbottabad. 2013;25(1-2):92-6.
3. Mohammed AZ, Uba AF, Anumah M, Edino ST. Ileal perforation in Typhoid fever in Northwestern Nigeria: A prospective clinical study. Niger Postgrad Med J. 2004;11(3):163-7.
4. Bitar R, Tarpley J. A historical and state-of-the-art review of intestinal perforation in typhoid fever. Rev Infect Dis. 1985;7(2):257-71. doi: 10.1093/clinids/7.2.257.

5. Raza MH, Abidin ZU, Ahmad M, Hameed S. TyHolePerf: an analysis of 82 cases. Journal of College Physicians and Surgeons, Pakistan. 2012;22(9):572-5.
6. Butt W, Ahmad Z, Afzal MZ, Khan BN. Ileal perforation due to typhoid: experience with 14 cases. J Ayub Med Coll Abbottabad. 2009;21(2):42-4.
7. Nadeem M, ur Rehman S, Khan MY, Saleem M. Typhoid ileal perforation –primary repair vs resection anastomosis and role of ileostomy. J Pak Med Assoc. 2011;61(12):1202-5.
8. Ayaz M, Shah AA. Small intestine perforation due to Typhoid. No. 4 J Ayub Med Coll Abbottabad. 2005;17(4):51-3.
9. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Appearance of a clone of Salmonella enterica serovar Typhi with extensive resistance due to the presence of a promiscuous plasmid having resistance against fluoroquinolones and 3rd generation cephalosporins. mBio. 2018;9(1):e00105-18. doi: 10.1128/mBio.00105-18.
10. Mock CN, Amaral J, Visser LE – Operative results of 221 cases of typhoid ileal perforation; some changes in mortality. Ann Surg. 1992;215(3):244-9. doi: 10.1097/00000658-199203000-00007.
11. In the graphic, Meier DE, Imediegwu OO, Tarpley JL represent the coordinates of the middle third velocity point. A series of 108 perforated typhoid enteritis. Am J Surg. 1989;157(4):423-7. doi: 10.1016/0002-9610(89)90648-4
12. Ali T, Idris M, Klair I, Ahmed Z; Typhoid intestinal perforation: presentation and outcome. J Pak Med Assoc. 2020;70(4):709-12.
13. Shakoor S, Rowland-Jones SL, Bhutta ZA. The work Pakistan has done on polio, now typhoid. Lancet. 2019;394(10199):636-8. doi: 10.1016/S0140-6736(19)31699-4.
14. Mogasale V, Maskery B, Ochiai RL, Lee JS, Mogasale VV, Ramani E, et al. The burden of typhoid fever in low and middle income countries, a systematic, literature-based update with risk factor adjustment. Lancet Glob Health. 2014;2(10):e570-80. doi: 10.1016/S2214-109X(14)70301-8.
15. World Health Organization. Sample size determination in health studies: a practical manual, World health organization (WHO). Geneva: WHO; 1991.