

Original Article

# Surgical Management of Typhoid Ileum Perforations: A Systematic Review

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## ABSTRACT

**Background:** Typhoid is a disease caused by a gram negative bacterium *Salmonella typhi*. Prolonged infection leads to necrosis in the Peyer's patches of the antimesenteric border of bowel leading to intestinal perforation. Various surgical procedures have been described for the treatment of these perforations. Typhoid intestinal perforations are still associated with high case fatality rates averaging 15.4%.

**Objective:** To identify current surgical management options for typhoid ileal perforations and to describe the best surgical management in relation to mortality and complications.

**Methods:** A systematic review was done using PRISMA guidelines. Common search terms used were typhoid perforation/typhoid ileal perforation management. A narrative synthesis of the findings from the included studies structured around the type of intervention, target population characteristics, types of outcome and intervention content was done.

**Results:** Primary closure of ileal perforations was the most commonly performed procedure. Ileostomy is the choice of surgery for severe abdominal contamination and when the patient has poor general health. Most studies found mortalities and complications to be unrelated to surgical procedure done. Mortality was significantly associated with the number of perforations and abdominal contamination.

**Conclusions:** Individual studies support particular surgical interventions but the review showed that complications and mortality are not related to the type of surgical intervention alone but to a number of

other non-surgical factors. There is need for further level 1 studies on this topic.

## INTRODUCTION

Typhoid fever, also known as enteric fever, is a potentially fatal multisystemic illness caused primarily by *Salmonella enterica*, subspecies *enterica* serovar *typhi* and, to a lesser extent, related serovars *paratyphi* A, B, and C.

Patients with perforations are diagnosed clinically with signs of peritonitis and radiologically with simple plain x-rays and ultrasound. Diagnosis is difficult as patients are ill for a while prior to perforation which usually occurs in the second week of illness. Ileal perforations due to typhoid have posed a management challenge to surgeons and have high case fatality rates averaging 15.4% amongst hospitalized patients.

The purpose of this review is three fold: (1) to identify the current surgical treatment options for typhoid ileal perforations. (2) to identify the factors influencing the choice of treatment. (3) to identify the best treatment option (s) for typhoid perforation.

## Methods

A systematic review was done using PRISMA guidelines. Common search words of typhoid perforation/ typhoid ileum perforation management were used to search on PubMed, Cochrane library and Google Scholar. All retrospective and prospective studies between 2000 and 2018 were included. Titles and abstract screening was done by one researcher. Reviews of selected articles was done by two independent reviewers. Review protocol was registered on the PROSPERO register

of systematic reviews (Prospero review number CRD42018089394).

**Inclusion criteria:**

The inclusion criteria were:

- Level I, II, III and IV studies
- Studies with patients treated between 2000 and 2018.
- Only abstracts in English with available full papers.
- Human subjects
- Patients of all ages with Ileum perforations identified at surgery.
- Only patients with a positive microbiological test for typhoid or positive Widal's test.

**Exclusion criteria:**

The exclusion criteria were:

- Case reports and case series with less than 10 patients were excluded
- Studies that did not give details of surgical procedure.

Types of outcome measures:

Studies with details of complications and mortalities in relation to the surgical intervention were included. Studies in which a second surgical intervention was carried out were also included.

Analysis:

A narrative synthesis of the findings from the included studies structured around the type of intervention, target population characteristics, type of outcome and intervention content was performed. The review focused on the various surgical treatment options that were described in the selected studies. The factors leading to the choice of surgical treatment was described and categorized. Each treatment option was analysed in relation to mortality, complications and need for further surgical treatment.

Quantitative analysis of the data was done for 8 studies that had similar methodology and had clearly correlated the surgical intervention with the mortalities and complications observed. Odds ratios were calculated with 95% confidence interval and plotted on a forest plot for comparison of mortality with surgical intervention.

**RESULTS**

Studies included:

From the 71 studies identified with full text available, 24 studies were excluded as no confirmation of diagnosis was done for typhoid fever. Thirty one studies met the full inclusion criteria . Eight studies had quantitatively correlated the surgical intervention with mortality and complications. These included a randomized control trial and seven cohort studies. The 7 cohort studies that had quantitatively related the various surgical treatment options to mortality and complications were subjected to the Newcastle-Ottawa quality assessment for cohort studies as shown in Table 2 below.

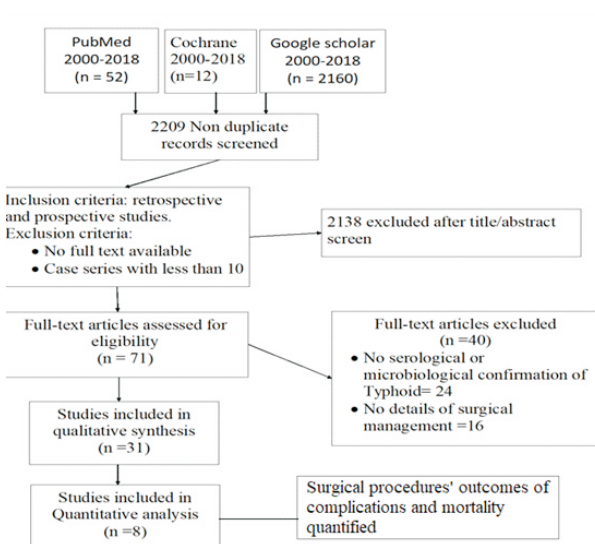


Diagram 1: Flow diagram of the study selection process

**Table 2: Newcastle-Ottawa Quality Assessment Form for Cohort Studies included**

Study	Selection ****			Comparability **		Outcome ***		
	Representative of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start	Comparability of the cohorts	Assessment of outcomes	Follow up long enough	Adequacy of follow up
Arshad et al (3)	*		*	*	*	*	*	
Bashir et al (10)	*		*	*	*	*		
Choudhury et al (12)			*	*		*		
Tariq et al (16)	*	*	*	*	*	*	*	*
Steven et al (23)	*		*	*		*		
Sagar et al (28)	*		*			*	*	
Udai et al(18)	*		*	*	*	*		

Quality assessment using the New-Castle Ottawa Scale for cohort studies included for quantitative analysis. An asterisk [\*] indicated that a measure was adequately addressed in this study. A maximum of one star was awarded for each numbered item within the selection and outcome categories while two for the comparability.

Two studies were rated as good quality , two studies were fair quality (12, 20) and three were poor quality (14, 25, 30) according to the Newcastle-Ottawa quality assessment for cohort studies. Based on this assessment, a meta-analysis was not carried out.

*Surgical treatment options*

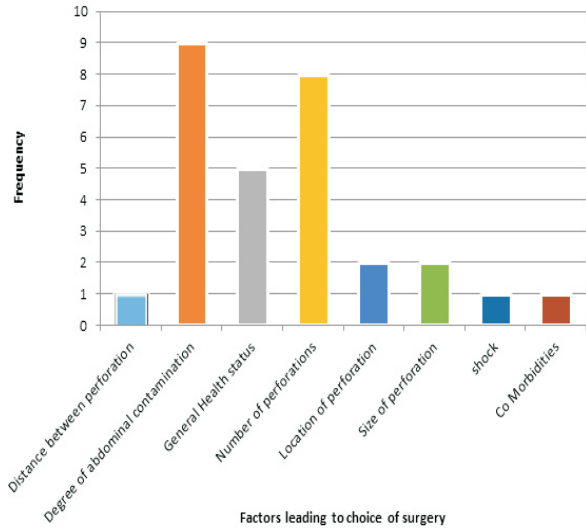
All eligible studies used an open approach. Table 3 lists the surgical options that were employed.

**Table 3: Surgical treatment options identified.**

Surgical procedure	Number of studies N=31
<b>Primary closure (repair)</b>	22
<b>Resection and anastomosis</b>	15
<b>Loop ileostomy at perforation</b>	10
<b>Proximal end ileostomy with perforations repair</b>	9
<b>Right hemicolectomy</b>	7
<b>Resection and Ileo-transverse anastomosis</b>	5
<b>Primary closure with omental patch</b>	4
<b>Ileostomy with distal mucous fistula</b>	2
<b>T tube drainage</b>	1

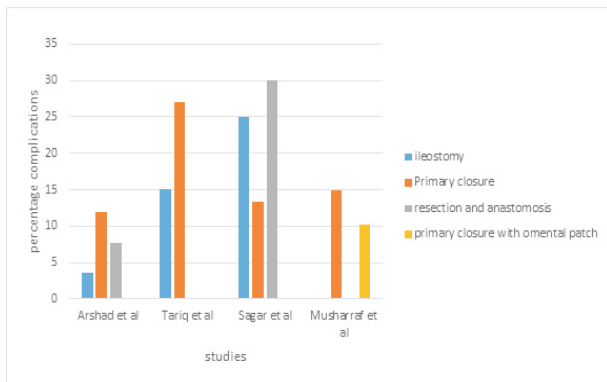
*Factors influencing choice of surgical procedure*

The factors influencing the choice of surgical intervention from the studies in the review were categorised and tallied as shown in figure 1.

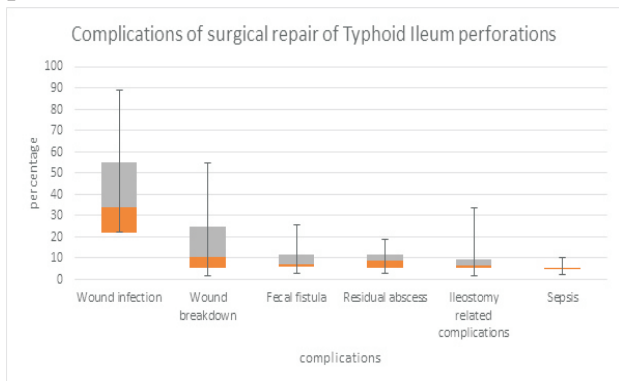


**Figure 1: Factors influencing the choice of surgery**

*Complications*



**Figure 2: Complications with various surgical procedures**



**Figure 3: Box plot of early and intermediate complications of surgical management of typhoid ileum perforations.**

*Mortality*

Mortality rates in patients with typhoid perforations have shown a declining trend. Authors have described various factors that are significantly related to mortality. Figure 3 shows 8 studies that correlated mortality to various surgical procedures used in the treatment of typhoid ileum perforations.

**Figure 4: Forest plot comparing mortality rates among various surgical procedures (see figure on the next page)**

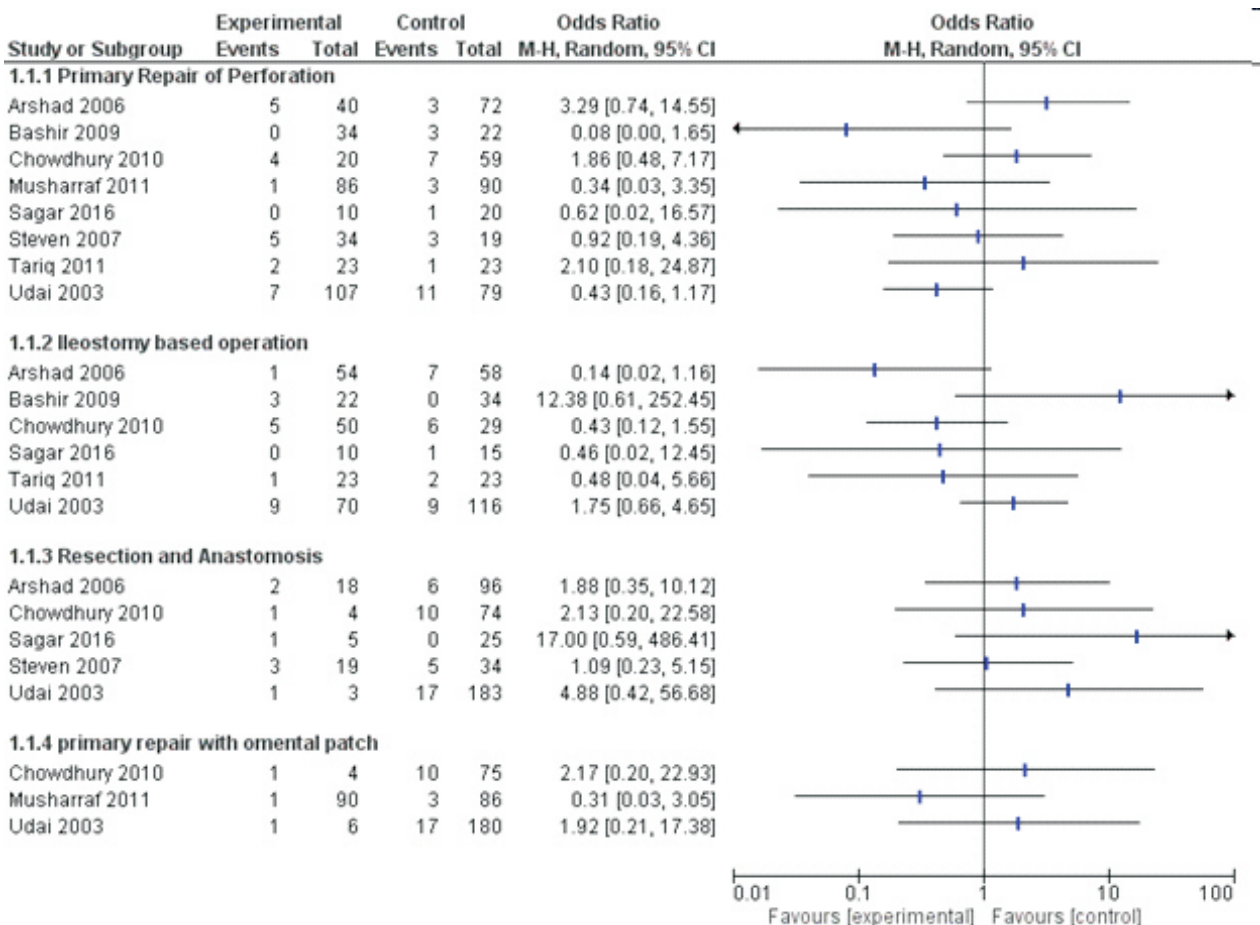
**DISCUSSION**

Overall case fatality rates have reduced for hospitalized patients with typhoid ileum perforations. Mogasale et al in 2013 found a case fatality rate (CFR) for hospitalized patients with typhoid ileum perforations at 15.4%. The average case fatality for studies in the review from January 2014 to January 2018 dropped to an average of 11.6% in these studies.

Early presentation to hospital, adequate preoperative resuscitation with intravenous fluids and blood products, antibiotic treatment, employment of damage control surgery were associated with improved outcomes (6-9, 14, 24, 26, 27)

The use of primary repair as the choice of surgical treatment of ileum perforations due to typhoid is recommended because it is simple, quick and cost effective. . Patients presenting with single perforations were more common than multiple perforations in all studies except for the study by Ekenze et al that showed an equal distribution of patients . All studies that were testing primary repair as a surgical treatment option recommended it to be the treatment of choice for single perforations . The only exception to this was in the presence of severe abdominal contamination when exteriorisation of the perforation was the preferred choice of surgical intervention . Primary repair with omental patch was described in 3 studies including a randomized control trial (RCT) by Musharraf et al . No blinding was done in the RCT that compared primary repair alone to primary repair with omental patch. For the omental patch repairs, the perforation was first repaired in 2 layers with vicryl 3/0 for the inner layer and silk 3/0 for the outer layer. The omentum was fixed with vicryl 3/0 over the repair as a patch.

**Figure 4: Forest plot comparing mortality rates among various surgical procedures**



Musharraf et al used this only for patients with single ileum perforations due to typhoid.

Complications were noted to be increased with primary repair according to Arshad et al . These mostly included wound infection, residual abscess and faecal fistula. Faecal fistulae were a result of repair breakdown or re-perforations. Uba et al and Faisal et al however found less complications in patients treated with primary repair . The majority of studies found no significant correlation between primary repair and occurrence of complications in comparison to other surgical treatment modalities . Primary repair was not significantly correlated with

mortality and complications based on level II and III evidence.

Faisal et al recommended primary repair as the choice of treatment for patients presenting with symptoms of bowel perforation of less than 48 hours duration .

Resection and anastomosis was the choice of surgical procedure in the presence of multiple perforations . Right hemicolectomy was done with ileotransverse anastomosis when the perforation was within 15cm of the ileocecal junction (8, 27). This review noted that there was no significant difference between mortality in patients treated with

resection and anastomosis as opposed to those treated with other surgical methods but this evidence is considered level II. With regards to complications, resection and anastomosis was significantly associated with increased number of complications. Ugwu et al advised not to attempt resection and anastomosis within 15cm of the ileocecal junction as this was associated with increased complications.

Various types of ileostomies were described in the review including loop ileostomy via perforation, end ileostomy and primary repair with proximal loop ileostomy. T-tube ileostomy in paediatric patients of typhoid fever with multiple ileal perforations and poor general condition can be used as an alternative to bowel ileostomy. Given the better outcome with T-tube, it may be necessary to include patients with single perforation and poor general condition among those who may benefit from T-tube in future studies. Anand et al had no mortalities and there was no need for a second operation with the use of a T-tube.

Ileostomies were the choice of surgical intervention in the presence of multiple perforations and severe abdominal contamination based on level II evidence. There was a significantly reduced mortality amongst patients surgically treated with ileostomy compared to other surgical procedures. However enterostomies were associated with increased stoma related complications such as stoma prolapse (4, 24). Long term complications such as incisional hernia, late adhesive intestinal obstruction and hypertrophic scar or keloid formation were only comprehensively assessed in one study by Phillip et al and hence no conclusion could be made on long term complications in typhoid ileum perforation. This study did not correlate these long term complications to the exact type of surgical intervention.

With no surgical intervention standing clearly above the other interventions and the relatively high mortality rate in patients with typhoid ileum perforations, it is recommended that prevention of

this condition should be done when possible. This mainly involves breaking the faecal-oral cycle by means of good hygiene. With social-economic challenges, this may also be difficult to achieve.

One of the limitations of this review was that only articles in English were included.

## CONCLUSION

The choice of surgical procedure for treatment of typhoid ileum perforation is dependent on the number of perforations and the level of peritoneal contamination. Aggressive resuscitation and prompt surgical treatment are key to better outcomes. Complications and mortality are not related to the surgical procedure alone but to a number of non-surgical factors. There is need for further level 1 evidence on this topic.

## FUNDING

No funding was required for the review.

## CONFLICTS OF INTEREST

There were no conflicts of interest to be declared.

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