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**Original Research Article**

# Retrospective case control study on typhoid and non-typhoid small bowel perforation

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## ABSTRACT

**Background:** Out of several causes of small bowel perforations, Typhoid is the commonest cause in tropical countries claiming a higher morbidity and mortality profile. In Spite of conducting a good clinical examination and a battery of investigatory procedures, the etiology of perforation still remains obscure in a good number of cases. This retrospective case control study was conducted with an objective to evaluate the causes of small bowel perforation and to compare the surgical procedures and the outcomes in patients of typhoid and non-typhoid small bowel perforations.
**Methods:** This study was based on hospital records for the last 3 years from April 2003 to April 2006. All the cases that were admitted with perforations had undergone a battery of tests to rule out the causes. 69 patients had one or the other test positive for typhoid (cases); the other causes of perforation were taken as control (n=43).
**Results:** In typhoid perforations, although none of the operative procedures are clearly advantageous over the other, but anastomoses including the by-pass procedures are associated with more of complications wound dehiscence (p value 0.004), anastomotic leakage (p value 0.04), intra-abdominal collections (p value 0.009) with a longer hospital stay and hence to be avoided as practicable.
**Conclusions:** Typhoid ileal perforation still has a poor prognosis with high morbidity and mortality. Late presentation, delayed surgery, multiple perforations, severe peritoneal contamination, and post-operative faecal fistula are factors that have an adverse effect on mortality. Most deaths occur during the early post-operative period, with survivors having a prolonged hospital stay.

**Keywords:** Anastomosis, Bypass, Non typhoid small bowel perforation, Typhoid

## INTRODUCTION

Typhoid ileal perforation is still very common in the tropical countries like India with high morbidity and mortality. The mortality ranges between 9 and 43%, with survivors having severe wound infection and a history of long hospital stay.[1-4] Many factors, such as late presentation, inadequate pre-operative resuscitation, delayed operation, the number of perforations, and the extent of faecal peritonitis, have been found to have a significant effect on the prognosis.[5-9] Various operative procedures, such as simple closure of perforation, wedge resection, resection anastomosis and Ileo colic bypass were statistically analyzed with respect to the morbidity in terms of wound infection, wound dehiscence, intra-abdominal collection, and anastomotic leakage with resultant fistula. The present effort was to compare the outcomes in typhoid and non-typhoid perforations in terms of morbidity, mortality and duration of hospital stay to find out the ideal operative procedure.[10]

## METHODS

It was a retrospective case control study. A total of 112 patients with small bowel perforation were included in the study. As per the inclusion criteria, all the patients

with small bowel perforations were grouped into typhoid or non-typhoid perforation group. Perforations secondary to obstruction were excluded from study. Patients were admitted with signs and symptoms pertaining to hollow viscus perforation, vitals monitored and subjected to a battery of investigatory procedures.

The entire patients were subjected to plain X-ray abdomen for Pneumoperitoneum, Widalserology, stool / urine culture; blood cultures were done along with selective tissue biopsy culture. Bone marrow aspiration culture, being an invasive and painful procedure, was selectively advised to patients suspected of typhoid perforation. Stool and urine culture was advised to both case and control subjects. Histopathology suggestive of erythrophagocytosis and mononuclear cell infiltration was helpful in excluding other causes for perforation.

Typhidot test to detect the IgM and IgG antibodies against the outer membrane protein (OMP, A 50k Dalton protein) of Salmonella typhi was employed to screen out the typhoid cases. The cases, where etiology could not be established in spite of conducting all the aforementioned tests were grouped under the umbrella of non-specific small bowel perforation.

The outcomes of both cases and controls were compared against the operative procedure performed. Simple closure and the wedge resection were the commonest surgical procedure done. Resection anastomosis and ileotransverse bypass was done in selected cases with regard to the location of the perforation, number of perforations, the associated co morbid conditions and the operating surgeon's judgement. The complications observed were those of wound infection, wound dehiscence, leakage from the anastomosis, intra-abdominal collection, and respiratory complications. The outcome was recorded in the form of cure of the disease, to leave against medical advice or death of the subject analyzed against the weeks of hospitalization.

***Statistical analysis***

The various parameters were tabulated and analyzed. Patients who had typhoid small bowel perforations were compared with non-typhoid small bowel perforations for presentation, occurrence of complications and mortality. Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) software version 10.0 A 'p' value less than 0.05 was considered significant for the purpose of the study.

## RESULTS

A total of 112 small bowel perforations were included in the study, out of which, 69 (61.60%) were diagnosed based on laboratory tests as typhoid perforation and 43 (38.4%) as non-typhoid perforation. Amongst the causes of non - typhoid small bowel perforations were trauma 25 (22.3%), tuberculosis 4 (3.6%) and radiation enteritis 1 (0.9%) and non-specific accounting for the rest 13 cases (11.6%).

**Table 1: Preoperative laboratory parameters in typhoid and non-typhoid small bowel perforation cases.**

| | | n | Mean | Std. Deviation | P value |
|---|---|---|---|---|---|
| Hb (gm%) | Typhoid cases | 69 | 9.02 | 1.68 | 0.920 |
| | Non typhoid cases | 43 | 9.06 | 1.87 | |
| TLC (cells/mm$^3$) | Typhoid cases | 69 | 8,896.23 | 2,117.52 | 0.029 |
| | Non typhoid cases | 43 | 7,938.13 | 2,411.64 | |
| Neutrophil | Typhoid cases | 69 | 62.17 | 7.60 | 0.853 |
| | Non typhoid cases | 43 | 62.44 | 7.11 | |
| Lymphocyte | Typhoid cases | 69 | 26.30 | 6.03 | 0.673 |
| | Non typhoid cases | 43 | 26.76 | 4.89 | |
| Urea (mg%) | Typhoid cases | 69 | 46.07 | 7.59 | 0.094 |
| | Non typhoid cases | 43 | 48.60 | 7.88 | |
| Creatinine | Typhoid cases | 69 | 1.16 | 0.39 | 0.039 |
| | Non typhoid cases | 43 | 1.30 | 0.31 | |

p value<0.05 is statistically significant; The preoperative laboratory parameters were almost similar in both cases and control subjects.

In the present study, Typhoid perforations mostly occurred in the 3rd and 4th decade of life with a male preponderance of 2:1. Perforations mostly occurred in the 2nd and 3rd week of illness which is statistically significant (p value<0.001). Fever was the presenting symptom in 57 out of 69 cases of typhoid perforations (p value=0.004) compared to 25 out of 43 cases of non-typhoid perforations. In the present study the Widal test had a sensitivity of 49.27% compared to 84.05 % sensitivity of Typhidot test though both tests are statistically significant (p value<0.001) in diagnosing typhoid perforations. The negative predictive value of

Widal test was 55.12% compared to 79.62% in Typhidot test. Culture yields were generally poor; tissue biopsy culture showed the highest positivity (25%) compared to all other cultures. In spite of conducting a battery of tests, we could not find the etiology in 13 (11.6%) cases of small bowel perforations establishing the entity of non-specific cause of small bowel perforation. Overall complication rates were significantly higher in typhoid small bowel perforations compared to non-typhoid perforation. The complications that occurred more commonly in typhoid group were wound dehiscence (39.13%), anastomotic leakage (40.57%) and intra-abdominal collection (42.02%) and respiratory complications (39.13%). Simple closure and wedge resection fetch better results compared to the gut anastomotic procedures though none of the operative procedures are absolutely free from complications. Weeks of hospitalization were significantly higher in typhoid perforation group (p value 0.008).

**Table 2: Outcome of operative procedures in typhoid and non-typhoid perforation cases.**

| | Typhoid cases, (n=69) | Non-typhoid cases, (n=43) | D.F | Chi-square value | P value |
|---|---|---|---|---|---|
| **Simple closure** | | | | | |
| Wound infection | 12 | 5 | 1 | 5.123 | 0.024 |
| Wound dehiscence | 9 | 1 | 1 | 0.161 | 0.688 |
| Anastomotic leakage | 9 | 2 | 1 | 0.341 | 0.559 |
| Abdominal collection | 9 | 2 | 1 | 0.585 | 0.444 |
| **Wedge resection** | | | | | |
| Wound infection | 23 | 14 | 1 | 0.174 | 0.676 |
| Wound dehiscence | 10 | 4 | 1 | 2.658 | 0.103 |
| Anastomotic leakage | 12 | 4 | 1 | 0.777 | 0.378 |
| Abdominal collection | 12 | 2 | 1 | 1.248 | 0.264 |
| **Resection anastomosis** | | | | | |
| Wound infection | 10 | 7 | 1 | 6.237 | 0.013 |
| Wound dehiscence | 8 | 2 | 1 | 8.201 | 0.004 |
| Anastomotic leakage | 7 | 3 | 1 | 4.198 | 0.040 |
| Abdominal collection | 8 | 2 | 1 | 6.921 | 0.009 |
| **Ileo transverse bypass** | | | | | |
| Wound infection | 8 | 2 | 1 | 4.826 | 0.028 |
| Wound dehiscence | 6 | 1 | 1 | 4.888 | 0.027 |
| Anastomotic leakage | 7 | 1 | 1 | 8.262 | 0.004 |
| Abdominal collection | 8 | 1 | 1 | 12.482 | <0.001 |

p value<0.05 is statistically significant; D.F.=Degrees of freedom.

**Table 3: Morbidity and mortality profile of typhoid and non typhoid perforation.**

| Morbidity/mortality | Typhoid cases, (n=69) | Non typhoid cases, (n=43) | D.F | Chi square value | P value |
|---|---|---|---|---|---|
| Wound infection | 45 | 26 | 1 | 0.258 | 0.612 |
| Wound dehiscence | 27 | 7 | 1 | 6.543 | 0.011 |
| Anastomotic leakage | 28 | 9 | 1 | 4.624 | 0.032 |
| Abdominal collection | 29 | 6 | 1 | 9.719 | 0.002 |
| Respiratory complication | 27 | 9 | 1 | 4.023 | 0.045 |
| Death / left against medical advice | 11 | 5 | 1 | 0.638 | 0.727 |

p value<0.05 is statistically significant; D.F.=Degrees of freedom

Single perforations predominated (45 out of 69 cases) in typhoid group.

Multiple perforations were found in 24 cases. The mortality for both typhoid and non-typhoid perforation cases was 16. Out of 69 typhoid cases 58 patients got cured, 3 left against medical advice, and 8 patients died. Out of 43 non-typhoid cases, 38 patients got cured, 2 left against the medical advice and 3 patients died. 38 out of 69 cases had a hospital stay for >3 weeks compared to 9

cases out of43 for >3 weeks of hospitalization. In present study, the mortality rate amongst male and female did not differ statistically.

## DISCUSSION

Typhoid fever still continues to be an enigma for the surgeons working in the developing countries like India in terms of the associated morbidity and mortality. The most lethal complications of typhoid fever is ileal perforation resulting from the necrosis of the Payer's patches in the terminal ileum.[18] Perforation has been reported to occur in 0.9% to 39% of cases of typhoid fever with wide variation, often dependent on the geographic location.[18,20] Typhoid perforation is more common in males and is similar to the findings as observed in the previous studies.[10]

India is the second most populous country of the world with majority inhabiting in the rural areas with little access to modern diagnostic tools. Blood culture and Widal test are routinely employed investigations in all clinical settings. Blood cultures are positive in only 3% to 34% cases of typhoid perforations.[23,27] And cultures of the stool and peritoneal fluid are usually negative for the organism.[27,31]

The standard serological test use for the diagnosis of typhoid fever is the Widal reaction, which measures agglutinating antibodies against flagellar and somatic antigens of the causative organism. The sensitivity and specificity of the Widal test was 70 to 75% and 80 to 95% respectively.[18,20] Duthie et al reported that the sensitivity and specificity of the Widal test was 78% and 99% respectively with a positive predictive value of 66% and a negative predictive value of 99%.[11] A positive diagnosis can be made from seventh to tenth day. Santillana et al reported Widal test is positive in 38% of patients with small bowel perforation.[12] Rising tires might be more useful. Four-fold rise in titers might be of more value but the rise might be blunted by early antibiotic therapy.

The Typhidot test is a dot enzyme immunoassay (EIA) kit, which detects IgM and IgG antibodies against *S.typhi* -specific outer membrane protein (OMP). This is as sensitive as and more specific than the Widal test in the diagnosis of enteric fever. It is easier and quicker to perform in order to increase diagnostic accuracy in an area of high endemicity.

With culture used as the gold standard, the dot EIA is as sensitive as the Widal test (95% vs. 98%), has a similar high negative predictive value (96% vs. 98%) and is more specific (75% vs. 67%). Jesudason et al reported that the Typhidot test was performed on 30 Widal positive sera, and 60 Widal negative sera; out of 30 Widal positive sera 27 gave a positive Typhidot test and out of 60 Widal negative sera, 58 were also negative for the Typhidot test.[13] Typhidot test, being a highly sensitive and specific rapid, inexpensive test with a high negative predictive value is recommended as the screening tool of choice in typhoid perforations.

Nonspecific cause of small bowel perforation is documented in reports by Dixon et al (25.9%), Chaik of et al (18.4%), Nadkarni et al (56.12%), Karmarkar et al (23.33%).[14-17] No causal relationship could be established between the nonspecific small bowel perforation cases to the operative complications like wound infection, wound dehiscence, anastomotic leakage or intra-abdominal collection. It is now universally accepted that the treatment of typhoid perforation must be Surgical.[18] Adequate resuscitation, correction of electrolyte disturbance, appropriate antibiotic therapy and surgery have proven to be essential for a successful outcome.[1-3]

Early surgical intervention sharply reduced mortality from 70-100% to about 30%.[3-5] Many surgical options have been used, ranging from simple peritoneal drainage under local anaesthesia in moribund patients.[2,4,19] Excision of the edge of the ileal perforation and simple transverse closure, either in a single layer or in two layers, have been widely practiced by many workers.[2,20-23] Added to this is generous intra-operative irrigation, but the value of continuous post-operative peritoneal irrigation, introduced by Mckeena et al in 1970, is doubtful.[24,25] Two-layer closure of the perforation with or without an omental patch has been most successful.[22,23]

Patients are managed on the dictum of "Doing as much as necessary but as little as possible." A swift, effective procedure was advocated to halt contamination and remove the existing collection is achieved by laparotomy, excision, and simple closure of the perforation, peritoneal irrigation and closure of the abdominal wall Welch and Martin recommended wedge excision and segmental resection, and end-to- end anastomosis of the diseased perforated ileum because of frequent reperforation in their patients.[26]

Many workers claimed that segmental resection of the involved bowel may be necessary in the presence of multiple perforations and a severely diseased terminal ileum.[19,23] Eggleston et al advocated closure of the perforation with end-to-side Ileotransverse colostomy; this takes the involved bowel out of the intestinal stream.[27] Although the mortality rate has not been improved by this method, a lowering of the morbidity rate has been achieved. The need for a second operation to restore ileal continuity has made the procedure less popular, and thus some workers prefer the use of side-to-side ileotransverse colostomy.[28]

None of the operative procedures are free from complications in terms of operative site infection, enterocutaneous fistula formation or respiratory co morbidities in accordance with previous studies.[1-10,29-32] Mortality is related to toxemia, septic shock and multiple organ failure. These uncontrollable factors make the

evaluation of the result of any surgical procedure for this condition difficult.

The post-operative complications had serious effects on each other. While wound infection adversely affected the presence of residual intra-abdominal abscess and faecal fistula, the incidence of residual intra-abdominal abscess was enhanced by the presence of faecal fistula. The presence of wound infection also significantly contributed to wound dehiscence. The presence of faecal fistula had a significant effect on mortality. Most patients died in the early post-operative period and survival beyond the 2nd week was associated with a high chance of complete recovery.

## CONCLUSION

We conclude, therefore, that widal and blood cultures alone are not sufficient to diagnose typhoid small bowel perforations.

Typhidot test being an reproducible, in expensive, noninvasive diagnostic test with high sensitivity is recommended as an excellent screening tool for rapid diagnosis of typhoid small bowel perforations, the yield is further improved by tissue biopsy culture. There appears to be a definite entity of non-specific small bowel perforation, which cannot be attributed to any other cause. Whether they represent an undiagnosed subset of typhoid perforation is to be further researched. Wound infections, intra-abdominal collections, anastomotic leakage and respiratory complications do not depend on the operative procedure performed. Simple closure and wedge resection are definitively the best operative procedures for singulate perforations of the terminal ileum in typhoid perforations.

In conclusion, typhoid ileal perforation still has a poor prognosis with high morbidity and mortality. Late presentation, delayed surgery, multiple perforations, severe peritoneal contamination, and post-operative faecal fistula are factors that have an adverse effect on mortality. Most deaths occur during the early post-operative period, with survivors having a prolonged hospital stay.

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