Review of Paediatric Typhoid Perforation Cases Managed at a Tertiary Care Centre

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

ABSTRACT

Background: Any criteria (clinical, pathologic, microbiological or histo-pathologic) attributing a case of Paediatric gastrointestinal perforation to Typhoid would be of help in reaching a proper diagnosis to guide appropriate management.

Aims and Objectives: To review all cases of Typhoid perforation for their clinical, pathologic and intra-operative findings.

Materials and Methods: A retrospective study was conducted on all cases of typhoid perforation (gastrointestinal perforation with positive Widal test) operated at a tertiary care centre from September 2015 to September 2018. Data regarding their clinical findings, investigation results, intraoperative findings, nature of the surgical intervention, postoperative results and histopathological findings were collected from their records and analysed.

Results: A total of 13 patients were operated during this period with positive Widal’s test at presentation. 6/13 had single ileal perforation; two patients had multiple ileal perforations; perforation at atypical sites were found in four patients (one each at gastric, duodenal, caecal and rectal); one patient presented with Meckel’s band obstruction with multiple ulcers – this patient was sick and died despite a diverting ileostomy in the postoperative period. While 8/13 patients had

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primary closure of the perforation site, diversion through ileostomy was performed in five patients. All patients did well in the post-operative period except one patient of multiple ulcers and obstructing Meckel’s band who died in the post-operative period.

**Conclusion:** On encountering a gastrointestinal perforation, no definite symptomatology or its pattern, no clinical examination findings, no intraoperative characteristics of the perforation and no biopsy can definitively point towards Typhoid as the cause. Therefore, we still have to depend on serological tests in correlation with clinical features to reach a conclusive diagnosis. Cultures and PCR, although sensitive are either time-taking or expensive to guide management. Typhoid perforation can have vivid and atypical presentation depending on the number and site of perforation.

**Keywords:** Culture; perforation; serological test; typhoid; widal.

### 1. INTRODUCTION

Besides being an important public health disease, surgical complications (Enteric perforation, haemorrhage, ulcers) in typhoid still are difficult to diagnose, manage and are a source of morbidity in the developing world. When a case of Typhoid presents with features of Acute Abdomen, it is almost impossible to think of Typhoid fever as the primary cause due to non-specificity of symptoms and lack of any instant diagnostic modality. Intra-operative findings are also not specific for Typhoid on most occasions. Although different cultures (Blood, stool, urine and bone marrow aspirate) have been reported to have different sensitivity and specificity, they are time taking and not helpful in emergency diagnosis. While newer techniques like Polymerase Chain reaction (PCR), Nested PCR is not readily available, rapid diagnostic kits like Typhidot, TUBEX and Test-it are often imprecise in diagnosis. Considering all this, how should a surgeon who has encountered an enteric perforation or bleeding ulcers in bowel think of Typhoid as the cause is an important question to guide appropriate management. We present our experience regarding this diagnostic dilemma over the last three years in all patients of typhoid who presented with positive Widal test and acute abdomen which necessitated emergency surgery.

### 2. MATERIALS AND METHODS

This was a retrospective study of three years duration from September 2015 to September 2018. Using a standardized data collection form, we abstracted data from the medical records of all inpatients with typhoid fever and acute abdomen hospitalized over 3 years (September 2015 to September 2018). The diagnosis was based on a standardized clinical definition (i.e., persistent fever and at least two of the following: constipation or diarrhoea, anorexia, abdominal pain, abdominal rigidity, relative bradycardia, and change in consciousness) and intra-operative findings (ante-mesenteric perforation of the gastrointestinal tract with histologic evidence of inflammation in the tissue. Typhoid ileal perforations (TIPs) were diagnosed clinically by peritonitis which was supported by a positive Widal test. Non-ileal Typhoid perforations (NITPs) were diagnosed clinically by peritonitis which was also supported by a positive Widal test. All other causes of perforation like appendicular and traumatic were excluded.

All patients were resuscitated, prepared physically and psychologically before surgery; they received antibiotics (Piperacillin+ Tazobactum – 100 mg/kg/dose, slow intravenous in infusion thrice a day along with Metronidazole – 10 mg/kg/dose intravenous thrice a day and Amikacin – 15 mg/kg intravenous once daily), analgesics, fluid and transfusion as per need and had nasogastric (NG) tube insertion, urethral catheterisation. Piperacillin+Tazobactum was chosen as the antibiotic because all our patients were referred patients who already had Ceftriaxone administered outside and at our institution, high incidence of Nalidixic acid-resistant Salmonella Typhi (NARST) infections have often been reported in cultures. Intravenous antibiotics were given for 7 to 10 days and depending on the patient's oral intake, oral Azithromycin (20 mg/kg once a day) was given for 5 days. Emergency laboratory tests including hemogram, electrolytes, renal function tests, blood /urine and stool analysis and sickling tests were done. All patients were admitted in emergency and surgery was performed within 6 hours, after resuscitation and primary laboratory workup. Postoperatively, all patients were monitored carefully with adequate hydration. Appropriate antibiotics were instituted post-operatively based on the culture and sensitivity
results. All operated patients did well in the postoperative period except one patient who expired on the second day of surgery. Blood transfusion was done in all patients.

3. RESULTS

Out of all Paediatric surgery admissions, only 13 patients were documented to have typhoid fever with perforation peritonitis (12) and intestinal obstruction (01) and all were operated. These patients were in the age group between 3 years to 10 years, with M: F ratio of 9:4.

Duration of illness: All the patients were brought to the hospital by their relatives and their history of illness was between 13 days to 28 days.

Table 1. Demographic results

| Total No. of Pts. With Typhoid Perforation | 13 |
| Age range | 3 – 10 years |
| M: F | 9:4 |

These patients were referred to cases and were already on antibiotic treatment. Most patients had already had Ceftriaxone outside. They presented to us with positive Widal test, important laboratory tests (Hemogram, serum electrolytes, creatinine and liver function tests) and abdominal & pelvic X-ray. In twelve patients, free intraperitoneal gas was seen and in one multiple air-fluid levels was observed.

Out of all 12 patients, 8 had a typical perforation of the ileum (single perforation = 6; multiple perforations = 2); remaining 4 patients had atypical perforation sites (gastric, duodenal, caecal and rectal perforation one each). Fig. 1 shows the clinical pictures of a few atypical perforations in our series. Two patients with multiple perforations are important; one had six perforations involving both jejunum and ileum, while the other one had eight perforations in the ileum.

One patient was toxic at presentation and had acute intestinal obstruction; on exploration, he had Meckel’s band obstruction with three impending perforations that were perforated during the release of the Meckel’s band and 11 ulcers one at Meckel’s diverticulum, five at the jejunum and five at the ileum.

Ileostomy was performed in five patients (Loop ileostomy-2; double-barrel ileostomy-3). All four patients with atypical perforation sites were managed by primary repair of perforation after freshening of the margins and tissue from margins were sent for Histopathological examination (HPE). Enlarged mesenteric lymph nodes were sent for HPE in all the cases. HPE revealed evidence of acute inflammation with fibrino-purulent exudates on the serosa of the intestine. There was evidence of villous blunting and crypts elongation which was suggestive of chronic mucosal injury. Fig. 2 shows the features at histopathology in two patients.

Table 2. Symptoms at presentation to the hospital

<table>
<thead>
<tr>
<th>Complaints for which they were on treatment</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (body temperature &gt; 38.5°C)</td>
<td>13</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>10</td>
</tr>
<tr>
<td>Generalised Weakness</td>
<td>13</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>09 (1 Rectal Perf. + 8 Ileal Perf.)</td>
</tr>
<tr>
<td>Pain abdomen</td>
<td>13</td>
</tr>
<tr>
<td>Vomiting</td>
<td>08 (1 Gastric Perf. + 1 Duodenal Perf. + 2 Multiple Perf. + 3 Ileal Perf. + 1 Acute Intestinal Obstruction)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>03</td>
</tr>
<tr>
<td>Bleeding per rectum</td>
<td>04 (2 Multiple Perf. + 1 Rectal Perf. + 1 Acute Intestinal Obstruction)</td>
</tr>
</tbody>
</table>

Table 3. Results of available lab tests at admission

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Widal test</td>
<td>13</td>
</tr>
<tr>
<td>Leucocytosis (&gt;11,000/cumm)</td>
<td>09</td>
</tr>
<tr>
<td>Leucocytopenia (&lt;4000/cumm)</td>
<td>04 (2 Multiple Perf. &amp; 1 Rectal Perf. + 1 Ileal Perf.)</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;100,000/cumm)</td>
<td>04 (2 Multiple Perf. &amp; 1 Rectal Perf. + 1 Ileal Perf.)</td>
</tr>
<tr>
<td>Anaemia (Hb% &lt; 9 gm %)</td>
<td>13</td>
</tr>
</tbody>
</table>
Table 4. Exploratory laparotomy findings

<table>
<thead>
<tr>
<th>Exploratory laparotomy findings</th>
<th>Surgery performed</th>
<th>N = 13</th>
<th>Postoperative Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single ileal perforation</td>
<td>Primary closure=4; Loop ileostomy=2 (Lymph node biopsy sent for HPE in all)</td>
<td>n = 6</td>
<td>-1 Wound infection (conservative management)</td>
</tr>
<tr>
<td>Multiple ileal perforations</td>
<td>Double barrel ileostomy (Lymph node biopsy sent for HPE in all)</td>
<td>n = 2</td>
<td>- 1 Peristomal skin excoriation (conservatively managed)</td>
</tr>
<tr>
<td>Gastric Perforation, duodenal</td>
<td>Primary closure was performed (Both Tissues from margins of perforation and lymph</td>
<td>n = 4</td>
<td>- 1 Distal stomal mucosal prolapse</td>
</tr>
<tr>
<td>Caecal perforation and rectal</td>
<td>node biopsy were sent for HPE)</td>
<td></td>
<td>- Both cases healthy after stoma closure</td>
</tr>
<tr>
<td>perforation (one each)</td>
<td>Primary repair of ulcers and double barrel ileostomy (Both Tissues from margins</td>
<td>n = 1</td>
<td>- Uneventful</td>
</tr>
<tr>
<td>Acute intestinal Obstruction*</td>
<td>of perforation and lymph node biopsy were sent for HPE)</td>
<td></td>
<td>- Expired on day 2 due to sepsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MecKel’s band obstruction with three impending perforations, 11 ulcers one at Meckel’s diverticulum 5 at the jejunum, 5 at the ileum*
Fig. 1. Atypical perforation in a few patients

HPE of mesenteric lymph nodes sampled during surgery showed evidence of follicular hyperplasia and markedly distended sinuses containing numerous histiocytes. Granulomas were absent in most cases. However, none of these findings was specific for typhoid affection.

4. DISCUSSION

Although Typhoid has been an important public health problem, its diagnosis is still challenging. Blood, stool and urine cultures along with antibody tests like Widal have been reported to have variable sensitivity and specificity concerning the time of presentation of the patient in the natural course of this disease. Several studies have reported positive cultures and PCR as the gold standard against which other investigations like antigen/antibody assay have been compared [1-4]. However, cultures take a long time to be reported and PCR is not readily available at all places. A recent Cochrane
may be due to faecal contamination. Cases, E.coli was the isolated organism which fluid for culture and sensitivity but in almost all practical in emergency cases. We sent peritoneal

turine, bone marrow or bile. Though Bone marrow in infectious agent may also be obtained from stool, Ceftriaxone/Ciprofloxacin). Culture of the already had received antibiotic coverage (mostly referred to cases from other centres where they did not go for blood culture as our

referred to cases from other centres where they did not go for blood culture as our

considered to be significant when considering these patients to be Widal positive. In a study on Bangladeshi Children, Saha et. al. concluded that a positive Widal test is still of diagnostic importance in diagnosing Typhoid fever in an endemic area and that both the agglutinins should be considered to be important [8].

Blood cultures are the diagnostic test of choice, and the results can be positive in 50–80% of patients, provided that a large volume of blood (typically 25-30 ml for adults) is cultured [1]. We did not go for blood culture as our patients were referred to cases from other centres where they already had received antibiotic coverage (mostly Ceftriaxone/Ciprofloxacin). Culture of the infectious agent may also be obtained from stool, urine, bone marrow or bile. Though Bone marrow is the most sensitive source (80-95%), it is not practical in emergency cases. We sent peritoneal fluid for culture and sensitivity but in almost all cases, E.coli was the isolated organism which may be due to faecal contamination.

Not only the investigative tools but also the clinical findings in patients of Typhoid are non-specific and often unreliable. In the first week of typhoid fever, non-specific headache (80%), malaise and rising remittent fever are variably seen [1,9]. Patient may have constipation (16%) or diarrhoea (28%) [9]. Constipation is more common in cases of adults whereas, diarrhoea is more prominent in children [9] as in our study 9/13 cases presented with diarrhoea (8 of ileal perforation and 1 of rectal perforation). Rose spot rash is located primarily on the trunk and chest, evident in 30% of patients at the end of the first week and resolves after 2–5 days (difficult to detect in dark-skinned person and late presenters) [1,9] as in our series. Patients can have two or three crops of lesions, and Salmonella can be cultured from punch biopsies of these lesions [1]. During the second week of the disease, the patient looks more toxic with sustained temperature; abdominal distension and splenomegaly. In the third week, development of continuous high fever and a delirious confusion state with pronounced abdominal distension, ileus, or diarrhoea may occur, with liquid, foul green-yellow stools [1,9]. The patient is likely to become obtunded and hypotensive and crackles may develop over the lung bases. Death may occur at this stage from overwhelming toxemia, myocarditis, intestinal hemorrhage or perforation [1]. In our study, there is no clear cut timeline of 3 weeks at presentation; this may be because in almost all cases, history was given by their distant relatives, who may have been unaware of the exact period. The symptoms may mimic other common illnesses, such as malaria, sepsis with other bacterial pathogens (tuberculosis, brucellosis, tularemia, leptospirosis and rickettsial disease) and viral infections (dengue, acute hepatitis and infectious mononucleosis) [1,10].

In only 16-46% of cases, leucopenia and neutropenia [9] can be detected; in our study, leucopenia was reported in 4/13 patients. Leukocytosis was more common among children (9/13), similar to other studies, during the first 10 days of illness and in cases complicated by intestinal perforation or secondary infection.

Although, intestinal haemorrhage is the most common complication of typhoid fever it usually occurs 14 to 21 days after the onset of the illness and is often silent. The patient may bleed from several areas of the intestine, or there may be massive haemorrhage leading to shock.
Intestinal perforation continues to be the most frequent cause of high morbidity and mortality. In general, haemorrhage and perforation occur in terminal ileum secondary to ulceration and necrosis of Paeyer’s patches at 2-3 weeks after the onset of the disease. Mortality rates of TIP cases are reported to range from 5% to 62% [11,12]. TIP remains a very severe condition in tropical countries. Its incidence ranges from 0.9% to 39%, with a high mortality rate [13]. In our study, we found 8/13 cases of ileal perforation and one case of acute intestinal obstruction with impending multiple ileal perforations; if we include this as perforation, total 9/13 cases of ileal perforation and four cases of atypical sites of perforation. Review of relevant literature during our study revealed sporadic case reports of multiple typhoid, ileal and caecal perforations [12]; few cases of Caecal [14], sigmoid [15] and rectal [16] perforation but typhoid gastric perforation could not be found. Also, there is no reporting of combined jejunoileal perforations along with Meckel’s band obstruction and Meckel’s diverticular perforation. Chalya P et. al., in a review of 109 Typhoid perforation patients reported the sites of perforation to be Ileal, Jejunal, Caecal, appendicular and ascending colic in that order [14]. The exact cause of gastric perforation in enteric fever is not known however the best possible explanation may be stress factor due to illness, as stress gastric perforations are well documented in the literature. The ileum is the most common site of multiple perforations due to abundant lymphoid follicles in Paeyer’s patches. In our case, the cause of multiple jejunoileal perforations may be due to pressure effect caused by simultaneous Meckel’s band obstruction. The cause of death in this patient is the delayed presentation (more than 72 hours of symptoms) and improper treatment leading to hemorrhagic syndrome and endotoxic shock.

The only death in our series was that of a patient having multiple ulcers and impending perforation who presented with intestinal obstruction. We believe that this observation is in line with that of other investigators who have noticed an increased mortality rate in the case of multiple perforations [14,17-19].

As far as Histopathological guidance towards diagnosing Typhoid is considered, our results did not reveal any specific finding other than inflammatory changes, changes in mucosa and villi of the small intestine and Paeyer’s patches involvement in a few cases. None of these conclusively point towards Typhoid as the cause for perforation. However, several studies have now shown evidence for the detection of S.Typhi DNA in gut biopsy samples by PCR [20]. Unfortunately, not many centres in our country including our centre provide this facility.

5. CONCLUSION

We concluded that on encountering a gastrointestinal perforation, no definite symptomatology or its pattern, no clinical examination findings, no intra-operative characteristics of the perforation and no biopsy can definitively point towards Typhoid enteric fever as the cause. Therefore, we still have to depend on serological tests in correlation with clinical features to reach a conclusive diagnosis in time. Cultures and PCR, although sensitive are either time-taking or expensive to guide management. Typhoid perforation can have vivid and atypical presentation depending on the number and size of perforation.

CONSENT

Consent was taken from every patient or his parents before including their details in the study.

ETHICAL APPROVAL

As per international standard or university standard was written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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3. Tran Vu Thieu N, Trinh Van T, Tran Tuan A, Klemm EJ, Nguyen Ngoc Minh, Voong


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