Repeat Laparotomy in Typhoid Intestinal Perforation Patients: Experience from a Developing Nation

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Abstract: Typhoid intestinal perforation constitutes one of the major indications for admission into emergency unit in areas of low socio economic environment. Its associated with many post operative complications, some requiring repeat laparotomy. Study was carried out to review of all cases of TIP between 2003 and 2011 in two hospitals (LTH & AMC both in Osogbo). The case files of 216 out of 235 patients treated for TIP between 2003 to 2011 at the study centres were evaluated. This consisted of 63.5% males and 80% in the first two decade of life. There were 24 RL in 21 (9.99%) patients, all the in the first 2 decades but significantly higher in the first decade (p=0.0266) and patients with serum urea greater than 10 mmol/l (p=0.0000, RR 3.67), PCV less than 20% (p= 0.0000, RR 21) and those presenting after 5 days after perforation (p = 0.000)but not with jaundice (p= 0.3967, RR 3.01. Perforations closer to the ICJ (>5cm) (p=0.0266), faecal or frank intra abdominal pus collection (p = 0.037 , RR = 2.3) significantly predispose to RL (x^2= 4.9123), but no significant difference in the incidence of those with 1 or 2 intestinal perforations compared to those with 3 or 4.( x^2=0.03, p= 0.862). Indications were intra abdominal abscess, wound or anastomotic dehiscence, re-perforation, adhesive obstruction and persistent entero-cutaneous fistula. The mean LOS is significantly prolong and mortality significantly higher (X^2=9.454, p value 0.0006) in those with RL. Late presentation, anaemia, renal impairment, perforations in the high pressure zone predisposes to RL which worsens prognosis and prolongs hospital stay in patients with TIP.

Keywords: Repeat laparotomy, Typhoid intestinal perforation, anaemia, late presentation, renal impairment.

INTRODUCTION

Typhoid intestinal perforation (TIP) constitutes one of the major indications for admission into emergency units in areas of low socio economic environment. It is one of the most dreaded surgical complications of typhoid enteritis seen commonly in developing countries [1, 2]. Most of the post operative surgical complications associated with typhoid enteritis were often due to delay in presentation, prolong suspected perforation- operation interval, and others requiring repeat laparotomy [3, 4]. Repeat laparotomy (RL) is associated with additional risk of anaesthetic and other post operative complications as it constituted additional surge of metabolic response, this worsens the prognosis, morbidity and mortality wise in already debilitated patients. Intra-abdominal sepsis from perforated viscous results from direct spillage of intestinal contents into the peritoneal cavity in these patients. The spillage of the contents, gram-negative and anaerobic bacteria, including other common gut flora, enters the peritoneal cavity. Endotoxins produced by gram-negative bacteria lead to the release of cytokines that induce cellular and humoral cascades, resulting in cellular damage, septic shock, and multiple organ dysfunction syndrome (MODS). The latter poses a lot of challenges in the management of patients with TIP in the developing world.

The condition affect all age groups with higher incidence in young adult and children who are even more susceptible to overall morbidity and mortality of this condition [2]. The purpose of this study was to determine the factors associated with repeat laparotomy and its outcome in LAUTECH teaching Hospital and Abake Medical Centre both in Osogbo, Osun state of Nigeria.

METHODOLOGY

This is a retrospective assessment of all cases of TIP treated between the year 2003 and 2011 in the two hospitals, a teaching hospital and a private hospital with the standard of a modern general hospital in Osogbo metropolis. The study utilised the records of all patients who were operated upon with intraoperative diagnosis of intestinal typhoid perforation. All recruited patients were operated upon by surgical residents and
consultant staff of the hospitals, following initial resuscitation and therapeutic antibiotics administration. The patients socio-bio demographic data, clinical diagnosis, previous treatment obtained, ASA status, suspected perforation presentation interval, suspected operation perforation interval, intraoperative findings, surgical options, duration of the operation and type of anaesthesia, indications for repeat laparotomy and final outcomes. It was noted that prior to the first surgical procedure and repeat laparotomy procedure most patients had the following investigations done: full blood count, plain abdominal X-rays, electrolytes, urea ± creatinine, grouping and cross matching of blood, urinalysis. The duration of hospital stay and outcome were entered into a paper proforma and analyzed.

All patients who underwent laparotomy with intraoperative diagnosis of typhoid perforation based on anti mesenteric perforation of the gut were included. All patient included had intravenous antibiotic and follow up with oral antibiotic for minimum period of two weeks, the choice of antibiotics was based on the discretions of the surgeons and affordability and patient response (most commonly used was a combination of ciprofloxacin /gentamycin /metronidazole). Other postoperative management such as resumption of oral feeding, discontinuation of intravenous fluid, repeated investigations and use of other drugs were all based on patient response. The outcome was based on the patient status at the time of discharge or documented last clinic visit.

Data obtained were subjected to statistical analysis using Epi-info 7 packages, setting p value at ≤0.05. Significance testing was done using either Student’s t-test, or Chi-square as appropriate. The risk ratio of some of the possible risk factors for RL was also calculated where necessary using the same package, while tables and figures were also drawn.

RESULTS

The case files of 216 out of 235 patients treated for TIP from year 2003 through 2011 at LTH Osogbo and Abake medical centre were evaluated. This consisted of 134 males (63.5%). All were adequately resuscitated and had laparotomy done, they all had copious peritoneal lavage with warm normal saline after simple closure or ileal resection and anastomosis or occasionally a limited right hemicolectomy.

About 80% of all patients are in the first two decade of life; among these, 21 (9.99%) had repeat laparotomy (RL) and only three had second repeat laparotomy (SRL). Repeat laparotomy was significantly higher in the first decade of life ($X^2 = 10.91$, p-value= 0.0009). All the SRL occurred in the first 2 decades of life (age distribution of TIP and RL (Fig. 1).

Eighteen of the 21 first repeat laparotomy (FRL) was done within days 7 – 12 after the initial operation. The indications included 9 cases of intra abdominal abscess, 5 cases of wound dehiscence, 3 cases of anastomotic breakdown/leakage and a single case of re-perforation. A case of adhesive obstruction and two cases of persistent enterocutaneous fistula accounted for the FRL at about the end of the first month post operative. The second repeat laparotomy was for anastomotic leakage and wound dehiscence (Table 1).

Fourteen of all FRL and all SRL occurred in patients with serum urea greater than 10 mmol/l ($X^2 = 21.92$, p=0.0000 RR 3.67). Similarly 12 of all 17 patients presenting with Packed cell volume less than 20% (Hb < 7) had a repeat laparotomy ($X^2=68.67$, P=0.0000, RR 21) (Table 2).

Clinical jaundice was found reported in 8 patients on admission, one of them had repeat laparotomy and SRL for abdominal wound dehiscence with evisceration and another had FRL for residual abscess. $X^2=0.7181$, p=0.3967, RR 3.01).

Three of the 6 patients with perforation less or equal to 5cm from ileo-cecal junction (ICJ ) had repeat laparotomy for re collection and anastomotic break down compared to only 12 of 114 with perforation greater or equal to 20cm from ICJ ($X^2= 4.9123$, p=0.0266) (Table 2).

Thirteen of the 87 patients that had 2 perforations needed repeat laparotomy, while only 3 each of 72 with one perforation and 33 with 3 perforations had repeat laparotomy. Two of the 19 patients with 4 or more perforations had RL. There is no significant difference in the incidence of RL in patients with 1 or 2 intestinal perforations compared to those with 3 or 4 . ($X^2=0.03$, p=0.862) (Fig. 2).

Eleven of the 68 patients which had a feculent or frank intra abdominal pus collection when compared to 10 of 143 with straw colour or turbid intra-abdominal collection had repeat laparotomy ($X^2 = 4.38$ p = 0.037 , RR = 2.3)

None of the 21 patients with suspected perforation - operation interval of 48hrs or less required repeat laparotomy compared to 14 of 42 who had operation after 5 days. Most patients 147/211 (69. 7%) presented within days 3 – 5, 7 of them had RL (7 / 169 against 14 / 42, $X^2 = 28.81$, p= 0.000) (Fig. 3).

The range of hospital stay for all patients was 7-57 days (mean 13.3). All patients who had re-lap stayed for more than 15days, the longest being 57days (mean 18.1days).
We recorded 8 deaths out of the 21 patients that had RL (38.09%) compared to about 13.74% mortality amongst all patients and 11.05% of those without RL. Comparison of mortality in those with and without RL (i.e. 8/21 and 21/190) shows high level of significance ($X^2 = 9.454$, p value 0.0006).

**Table 1: Indications for repeat laparotomies**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Number of FRL</th>
<th>N=Number of SRL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra; Abdominal Abscesses</td>
<td>9 (42.8%)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Anastomatic Leakage/ Dehiscences</td>
<td>3 (14.3%)</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Wound Dehiscence/ Evisceration</td>
<td>5 (23.8%)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Reperforation</td>
<td>1 (4.76%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Glo Adhesive obstructions</td>
<td>1 (4.76%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Persistent Entero-Cutaneous Fistula</td>
<td>2 (9.5%)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>21 (100%)</td>
<td>3</td>
<td>24</td>
</tr>
</tbody>
</table>

FRL= First repeat laparotomy, SRL= Second repeat laparotomy

**Table 2: Serum Urea level, Packed cell volume & Perforation location in 211 patients with TIP**

<table>
<thead>
<tr>
<th>Pre-op Serum Urea level</th>
<th>No. of TIP patients</th>
<th>No. of First Repeat laparotomy</th>
<th>No of patients with second repeat laparotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3.5 - 5</td>
<td>46</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>5.9</td>
<td>101</td>
<td>s</td>
<td>0</td>
</tr>
<tr>
<td>10.15-15</td>
<td>17</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>&gt;15</td>
<td>28</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>192</td>
<td>21</td>
<td>3</td>
</tr>
</tbody>
</table>

Packed cell volume (PCV) on Admission

| <20                     | 17                  | 12                            | 1                                           |
| 20.25                   | 63                  | 5                             | 1                                           |
| 26-30                   | 40                  | 2                             | 1                                           |
| >30                     | 91                  | 2                             | 0                                           |
| Total                   | 211                 | 21                            | 3                                           |

Perforation Distance proximal to the ICJ(cm)

| <5                      | 6                   | 3                             | 1                                           |
| 5-10                    | 11                  | 2                             | 1                                           |
| 11-20                   | 80                  | 4                             | 0                                           |
| >20                     | 114                 | 12                            | 1                                           |
| Total                   | 211                 | 21                            | 3                                           |
DISCUSSION

Scanty reports exist in the literature regarding RL especially in relationship to TIP. TIP is very common in the developing world, more common in the males [3, 5] and in the first three decades of life [6]. The patients tend to present late [7, 8] with severe toxæmia from generalised secondary peritonitis. It is associated with high rate of morbidity and mortality, the later ranging from 10% to even 60% [3, 4, 9-11]. Common intra abdominal findings tend to include pus, turbid peritoneal fluid, free intestinal contents including herbal concoction components and even free dead and live round worms. The finding of close to 80% of all TIP patients being in the first three decades of life is in keeping with findings all over the world [6]. The main objectives of re laparotomy include further evacuation of purulent exudates and necrotic materials, eventual intervention on the source of peritonitis and the inflammatory process, repeat copious peritoneal larvage; all aiming at improving the source control, thus improving the prognosis in these critically ill patients.

Most RL done are usually unplanned in the developing world. Reported studies on RL are commonly pre-planed in the developed world for various causes of peritonitis including trauma, severe acute pancreatitis, peritonitis of gynaecologic origin, post operative peritonitis, intestinal pathologies, etc. For the purpose of laparostomy, authors have used various approaches including Bulgarian Antibacterial Polyamide Mesh (BAPS) fixed to the abdominal wall or the use of ZIP, or polyethylene sheet sandwich method of scheme, Velcrolike closure devices, VAC devices or even large gauze [12-15]. These allow for easy access to the peritoneal cavity for the purpose of re-exploration. Ivatury et al concluded that the open technique is feasible, effective, and worthy of consideration in patients with extensive wound necrosis and uncontrolled abdominal sepsis [16].

Patients with TIP and diffuse generalised purulent peritonitis should be regarded as having “a great abscess with many pouches”. Open laparotomy for proper elimination of source of peritonitis and proper larvage with copious amount by warm saline which can be as much as 8 litres, or till the final effluent becomes clear. This could be followed with partial closure leaving the skin un-sutured. Loss of
electrolytes, water and proteins are quite significant after copious peritoneal larvage while removal of fibrin deposits and necrotic residues is frequently associated with risk to bowel loops, risk of bleeding from inflamed intra abdominal organs, thus creating good media for the growth of bacteria. These may be accompanied by translocation of bacteria, endotoxin and cytokines to the lymphatic and systemic circulatory systems.

About 10% of all cases of TIP in this study had RL, this may be due to the fact that almost 20% of patients came in 1 week after suspected perforation. TIP tends to generally portend worse prognosis [7]. The need for RL was significantly higher for patients in their 1st decade of life, keeping in mind, the relatively low immunity in children, as well as late presentation due to ignorance and possibly neglect on the side of the parents could account for this.

Severe anaemia in TIP patients could arise from haemolysis due to septicaemia and hypoproteinaemia from hyper-catabolism of severe illness. Low haemoglobin concentration has significant effect on wound healing, leading to wound dehiscence and possible evisceration requiring unplanned RL.

Above 60% of all First Re Laparotomy (FRL) in this series occur in patients with serum urea > 10, in fact, all those who needed to have Second Re Laparotomy (SRL) fall into this category as well. Similarly more morbidity was recorded by Akoh JA in a TIP series from Nigeria [11]. Dehydration from severe third space loss and renal impairment from toxemia of the pan-systemic infection could account for this. The serum creatinine would have been more apt in assessing for renal impairment; this was recorded for few of the cases. High serum urea is known to impede healing and also affect the activity of the polymorphonuclear leucocytes whose functions is essential during the lag phase of wound healing. Fibroblast activities are also known to be impaired, thus laying down of collagen and modelling are greatly affected.

Severely impaired renal activity in three of our patients required haemodialysis which greatly improved their renal function and final prognosis. It should also be noted that typical hyper-kalaemia in patients with acute renal shut down may not be routinely seen in patients with TIP in view of the severe loss of potassium into the 3rd space, into the distended bowel and also the associated diarrhoea and vomiting. Guided volume resuscitation measures using invasive or non-invasive hemodynamic monitoring is important in the prevention of secondary organ system dysfunction in patients with intra-abdominal infections while correction of existing serum electrolyte disturbances and coagulation abnormalities as best as possible is encouraged before surgical intervention to reduce intra and post-operative mortality [10].

Most of the FRL were done within the first two weeks after the initial operation. Residual intra abdominal abscesses accounted for half of these. This along with wound dehiscence, anastomotic dehiscence necessitated early FRL. The late FRL took place close to a month after the initial operation. These were for persistent entero-cutaneous fistula or adhesive obstructions. Most adhesion obstructions are treated conservatively, but presence of peritoneal signs, fever and leucocytosis are strong indications for early surgical intervention. It commonly present after two weeks of initial operation and may be observed for as long as 10 days if there are no signs of complications [17].

Anastomotic dehiscence can appear clinically silent, but can be severe enough to cause severe sepsis associated with abscesses or peritonitis causing mortality ranging between 10 and 50% [18]. Common surgical options include resection of the anastomosis with proximal diversion, simple drainage of the anastomosis and proximal diversion with a loop ostomy.

Unplanned SRL are required for cases of anastomotic leakage and wound dehiscences which are features of severely impaired wound healing; parenteral feeding or intravenous hyper-alimentation could be helpful in preventing the need for this [19]. A planned second re-opening through laparostomy, exteriorisation of involved part of intestine are other useful approaches. Higher number of RL in a patient portends higher mortality [20], hence early planed reexploration through laparostomy or CT-guided aspiration of localised abscess [21] or drainage and or adhesiolysis using laparoscopy will be better alternatives [22]. The high possibility of injury to adherent omentum and bowel during the laparoscopic procedure should always be borne in mind since intestine-parietal adhesions are common findings post laparotomy [23].

TIP in the region of high pressure zone (distal 5 cm of the ileum) could predispose to anastomotic leakage, hence RL. Limited right hemicolecetomy is advised in such situations especially when there is associated gross soilage. Most of the initial laparotomy were commonly led by a senior registrar, few of whom might not be experienced enough to undertake a hemicolecetomy, hence the need for close supervision by the supervising consultant so as to mitigate against the need of RL. Appropriate timing and adequacy of surgical source control is crucial, because an untimely, or incorrect operation may have a serious negative effect on outcome.

The number and size of perforation(s) determine the degree of peritoneal soilage and third space loss, hence toxicity and electrolyte derangement will be worse in those with large number and sizes [4,
Bowel resection with copious larvage at first surgery may obviate the need for RL compared to multiple single closures when we have more than two perforations [9, 24].

The risk ratio for RL is quite high when the peritoneum is soiled with faeculent materials or frank pus. These could arise from late presentation [11, 20] or massive perforations especially when the large bowel is involved. The toxoaemia of the disease, release of cytokines, TNF, IL among others hamper wound healing, thus increases risk of wound dehiscence. The possibility of incomplete evacuation of peritoneal contaminants especially in the recesses including the lesser sac, sub-phrenic spaces is much higher with grossly contaminated abdomen in severely ill patients who are usually poorly fit for the procedure.

A grossly contaminated abdomen predisposes to surgical site infection and dehiscence while moderate or severe distension brings about abdominal compartment syndrome (ACS). In the presence of ACS, the wound is under tension, thus leading to wound dehiscence, respiratory impairment or failure, impaired venous return, vascular insufficiency to bowel and other intra abdominal organs, paralytic ileus, etc. The normal intra abdominal pressure is 6-10 cm of water, pressure ≥ 20mm may be an indication for laparostomy with the use of Zip or the use of adjustable nylon ties for abdominal closure as described by Chavez-Cartava et al. [25]. Patients undergoing repeat laparotomy after trauma are known to be at increased risk for wound dehiscence especially when associated with intra-abdominal abscess and high injury severity score [26].

The significantly higher mortality recorded in the 21 patients that had RL is not unexpected in view of the poor clinical state of most of the patient who finally had RL [27]. Outcomes are known to be worse in patients who had unplanned reoperations for persistent or recurrent infections (30-50% increase in the mortality rate); however, patients undergoing early planned second-look operations do not demonstrate this trend [15].

The age of the patients, serum haemoglobin level, presence of jaundice, presence of renal impairment, the degree of peritoneal contamination and severity of distension in the face of severe toxoaemia do contribute to the possibility of a patient with TIP requiring RL. The role of expertise of the available surgeon, availability of supportive care e.g., parental nutritional support, dialysis and with intensive care support as well as the role of financial wherewithal cannot be over emphasized in the quality of management of TIP patients in the developing world. The practice of planned RL should be encouraged, rather than waiting for ominous signs before deciding on the need for a repeat laparotomy.

REFERENCES