

Original Article

## Typhoid perforation in children: an unrelenting plague in developing countries

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### Abstract

**Introduction:** Despite global scientific development, typhoid fever and subsequent typhoid perforation have continued to be common in developing countries. The aim of this study was to re-evaluate the pattern of presentation and management outcomes as well as morbidity and mortality of typhoid perforation among children.

**Methodology:** Children aged 15 years and under with clinical diagnosis of typhoid perforation were retrospectively studied by reviewing their hospital records between January 2006 and December 2015. Demographic and clinical data were analyzed with SPSS using descriptive statistics and the chi-squared test or Cramer's V for continuous and categorical variables respectively.

**Results:** 105 children had typhoid fever, 56 (53.3%) of them were diagnosed with typhoid perforation and 49 were confirmed intra-operatively. Of the children, 55.1% (n = 27) were school-aged while the remaining were adolescents; a majority had the classical triad of persistent fever (100%), abdominal pain (100%) and abdominal swelling (93.9%). Anaemia and hypokalaemia were common. The mean time duration for resuscitation was 16 hours (range 6-36 hours). Most perforations were single (n=36, 73.5%). There were more perforations in the school-aged than adolescent children (p = 0.845; V = 0.298). Wound infection (34.7%) was the most frequent morbidity but faecal fistula (10.2%) was most troublesome to manage. Death followed severe sepsis and chest infections in four children (8.2%).

**Conclusion:** Typhoid perforation continues to cause morbidity and mortality in children in developing countries. To stem this endemic disease, community health education and improved living conditions are required.

**Key words:** Typhoid perforation; children; developing countries.

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### Introduction

Pierre Charles Alexandre Louis (1787-1872), working in Paris in 1829, identified pathologic lesions of typhoid fever in the intestines, mesenteric lymph nodes and spleen [1]. Today typhoid fever remains a major health problem, particularly in developing countries where the lack of a potable water supply, poor environmental sanitation, increasing population and urbanization as well as poor health care delivery systems are rife [2]. The bacterial agent responsible for the spread of typhoid disease among humans is *Salmonella enterica* subspecies *enterica* serovar Typhi (*S. Typhi*) [3]. To date, the greatest burden of typhoid fever occurs in children [4]. Similarly, children comprise more than 50% of all cases of typhoid perforation (TP), the commonest severe complication of the disease [5]. Once TP has occurred, the overall management outcome becomes a function of several factors [6-7]. The aim of this study was to re-evaluate the pattern of presentation and management outcome as

well as morbidity and mortality of TP among children treated at University of Calabar Teaching Hospital, Nigeria.

### Methodology

This was a retrospective study of children aged 15 years and under with clinical diagnoses of typhoid perforation (TP) seen at University of Calabar Teaching Hospital between January 2006 and December 2015. The Paediatric Out-Patient (POP) clinic, Children Emergency Room (CHER) and ward registers were searched to identify all cases of typhoid fever seen during this period. The names and hospital numbers of those with clinical diagnoses of TP were retrieved. Their case notes were then obtained from the Health Records Department and reviewed to identify patients for whom the clinical diagnoses of TP were confirmed intra-operatively (i.e by surgical finding of anterior mesenteric perforation of the distal ileum). This finding was matched with the well-known clinical presentation

of the disease as well as compatible results of laboratory and radiological investigations. Patients who had no ileal perforations or whose perforations were due to appendicitis, duodenal ulcer or trauma were excluded from the study. The age, gender, clinical presentation, time interval between onset of abdominal pain and surgical intervention, operation findings, procedure performed, length of hospital stay, overall outcome and complications were then extracted and analyzed. Institutional consent was obtained from the hospital’s Research/Ethics committee.

Data analysis was carried out using Statistical Package for Social Sciences (SPSS) for Windows (IBM Corp. NY, USA) and Computer Programs for Epidemiologic Analysis (CPEA). Descriptive statistics (percentage tables, mean, median, standard deviation and interquartile range) were used to summarize variables. Chi-squared test was used for categorical variables. Cramer’s V [8], a chi-squared based adjustment with values as follows: small effect = 0.01, medium = 0.30, large = 0.50 was used to determine the strength of the relationship between categorical variables. Statistical significance was defined as  $p < 0.05$ .

**Results**

One hundred and five children aged 15 years and under with typhoid fever were managed during the study period, out of which 56 were clinically diagnosed as having TP, but only 49 had intraoperative

confirmation of the disease. Thus, seven children were excluded because their clinical diagnoses were at variance with intraoperative findings.

The age range was 5-15 years with a median age of 10 years. There were 29 males and 20 females giving a male: female ratio of 1.5:1.

More than half ( $n = 27, 66.1\%$ ) of the children were in the school-aged group (5-10), while the remaining ( $n = 22, 44.9\%$ ) were adolescent children (11-15). There were no infants or preschool-aged children (i.e. children aged below 5 years) (Table 1).

The median duration of abdominal pain before presentation was 72 hours with an interquartile range (IQR) of 48-96 hours. The majority ( $n = 32; 65.3\%$ ) presented 48 to 72 hours after onset of severe abdominal pain (Table 2). Only a few ( $n = 3; 6.1\%$ ) reported within 24 hours of onset of abdominal pain.

Forty-six (93.9%) children presented with the classic triad of TP: namely persistent fever, abdominal pain and abdominal swelling (Table 2). There were no cases with atypical presentation. The major physical findings exhibited by all patients were pallor, dehydration, elevated body temperature and generalized abdominal tenderness with guarding (Table 2). Abdominal distension and rigidity were the next most prevalent physical signs.

All ( $n = 49; 100\%$ ) patients were anaemic, but hypokalaemia and air under the diaphragm were observed in 28 (57.1%) and 20 (40.8%) children respectively (Table 3).

**Table 1.** Age and gender distribution of the number of perforations and degree of fecal soilage in children with TP ( $n = 49$ ).

| Characteristic   | No (%)              |           |           | p-value         |
|--|---------------------|-----------|-----------|-----------------|
|  | No. of perforations |           |           |                 |
| <b>Age</b>   | 1                   | 2-3       | ≥ 4       | $\chi^2 = 4.35$ |
| 5-10   | 17 (34.7)           | 7 (14.3)  | 3 (6.1)   | $p = 0.114$     |
| 11-15  | 19 (38.8)           | 1 (2.0)   | 2 (4.1)   | $V = 0.298$     |
| <b>Gender</b>  |                     |           |           |                 |
| Male   | 22 (44.9)           | 4 (8.2)   | 3 (6.1)   | $\chi^2 = 0.93$ |
| Female   | 14 (28.5)           | 4 (8.2)   | 2 (4.1)   | $p = 0.845$     |
|  |                     |           |           | $V = 0.083$     |
| <b>Degree of fecaloid peritoneal collection (mls):</b> |                     |           |           |                 |
| <b>Age</b>   | < 500               | 500-1000  | 1001-2000 | $\chi^2 = 0.93$ |
| 5-10   | 13 (26.5)           | 11 (22.5) | 3 (6.1)   | $p = 0.627$     |
| 11-15  | 8 (16.3)            | 12 (24.5) | 2 (4.1)   | $V = 0.138$     |
| <b>Gender</b>  |                     |           |           |                 |
| Male   | 12 (24.5)           | 13 (26.5) | 4 (8.2)   | $\chi^2 = 1.00$ |
| Female   | 9 (18.4)            | 10 (20.4) | 1 (2.0)   | $p = 0.060$     |
|  |                     |           |           | $V = 0.143$     |

**Table 2.** Clinical characteristics of children with TP (n = 49).

| Characteristic  | Number | Percentage (%) |
|---|--------|----------------|
| <b>Symptom</b>  |        |                |
| Persistent fever  | 49     | 100.0          |
| Abdominal pain  | 49     | 100.0          |
| Abdominal swelling  | 46     | 93.9           |
| Vomiting  | 34     | 69.4           |
| Diarrhea  | 11     | 22.4           |
| Constipation  | 5      | 10.2           |
| <b>Sign</b>   |        |                |
| Pallor  | 49     | 100.0          |
| Dehydration   | 49     | 100.0          |
| Elevated body temp (>38.3C)   | 49     | 100.0          |
| Abdominal distension  | 46     | 93.9           |
| Generalized tenderness  | 49     | 100.0          |
| Abdominal guarding  | 49     | 100.0          |
| Abdominal rigidity  | 46     | 93.9           |
| <b>Duration of onset of abd. pain prior to presentation (hours)</b> |        |                |
| < 24  | 3      | 6.1            |
| 24-48   | 10     | 20.4           |
| 49-72   | 22     | 44.9           |
| 73-96   | 11     | 22.5           |
| > 96  | 3      | 6.1            |
| Median  | 72     |                |
| IQR*  | 48-96  |                |

\*IQR = interquartile range.

**Table 3.** Results of investigations and outcome of management of children with TP (n = 49).

| Parameter                      | No. | Percentage (%) |
|--------------------------------|-----|----------------|
| <b>Laboratory findings</b>     |     |                |
| Air fluid levels               | 49  | 100.0          |
| Air under diaphragm            | 20  | 40.8           |
| Anemia (low Hb)                | 49  | 100.0          |
| Hypokalemia                    | 28  | 57.1           |
| <b>Duration of stay (days)</b> |     |                |
| 8-14                           | 19  | 38.8           |
| 15-20                          | 17  | 34.7           |
| 21-25                          | 7   | 14.3           |
| > 30                           | 6   | 12.2           |
| <b>Complications*</b>          |     |                |
| Wound infections               | 20  | 40.8           |
| Chest infections               | 5   | 10.2           |
| Enterocut. fistula             | 5   | 10.2           |
| Burst abdomen                  | 2   | 4.1            |
| <b>Overall outcome</b>         |     |                |
| Discharged home                | 45  | 91.8           |
| Died                           | 4   | 8.2            |

\*Wounds in 17 (34.7%) patients healed primarily.

Forty (82%) children had repeated unsuccessful medications for malaria and 25 (51.0%) of them had received native medications orally and via enema. Only a small number (n= 15; 30.6%) received oral antibiotics including chloramphenicol, albeit in inadequate doses.

The mean duration for resuscitation was 16 hours (range 6 to 36 hours). The estimated period from time of presentation to surgery ranged from about 18 hours to 4 days with an average of 2.2 days. Surgical operations delayed beyond 72 hours were associated with increased mortality.

The majority (n= 36; 73.5%) of the perforations were single. The highest number of perforations in a single patient was six (Figure 1), all limited to the terminal 60 cm of the ileum. The overall perforation rate (n= 49/105) was 46.7%. The mean size of the perforations was  $1.5 \pm 0.48$ cm. There were more perforations in the school-aged children (n= 27; 55.1%) than in those who were adolescents (n = 22; 44.9%). A chi-squared test for independence indicated no significant association between age and number of perforations.  $\chi^2 = (2, n = 49) = 4.35, p = 0.845, V = 0.298$  (Table 1). Similarly, more perforations occurred in males (n= 29; 59.2%) than females (n= 20, 40.8%). However, this observation failed to establish any statistically significant association between gender and number of perforations, and the effect of gender following Cramer's V adjustment was small.  $\chi^2 = (2, n = 49) = 0.34, p = 0.845, V = 0.083$ . (Table 1)

There was also no significant association between age and gender with degree of faecoloid peritoneal collection and the effect of these variables on this parameter was also small (Table 1).

In all, 30 (61.2%) patients had surgical operation within 24 hours of presentation. The surgical

procedures employed were excision of the edges of the perforations and simple closure in 36 (73.5%) children, segmental resection with primary end-to end anastomosis in 11 (22.4%) and right hemi-colectomy with ileo-transverse or ileo-colic anastomosis in only two (4.1%) patients.

Wounds in 17 (34.7%) children healed primarily without complications. The morbidity of TP was high. The most common complications were wound infections (n= 20, 40.8%), faecal fistula (n = 5; 10.2%) and chest infections (n = 5; 10.2%).

The mean duration of hospital stay was 17.45 days  $\pm 8.85$  days (range 8 to 45 days).

Overall, 45 (91.8%) children recovered and were discharged home. The mortality rate was 8.2% (n=4/49) and was associated with severe sepsis. Of the four (8.2%) children who died, two (4.1%) had troublesome uncontrolled faecal fistula while the remaining two (4.1%) had severe chest infections in association with burst abdomen.

## Discussion

Typhoid fever is a common infection that has remained a public health problem in many developing countries [9-10]. In endemic areas, the disease is said to predominantly affect school-aged children [11]. The results of our study were in support of this fact, as they demonstrated that school-aged and adolescent children were those commonly diagnosed with TP. Aside from poor sanitation and limited availability of clean and potable water, patronage of food hawkers at school who may be carriers of the disorder [12] are most commonly associated with a high prevalence of the disease among school-aged children. Similar to previous studies of TP in children, both boys and girls were equally affected [5,13].

The finding that there were no cases of TP among the under 5 age group of children agreed with those of others [13-14]. However, Sinha *et al.* [15] have challenged the view that typhoid fever was a disease of school-aged and adolescent children. They maintained that the incidence and age distribution of the disease varied between developing countries and even within the same country, and that typhoid was a common and significant cause of morbidity of children between 1 and 5 years of age. Consequently, reports from other studies [16-17], have shown that children under 5 years represent a high-risk group for TP. We therefore agree to the call for a reassessment of the optimum age of typhoid immunization and the choice of vaccines [15]. The current practice is that the injectable vaccine is approved for children aged two years and above while

**Figure 1:** Six perforations in the terminal ileum of a child.



the oral one is approved for children aged six years and above [18].

The occurrence of increasing abdominal pain in typhoid fever is thought to signify onset of intra-abdominal complication, most likely perforation [11]. Therefore, judging by the duration of onset of severe abdominal pain in the children prior to presentation, majority of them might have perforated several hours and even days previously, at home. This agreed with the observation that of the patients who perforate, most of whom are children, 90% do so outside the hospital [19]. This state of events may have been exacerbated by initial experimentation by parents with other drugs and native medications, as found in other studies [17,20]. Patients were then brought to hospital only when the experimental treatments failed. Hosoglu *et al.* [21] reported that inadequate and improper treatment increases the risk of perforation in typhoid fever. This fact and the attendant delay in commencement of treatment may have accounted for the very high perforation rate found in this series. Our study showed that almost all patients exhibited the classical triad of TP symptoms. This finding was similar to that of Uba *et al.* [22] where all patients manifested with the classical features of TP. Perhaps this could be attributed to late presentation of the patients at which time the clinical features were already well established. However, a high index of suspicion is required in all instances for early and accurate diagnosis because of the possibility of confusion with other diseases entities [11]. Among other risks factors of perforation reported by Hosoglu *et al.* was anaemia [21]. All our patients were already anaemic as at the time of presentation and blood transfusion formed part of the resuscitative measures in most instances. The pathophysiology of anaemia is said to be multifactorial and includes bone marrow suppression, haemophagocytosis, sepsis and malnutrition [11,17].

Similar to many other reports [5,17,22-23], the majority of perforations were singular in both genders. Our findings, in agreement with those of the Zaria series [5], showed that the perforation rate increased with age, though there was no significant statistical difference following this observation.

Similarly, our study showed that the volume of faecoloid peritoneal fluid collection was independent of age and gender. However, it is a known fact that faecoloid peritonitis, overwhelming septicaemia from *S. Typhi* and other intestinal bacteria are important prognostic factors [24-25].

Several operative modalities have been advocated in the management of children with TP [23,26]. In this

study, as in others [5,17,22-23], excision of the edge of the perforation and simple closure was the predominant surgical procedure performed. This is in agreement with the position that the simple, quick and effective procedure was the best choice because these were high surgical risk patients [17,27].

Overall, the majority of our patients survived and were discharged home. The mortality rate recorded in this series compared with that of an earlier report by Archibong *et al.* [20] from the same centre but is far lower than those from others [5,22]. Aside from variation in sample size, the difference in mortality rate may be due to availability of more recent and potent antibiotics to combat the systemic effects of the disease following surgical intervention.

Nevertheless, the morbidity still remained high, with the most frequent complication being wound infection as in other studies. [5,17,22-23]. However, the most challenging complication was entero-cutaneous fistula, as was also observed in other series [17,22].

The abdominal wound following surgery for TP is usually heavily contaminated [28]. This formed the basis for the practice of delayed wound closure by some authors [29-30]. All the wounds in this study were however closed primarily with acceptable outcome because of the logistic challenges of performing delayed wound closure in our setting, in agreement with earlier studies [31-32].

## Conclusion

Typhoid perforation, the commonest severe complication of typhoid fever, continues to cause high morbidity and mortality in children in developing countries. To stem this disease, community public health education is required to facilitate early presentation and management of children with persistent fever. There is need for improved sanitation and provision of safe water supplies as well as overall living conditions of those who are vulnerable.

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