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Typhoid perforation: Post-operative Intensive Care Unit care and outcome

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ABSTRACT

Background: Typhoid perforation ileitis is a serious complication of typhoid fever, a common and unfortunate health problem in a resource-poor country like Nigeria. Following bowel perforation, treatment is usually by simple closure or bowel resection and anastomosis after adequate aggressive fluid resuscitation and electrolyte correction. Postoperatively, some of these patients do require management in Intensive Care Unit (ICU) on account of sepsis or septic shock and to improve survival. **Patients and Methods:** This is a prospective observational study in which 67 consecutive patients who had exploratory laparotomy for typhoid perforation between August 2009 and October 2012 in the main operating theatre of the University College Hospital, Ibadan, were studied. The attending anaesthetists had the freedom of choosing the appropriate anaesthetic drugs depending on the patients' clinical condition. The reason for admission into the ICU, the types of organ support required and outcomes were recorded. **Results:** Twenty-five patients (37.3%) out of 67 required critical care. Reasons for admission among others included poor respiratory effort, hypotension, septic shock and delayed recovery from anaesthesia. Twenty-one patients (84%) required mechanical ventilation with a mean duration of 2.14 days (range 1–5 days). Fourteen patients required ionotropic support and the length of ICU stay ranged from 1 to 15 days (mean 4.32 days). Nineteen patients (76%) were successfully managed and discharged to the ward while 24% (6 patients) mortality rate was recorded. **Conclusion:** This study showed high rate of post-operative ICU admission in patients with typhoid perforation with a high demand for critical care involving mechanical ventilation and ionotropic support. In centres that manage patients presenting with typhoid ileitis and perforation, post-operative critical care should be available.

Key words: Critical care, Intensive Care Unit, outcome, typhoid perforation

INTRODUCTION

Typhoid fever, caused by *Salmonella typhi* and paratyphi, remains a serious systemic illness in underdeveloped and developing nations where unhealthy environmental conditions prevail as a result of poor public health measures. It is a multisystemic illness which is transmitted through the faecal-oral route by ingestion of contaminated food and/or water.[1] Typhoid fever is characterised by fever, headaches, joint pains, profound weakness, diarrhoea, acute respiratory symptoms (cough), a maculopapular rash and abdominal pain.[2] While control of the infection has been achieved in developed countries by effective public health measures, developing countries continue to bear the burden of the disease, principally because many communities still fall short of standards for drinking water, hygiene and sanitation.[3]

Intestinal perforation, most common in the ileum, is the most serious complication of typhoid fever and ileitis, with mortality rates ranging between 20% and 60% in the West African sub-region.[4] The rates of perforation have been reported in literature to vary between 0.8% and 18%. The high incidence of perforation in most developing countries has been attributed to late diagnosis and the emergence of

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multidrug-resistant and virulent strains of *S. typhi*.[3] The systemic involvement in typhoid fever can result in extra-intestinal complications such as encephalopathy, meningitis, hepatitis, myocarditis and pneumonia while the most common gastrointestinal complication is haemorrhage.[5]

Following intestinal perforation, the management involves aggressive fluid resuscitation and electrolyte correction, antibiotic therapy and surgical repair. Both surgical and anaesthetic management pose unique challenges to both the surgeon and anaesthetist as the patients are usually very sick, dehydrated, hypovolaemic and anaemic with varying degrees of biochemical derangement. Postoperatively, some of these patients may require further care in Intensive Care Unit (ICU) due to septic shock, poor respiratory effort, hypotension and delayed recovery from anaesthesia. Typhoid fever, in its complicated form, can therefore be regarded as a disease of poverty that requires expensive treatment especially when mechanical ventilation and haemodynamic support are needed in ICU.

Many studies have documented the surgical experiences and management of this unfortunate disease,[1-7] but little or no research has been done on the anaesthetic and post-operative critical care in our environment. We therefore undertook this prospective observational study to document the pattern of post-operative admission and intervention in ICU in a tertiary teaching hospital in Nigeria. The primary outcome measures were the intervention and survival in ICU, and the secondary outcome measure was to find out crucial factors that may determine survival/outcome.

PATIENTS AND METHODS

This was a prospective observational study in patients who had typhoid ileitis perforation. Sixty-seven consecutive consented patients who had exploratory laparotomy between September 2009 and October 2012 were recruited. Pre-operative resuscitative measures included intravenous hydration with crystalloids, broad-spectrum antibiotic coverage, correction of electrolyte derangement and correction of anaemia in some patients with unacceptably low packed cell volume. All patients had nasogastric tube inserted to decompress the stomach and urethral catheter to monitor the hourly urine output. These measures continued postoperatively.

Pre-operative laboratory investigations included full blood count, serum electrolytes, urea and creatinine and abdominal ultrasound scan. Attending anaesthetists chose the appropriate anaesthetic technique and drugs depending on the patients' clinical condition. Intraoperative monitoring included non-invasive blood pressure, oxygen saturation, continuous 5-lead electrocardiogram, end-tidal carbon dioxide and peripheral and core temperature. Blood transfusion was given when necessary.

At the end of surgery, patients were assessed for adequate recovery from anaesthesia and stability of the vital signs. Patients with inadequate recovery or hypotension on account of septicaemic shock were transferred to ICU for continuum of care.

Information obtained included the demographic, the American Society of Anesthesiologists' (ASA) status, blood loss and blood transfusion intraoperatively as well as intraoperative critical incidents. Other data collected were ICU admission and length of ICU stay, duration of mechanical ventilation, inotropic drugs used and outcome of ICU care. Data obtained were analysed using the Statistical Package for the Social Sciences (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Proportions and frequency tables were used to summarise categorical variables. The results are presented in simple tables and percentages. Test of associations for categorical variables was determined using Chi-square. Test of association for quantitative variables was determined using *t*-test and ANOVA. Level of statistical significance was set at $P < 0.05$.

RESULTS

We studied 67 patients with typhoid perforations presented for surgical operation over a period of 4 years (September 2009 to October 2012). There were 42 males (62.7%) and 25 females (37.3%) [Figure 1],

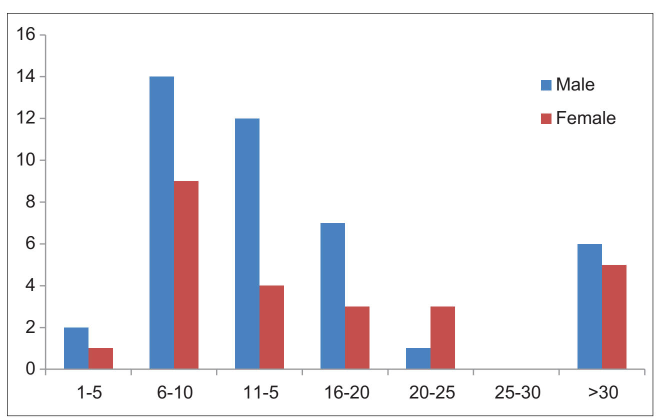

Figure 1: Age group distribution by sex

with a male:female ratio of 1.7:1. The age range was 3–64 years (mean 16.64 years). The peak age incidence was in 6–15 years age group which accounted for 58.2% of the cases [Table 1]. Seventeen patients (25.4%) were classified ASA II while 42 patients (62.7%) and 8 patients (11.9%) belonged to ASA III and IV, respectively [Table 2].

Intraoperative estimated blood loss ranged from 10 ml to 1600 ml (median 135 ml). Twenty-five patients were transfused with blood intraoperatively with a mean blood transfusion of 475.2 ml (range 100–1000 ml) [Table 2].

Postoperatively, 25 patients (37.3%) required ICU care [Table 3]. Twenty-one patients (84%) of 25 patients transferred to ICU required mechanical ventilation. Mechanical ventilation did not significantly affect the outcome in ICU, $P = 0.220$ [Table 4]. Of the 21 ventilated patients, 15 (71.4%) survived while 6 patients (28.6%) died. The mean duration of mechanical ventilation was 2.14 days (range 1–5 days), and the mean length of ICU admission was 4.32 days (range 1–15 days).

In ICU, 14 patients (56%) required inotropes to achieve or maintain cardiovascular stability. There was a significant association between the use of inotropic support in ICU and patients outcome, $P = 0.013$. Nearly 57.1% of 14 patients who required ionotropic support survived while 42.9% died [Table 4]. The ICU mortality rate in this study was 24% [Table 3].

Table 1: Age and sex distribution

Age group (year)	Male	Female	Frequency (%)
1-5	2	1	3 (4.5)
6-10	14	9	23 (34.3)
11-15	12	4	16 (23.9)
16-20	7	3	10 (14.9)
20-25	-	-	-
>30	6	5	11 (16.4)
Total	42 (62.7)	25 (37.3)	67 (100)

Table 2: Preoperative and intraoperative clinical characteristics

Variable	Frequency	%
ASA risk classification		
I	-	-
II	17	25.4
III	42	62.7
IV	8	11.9
Median EBL (range) ml	135 (10-1600)	
Median blood transfused (range), ml	475. 2 (100-1000)	

EBL: Estimated blood loss

Table 3: Postoperative ICU care

Variable	Frequency	%
Admission into ICU		
Yes	25	37.3
No	42	62.7
Mechanical ventilation		
Yes	21	84.0
No	4	16.0
Inotropic support in ICU		
Yes	14	56.0
No	11	44.0
Types of Inotrope used		
Dopamine only	6	42.9
Adrenaline only	3	21.4
Dopamine + adrenaline	5	35.7
Patients outcome		
Survived	19	76.0
Dead	6	24.0
Mean duration of mechanical ventilation (range), days	2.14 (1-5)	
Mean length of ICU stay (range, SD) days	4.32 (1-15)	

Table 4: Survival and ICU intervention

	Survived (%)	Died (%)	Total	*P* value
Mechanical ventilation				
Yes 21	15 (71.4)	6 (28.6)	21 (100)	0.220
No 4	4	0		
Inotropic support				
Yes 14	8 (57.1)	6 (42.9)	14 (100)	0.013
No 11	11 (100)	0		

DISCUSSION

The global burden of typhoid fever remains high in low- and middle-income countries (LMICs), especially in South Asia and Africa. The estimated number of typhoid fever cases in LMICs in 2010 after adjusting for water-related risk was 11.9 million (95% confidence interval 9.9–14.7) cases with 129,000 (75,000–208,000) deaths.[8] With such a high burden, typhoid ileal perforation is the most feared complication of typhoid fever due to its high morbidity and mortality rate.

Typhoid ileal perforation is more common in the paediatric age group. Children, 15 years and below, accounted for 42 patients (62.7%) of 67 patients operated upon during the study period. This is in agreement with other studies in which children constituted more than half of the cases of typhoid ileal perforation.[4,9,10] Children, 15 years or younger, constituted 55.4% of patients studied by Nuhu *et al.*[4] at the Federal Medical Center, Azare, Nigeria. At the University of Benin Teaching Hospital, Nigeria, children aged between 5 and 13 years constituted 70.6% in a study by Osifo *et al.*[1] We also observed a male preponderance of 62.7%, which is also similar to previous reports.[4,10] Chalya *et al*.[3] reported male:female ratio of 2.6:1 (72.1% vs. 27.9%) in North-Western Tanzania while Nuhu *et al*.[4] reported male:female ratio of 1.5:1 in North-Western Nigeria. Higher incidence of typhoid perforation in males has been attributed to the fact that men spend longer time and consume more food outdoors and this may lead to more frequent contact with the causative bacteria.[3]

Patients with typhoid perforation are usually very sick and at times moribund. Therefore, it is not surprising that 74.6% of the patients we studied belonged to ASA risk classification III and IV. Patients had emergency laparotomy with either simple closure for single intestinal perforation or bowel resection and anastomosis or hemicolectomy for multiple intestinal perforations. In a study by Bolaji and Kolawole,[11] bowel perforation in patients with typhoid fever was the most common indication for laparotomy (20 patients [20.6%]). Fifteen of these patients were in the ASA IV category while the remaining 5 were in ASA V category; however, none of our patients was in ASA V category.

Presenting with varying degree of septicaemia, all patients had aggressive fluid resuscitation, parenteral antibiotics and correction of electrolyte derangements and anaemia preoperatively. These measures most probably contributed to satisfactory anaesthetic outcome in 62.7% [Table 3] of patients, thereby reducing rate of admission into ICU. Notwithstanding optimal pre-operative preparation, we recorded ICU admission rate of 37.3%. The reasons for ICU admission were mainly cardiorespiratory problem due to septicaemia and septic shock (hypotension, anaemia and poor respiratory efforts) for support and stabilisation. In a report on post-operative intensive care admission of paediatric surgical patients, Bolaji *et al*. recorded 29.9% ICU admission rate following surgery for typhoid perforation.[12]

Postoperatively, some patients may require elective mechanical ventilation on account of respiratory insufficiency. Most of our patients (84%) admitted into ICU were mechanically ventilated. Bolaji *et al*. reported 40% rate of mechanical ventilation.[11] In another report by Bolaji *et al*.,[12] only 5 (20%) of 25 patients who required mechanical ventilation were ventilated while 75% could not be ventilated due to inadequate number or unavailability of mechanical ventilators in their ICU. This brings to the fore some of the challenges encountered in critical care in a resource-limited environment. The mean duration of mechanical ventilatory support in this study was 2.14 days (range 1–5 days).

Patients with typhoid perforation may develop various degrees of septic shock (often due to late presentation) requiring vasopressor and/or inotropic support. In this study, 14 patients (56%) received inotropic support. Dopamine only was used in 42.9%, adrenaline only in 21.4% while 35.7% of patients had both dopamine and adrenaline for haemodynamic support.

Septic shock is characterised by hypotension (mean arterial pressure [MAP] ≤65) and poor tissue perfusion which may manifest clinically by reduced capillary refill, oliguria and altered sensorium.[13] In septic shock, tissue hypoperfusion results not only from decreased perfusion pressure attributable to hypotension but also from abnormal shunting of a normal or increased cardiac output.[14] Despite adequate use of appropriate fluid challenge, 14 patients required the use of vasopressors to restore adequate arterial pressure and organ perfusion. The blood pressure of all the 14 patients was monitored non-invasively. The use of an arterial catheter provides a more accurate and reproducible measurement of arterial pressure where the resources are available and this will help in early intervention when necessary.

In this study, dopamine was used because of its vasopressor and inotropic effect. Dopamine, the natural precursor of norepinephrine and epinephrine, increases MAP and cardiac output primarily by an increase in stroke volume, and to a lesser extent by an increase in heart rate. It has also been shown to increase oxygen delivery to the tissues.[14] Dobutamine, the inotrope of first choice in septic shock for patients with measured or suspected low cardiac output, would have been preferable if available.

Alternative vasopressor drug that is useful in the management of shock is adrenaline (epinephrine). It is a potent α- and β-adrenergic agent that increases MAP by increasing both cardiac index and peripheral vascular tone. It increases not only oxygen delivery to the tissues but also oxygen consumption. The main concern with the use of epinephrine in sepsis is the potential to decrease regional blood flow, particularly in the splanchnic circulation, increase in lactate level and is also more arrhythmogenic than other catecholamines.[13] Another vasoactive drug that may improve haemodynamic stability is phenylephrine.

Typhoid perforation is associated with high morbidity and mortality. In the developing world, mortality rates from typhoid perforation have been reported to range from 9% to 22%.[3] We recorded 24% ICU mortality rate in this study which is comparable to the rates reported from resource-limited and developing countries like Nigeria. Chalya *et al*. reported mortality rate of 23.1% in Northwestern Tanzania, Irabor 21.3%, Ajao *et al*. 25% and Adesunkanmi and Ajao 25%.[3,6,15,16] According to Chalya *et al*., factors contributing to high mortality include high ASA (III–V), shock on admission and inadequate antibiotic treatment before admission[3]. Findings in our study also showed patients with high ASA, shock and respiratory insufficiency that required critical care.

Higher mortality rates of 31% and 36% were reported earlier by Olurin *et al*.[17] and Bohrer[18], respectively, while anecdotal low mortality rates below 10%[19,20] have also been reported. In the developed world where socioeconomic infrastructures are well developed, exceptionally low mortality rates of 1.5–2% have been reported.[21]

The high mortality rate associated with typhoid perforation in the developing countries has been attributed to three factors: disease, patient and environment.[6] The disease, typhoid fever, affects many organs (especially the heart, lungs, kidneys and intestinal tracts) and is mediated either via endotoxins and/or Shwartzman/Sanarelli type of hypersensitivity reaction leading to various degrees of septicaemia.[6] The patients are usually paediatric with less than optimum immune system, poverty-induced malnutrition, born to illiterate or semi-literate parents who obtain drinking or cooking water from any source, live in dwellings where sanitary disposal of human and animal is lacking.[6,20] All these occur in an environment (usually in the underdeveloped and developing countries) where pipe-borne portable water is lacking, with widespread sale and use of fake antibacterial drugs (thereby promoting multidrug-resistant strains) and lack of basic sanitary rules and socioeconomic infrastructures[6].

This study showed high rate of post-operative ICU admission. Mechanical ventilation and inotropic support contributed to better outcome from the disease; however, there is a significant association between inotropic support and ICU survival, $P = 0.01$.

CONCLUSION

The burden of typhoid fever still remains high in poor resource settings. Mortality arising from typhoid perforation is high due to late presentation and inadequate resources to properly manage it. ICU plays an important role in the management of typhoid perforation postoperatively. The study also highlights some of the challenges encountered in managing the complications of typhoid fever in the critical setting in a resource-limited environment.

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Conflicts of interest

There are no conflicts of interest.

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