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original article

Surgical intervention for intestinal typhoid perforation

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SUMMARY: **Surgical intervention for intestinal typhoid perforation.**

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Aim. *Typhoid perforation is the most fatal complication of typhoid fever in developing countries and is most often caused by the bacteria Salmonella Typhi. There are conflicting views as to which type of surgical intervention gives the best outcome. The aim of this study was to determine the mortality associated with the different types of surgical interventions employed in patients with typhoid perforation.*

Method. *This was a retrospective review of the medical records of adult and paediatric surgical patients treated in the general and paediatric surgical units of the Korle Bu Teaching Hospital. Information was obtained from medical records at the Korle Bu Teaching Hospital in Accra, Ghana, between January 2009 and April 2012. The data was analysed using IBM SPSS Statistics version 20 and 22.*

Results. *133 patients (median age of 21 years, 72.2% males) with typhoid perforation were included in the study. The typhoid perforation specific mortality rate was 12.8%. Males had a significantly lower mortality rate (7.3%) compared to females (27%). Simple bowel closure (85.7% of total) was the most common surgical intervention performed and patients operated upon with this method had a significantly lower mortality rate (9.6%) compared to patients with bowel resection (31.6%).*

Conclusions. *In this study, patients treated with intestinal resection were more likely to die from typhoid perforation and female gender was a risk factor for death. Simple bowel closure was the predominant surgical procedure.*

KEY WORDS: Typhoid perforation - Typhoid fever - Surgery.

Introduction

Typhoid fever is a systemic bacterial infection caused by *Salmonella typhi* and *Salmonella paratyphi* affecting mainly the young population in less industrialized countries (1, 2). The infection is primarily transmitted by the faecal-oral route and humans are the only hosts developing the disease (3). It is postulated that most adults develop immunity after repeated infections. Annually the disease affects 17-22 million people worldwide and up to about 600 000 die from the disease (4). Studies on typhoid perforation show differing mortality rates among patients in West Africa, ranging from 12.8 to 28.3% (1, 2, 5-7). In developed countries deaths are as low as 1.5-2% (1). Some studies show a seasonal variance in incidence correlated to rainy seasons (5, 8). *Salmonella typhi* infects Peyer's patches in the terminal ileum from where the bacteria reach the bloodstream and lymphatic system (3, 9). During this phase, the patient experiences a febrile illness, which generally occurs with chills and headache (3). After this initial bacteremia, the bacteria reinfect the Peyer's patches, causing an infiltration of mononuclear phagocytes resulting in ulceration, local necrosis, bleeding and bowel perforation (3, 9). The most feared complications following intestinal perforation are septicaemia and organ failure, which may lead to death (1, 2). The perforation usually occurs in the 2nd to 3rd week after infection, however in developing countries bowel perforation often occurs

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within the 1st to 2nd week (10). Typhoid perforation is usually single and located at the antimesenteric border of the terminal ileum, but may also be multiple and occur nearly all throughout the gastrointestinal system (9, 10). There is an ongoing debate about which surgical intervention gives the best survival (6, 9, 11). The aim of this study was to examine the mortality associated with surgical intervention in patients suffering from typhoid perforation at the Korle Bu Teaching Hospital (KBTH).

Patients and methods

Patients and data collection

Data was collected retrospectively from medical records of the general and paediatric surgery wards of the Korle-Bu Teaching Hospital in Accra, Ghana. The study was approved by the Ethical and Protocol Review Committee of the University of Ghana Medical School, 30th October 2013 (Protocol identification number: MS-Et/M.1-P3.4/2013-2014).

Patients registered in the admission books of the surgical ward between the 1st of January 2009 and the 23rd of April 2012 and in the paediatric ward between 1st of January 2010 and the 23rd of April 2012 with suspicion of intestinal typhoid perforation were noted. Inclusion criteria included patients with confirmed typhoid perforation in at least one of our sources of information (i.e. admission and discharge book, surgical theatre registry, mortality and morbidity conference records and mortuary records) and primary laparotomy documented confirming the typhoid perforation. Exclusion criteria were patients with presurgical or clinical diagnosis of typhoid perforation but unconfirmed at surgery or not operated on, and confirmed post-mortem diagnosis of typhoid perforation without prior surgical intervention.

Data from the surgical theatre registry and admission and discharge books were used to double-check and confirm the diagnosis, type of surgery, length of hospital stay and in-hospital mortality. Mortality and morbidity conference records and data from the mortuary were also used to confirm in-hospital deaths.

Informed consent

We acquired appropriate "prior informed consent" of patients and hospital administration used in the studies.

Diagnosis and treatment

At Korle-Bu Teaching Hospital, just like at many other hospitals in the region, typhoid perforation is mainly a clinical diagnosis. The main criteria are clinical features of acute abdominal pain, fever, generalized peritonitis and sepsis in addition to findings of perforation at the antimesenteric border of the terminal ileum mainly, but occasionally in the rest of the small bowel or colon at surgery or during post mortem examinations (2). Types of surgery performed are simple closure of the perforation or bowel resection and anastomosis i.e. ileal resection or right hemicolectomy. Generally, bowel resection is preferred when treating multiple perforations while for single perforations, simple closure is done. Patients with the above clinical features that subsided on medical treatment did not undergo surgery, thus were diagnosed as typhoid enteritis. Other secondary diagnoses could therefore not be ruled out.

Rainy season

The rainy season was defined as April-July and September-November (12).

Statistical methods

The data was analysed using IBM SPSS Statistics version 20 and 22. The distribution of confounding factors were analysed with Pearson Chi-square test and Mann-Whitney U test. Due to lack of information about children from the paediatric wards and theatre registry in 2009, age distribution was analysed in two different groups with cut off December 31st 2009. Logistic regression analysis was used to adjust for age and gender distribution in survival.

Results

Basic data

Of a total of 339 patients diagnosed with typhoid enteritis or typhoid perforation, 133 patients were included in the study. 206 patients were excluded, of which 8 were confirmed as imminent typhoid perforations at surgery, 93 had a preliminary diagnosis of typhoid enteritis but did not have confirmed perforation in theatre records and 105 patients were diagnosed with other acute abdominal states. 96 (72.2%) of the patients were males and 37 (27.8%) were females. There was a significant difference in sex dis-

tribution (p <0.001). Females had a lower median age (15 years) compared to males (24 years). The median age of all 133 patients was 21 years. Based on the material from January 2010 to April 2012, the median age of patients with typhoid perforation was significantly lower, 20.5 years compared to 26 years in 2009 (p = 0.004). There was no significant difference in mortality rates between the two time periods. No significant difference in the incidence of typhoid perforation was found when comparing the rainy season to the rest of the year (Figure 1).

Based on 98 valid cases, length of hospital stay ranged from 0-82 days with a median of 11 days. Non-survivors had a significantly shorter length of hospital stay with a median of 7 days compared to 12 days amongst survivors (p = 0.008) (Table 1).

Mortality Rate

The mortality rate was 12.8%. Of a total of 96 males, 7 died and out of 37 females, 10 died (p = 0.002) (Figure 2). When adjusted for surgical intervention and age, regression analysis showed a 6-fold risk for fatal events amongst females (Table 2 A). There was no significant difference in mortality rates between children (15 years or younger) and adults (p = 0.759). No cases of death were found between the ages of 14 to 24 years (Figure 3).

Surgery

The patients were divided into two groups, simple closure and intestinal resection. There was a significant difference in sex distribution between the surgical groups (p = 0.04). Among those undergoing simple

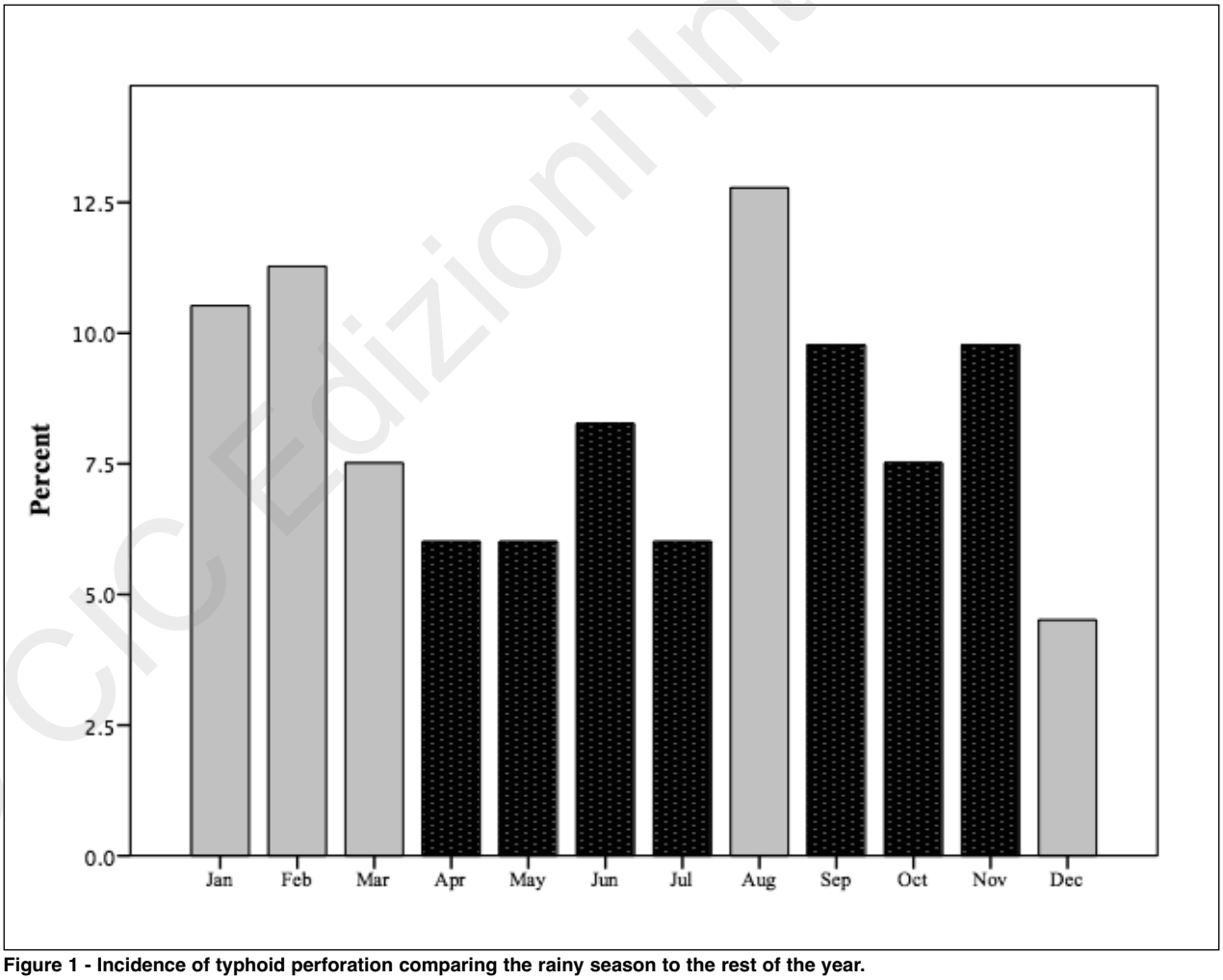

Figure 1 - Incidence of typhoid perforation comparing the rainy season to the rest of the year.

TABLE 1 - DESCRIPTIVE DATA BASED ON TYPE OF SURGICAL INTERVENTION. RESULTS ARE GIVEN AS N (%) OR MEDIAN (RANGE). P-VALUES ARE ANALYZED WITH PEARSON CHI-SQUARE OR MANN-WHITNEY U TEST WHERE APPROPRIATE.

		Simple closure *n*=114	Intestinal resection *n*=19	p-value	n(missing)
Sex					
	Female (*n*=38)		9 (47.4%)	0.04	133 (0)
	Male (*n*=96)		10 (52.6%)		
Age					
	2009	Median 25.5 (13-62)	Median 31.0 (31)	0.667	27 (0)
	Jan 2010-April 2012	Median 19.5 (4-76)	Median 22.0 (11-64)	0.076	104 (2)
Seasonal incidence					
	Rainy season	61 (53.5%)	10 (52.6%)	0.943	133 (0)
	Dry season	53 (46.5%)	9 (47.4%)		
Length of hospital stay		Median 11.0 (0-82)	Median 17 (1-40)	0.508	98 (35)
Mortality					
	Survivors	103 (90.4%)	13 (68.4%)	0.008	133 (0)
	Deaths	11 (9.6%)	6 (31.6%)		

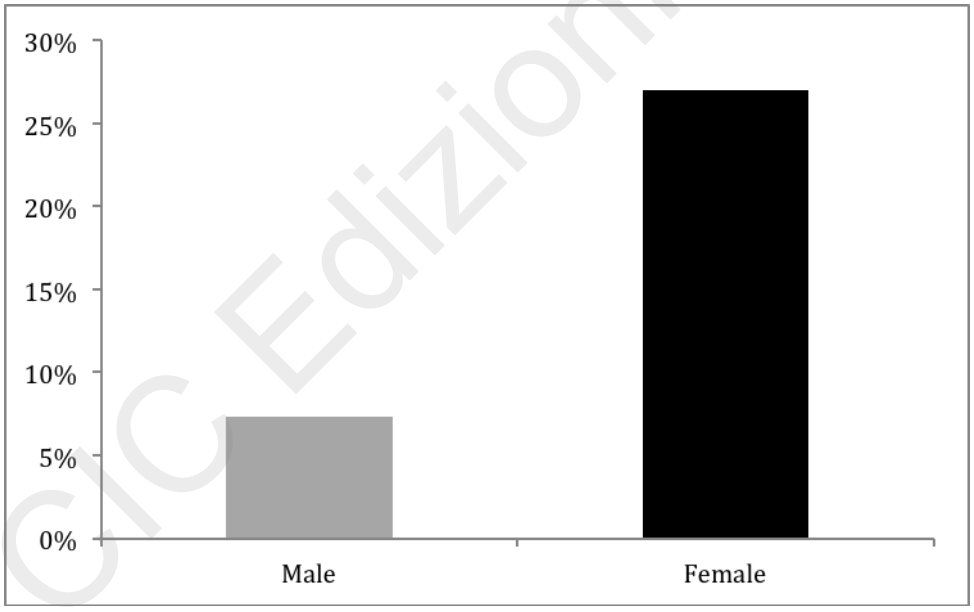

Figure 2 - Gender distribution of the population.

closure, 75% were males, compared to the group receiving bowel resection where equal distribution of both sexes was found. The distribution of age, seasonal incidence and length of hospital stay showed no significant difference between the two groups (Table 1). 114 patients (85.7%) were treated by simple closure, of which 11 (9.6%) died. 19 patients (14.3 %) were treated with resection, of which 6 (31.6%) died (Figure 4). There was a significant difference in mortality between the surgical groups (p

= 0.008), when adjusted for sex with logistic regression analysis. The risk of death was three times higher when treated with bowel resection. The difference in mortality between the surgical groups did not remain significant when adjusted for both sex and age (Table 2 B).

TABLE 2 - A) MALE-FEMALE DIFFERENCES IN MORTALITY. B) MORTALITY ANALYSES COMPARING TYPE OF SURGICAL INTERVENTION.

A)

	OR Crude (95% C.I.)	OR adjusted (95% C.I.)[a]	OR adjusted (95% C.I.)[b]
Male	1.00	1.00	1.00
Female	4.71 (1.64-13.56)*	4.04 (1.36-11.97)*	6.65 (1.91-23.16)*

[a]*Adjusted for surgical intervention*
[b]*Adjusted for surgical intervention and age*

B)

	OR Crude (95% C.I.)	OR adjusted (95% C.I.)[c]	OR adjusted (95% C.I.)[d]
Simple closure	1.00	1.00	1.00
Intestinal resection	4.32 (1.37-13.65)*	3.38 (1.01-11.29)*	2.59 (0.73-9.16)

[c]*Adjusted for sex*
[d]*Adjusted for sex and age*
* *significant results*

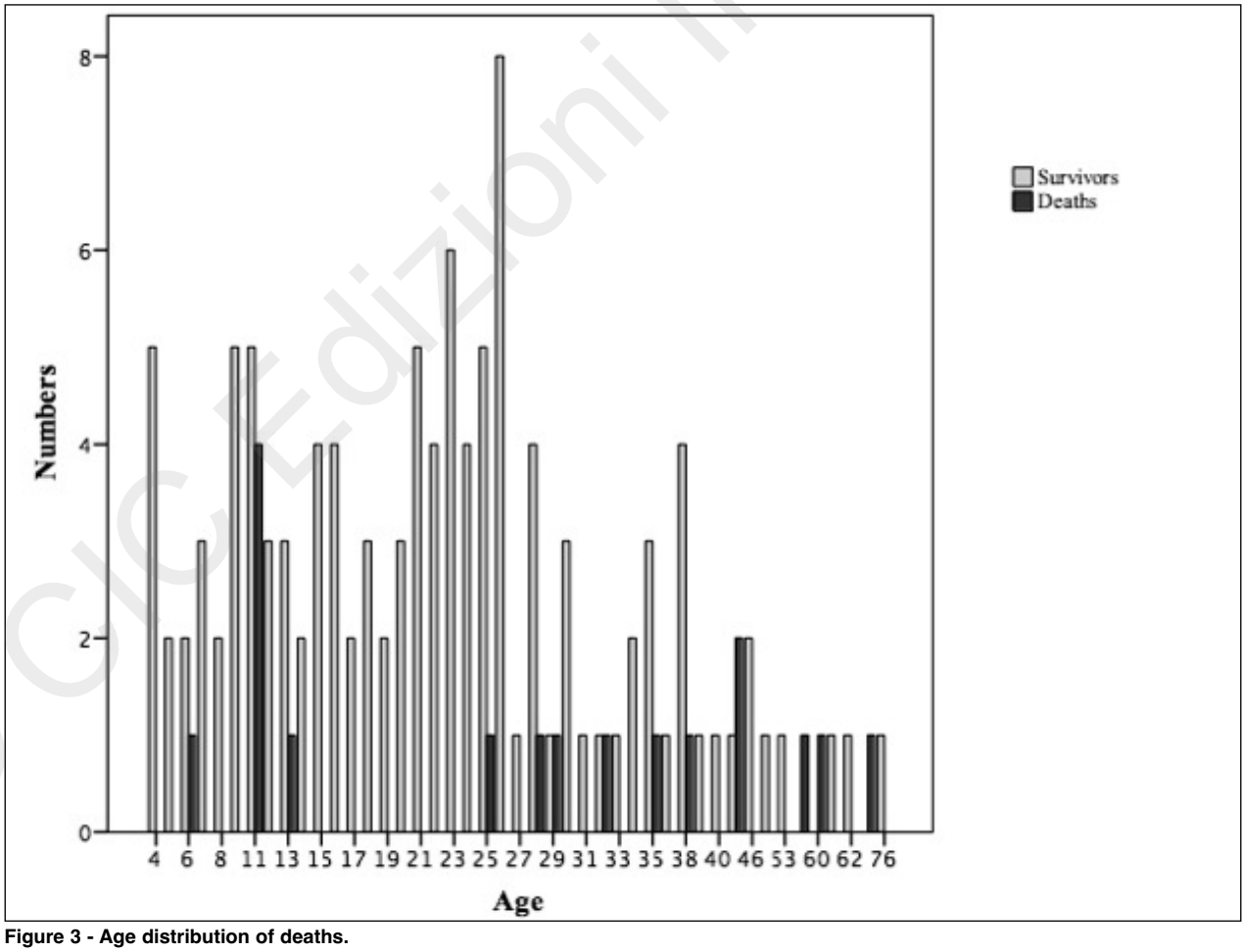

Figure 3 - Age distribution of deaths.

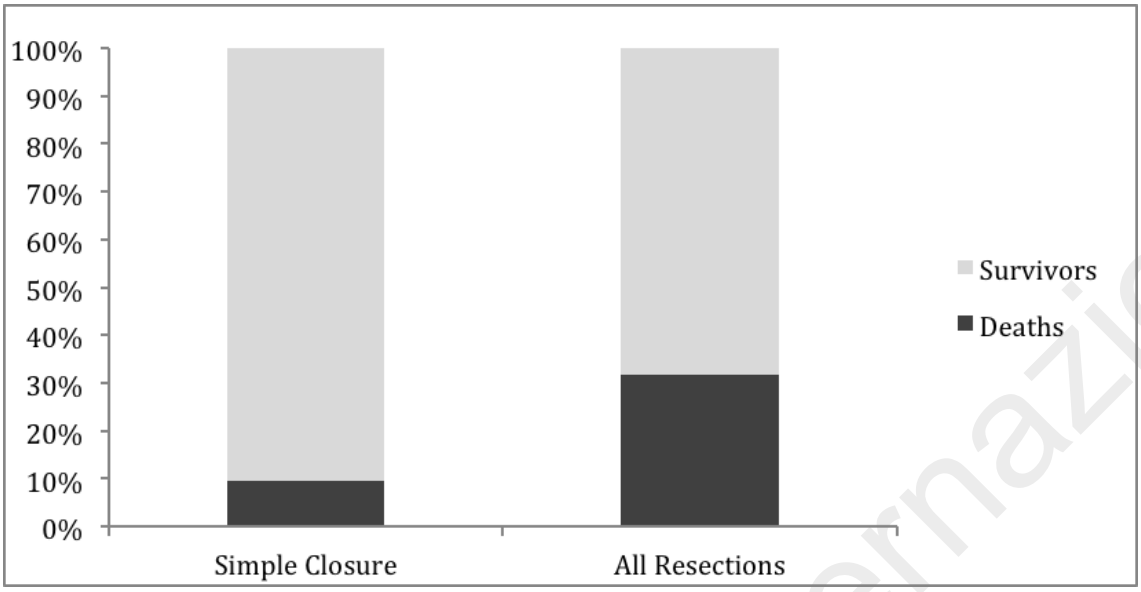

Figure 4 - Deaths and survival rate comparing the different treatment groups.

Discussion

The patients in this study were treated with simple closure or bowel resection as a primary surgical intervention. The results showed a total mortality rate of 12.8%. This compares with the rates found in previous studies in Ghana -11.69% (13) and also the West African subregion -12.8% to 28.3% (1, 2, 5-7). However, in developed countries deaths are as low as 1.5-2% (1). In addition to poor infrastructure, the high mortality rate from typhoid perforation in West Africa is thought to be due to late diagnosis, the presence of a more virulent strain and a higher frequency of multi-drug resistant strains of *Salmonella typhi* and lack of readily accessible supportive care (2). These factors also apply in Ghana.

In our study, the results showed a predominance of the simple closure procedure (85.7%) as in many other studies (2, 5, 6, 10). This type of surgery is time efficient, cheap and gives proportionately good results. While some studies maintain there is no correlation between type of surgery and mortality, others present a lower mortality rate with intestinal resection, whilst some show an advantage with primary ileostomy (6, 9, 11). Other studies also found like we did, that simple closure results in better outcomes (2, 8). Our study found a significantly higher mortality rate (31.6%) with intestinal resection compared to simple closure (9.6%). When adjusted for sex, bowel resection showed a significantly higher (triple) mortality risk. Adjusted for both sex and age, the results were no longer significant even though odds ratio still showed a two times increased risk of death. One explanation for the loss in significance, besides lack of causality, is that the number of cases and events were too few in this study. A limitation of this study was the absence of access to data on specific location and number of perforations as well as duration of symptoms, time to surgery and documentation of vital parameters e.g. ASA score. As to whether the numbers of perforations are a predictor of death is uncertain as studies show conflicting results (6, 9). Typhoid perforation is an illness infecting people throughout the year. Of two studies from Nigeria, one showed a seasonal peak in the rainy season with the other in the dry season (5, 8). Poor infrastructure and lack of proper sanitation facilities are thought to be some of the causes of the seasonal variation. Drinking water is easily contaminated during the rainy season by dirty water from choked gutters and drains. On the other hand the higher incidence during the dry season (8) is explained by the lack of water reservoirs resulting in poor supply of fresh and clean drinking water (8). The value of well-developed infrastructure in the struggle to fight the disease has been mentioned in several recent reports (5, 10).

However, no significant difference in seasonal incidence was found in our study.

Non-survivors had a significantly shorter length of hospital stay compared to survivors. This has also been shown by similar studies (2, 10). It has been explained that mortality from typhoid perforation occurs in the early postoperative period from sepsis related complications and multiorgan failure which explains the disparity in the length of hospital stay between survivors and non-survivors (2). There was a predominance of male patients suffering from typhoid perforation in this study, shown as a male-female ratio of 2.6:1. This is in keeping with results seen by many other researchers (2, 5, 10, 14, 15). Poor hygiene and more outdoor eating among young males is thought to increase exposure to infection (9, 10, 14).

Contrary to other studies, this study showed a significant correlation between gender and mortality from typhoid perforation with a higher mortality rate in the female population (1, 10). The mortality rate amongst males was 7.3%, while as many as 27% of the females died. When adjusted for age the relative risk of dying increases for the female gender indicating that female gender itself may be a risk factor for mortality. Poor prognosis in women may be due to the fact that other inflammatory gynaecologial conditions in the pelvis may have to be considered. This could be a factor in decision making probably leading to delayed surgery. Further, other factors influencing female mortality could be greater responsibility of domestic work and childcare leading to an unwillingness to leave home and seek medical care early in the disease process. Similar to a study conducted in Nigeria (1), there was no significant difference in mortality rates between children and adults. However other studies have shown higher mortality in children compared to adults (8).

Conclusion

In this study, compared to simple bowel closure, patients treated with intestinal resection were more likely to die from typhoid perforation and female gender was a risk factor of dying. To obtain more reliable causality between different types of surgical interventions, gender and mortality, prospective randomized studies need to be done.

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