



Surgical management of perforated bowel due to typhoid infection. What are the predictive factors for pre-operative diagnosis in the endemic area

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ABSTRACT

Perforated typhoid fever is a common cause of peritonitis in the endemic areas and associated with high mortality and morbidity if not managed properly. This prospective study included 75 patients with perforated bowel that operated upon in two years (2017-2018) and other 29 cases of non-perforated typhoid enteritis presented as acute abdomen. Of 75 cases, 13 (17%) presented as local peritonitis, while 63 (87%) as general peritonitis, which was confirmed by chest X-Ray/ gas under the diaphragm in 80%. 61(81%) patients were males. The age was 15-40 years in 54 (72%) patients. White Blood Cell count [WBC] is low or normal in all cases. 35(46%) patients were presented as an acute abdomen without fever. All patients had at least one perforation in the terminal ileum. There was single perforation in 47(62%) patients. The midline incisions were complicated by dehiscence in 15 (24%) of 54 cases and by wound infection in 35(64%). Six(8%) cases were complicated by fecal fistula and 3(4%) patients unfortunately died. Wound infection complicated 4 (26%) of 15 cases of gridiron incisions, but no wound dehiscence or incisional hernia. WBC is helpful in the diagnosis of perforated bowel due to typhoid infection. This is important for the proper choice of an incision. Grid iron incision is associated with minimal complications and is preferred to the midline one. Acute diffuse peritonitis indicates perforation in almost all cases, but only one-third of local peritonitis caused by perforation. Early limited surgery and the proper choice of antibiotics according to local microbiologist opinion or culture decreased the mortality to 4%.

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INTRODUCTION

There are 16 million new cases of typhoid fever (TF) around the world and approximately 600000 of

these die each year. It is an acute systemic disease of several weeks duration. Many cases of TF present as mild illness and low-grade fever and relapse is common (Chalya *et al.*, 2012). Intestinal perforation complicated up to 3% hospitalized cases and attributed to one-third of mortality. The perforation is usually single but multiples in 25% (Ukwenya *et al.*, 2011). The site of perforation is mainly in the lower terminal ileum, although perforation can affect any area in the small or large bowel. Diagnosis of perforation can be achieved based on a clinical picture in an endemic area and surgery is preferable to medical treatment (Abantanga *et al.*, 2009; Karmacharya and Sharma, 2006; Ewaid and Abed, 2017).

The typical patient presents with sudden, severe abdominal pain that complicated febrile illness for

2-3 weeks with peritoneal irritation. Gas under the diaphragm on Chest X-ray [CXR] confirms the perforations. The perforation affects males in a ratio of 4 or 3 to one and in young adult life, but it is very rare in children, especially below 10 years (Al-Grawi and Al-Awsi, 2018). Although most cases of TF are seen in those aged 3-19 years, most patients of perforated TF are seen in second or third decades. The occurrence of perforation is not related to the severity of the individual attack of the disease. In some cases, the perforation occurs in a mild episode and in the first week. The diagnosis of the TF depends on the blood culture, which was positive in 90% of cases in the first week or stool culture in the second or third week and become negative after antibiotics treatment. The detection of antibodies IgG and IgM are cheap and accurate investigations. A literature review of 57864 cases of TF in developing countries in the antibiotic era revealed that perforation developed in 2.5% of patients, a percentage that is very similar to the incidence of 2.8% reported in the pre-antibiotic era. The morbidity in the form of wound infection is common because it is a contaminated operation, in addition to wound dehiscence, fecal fistula, intra-abdominal abscess and incisional hernia. The complications had been on the gradual decline with the advance in medicine. The modern surgery and supportive care decreased mortality ratio from 50% in 1960 to single digit in the last years but still high in places like West Africa (16%) (Sheshe et al., 2018; Ewaid et al., 2019a,b).

PATIENTS AND METHODS

This is a prospective study done in two years [2017-2018] at our teaching hospital and included 75 cases of bowel perforation due to TF that were managed surgically. Operations were done by 8 surgeons, three of them consultants and other new specialists in general surgery.

The diagnosis of perforated TF was proved operatively. Some cases were operated upon depending on the clinical picture as acute peritonitis without investigations (see Table 3). The study also included the other 29 cases of TF that presented with sudden, severe, abdominal pain associated with tenderness and rebound tenderness and divided in two groups according to the options of surgeons in treatment.

Group C that included 16 cases presented with local peritonitis that was diagnosed on the clinical bases and investigations (serology IgM, IgG), and treated conservatively (presumed or impending perforation). Other groups included 13 patients that managed by operation, 11 cases by grid iron because of suspicion of acute appendicitis and was classified as group B.

The other two were operated upon by midline incision for generalized peritonitis. The operative finding in all cases shows severe ileitis, impending perforation, lymphadenopathy, in addition to fluid collection in two cases only, one case with sealed pinpoint perforation but no active perforation.

Our hospital had no experience in dealing with cases of perforation of the bowel due to TF for decades but suddenly, the surgeons faced a large number of cases in the non-familiar epidemic attack. We included 75 cases of perforations during two years and many other patients were excluded due to insufficient data and being considered not eligible for this study.

Some cases were diagnosed as typhoid fever by a physician and complicated by the acute abdomen and referred to the surgeons. Other cases presented or referred to the surgeons as acute appendicitis, perforated duodenal ulcers and peritonitis of unknown cause.

RESULTS

61 patients (81%) of perforated bowel were males, while no case was reported below 10 years, 5 cases between 10-14 year. 54 (72%) of cases between 15-40 years, 14 (18%) cases between 40-60 years, and two cases above 60 years. (see Table 1). 48 (64%) patients were presented with single perforation, while 27 (36%) cases are presented with multiple perforations. Females are older than males and two-thirds of females were with multiple perforations that occur in only one-fifth of males (see Table 2). All the perforations were in the small bowel and the single perforation always located in the terminal ileum, while in multiple perforations, there was also at least one perforation in the terminal ileum while the others located proximally (to be in the jejunum in a case with 7 perforations).

No perforation was reported in the large bowel or appendix and also no single perforation reported in the jejunum or proximal half of ileum.

In 22 cases, in addition to with the perforation closure, an appendectomy was done.

11 cases of appendectomy done in non-perforated TF, which were wrongly diagnosed as appendicitis. So, the total number of an appendectomy was 33.

All the cases with a perforation that were investigated by WBC, which were 57 (76%) cases, showed low or normal count (see Table 3). Also, WBC is low in all 27 patients with local peritonitis but without definite macroscopic perforation (see Table 5). WBC is also low in 2 cases of non-perforated TF but presented as generalized peritonitis.

Table 1: The number of patients with perforation according to the age

0	0-10 years
5	10-14 years
54	15-40 years
14	40-60 years
2	Above 60 years
75	total

Table 2: The gender ratio and the differences between them in perforated cases

Range of age	Median age	Multiple perforations	Single perforation	Total number	gender
25-45 years	30 years	9	5	14	female
10-70 years	25	18	43	61	male

Table 3: The investigations that done preoperatively in perforated cases (peritonitis)

Negative findings	Positive finding	Total number of cases that investigated	Methods of investigation
9	42	51	Air under diaphragm by plain abdominal x-ray
3	31	34	Ultrasound of the abdomen
No cases presented with a marked increase in WBC	In all cases, the count is low or normal	57	White cells count N.B. : WBC expected to increase in nonspecific bacterial peritonitis due to perforation

Table 4: Some complications of perforated bowel according to types of abdominal incisions

Fecal fistula	Burst abdomen	Wound infection	Total number	Types of incision
6	15	35	54	Midline incision
0	0	3	6	Right Paramedian incision
0	0	4	15	Grid iron incision
6	15	44	75	Total

CXR showed gas under the diaphragm in 42(82%) of 51 cases(see Table 3).

Of the 54 patients operated upon by midline incisions,15(24%) complicated by abdominal wound dehiscence,2(3.7%) incisional hernia after three months, 35(46%) cases complicated by wound infection, 6 (8%) cases complicated by fecal fistula. While of 15(20%) cases operated by grid iron (in 13 cases, the preoperative diagnosis was appendicitis, 2 cases the preoperative diagnosis was perforated TF), no case was complicated by wound dehiscence and 4 patients were diagnosed with mild infection (see Table 4).

Table Legends

1. Table 1 -shows the number of perforation according to age
2. Table 2 -shows the gender ratio and the difference between them in perforated cases.
3. Table 3 -shows the investigations that done preoperatively in perforated cases.
4. Table 4 -shows some complications of perforated bowel according to the type of abdominal incisions.

Table 5: Compare among three groups that presented with localized peritonitis.

Final diagnosis	Ultrasound	Chest x-ray	Low or normal White cells count	Preoperative diagnosis	Clinical feature	Number of cases
Perforated typhoid enteritis	Done in 8 cases and there is fluid in 6 cases	Not done because the diagnosis is appendicitis	10 of 10	Acute appendicitis	Rh. and central pain, tenderness and localized guarding	13 cases operated by Grid iron incision
Non-perforated typhoid enteritis -normal appendix	In 7 cases done but no collection except one case	Not done	11	Acute appendicitis	Rh. And central pain and localized tenderness	11 cases operated by grid iron incision
Typhoid enteritis with or without perforation	No fluid collection	No air under the diaphragm	16	Typhoid enteritis	Localized abdominal pain with localized tenderness	16 cases managed conservatively

Table 6: Antibiotics sensitivity and resistant of strains of S.typhus in Aldywania city in 78 patients in the same period of study and included some of the patients that complicated by perforation while the other non-perforated cases

Ratio of sensitivity	Resistant	Sensitivity	antibiotics
88.5 %	9	69	Meropenem
91 %	8	71	Imipenem
19 %	63	15	ciprofloxacin
62 %	29	49	Cefotaxime
57.8 %	33	45	Ceftriaxone
70.5 %	23	55	Cefixime
16.5 %	65	13	Azithromycin
65 %	27	51	Chloramphenicol
48.7%	40	38	Validixic acid

5. Table 5 -shows compare among three groups that presented with localized peritonitis.

6. Table 6 -shows antibiotics sensitivity and resistant of S. typhus in Aldywania city in 78 patients in the same period of study and included some of the patients that complicated by perforation while the other non- perforated cases

Discussion

In 62 (82%) patients of perforated typhoid enteritis presented as acute severe diffuse abdominal pain associated with signs of generalized peritonitis. The other 13(18%) cases presented as right lower and central abdominal pain with tenderness, rebound tenderness and local rigidity, a feature of localized acute peritonitis. In 40(54%) of cases, the acute

peritonitis developed after long history of fever, more than 10 days up to two months, and during this period, were treated as TF but inadequately or not responding; while in 35(46%) of cases, the fever is not consistent feature or of few days duration and the patients presented to the surgeons because of acute abdomen ([Amalraqibshamran et al., 2018](#); [Chalap and Al-Awsi, 2019](#)).

These did not present as TF, but accurate post-operative history revealed mild fever and ill health before the acute abdomen. According to that, all the cases of bowel perforation presented with generalized or local peritonitis but not necessary with typical clinical features of TF ([Al-Zaidy et al., 2019](#); [Al-Grawi and Al-Awsi, 2018](#); [Al-Awsi et al., 2019](#)). Analysis of 52 articles by R. stockenbrugger (3) showed

the diagnosis of perforated bowel by typhoid in endemic area depended on accurate history and physical examination, which was seen in our study that is supported also by the statement that acute abdominal pain and the alarming signs in treated typhoid fever should be regarded as typhoid perforation till proven otherwise. Two cases of generalized peritonitis of TF, although abdominal ultrasound scan (USS) showed fluid collection, operative finding showed no perforation, so general peritonitis without perforation occurs in nearly 3%, corresponding to other study showing 5.5% of generalized peritonitis developed without perforation (Chalap and Al-Awsi, 2019; Chillab *et al.*, 2019). Local peritonitis is less sensitive to diagnose perforation (half of the cases that operated, without perforation).

In our study 40 cases presented as local peritonitis (see Table 5) and divided into three groups (A, B, C) and in 75% not preceded by typical TF but mainly as acute surgical diseases, so two-thirds were diagnosed wrongly as appendicitis and operated by grid iron incision (group A and B) while group C diagnosed as TF complicated by localized peritonitis and managed as presumed or impending perforations. Group A of 13 patients (34%) operated by grid iron and the finding is terminal ileitis with perforations (Talwar *et al.*, 1997a; K Pujar Anupama *et al.*, 2013). Group B of 11 patient (27%) also operated as appendicitis but without perforation so if the acute appendicitis is excluded, the most difficult problem regarding management is to differentiate perforated terminal ileitis that was surgically managed (group A) from non-perforated terminal ileitis or pinpoint perforation that was managed conservatively (group B and C). As seen in our study, the perforation is either impending or of different size from pinpoint to that involved half circumference of the diameter. Impending and pinpoint perforation was not associated with fluid in peritoneal cavity or gas under diaphragm. It was associated with less signs of peritoneal irritation as seen in group B and C, (see Table 5) and responded to the conservative treatment in the form of antibiotic, nothing orally, intravenous fluid but if the pain is getting worse, tenderness spreading with guarding, and USS showed collection (6 of 8 cases), these patients needed surgical treatment as seen in group A (see Table 5). CXR is indicated in all cases of localized peritonitis when the perforation is suspected for evidence of gas under diaphragm.

The radiological investigations, in most cases, confirmed the perforation (see Table 3). 51 (82%) of our cases that were investigated by the CXR showed gas under the diaphragm; this finding were seen in other

studies. The USS were done for 40 (53%) of perforated cases and showed a collection of fluid with lymphadenopathy, increase the thickness of bowel, and enlargement of spleen in 37 (91%) similar to a study on 104 cases that was positive in 85.7%.

WBC count especially the neutrophil is low or normal in TF and it is not specific finding and not of value in diagnosis, but the story is different when the disease is complicated by perforation because, in spite of acute peritonitis by intestinal flora, the bone marrow does not react by leukocytosis as seen in other causes of perforation like perforated duodenal ulcer or appendicitis. 57 (76%) cases with perforation were investigated by WBC; all of them showed low or normal count. The precise preoperative diagnosis of TF as a cause of perforation, in the cases not diagnosed as TF and presented as an acute surgical emergency, is important because it helped in the choice of an abdominal incision as in our study. This finding of low WBC is corresponding with other studies that was done in Turkey which showed that leukopenia was not only finding but also a risk factor for perforation (12), and in other studies from Nigeria that included 86 cases and show white cells count was 4200 in 88.4% of cases (10). Also, the low WBC is of value in the exclusion of appendicitis as a cause of local peritonitis. Appendicitis was suspected as a cause in two-third of our cases and its exclusion as a cause leads to avoid operation in group B. WBC is low or normal in all cases [A, B, C] while in severe appendicitis, there is leukocytosis or relative increasing in neutrophil. The diagnosis of perforated TF need, in most of the cases, clinical diagnosis of peritonitis that indicates the perforation of the bowel and confirmed in most cases by CXR (gas under diaphragm) with 1-Fever preceded the peritonitis 2-Low, normal white cells count, although the localized peritonitis is less sensitive in the diagnosis of perforation.

The average fever-clearance time is less than 4 days with effective medications, but as the above figures shown, in 40(%) cases, the perforations developed while the patients on treatment for 1-4 week (resistant cases). This fact must be regarded in the postoperative period by review the antibiotics and used new antibiotics. Otherwise, the disease is still active in the postoperative period leading to increased mortality and morbidity. In 35(46%) cases, the diagnosis of perforated typhoid enteritis was intra-operative one, which means that patients not received specific antibiotic treatment. Culture, in these cases, is essential not for diagnosis but for treatment because the patient is critical and no time to loss by random choice of antibiotics. All perforations developed either in untreated patients or

resistant to antibiotics; this is consistent with the previous study, antibiotics must be started early and to be used for a proper time to cure the disease; otherwise, the incidence of perforation increases. Another article also showed that perforation was extremely rare in developed countries.

Salmonella typhus characterized by the formation of the resistance to antibiotics that transmits by plasmid and this resistance is different according to place and time. The perforation usually develops in resistant or undiagnosed cases, as discussed above, and could make it worse, so the control of the primary disease in the postoperative period with effective antibiotics is essential. The analysis of 78 cases of blood culture in the same area and in the same time (most of them not included in our study), showed most cases were resistant to the ciprofloxacin (81%) and nalidixic acid but were sensitive to the imipenem and meropenem (see Table 6). Post-operative use of meropenem in 30 cases (40%) showed a good postoperative course regarding morbidity and mortality in comparison with other used other antibiotics. The post-operative choice of antibiotics according to this table had dramatic effect because the empiric use of antibiotics according to the sensitivity of strain of microorganism in the area of epidemic attack which is different from other areas so local rather than global study of sensitivity and resistant strains of bacteria must be the base for choice of empiric antibiotics.

No case was reported below 10 years. This is similar to the other study in Europe in the pre-antibiotic era, but this finding is not seen in Africa. Only two cases above the age of 60 years. 72% of patients were between 15-40 years, 90% were males (a group of good immunity and strong inflammatory response) (see Table 1), and in 45% cases the systemic manifestations of disease were mild (walking typhoid), site of perforation in lymphoid follicle, and no reported case in colon. All these findings suggest that perforation did not reflect the virulence of microorganism and severity of systemic infection but it was caused by exaggerated local inflammation, immunologically mediated, in lymphoid follicles due to repeated exposure to antigen in an endemic area, lead to necrosis and even perforation, so it is not necessary associated with severe systemic symptoms. The absence of systemic manifestation explains why the disease, in some cases, was confused with an acute surgical emergency like a perforated duodenal ulcer or acute appendicitis and 45% of cases presented as acute abdomen to the surgeon rather than as typhoid fever. Wound infections were common finding that occurs in 39(65%) of 60 cases of

median and para-median incisions, while in grid-iron incision the incidence is 4 of 15 cases (26%) and overall incidence is 57%. This high incidence of infection is seen in other studies, although the percentage of the wound infection is different from one area to other but all the studies showed high incidence of wound infection, maybe because the field of operation regarded as dirty wound in addition to the effect of primary disease. Grid iron incision in our study showed a low incidence of infection, at the same time gives a good approach to the pathology, this finding was supported by other study concluded that the use of Mcburney incision may provide better results in term of subsequent wound healing. Abdominal wound dehiscence was reported in 15 (24%) patients operated by midline incision (see Table 3); a finding is seen in another study but in different percentages. Two (3.7%) incisional hernia detected after 3 months, although there is no longer a follow up with most of the cases. While no reported cases of wound dehiscence were complicated gridiron incision, this was confirmed by other studies with a low incidence of wound dehiscence in gridiron incision with extension in comparison with other papers. The healing of the gridiron incision is better with a low incidence of infection and no dehiscence; at the same time, it gives good access to the pathology, so it is preferable to a midline incision. The precise preoperative diagnosis of the cause of perforation is needed (as discussed above) to choice proper incision. Gridiron incision was a good option in case of precise preoperative diagnosis of perforated TF and preferred to the midline in terms of good wound healing but not proper one if the cause of the perforation is unknown. Appendectomy that done in 33 cases had no adverse effect specific to the removal of the appendix. Only two (2.6%) cases were complicated by the intra-abdominal collection, which was a response to conservative treatment. Closure of the perforations were done in 50 cases with single perforation or multiple perforations when present along a long segment of bowel while resection and anastomosis were done for multiple perforations in 21 cases that presented together in short segment, and 4 cases in single perforations. No ileostomy was done. Copious irrigation and drainage of the abdominal cavity with a good peritoneal toilet is essential and was done in all cases. The technique of surgery plays no rule in mortality or morbidity in our study and no need for complicated procedures, so limited surgery (no more than the closure of perforation) with good peritoneal toilet and good drainage post-operatively give the best result if associated with proper post-operative antibiotics. Although the study showed

resection and anastomosis decreased the mortality while in one of the larger series on 352 cases by Rthene showed extended resection of the bowel 10 cm proximal and distal to perforation decrease the mortality. In our study, no reported death case in simple closure. The postoperative fecal fistula was reported in all articles of perforated typhoid fever but in a different ratio. In our study, the fecal fistula complicated 6 cases in a ratio of 8% and all reported in multiple perforations. The development of postoperative fecal fistula is significantly increased the mortality rate and was complicated all cases of postoperative mortality in our study; this finding is seen in other studies. 5(18%) cases of fecal fistula developed in 27(%) cases with multiple perforations, but only one case (2%) is reported in 48 cases with single perforation. This finding was also noticed in other studies. The surgeon must deal carefully with fecal fistula. Only 3 (4%) cases of perforated typhoid that operated had died. In all mortalities, there was no response to the antibiotics due to resistant strains, and all of them were associated with multiple perforations (Adesunkanmi and Ajao, 1997) and also all complicated by fecal fistula.

Another important reason of successful management was short interval time between the perforation and operation, nearly 60% of all cases operated within 24 hours after perforation, in addition to the good quality of medical care. All fatalities presented late after 4 days of perforation with septic shock and were not responding to the post-operative antibiotics. The mortality rate on gradual but variable decline worldwide, it decreased from 50% in 1960 to single digit in last decade (Sheshe et al., 2018) as seen in study on 102 cases in Bir hospital in Nepal around 6.68% (Talwar et al., 1997b), but West Africa still lagging behind at 16%. No reported mortality in a study done on 40 cases in which 57% diagnosis was achieved in the first week and operated within 6 hours (Parry et al., 2002). This worldwide improvement in prognosis due to the good quality of medical service in diagnosis and treatment, as seen in our study.

CONCLUSIONS

Nearly all cases of acute general peritonitis complicating typhoid fever are due to perforation, while only one-third of localized peritonitis caused by perforation and x-ray confirms that in 80%. Low or normal WBC count is essential for the diagnosis of typhoid fever as a cause of acute abdomen with atypical presentation of TF and the preoperative diagnosis is useful because it helps in the choice of a proper incision. Gridiron incision is the preferable

option to midline incision as it associated with low wound complications. Early surgical interference in the form of the limited surgery with postoperative choice of antibiotic against resistant *S. typhus*, according to local microbiologist opinion or culture (and not according to global study), is essential to decreased mortality and morbidity.

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