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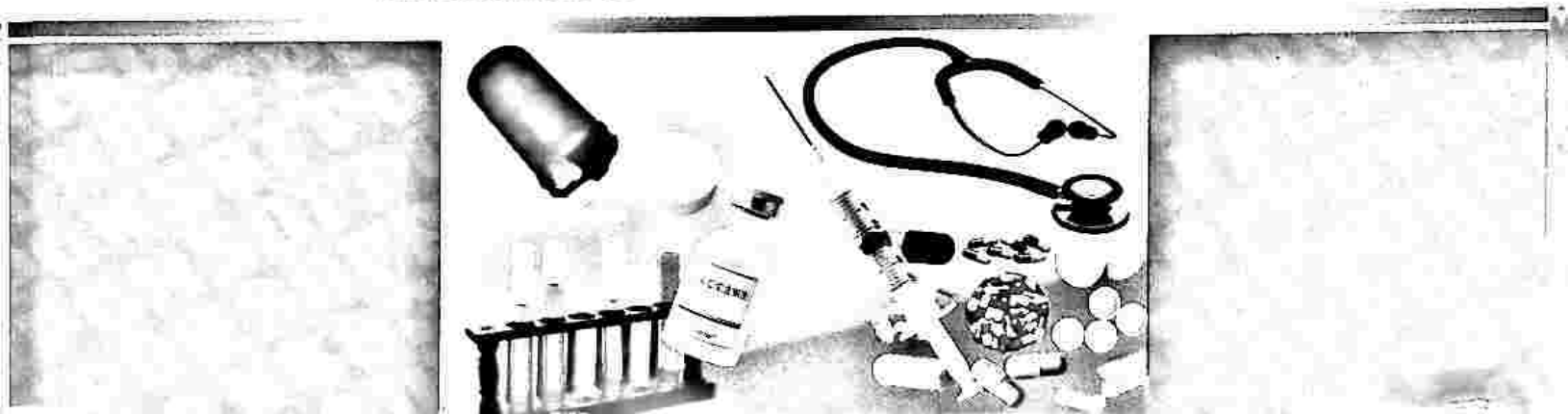

PATTERN OF TYPHOID PRESENTATIONS IN CHILDREN AND SURGICAL OUTCOMES OF PERFORATED CASES IN A TERTIARY CENTRE IN NORTH CENTRAL, NIGERIA

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Key words: Typhoid perforation, Health-Related Quality of Life (HRQoL). Quality of life (QoL), Length of Stay (LoS)

Conflict of interest: We declare that we have no financial or personal relationships, which may have inappropriately influenced us in writing this paper.

ABSTRACT

Background: Mortality in children with typhoid perforation is four (4) times higher than those without perforation in Nigeria. A high index of suspicion and early surgical intervention reduces morbidity and mortality in children with typhoid fever with and or typhoid perforation.

Methods: To determine the pattern and treatment outcome of typhoid enteritis with ileal perforations, leading to observed improvement of treatment of perforation due to prompt simple surgical management and determine whether the mortality of perforation in typhoid was still adamantly 4 times as high as before. A 5-year retrospective study of all managed children with perforated typhoid enteritis between March 2012 and March 2017 at Bingham University Teaching Hospital, Jos, North-Central Nigeria was undertaken. Effect of duration of illness at home before referral to hospital, impact of time lapse between perforation, operation and management were investigated.

Results: Sex differential of the152 admitted children was female 53(36%) and males 96 (64%) ratio F: M of 1:1.8 aged from 0.6 to 17 years. We had a mortality of nine cases (6 %) M: F ratio of 2:1.Age range of the group was 16.4; median was 8.0, standard deviation of 3.48, min of 0.6 and max of 17 and variance was 12.11.LoSwas highest for male children. The QoL of the children and parents/guardians were better.

Conclusion: Quick diagnosis, immediate resuscitation and prompt surgical decision and simple surgical intervention were vital to the improved morbidity and mortality recorded in this study.

INTRODUCTION

Intestinal bleeding and perforation from necrosis of Peyer's patches in the terminal ileum in typhoid fever (enteric fever) are severe complications, which very often end up lethal.[1]

The impact on resource-poor countries is devastating.[1,2] Regions with contaminated water supplies and inadequate waste disposal have a high incidence of typhoid fever.[1,2,3]

In that the clinical diagnosis of typhoid fever is not yet clear because of its protean manifestations with numerous differential diagnosis makes the diagnosis of typhoid fever difficult to differentiate from malaria, brucellosis, which are endemic all over West African subcontinent.[1,3]

With a high index of suspicion, the diagnosis of typhoid and its perforation could be made with a high level of accuracy based on clinical features, basic laboratory findings and imaging investigations; the use of the Centre for Disease Control (CDC) and Prevention case definition for typhoid fever further helps in making the diagnosis. [2, 3]Clinical, radiological and ultrasound examination assist in the diagnosis of perforation.

After vigorous resuscitation, simple surgical closure of the perforation and abdominal irrigation and drainage of operation site will suffice for most cases.[2] Antibiotics effective against S. typhi, coliforms and anaerobes are required.[4,5]

The risks factors for enteric perforation have not been standardized [1,2, 3, 5], making it mandatory for the plethora of diagnostics like cultures of blood serum, bone marrow aspirate, stool and urine to be taken on day of presentation in the clinic mandatory.[3,4]

Although the isolation of S. typhi and its subspecies is gold standard in the diagnosis of typhoid fever, yet a high index case of suspicion, radiographic and US examination of abdomen are enough to make a rapid diagnosis.[1,2,5,6]

Ultrasonography and radiography of abdomen that shows air under diaphragm clinch the diagnosis with high level of accuracy.[2]Culture of blood either from bone marrow or of peripheral blood, and even culture of intra-abdominal faecal soilage have high false negative results of up to 70%.[3] This may be due to prior self-medication with antibiotics especially in urban regions.[1,3]

Mortality being still very high in perforated typhoid fever of children, the purpose of this study therefore was to demonstrate clearly, which factors were modifiable in the management of typhoid perforations in the local environment. Was it possible to forestall perforations from onset of the disease and determine what these measures are that could prevent such a very lethal complication from occurring?

We therefore took a second look at the data of all typhoid perforations in children who were admitted in the Paediatric Ward of BHUTH, Jos, Nigeria within a period of five years. We knew mortality in children with typhoid perforation was four (4) times those without perforation.[2,6] We wanted to know the present trends. Was management of perforated typhoid getting better or worse?

ETHICAL CONSIDERATION

Ethical clearance was obtained from the hospital's Ethical and Research Committee and written informed consent from parents/guardians of patients was also obtained.

PATIENTS AND METHODS

We retrospectively analysed 152 children infected with typhoid fever, all from 0.6 years to 17 years of age, who were admitted at the Paediatric Department of the Bingham University Teaching Hospital (BHUTH), Jos, Nigeria over a 5-year period from March 2012 to March 2017.We extracted and analysed data from the folders retrieved from the Health Information Management Department (Records Department) of the Hospital. For this purpose, we used dictionary definition of the child as being biologically a human being between the stages of birth and puberty.[7,8]

We classified the perforated cases as the index cases and the non-perforated cases as the control groups.[1]We checked Quality of life (QOL), length of hospital stay (LOS), and parents' satisfaction after patients' management.

Patients on arrival at paediatric ward had focused history taking by doctor on call from parents or guardians about length of illness and type of management at point of referral, especially antibiotics given before referral to BHUTH.

Demographics, clinical presentations, and management were analysed and antibiotics changed if necessary, to 3rd generation injectable cephalosporins, aminoglycosides and metronidazoles from reputable pharmaceutical companies in sufficient dosages.

Laboratory investigations consisting of blood packed cell volume (PCV), blood grouping and cross matching, Urinalysis, Serum electrolytes and creatinine, urea, Liver function tests (LFT) were done.

Diagnosis of typhoid fever was casehardened using the Centre for Disease Control (CDC) and Prevention case definition for Typhoid fever. Widal agglutination screen test was not done. Such brought in results were also considered for final diagnosis particularly if the Salmonella typhisero-antigen titers were higher than 160 under O and confirmed with a titer of over 1: 80 under H. Culture of bone marrow aspirate was not done for lack of equipment and its low positivity yield.[3,6,9]

Imaging consisted of radiograph of chest and of abdomen in standing, if child was not too frail. Ultrasonography of abdomen done regularly. The cardinal diagnostic proof for perforation was air under the diaphragm and clinical evaluation; [2, 3, 4]Fever, vomiting or even haematochesia were not specific.[3,6,9]

Clinical features were recorded at this stage. See Table 1All patients had abdominal pains and guarding, even though some abdomens were also doughy. Some parents/guardians asserted that severe abdominal pains that lasted for a long while followed by sudden relief, as inference of intestinal perforation especially for patients whose radiographic examination of abdomen were negative for air under diaphragm.

Pain evaluation: Evaluation of pain level showed which procedure could be shortened in the questioning stages. From the numerous pain evaluation methods we were satisfied with those used in clinical settings such as the Brief Pain

Inventory.[10] Patients received opioid analgesics.

Exclusion of patients: Patients without definite index of suspicion for perforation, without air under diaphragm who felt immediately better after resuscitation and use of analgesic were excluded from surgery .Moribund patients were also excluded from the surgery and managed in the Intensive Care Unit (ICU) until fit for operation.[2] Operative procedure was emergent if a high index of suspicion for perforation existed.

We secured written informed consent from parents/guardians of patients for all operative cases. ASA-grading were documented. Patients whose ASA grading permitted for immediate surgical intervention continued with resuscitation. Blood transfusion was started preparatory to surgery. A proper checklist procedure preceded every surgery. They had bladder and nasogastric tubes placed before ***sign-in*** or ***time-out checklist*** requirements were completed in the operating room.

Trainee Registrars formed the bulk of the lead surgeons expertly supervised by Consultant General or Paediatric surgeons. All patients had General Anaesthesia and continued with the broad-spectrum antibiotics medication, which they had already started receiving in the ward as infusions, but latest at **sign-in** time. Immediate post-operative care of patients was at the ICU until they could feed orally.

Operation results: Operation results were best for perforations of less than 24 hours duration.[2,16] Simple transverse surgical closure of the antimesenteric perforation was done with absorbable suture materials.[2,6,16]

ANALYSIS AND STATISTICS

Statistical analysis was done with SPSS 22 Edition. Test of significance was done using Chi square test from EXCEL 2013 where applicable.

Children in the age group differentials of 6 – 10 years (F: M ratio of 1:1.96) made the highest representation with a frequency of 75 and a valid percentage of 50.0% followed by those in the age group of 1 – 5 years (F: M ratio of 1:2.07) with a frequency of 40 and a valid percentage of 26.7%.

RESULTS.

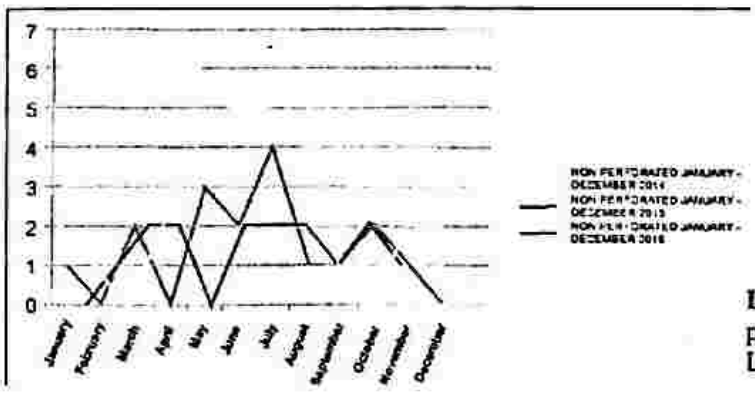
Epidemiology: Sex differentials of the 152 admitted children between March 2012 and March 2016 was female 55(36.2%) and males 97 (63.8%) in the ratio F:M of 1:1.8There were 76 cases of perforated typhoid and 76 cases of non-perforated typhoid in the ratio of 1:1(50%).

Age range of the group was 16.4; median was 8.0, standard deviation of3.48, min of 0.6 and max of 17 and variance was12.11

The social class distribution was a mix-up and not only of mostly low wage earning parentage as few mid class parentage was always supposed.[2,3,5] There were also children of high-class politicians judging from the schools the children attended. Few children came from highbrow areas of town. Their parents had private sewage disposal systems, deep boreholes for water production and private use and yet had typhoid intestinal infection. They could have eaten retail snacks at school contaminated by Salmonella typhi carriers. We did not find typhoid fever actually wearing the face of the poor anymore as it usually was.[2]

It appeared that the hand-washing propaganda of the government because of Ebola crises had a positive drag-effect on the spread of intestinal typhoid infection. Infection rate dropped. Most schools, banks and offices had imbibed Hand-washing propaganda and therefore installed hand-washing kits at schools, shops and places of religious worship and enforced washing of hands. Bottles of hand disinfectants were distributed freely at these centres.

As shown in our graphs and charts, most incidences of intestinal typhoid infections and admissions, which normally occurred during raining season from May to end of August declined yearly steadily from time of EVD out-break. The curves showed similar trends but maintained August as the peak of highest typhoid outbreak. See Line Charts 1



Line Charts 1: Frequency of Admitted Non-perforated Tyhoid Cases From Jan. –Dec. in the Last Three Consecutive Years

Features at Presentation: Lead symptoms were abdominal pains, fever and vomiting.

Fever, vomiting, abdominal pains and anaemia were the most common found features.

Fever lasted in some cases as long as two weeks. Constipation, and especially pain and diarrhoea mixed with blood, seemed what prompted parents to seek alternative management centres. A sudden remission of these severe abdominal pains in a cycle of such pains with resultant doughy abdominal coverage indicated a time of perforation to these parents, which phenomenon has not been scientifically correlated, but appears plausible even if not reliable.

See TABLE 1

Table 1:CLINICAL/LABORATORY FEATURES ON ADMISSION

FEATURES	No of Patients	Percentage
Pain	152	100
Fever	152	100
Vomiting	91	60
Diarrhoea	85	56
Mixed with blood	35	23
Anaemia	67	44.1
Psychosis	1	0.6
>4 days of illness before referral	146	96.1
Haematochesia	3	2
Leucocytosis	86	56.6

Investigations and Laboratory workup: Laboratory results showed low values of PCV in the range of 20%and less before operation in over 44% of available documented laboratory results that justified blood transfusion for all operated 73(100%) cases.

Laboratory investigations consisting of blood packed cell volume (PCV), blood grouping, cross matching, urinalysis, serum electrolytes and creatinine, urea, liver function tests (LFT) were done. Diagnosis of typhoid fever was hardened using the Centre for Disease Control (CDC) and prevention case definition for Typhoid fever. Widal agglutination screen test was not done as several authors found it useful only to prove non infection. We did not find HIV reactivity.

Bone marrow aspiration was not done for lack of equipment. It caused the children needless pains apart from its low positivity yield.[3,6,7]

Imaging consisted of radiographic chest examination and occasionally abdomen in standing and supine, if child not too frail. Ultrasonography of abdomen was carried out. The cardinal diagnostic proof for perforation was air under the diaphragm and clinical evaluation;[2,3,4] Fever, vomiting or even haematochesia were not of high value in the specific diagnosis.

Surgical findings: We operated all 74 (49.3%) cases with intestinal typhoid perforations (F: M= 1:2.2) within 24 hours of arrival. Most cases (numbers not seen in folders) had perforated on arrival and others soon after arrival. The non-perforated cases 79 (51%) F: M ratio of 1:1.5, improved dramatically within 2-3 days following vigorous resuscitation and drug administration.[5]

Operative manoeuvre: Abdominal entry was by median incision beginning from about 4 cm below the umbilicus down to the supra-pubic region care taken not to breach the urine bladder.
Incision was increased when found necessary.

Intra-abdominal soilage with stool and blood was usual finding in all perforated cases. Samples for culture workup for identification of Salmonellatyphi were taken. The caecal-pole was inspected for perforations. Most perforations were ileal and antimesenteric. Perforations were found up to or even higher than 20cm above the ileo-Caecal joint. Literature evaluation have reported of up to 24perforations of the ileum necessitating resection, continuity anastomosis and the performance of temporary ileostoma.[11]

The typical longitudinal antimesenteric perforations were closed by a simple all layer transverse sutures with vicryl® so as not to narrow the intestinal lumen.[2] Perforation edges were trimmed and reserved for culture investigations. The results were not always positive for Salmonella typhi[2,4]

Copious irrigation of abdomen with Normal Saline and drainage of operation site with soft silicone tube or flat rubber so then followed by replacement of viscera into situs. Preferred was mass closure of abdomen up to the fascia. Some surgeon left the skin for delayed closure while others closed immediately after abdominal drainage. Patients returned to the ICU. We preferred to wait for the passage of flatus as signs of commencement of bowel movements before allowing graded oral feeding.

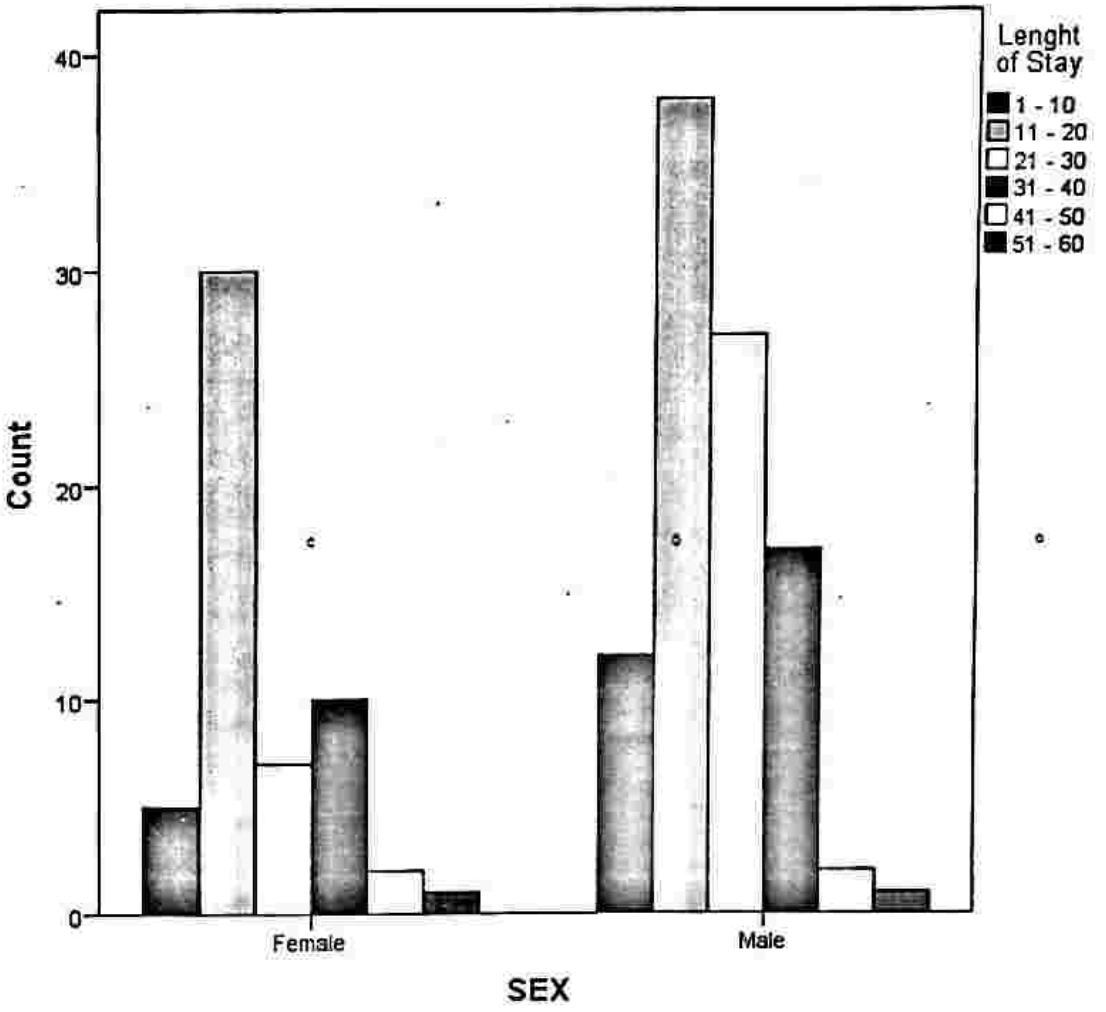
We found 75 (48.7%) cases F: M ratio of 1:2.2 with intestinal typhoid perforations operated. Most cases had perforated on arrival. The non-perforated cases 79 (51%) improved dramatically within 2-3 days after admission following vigorous resuscitation and drug administration.[5] Two cases perforated with 48 hours of arrival in the F: R ratio of 1: 1

Mortalities and morbidities:
Nine (9) mortalities (12.3%) F: M ratio of 1:2were recorded among the operated cases only and 138 (90.8%) children (F: M) were discharged home, of which Five patients (3.3%) left our medical services by way of referral or left against medical advice.

One (1) male child (0.7%) of 7 years of age was readmitted for further management.
Three (3) patients were statistically not recognized and two patients were referred out.
Length of hospital stay (LoS), Is a term that describes the duration of a single episode of hospitalization of a patient mostly in a hospital.[21] LoSwas highest for the group of male children, whether operated or managed conservatively.

See Bar Chart 4 below:

Bar Chart 4: Los/Sex Frequency Distribution



One female case of 7yearshad 8 bags of erythrocyte-concentrate transfused peri-operatively. She had two ileal perforations with the longest LoS of 59 days. She survived.

DISCUSSION.

Mortalities:

We had a mortality of nine 9 (5.92%) M: F ratio of 2:1. This mortality is by no means as high as 4 times of mortality in children of few years back.[6,14,16]

In BHUTH, clinical diagnosis of typhoid based more on the high index of suspicion in compliance with CDC definition of index case of typhoid fever and imaging tests showing air under diaphragm, and less than isolation of Salmonella typhi from cultures that takes over 72 hours.

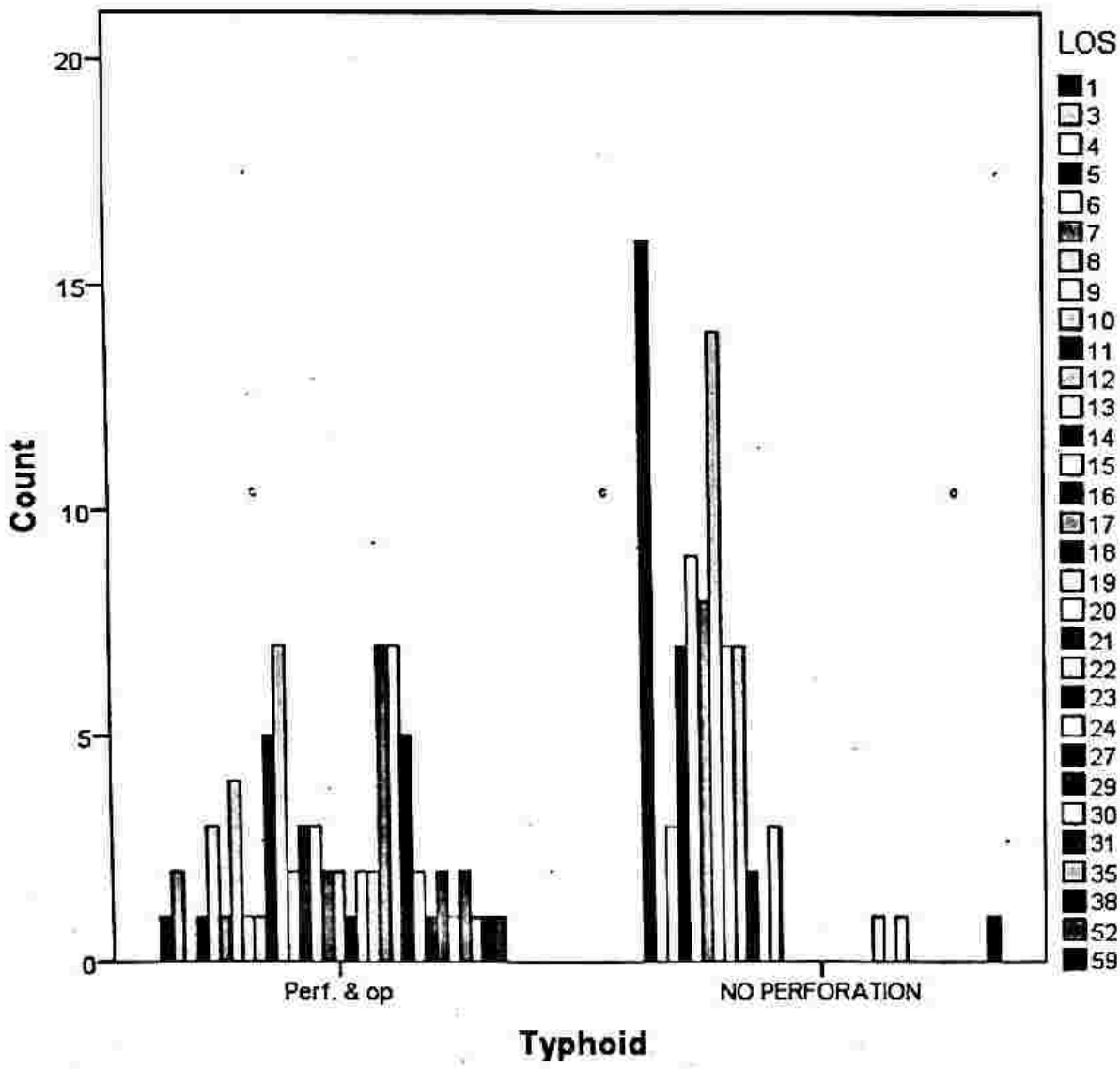
Our study results showed typhoid perforation not only in the school age children, toddlers, but also even in infants. We had three infants. One (1.3%) infant's age 0.7 years had intestinal perforation confirming some studies[6] in variance to other findings.[1]

Our study showed higher rate of typhoid intestinal perforations in the male than the female but gender was not necessarily a causative factor for the perforation in males, as the males were more in number, perforation should be expected to be more in number in the male group.[15,16]

Leukocytosis did not seem to warrant a higher risk for perforation as disputed by some authors.[1] All 79 non-perforated typhoid cases (51.3%) showed leukocytosis.

LoS: The non-perforated children had overall longer LOS than the operated perforated cases.[17]
See Bar Chart 7.

Bar Chart 7: Comparism of LoS between Operated Cases Male and Female / Non-Operated Cases Male and Female Respectively



Surgical intervention with thorough irrigation during surgery may have reduced the bacterial load in the system coupled with effective antibiotics use under a low bacterial load.

QoL: The QoL of the children and parents/guardians were better if happiness and joy are measures of Qol in any form. Most children had resumed school by our latest checking after 2 to 3 months except the lone male child who had an ileostomy reverted after 2 months at home. He spent yet another 2 months and was back to school with satisfactory weight gain. This measures well against CDC Health-Related Quality of Life (HRQoL) definition. The CDC has defined HRQoL as "an individual's or group's perceived physical and mental health over time."[20]

Young children in the age group differential of 6 – 10 years (F:M: M ratio of 1: 1.96) made the highest perforation rate with a frequency of 75 and a valid percentage of 50.0%. Those in the age group of 1 – 5 years (F: M ratio 1: 2.07) with a frequency of 40 and a valid percentage of 26.7% were next. These findings are in tandem with findings of Rabasa AI, Mava Y, Pius S, Timothy SY, Baba UA and other workers.[2,3,16]

Sex differentiation:
Our study showed higher typhoid infection and perforation in the male than the female in a ratio M: F of 2.2: 1. A genetical connection has been discussed by some authors.[3]

Late presentation:
As usual with surgical diseases in the sub-region, late presentation (fever and abdominal symptoms > 2 weeks) was observed in this study demonstrated by the high percentage (50%) of perforation in cases with delayed referral. Making a diagnosis in these Health Centres may have been difficult because of the protean nature of manifestation of symptoms and signs of typhoid illness which mimic malaria, brucellosis, Lyme disease that are ubiquitous in this region.[3,9]

Good results of typhoid management depend on early diagnosis, effective and prompt initiation of vigorous resuscitation and correct antibiotics medication in the correct doses.[2,4,6] Medication was mostly methronidazole, genticine and cephtiazole. We recorded only two (2.5%) cases of perforated typhoid out of 79 admitted non perforated intestinal enteritis 48 hours after admission at BHUTH consequent upon early diagnosis and effective and prompt conservative treatment.[2,6]

Surgical management was by freshening of the edges of the perforations and doing a simple 1-layer transverse closure.[2, 17, 18] Non-aggressive surgery with minimal use of cautery was done. Exact haemostasis at the perforation site, together with copious abdominal lavage with normal saline mixed with gentic in and drainage of operation site, gave good healing.[2, 6, 16] We saw low rate of intra-abdominal abscess formations during reoperations. Six (8.2%) cases of low output entero-cutaneous fistulae were recorded which healed by secondary intention except in one 1(0.7%) who was readmitted after two months and re-operated.

There was 1 (1.3%) case of burst abdomen and 12 (16.4%) of primary surgical skin infections (SSI).
In 1 (1.3%)other case an ileostomy was fashioned because closure of one of the two (2) perforations of the distal ileum, 1.5cm x 4cm large, proved difficult to close by the principle of simple closure.[18,19] A successful reversal of the ileostomy was done after 2months without complications.

Strengths and weaknesses of the study design:
The major weakness was its retrospective design. Our strength was reduction in mortality from 1: 4(25%) mortality for perforated typhoid children to just 1:9(11.1%).[6, 16] We registered 16.4% (12 patients) whose abdominal incisions healed by primary skin closure. Positive demonstration of typhoid infection by isolation of Salmonella typhi was not awaited before the laparotomy in this Centre. Surgeries were emergent, which though was a weakness. However, the end justified the means as 100% of patient had actually perforated before laparotomy.

Significance and implication of the findings:
We found that not all cases who had early diagnosis of typhoid fever, effective resuscitation, the use of right choice of antibiotics, perforated even if with longer LOS. Those cases of perforated typhoid who however had in addition prompt simple closure of perforations healed well with shorter LOS.[17]

The main limitations in this study were that culture results did not come in early enough to be of worth. Blood samples from bone marrow were not sent for culture because of non-availability of facilities. The Widal agglutination screening did not help matters either.[3,11,12]

CONCLUSION

The surgery of typhoid perforation is improving. It is now certain that early diagnosis, prompt attention, simple surgical closure of perforation and sufficient use of adequate antibiotics are factors critical to sustaining improvement amongst people with enteric fever with perforation.

ACKNOWLEDGEMENT

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