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# Mild typhoid fever

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SUMMARY A series of 100 Zimbabwean children aged between 5 months and 13 years with culture positive typhoid fever is presented. The disease was found to be fairly mild with a low prevalence of complications, and no patient in the series died. Possible explanations for the relative mildness of typhoid in this paediatric population are discussed.

There are few reported studies of typhoid fever in children, and the available data suggests that its manifestations differ from those in adults.[1–4] There is also considerable geographical variation in the prevalence of complications and mortality in reported series.[1–3] An impression of a rather better outcome than is suggested by other reports prompted this review.

## Patients and methods

The 100 cases were selected by retrospective review of admissions to the Harare Infectious Diseases Hospitals, and criteria for selection were that patients were: (a) below the age of 14 years; (b) symptomatic; and (c) culture positive for *Salmonella typhi*.

Patients were investigated in a standard manner. A single blood, three stool, and three urine specimens were cultured for *S typhi*. Stool and urine samples were also examined for ova and parasites. A full blood count, including platelet and reticulocyte counts, was performed on admission and repeated every seventh day during treatment. Other investigations were performed as dictated by the clinical findings and course. Antimicrobial treatment with chloramphenicol was routinely administered for 21 days by mouth unless vomiting precluded this, in which case it was given intravenously. Seventy two hours after completing treatment three stool and three urine specimens were cultured on consecutive days. If these were negative for *S typhi* the patient was discharged and was requested to attend for repeat cultures after one, three, six, and 12 months. Default from follow up was, however, the norm.

## Results

**Age, sex, and weight.** The mean age of the 100 children was 7 years with a range of 5 months to 13 years. Figure 1 shows the distribution of patients throughout the age range, and while there was considerable variation between the different years there were no specific age peaks of incidence. There were 52 boys and 48 girls. The weight was recorded in 93 children, and in 53 (57%) it was below 80 per cent of the Boston 50th centile for weight. In six children (6%) the weight was below 60 per cent of the 50th centile.

**Source of patients.** Fifty nine of the patients came from rural areas within 250 km of Harare and 41 from the municipal area of Harare. In 23 patients one or more household contact was either a carrier or developed the disease.

**Seasonal prevalence.** Typhoid cases presented throughout the year but, as shown in Figure 2, which represents the 1984 admissions, there was a peak from December to February during the rainy season and a smaller peak in June.

**Presentation.** The mean duration of symptoms at presentation was 11 days (range 1–120). Fifty five

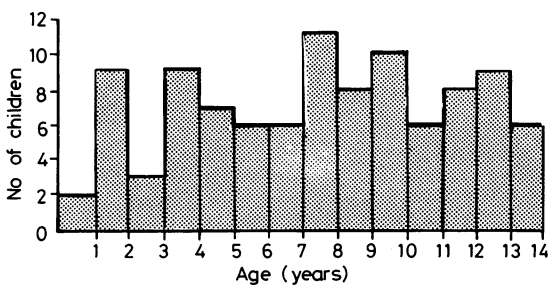


Fig. 1 *Age of presentation in 100 children with typhoid fever.*



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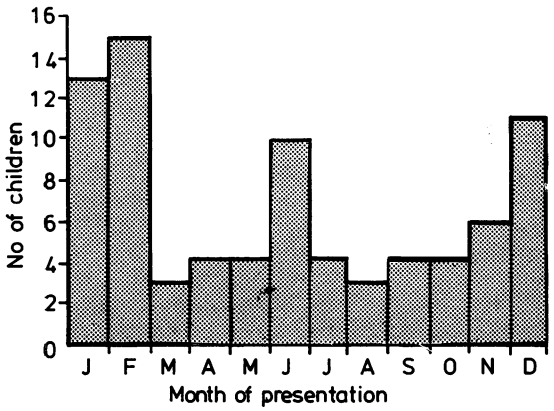


Fig. 2 *Seasonal prevalence of presentation in 100 children with typhoid fever.*

patients presented within seven to 14 days of the onset of symptoms. Table 1 shows the incidence of symptoms reported. Fever, headache, diarrhoea, and abdominal pain were the most common complaints. Three children were jaundiced on admission, and two of these had homozygous sickle cell disease. The other jaundiced child had raised transaminase activity, and *S typhi* was cultured from her blood.

One child presented with intestinal bleeding, and her haemoglobin concentration on admission was 42 g/l. The bleeding settled within 24 hours of beginning treatment with blood transfusion and chloramphenicol. Another child with positive *S typhi* culture from the urine presented with features of the nephrotic syndrome, which resolved on treatment with chloramphenicol alone. A raised blood urea concentration of 22·6 mmol/l (136 mg/100 ml) was recorded in one child who was not clinically dehydrated, and this fell into the normal range after a few days of treatment.

One child presented with fever and extreme drowsiness, and another had slurred speech on admission, which resolved after seven days of treatment; another experienced auditory hallucinations for five days after admission and also had an abnormal electrocardiogram showing ventricular ectopic beats, which disappeared after a few days of treatment. A single case of meningitis was seen in a 5 month old baby who had a cerebrospinal fluid pleocytosis of more than 2000 white blood cells per centimetre but no growth on culture, though *S typhi* was isolated from the blood.

**Clinical features.** Table 2 shows the incidence of various clinical features. In common with other reports on paediatric typhoid fever there was no evidence of the temperature-pulse dissociation seen in adults.[2 4] Similarly, the leucopenia (white blood cell count less than $5\times10^9$/l) seen at the onset of adult typhoid fever was fairly uncommon and seen in only 26 patients. Splenomegaly was observed in 13, and a rash was seen in none. The typhoid state, characterised by blank facies and withdrawn demeanour, was seen in 17.

**Laboratory investigations.** The mean haemoglobin concentration on admission, excluding three children with homozygous sickle cell disease, was 99 g/l (range 36–141) and the mean total white cell count on admission was $7{\cdot}2\times10^9$/l (range 2·1–31·1). Anaemia was common, and 32 of the 100 patients had an initial haemoglobin concentration of less than 90 g/l. The anaemia in most cases was normocytic and normochromic; the mean reticulocyte count on admission in 22 patients was 1·3%. Thirty six patients received a blood transfusion at some stage of the illness.

*S typhi* was cultured from the blood in 58 patients,

Table 1 *Presenting symptoms in 100 children with typhoid fever*

| *Symptom* | *No of children presenting with symptom* |
|---|---|
| Fever | 89 |
| Headache | 37 |
| Diarrhoea | 37 |
| Abdominal pain | 35 |
| Vomiting | 23 |
| Cough | 23 |
| Limb pain | 7 |
| Weakness | 4 |
| Constipation | 4 |
| Jaundice | 3 |
| Gastrointestinal bleeding | 1 |
| Convulsions | 1 |

Table 2 *Clinical features in 100 children with typhoid fever*

| *Feature* | *No of children with feature* |
|---|---|
| Fever | 95 |
| Anaemia | 32 |
| Admission white blood cell count $<5\times10^9$/l | 26 |
| Hepatomegaly | 22 |
| Pulse rate <100 beat/min | 17 |
| Typhoid state | 17 |
| Splenomegaly | 13 |
| Chest signs | 10 |
| Abdominal tenderness | 10 |
| Dehydration | 5 |
| Confusion | 3 |
| Drowsiness | 3 |

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from the stool in 50, and from the urine in 12. Positive cultures were obtained from both blood and stool in 13 patients, from blood and urine in two, from stool and urine in three, and from all three cultures in one. Other pathogens were grown from the urine of four children; untyped coliforms in three and a salmonella species in one. Other stool pathogens were isolated on admission in four children; a Group C salmonella in two, a Group B salmonella in one, and in the fourth child both Group B and C salmonella. *Schistosoma haematobium* was detected in the urine of three children and *Schistosoma mansoni* in the stools of two.

Widal agglutination titres were measured in 43 patients. Eight had insignificant titres, while 35 had *S typhi* 'H' titre of 1/80 or an 'O' titre of 1/160 or higher. Sixteen had an 'H' titre and six had an 'O' titre of greater than 1/1280. Titres were measured on one occasion only in seven of the eight with insignificant titres and in 24 of the 35 with significant titres.

**Chloramphenicol dosage.** The mean dose of chloramphenicol per kilogram body weight per day was 64 mg (range 34–117). Most patients remained on the same dose throughout, but a proportion were reduced to 75% of the initial dose after one week of treatment.

**Response to treatment.** The mean period from onset of treatment to defervescence was five days (range one–12). Six patients failed to respond completely to treatment, in that 72 hours after stopping treatment they were still positive for *S typhi* –five in urine and one in stool. One of the six had a low grade fever, but the remaining five were asymptomatic and were therefore early carriers. Two late carriers were identified one month and two months after treatment, and symptomatic relapse occurred in two at one week and two months, respectively.

**Mortality.** None of the 100 patients in this series died. The zero mortality was conceivably due to the more seriously ill patients dying of typhoid fever at the two central hospitals before they could be transferred to the infectious diseases hospitals. A review was therefore undertaken of all typhoid admissions below the age of 14 to the central hospitals during the period of study, and only one death due to proved typhoid fever was encountered. This was due to intestinal perforation. Several other cases were recorded as typhoid deaths but no bacteriological, serological, or histological evidence confirmed the diagnosis.

## Discussion

Typhoid fever is said to be milder in infants and young children,[5 6] and certainly the findings of this series suggest that this is so. It was previously thought to be rare below the age of 2 years,[7 8] but the Durban series[1] reported that 9% of their patients were under 2 years, which is close to the figure of 11% in this series. Other series have reported a similar pattern of presentation.[1–3] Gastrointestinal bleeding was seen in only one child, and other series report incidences between 0 and 13%.[1–3 9] Intestinal perforation was not seen in this series, and it has been suggested that perforation occurs less commonly in young children due to anatomical differences that result in more superficial ulceration of the Peyer's patches than occurs in older patients.[4] In this series 30 of the children were aged below 5, and in one Nigerian report no perforations were seen in 57 children below the age of 5 with typhoid fever.[10] In another Nigerian study no perforations were seen in children below 4 years.[9] A high incidence was reported from Ibadan, however, where 39% developed intestinal perforation.[3] A possible explanation is that only 17% of the 117 patients in that series were below the age of 5.

In conclusion, the severity of typhoid fever in children in this series was less than that described elsewhere,[1–3] and no deaths occurred. Case fatality rates in other recent series range widely from 0 to 32%.[1–3 9 10] There is no evidence to suggest that early referral was a factor in the generally favourable outcome as the mean duration of symptoms at presentation was similar to that reported in other series.[1–3] Nutritional state may be relevant in the outcome of this disease, but other studies have not specified the nutritional state of their patients to a degree that would make comparison possible. In spite of the fact, however, that 53 of these 100 children would be classified as undernourished by current definitions, response to treatment was in general satisfactory. The relative mildness of the disease in this study is possibly related to the intermediate state of sanitation currently prevailing in Zimbabwe. Exposure to *S typhi* early in life may provide a degree of immunity that reduces the severity of the disease occurring at a later stage.[5 8] Evidence for this was reported from this country by Wicks *et al*,[11] who found that over half of their 243 typhoid patients had *S typhi* 'O' or 'H' titres above 1/480 within seven days of the onset of symptoms, suggesting a primary immune stimulus in the past.

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