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Typhoid Fever in Children – A Retrospective Study of 54 Cases from Malaysia

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ABSTRACT

Background/Aim of Study: Typhoid fever, which is endemic in Malaysia, affects all age groups and it has been stated that classical features described in textbooks were absent in children. The aim of this study was to find out whether this was true in the local setting and hence a retrospective study was undertaken.

Methods: Fifty-four paediatric patients satisfied the inclusion criteria and all were seen consecutively during the study period of 10 years. Patients' records were reviewed for demographic data such as age, sex, ethnicity, clinical features, therapy and results of laboratory tests.

Results: Fever was the most common presenting symptom and diarrhoea was more common than constipation. Isolation of *S typhi* from blood and/ or stools was the most important diagnostic tool *85.2%) and of these 99% had significant Widal titres. Clinical and bacteriological relapse occurred in 5 children (3%) who were successfully treated with ceftriaxone. The absence of mortality and low level of complications indicates either a mild nature of the disease or to early recognition or prompt and appropriate therapy.

Keywords: fever, bacteriological isolation, Widal test, relapse

INTRODUCTION

Typhoid fever is an important public health problem in many of the underdeveloped and developing countries. It has been estimated that 33 million cases and more than half a million deaths due to typhoid fever occur throughout the developing world annually, mainly in school-going children[1]. It is endemic in Malaysia, and periodically gives rise to outbreaks. There was a range of 1,715 to 2,962 reported cases from 1978 to 1990 with an annual incidence of 10.2 to 17.9 per 100,000 population[2]. It affects all age groups and although the clinical characteristics are fairly typical in adults, it has been stated that classical features described in textbooks were absent in children[3]. The endemic nature of the disease in Malaysia sufficiently warrants a review of the special features of typhoid fever in children. Hence this retrospective study was undertaken. Over a period of 10 calendar years from 1981 – 1990, 74 children were admitted to the paediatric wards of the University Hospital, Kuala Lumpur with a clinical diagnosis of typhoid fever. However, only 54 patients satisfied the inclusion criteria and all were seen consecutively during the study period.

PATIENTS AND METHODS

Paediatric patients are defined as children below 12 years of age. The cases were diagnosed as typhoid fever based on the following criteria: (a) positive blood and/ or stool cultures for *Salmonella typhi*; (b) significant "O" and "H" Widal titres of $\geq$ 1:640 for *S typhi*; and (c) a four-fold rise in Widal titres together with clinical manifestations of infection. *S typhi* was isolated and identified by routine bacteriological methods and Widal agglutination was carried out using stained antigens (Wellcome Reagents Ltd, England). No history of typhoid immunisation was obtained from any of the cases.

Patients' records were reviewed for demographic data such as age, sex, ethnicity, as well as for clinical features, therapy and results of laboratory tests.

RESULTS AND COMMENTS

Fifty-four patients satisfied the inclusion criteria. Both sexes were equally affected and there were 27 boys and 27 girls. Their ages ranged from 2 months to 12 years (mean 7.2 years). Most cases clustered around the 9 – 10 years age group and only 3 patients (5.5%) were less than 2 years old. The ethnic breakdown consisted of 27 Malay children (50%), 16 Chinese (30%), 9 Indians (17%) and 2 Orang Aslis. For the year 1987, the population of Peninsular Malaysia consisted of 57% Malays, 32% Chinese and 10% Indians. There was no obvious seasonal variation but about half the cases (53%) were admitted during the dry months of May, June and July.

Clinical features

The duration of symptoms before admission to hospital ranged from 2 to 28 days (mean period of fever was 13 days). On admission, fever was present in almost all the children (98%) as shown in Table I but a step ladder pattern of fever was not observed.

Abdominal pain and mild diarrhoea lasting 2 – 3 days was present in 46.2% and 44.4% of cases respectively but constipation was noted in only 22%. Unproductive cough was present in 31% of the children. Hepatomegaly and splenomegaly were seen in 56% and 38.8% of cases respectively. Rose spots and relative bradycardia were rarely observed.

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Table I – Frequency of clinical findings among 54 children with typhoid fever.

Symptoms & Signs	Number	Percent
Fever	53	98
Hepatomegaly	30	56
Abdominal pain	25	46.2
Diarrhoea	24	44.4
Splenomegaly	21	38.8
Cough	17	31
Vomiting	13	24
Constipation	12	22.2
Headache	9	16.6
"Toxic looking"	6	11.1
Joint pain	4	7.4
Rose spots	4	7.4
Petechial rash/bleeding gums	2	3.6
Relative bradycardia	2	3.6
Neurological	2	3.6

Laboratory findings

Bacteriology:
S typhi was isolated from 46 (85%) patients. Information on prior antibiotic therapy was not available. There were 19 patients whose blood and stool cultures were positive, 12 patients with only positive blood cultures and 15 patients with only positive stool cultures. The frequency of isolation from blood ie. 31%, was highest in the first 2 weeks of illness (83.3%), with 48.4% being positive during the first week of illness. All urine cultures were negative for *S typhi*. In 3 of the patients, non-typhoidal *Salmonellae* was isolated from stool and in one child, both *S typhi* and non-typhoidal *Salmonella* were isolated from the stool. Carriage of non-typhoidal *Salmonellae* does occur and concomitant disease or other infections or antibiotic therapy can cause excretion of these organisms in the faeces. Post-treatment stool cultures were negative in all except 12 patients who defaulted and were lost to follow-up.

Widal agglutination test was carried out in 51 (94%) patients. In 8 patients (15%), the diagnosis was based solely on a positive "O" and "H" titre of $\geq$ 1:1280 against *S typhi*. Of the 42 cases which were culture positive, 41 (99%) had positive Widal titres of $\geq$ 1:640 or a four-fold rise in titres between acute and convalescent sera.

Haematology

On admission, leucopaenia (4 x E9/L) was noted in only 27.7% of patients and leucocytosis (>10 x E9/L) in 9.2% of the cases. Thrombocytopaenia (< 150 x E9/L) was found in 8 (14.8%) patients with most cases having a platelet count of >100 x E9/μL. These low counts are usually transient as shown by the normal bone marrow in the second patient. It is possible that these low counts may be related to a more protracted course of illness but we have no evidence for this. Bleeding gums and petechial rash were the presenting features in two patients. Their platelet counts were 31 and 41 x E9/μL respectively. One of them was a 10-year-old female Orang Asli who had a concomitant gram negative septicaemia and DIVC in whom pancytopaenia was present (Hb 8.6 g/L, platelets 31 x E9/L and WBC 3.6 x E9/L). Her bone marrow was reactive with no evidence of aplastic anaemia. She recovered with antibiotic therapy. Transient rise in hepatic enzymes (SGOT x 4 normal value) were noted in 6 patients and in 2 the liver was tender on palpation.

Treatment and Outcome

All patients received intravenous antibiotics except for 2 who were treated with oral antibiotics as outpatients. Chloramphenicol was used in the majority of patients (67%), initially given as 100 mg/kg/day intravenously followed by 50 mg/kg/day once fever had settled. Co-trimoxazole (trimethroprim 8 mg/kg/day) and ampicillin (100 mg/kg/day) were used in 40.7% and 22% of patients respectively. In 21 patients (38%), a combination of antibiotics was used. Recently in 1989 and 1990, ceftriaxone at 80 mg/kg/day for 3 – 7 days was introduced and was used in 5 patients who had a clinical relapse of typhoid fever after full treatment with chloramphenicol for two weeks.

Most patients showed constitutional improvement before resolution of fever which settled after a mean of 6.5 days and a range of 1 – 17 days.

Clinical relapse, defined as the return of clinical signs and symptoms after its apparent abatement, occurred in 5 cases of in-patients after 2 weeks' treatment with chloramphenicol and after 3 convalescent stool cultures were negative. In all the 5 cases, the *S typhi* isolated from stool cultures were found to be sensitive to chloramphenicol. All 5 patients were successfully treated with ceftriaxone 80 mg/kg/day for 3 – 7 days.

Two patients (3.7%) developed complications. One had gangrenous cholecystitis and underwent cholecystectomy. The other child developed secondary septicaemia due to *E coli* and *Klebsiella sp* after two weeks of oral ampicillin. Both responded to appropriate intravenous antibiotic therapy. During the 10-year study period, there were no deaths due to typhoid fever.

DISCUSSION

Typhoid fever which is endemic in Malaysia, has an annual national incidence of 10.9 per 100,000 population but it can be as high as 50.3 per 100,000 in some states such as Kelantan[4,5]. The incidence of typhoid fever is uncommon in infants and toddlers as only 3 of our 54 cases (5.5%) were less than 2 years old. This is consistent with other published series[3,6,7]. Although the incidence of typhoid fever increases during the rainy seasons in Africa[3], however in our series, there was a slight increase during the hot dry season, similar to that seen in the state of Kelantan[6].

Fever, recorded in 98% of the children, was the single most common presenting symptom and about 11% of these children were toxic on admission. Diarrhoea (46.2%) was more commonly noted than constipation (22.2%) which is similar to other published reports[3,6,8,9].

Rose spots were uncommonly seen in Malaysian children (7.4%). This is probably due to the darker pigmentation of Asian skin. Unlike adult patients, relative bradycardia was observed in only 2 (3.6%) children which concurs with other published reports[3,6] in contrast to 33% of adults with bradycardia reported in our hospital[10]. None of the children presented with febrile convulsions and only one was delirious on admission.

Haematological manifestations or complications were not common. Two patients developed bleeding of the gums secondary to thrombocytopaenia. One was due to secondary bacterial (*E coli and Klebsiella pneumonia*) septicaemia. The other child was referred to the hospital as a case of leukaemia but bone marrow aspiration showed no evidence of the disease. Both children recovered with appropriate antibiotic therapy. Leucopaenia and blood counts were not helpful in the diagnosis as only 27.7% had leukopaenia and 60% of the patients had normal blood counts.

Isolation of the organism (blood and/or stool) was the most important diagnostic tool with 85.2% yielding positive results. Of the 15% that were culture negative, we are unable to state whether this may have been due to prior antibiotic therapy before admission to hospital. We found the Widal test to be fairly sensitive as 99% of the culture positives had a significant titre above 1:640.

Although chloramphenicol has been the drug of choice, we recorded 5 cases of relapse with this antibiotic although the dosage and duration of therapy were adequate. However, blood levels of chloramphenicol were not monitored. Ceftriaxone used successfully in these cases though expensive is being recognised increasingly as the drug of choice and first line therapy for typhoid fever. There is increasing anectodal reports of short-course quinolones being used successfully to treat typhoid fever in children, but published reports of clinical trials are not available.

The absence of mortality and the low incidence of complications may be due to the mild nature of the disease in this country or more importantly, to the early recognition and prompt treatment as a clinical diagnosis of typhoid fever is usually made and treatment commenced before bacteriological or a serological diagnosis is made.

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