

SALMONELLA TYPHI INFECTIONS

A 10 - Year Retrospective Study*

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Enteric fever is still a common health problem in many countries, especially in children. Thus a ten-year retrospective study was carried out to evaluate the clinical and laboratory properties of enteric fever and the incidence of antimicrobial resistance in children. Throughout the past 10 years, Salmonella was isolated in 105 patients by blood culturing, 27 of which were Salmonella typhi. Most of the patients were above the age of two. Besides the typical symptoms and signs of enteric fever, 29.2% of the patients had some neurologic findings. Besides, 68.5% had elevated liver enzymes while only 44.4% had hepatomegaly with or without splenomegaly. Anemia was present in 44%, leukopenia in 16% and leukocytosis in 11.1% of the cases. The emergence of antimicrobial resistance during the last five years against ampicillin, chloramphenicol and trimetoprim-sulfamethoxazole has created a challenge in treating these infections.

Key words: salmonella typhi, clinical properties.

Enteric fever is caused mainly by S.typhi and paratyphi serotypes and is still a great problem, especially in children¹. In recent years, the extended use of various antibiotics for salmonella infections has caused not only an increased incidence of the carrier state but also the emergence of multiple antibiotic resistance¹⁻³. Thus, the management of salmonella infections is very important, both for the patient and the public health point of view.

Here, we present a 10-year retrospective study of patients with Salmonella typhi infections, including the signs and symptoms, clinical pictures, laboratory findings, complications and the incidence of resistance to antimicrobial agents.

Material and Methods

Between August 1982 and September 1992, Salmonella was isolated from the blood cultures of 105 inpatient cases at Hacettepe Children's Hospital. Out of

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105 blood isolates, 74 (70.5%) were *S.typhimurium*, 27 (25.7%) were *S.typhi*, three (2.9%) were *S.paratyphi* B and one was *S.choleraesuis*. The clinical and laboratory properties of the 27 *S.typhi* blood isolates were documented retrospectively from the records.

Cultures, serotyping and antibiotic resistance studies were performed by the Microbiology Department of Hacettepe Children's Hospital. Information was obtained from the medical records of each patient. The age and sex distribution, signs and symptoms, clinical pictures, complete blood count (CBC), liver function tests, fatality rate and resistance to antimicrobial agents were evaluated retrospectively.

Results

Salmonella typhi was isolated from the blood cultures of 27 cases. In addition to blood cultures, eight had positive stool and three had positive bone marrow cultures. Out of the 27 blood isolates, 16 (59.3%) were diagnosed in the first five years (1982-1987) and 11 (40.7%) in the second five-year period (1988-1992). There was no seasonal variations in the number of cases.

As shown in Table I, most of the cases were above two years of age (77.8%) and the mean age was 6.35. The youngest patient was 15 days old and the oldest, 13 years. Sixteen cases were males and nine were females.

Table I: Age Distribution of Patients with *Salmonella Typhi* Infection

Age (months)	Number of Patients
< 1	2
1-6	1
7-12	1
13-24	2
> 24	21
Total	27

Seven of the *S.typhi* blood isolates had an associated disease (two congenital heart disease, two mental retardation and three malignancy); types of cancer included acute lymphoblastic leukemia (ALL), acute non-lymphoblastic leukemia (ANLL) and non-Hodgkin's lymphoma (NHL).

The symptoms of patients at presentation were fever (23 cases, 85.1%), diarrhea (13 cases, 48.1%), vomiting (10 cases, 37%), malaise (five cases, 18.5%), abdominal pain (three cases, 11.1%), jaundice (two cases, 7.4%), abdominal distention (two cases, 7.4%), headache (two cases, 7.4%), and neurologic symptoms (eight cases, 29.2%). Neurologic symptoms included convulsions (three cases, 11.1%), aphasia (two cases), stupor (one case), ataxia (one case) and behavioral abnormality (one case) (Table II).

Table II: Symptoms of Patients with Salmonella Typhi Infection

Symptoms	No. and Percentage of Patients
Fever	23 (85.1%)
Diarrhea	13 (48.1%)
Vomiting	10 (37.0%)
Malaise	5 (18.5%)
Abdominal pain	3 (11.1%)
Jaundice	2 (7.4%)
Abdominal distension	2 (7.4%)
Headache	2 (7.4%)
Neurologic symptoms	8 (29.2%)
• convulsions	3
• aphasia	2
• stupor	1
• ataxia	1
• behavioral abnormalities	1

On physical examination, seven (25.9%) had hepatosplenomegaly, four (14.8%) had only hepatomegaly, three had encephalopathy, one had ataxia and two had aphasia (Table III). None of the patients had isolated splenomegaly without hepatomegaly.

Table III: Physical Findings of Patients with Salmonella typhi Infections

Physical Findings	No. and Percentage of Patients
Hepatosplenomegaly	7 (29.5%)
Hepatomegaly only	4 (14.8%)
Splenomegaly only	0
Encephalopathy	3 (11.1%)
Aphasia	2 (7.4%)
Ataxia	1 (3.7%)

In the laboratory studies, 13 (48.1%, including one patient with ALL and one with NHL) patients had anemia, three (11.1%) had leukocytosis and five (15.4%, including a patient with ALL) had leukopenia⁴. When the patients with ALL and NHL were excluded, 44% of the patients had anemia, 16% had leukopenia, 11.1% had leukocytosis and 72.9% had normal leukocyte counts (Table IV). In 19 cases, liver enzyme levels were measured and 13 (68.5%) had elevated SGOT. Ten (52.6%) had elevated SGOT and SGPT, while three (15.9%) had only elevated SGOT levels (mean for SGOT: 487.5 IU, range: 12-7455 IU; mean for SGPT: 226.8 IU, range: 16-2682 IU).

Table IV: Laboratory Findings of Patients with Salmonella Typhi Infection

Laboratory Findings	No. and Percentage of Patients
Liver enzymes*	
• increased SGOT	13 (68.5%)
• increased SGOT and SGPT	10 (52.6%)
• increased SGOT only	3 (15.9%)
• increased SGPT only	0
CBC**	
• Anemia	11 (44%)
• Normal Hb	14 (56%)
• Leukopenia	4 (16%)
• Leukocytosis	3 (11.1%)
• Normal WBC count	18 (72.9%)

*: Data on only 19 patients were available.

**: Cases with ALL and NHL are excluded.

Complications included subdural effusion (one case) and hemolytic anemia (one case). A total of four (14.8%) cases died, and the age distribution of the deaths is shown in Table V.

Table V: Distribution of Deaths According to the Age of Patients with Salmonella Typhi Infections

Age in Months	No. of Patients	No. of Deaths
< 1	2	1
1-6	1	0
7-12	1	0
13-24	2	0
> 24	21	3
Total	27	4

The antimicrobial resistance of S.typhi was strikingly different in the first and second five-year period of the study (Table VI). There was no antimicrobial

Table VI: Antimicrobial Resistance of Patients with Salmonella Typhi Infections

Antibiotics	Frequency of Resistance (%)	
	1982 - 1987	1988 - 1992
Ampicillin	—	23.5
Chloramphenicol	—	17.6
Trimetoprim - sulfamethoxazole	—	17.1
Cephaperazone	—	—
Ceftriaxone	—	—

resistance detected during the period between 1982 and 1987. However, between 1988 and 1992, antimicrobial resistance was found to emerge against ampicillin (23.5%), chloramphenicol (17.6%) and trimetoprim-sulfamethoxazole (TMP-SMX) (17.1%), but there was still no resistance against third-generation cephalosporins such as cefoperazone and ceftriaxone.

Discussion

Human *Salmonella* infections are important at any age, but especially important in children. In our study, most cases were above two years of age, which may be attributed to the protective effect of breastfeeding.

The signs and symptoms of our cases were similar to those in other reported series^{2,5-7}. However, ataxia, aphasia and behavioral abnormalities are not classical findings of enteric fever although reported occasionally². This emphasizes that in patients with unusual neurologic findings in addition to signs of infection such as fever, diarrhea and organomegaly, enteric fever should be considered.

In the laboratory findings, 68.5 percent of patients had increased SGOT and/or SGPT while only 44.3% had hepatomegaly and/or splenomegaly; these findings show that the liver may be involved even in the absence of hepatomegaly. Thus, liver enzyme levels may be a helpful laboratory test in the diagnosis of salmonellosis and should be measured in all suspected cases. On the other hand, anemia was detected in 44 percent of the cases while 56 percent had normal hemoglobin counts according to age standards. Leukopenia was detected in 16 percent of patients and leukocytosis in 11.1 percent, while 72.9 percent had normal leukocyte counts. Although similar results were reported in a study from Singapore⁷, our results are somewhat different from the other reports indicating leukopenia as more common^{2,8}. In another study it has been shown that leukocytosis is as common as leukopenia in children with typhoid fever, but most have normal leukocyte counts in contrast to adult patients⁹.

In this study, it has been found that there was no antimicrobial resistance of *S.typhi* serotype between 1982-1987, while resistance against ampicillin, chloramphenicol and TMP-SMX developed after 1987. On the other hand, resistance against third-generation cephalosporins, being the newly introduced antimicrobial agents, has not yet developed. Thus, third-generation cephalosporins may be good alternatives for resistant cases^{10,11}. In addition to third-generation cephalosporins, response to ciprofloxacin has been very satisfactory³. However, wide use of these agents should be avoided, otherwise emergence of resistance will be inevitable in the near future. Since most cases in this study were lost to follow-up, we could not detect the carriers in our series.

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