

PROGNOSTIC FACTORS IN SALMONELLA TYPHIMURIUM SEPTICEMIA A 10 - Year Retrospective Study*

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SUMMARY: Semeer G, Kanra G, Cemeroėlu AP, zen H, Ceyhan M, Ecevit Z. (Infectious Disease Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Prognostic factors in Salmonella typhimurium septicemia: a 10-year retrospective study. Turk J Pediatr 1995; 37: 229-233.

In this study, 74 S.typhimurium septicemia cases were evaluated retrospectively from their records, and the age and sex distribution, presence of underlying disease, signs and symptoms, complete blood count, liver function tests and case fatality rate were documented and prognostic factors determined. It has been shown that S.typhimurium is the most common strain causing Salmonella septicemia, which is more fatal in the newborn period and in the presence of an associated disease, while hemoglobin and leukocyte counts do not play an important role in the prognosis. In Salmonella septicemia, congenital heart disease was the second-most common associated disease, which may be attributed to probable underlying immunodeficiency. *Key words:* Salmonella typhimurium, septicemia.

Non-typhoidal Salmonella infections (NTS) are still a major health problem in children, particularly those with certain underlying diseases¹⁻⁸. Two-thirds of NTS infections present with gastroenteritis and fever, but septicemia occurs only in approximately 5-18 percent of cases^{2, 3}. S.typhimurium is the most common strain isolated as the cause of Salmonella septicemia in many countries^{1, 2}.

S.typhimurium septicemia is frequently encountered in patients with underlying disease, especially when cellular immunity is compromised, such as in Hodgkin's disease, renal transplantation, acquired immune deficiency syndrome (AIDS), leukemia and malnutrition⁴⁻⁸. Salmonella typhimurium septicemia is still quite fatal in these patients and in newborns⁴⁻⁹.

In this study, we investigated the clinical and laboratory findings of S.typhimurium septicemia retrospectively to determine the course and prognostic factors for the past ten years. Antibiotic therapy used in these patients was not taken into consideration.

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Material and Methods

Between August 1982 and September 1992, *Salmonella* species was isolated from the blood cultures of 105 cases at Hacettepe Children's Hospital. The clinical and laboratory features of 74 *S.typhimurium* blood isolates were documented retrospectively from the records, and the prognostic factors were determined.

Cultures and serotyping were performed by the Microbiology Laboratory of Hacettepe Children's Hospital. Information was obtained from each patient's medical records. The age and sex distribution, presence of underlying disease, signs and symptoms, complete blood count (CBC), liver function tests and case fatality rate were evaluated retrospectively for *S.typhimurium* septicemia cases. The blood isolates were accepted as septicemic when the patients had additional signs and symptoms such as fever, convulsion, stupor, malaise, vomiting, irritability, hepatosplenomegaly or elevated liver enzymes. According to these criteria, all of the patients with *S.typhimurium* infection were found to be septicemic.

Statistical analyses were performed using student's t-test, chi-square test and exact chi-square test.

Results

Salmonella species was isolated from the blood cultures of 105 inpatient cases. Seventy-four (70.5%) were *S.typhimurium*, 27 (25.7%) were *S.typhi*, three (2.9%) were *S.paratyphi* and one (0.9%) was *S.choleraesuis*. In addition to blood cultures, stool cultures of 18 (out of 46, 39.1%), bone marrow cultures of two (out of two) and cerebrospinal fluid (CSF) cultures of one (out of four) patient also revealed *S.typhimurium*.

Of 74 patients with *S.typhimurium* septicemia, nine (12.15%) were newborns, 35 (47.3%) were between one and 12 months of age, nine (12.15%) were between 13 and 24 months, and 21 (28.4%) were more than two years old (Table I). Thirty-three (44.6%) were female and 41 (55.4%) were male.

Table I: Age Distribution of *Salmonella Typhimurium* Septicemia Cases

Age (months)	No. of Patients	(%)
0-1	9	12.15
1-6	23	31.1
7-12	12	16.2
13-24	9	12.15
> 24	21	28.4
Total	74	100.0

In the *S.typhimurium* septicemia cases, 39 (52.7%) had an associated disease, such as malnutrition (16.2%), congenital heart disease (9.5%), malignancy (8.1%), mental retardation (2.7%) or other miscellaneous diseases (Table II).

Table II: Distribution of Patients with an Associated Disease

Disease	No. of Patients	(%)
Malnutrition*	12	16.2
Congenital heart disease	7	9.5
Malignancy	6	8.1
Mental retardation	2	2.7
Miscellaneous**	12	16.2
Total	39	52.7

* Four third-degree, two second-degree and six first-degree.

** Trisomy 13, prematurity, congenital immunodeficiency, aplastic anemia, Leiner's disease, nephrotic syndrome, polyarteritis nodosa, hemophilia, thalassemia major, congenital adrenal insufficiency, miliary tuberculosis and measles; one in each group.

The most common signs and symptoms were fever (70.2%), diarrhea (56.8%), vomiting (29.7%), cough (18.9%) convulsions (12.2%), stupor (9.5%) and hepatosplenomegaly (28.4%). In 38 patients, liver enzymes were measured; 20 (52.6%) had elevated SGOT (> 50 IU), 13 (34.2%) had elevated SGPT (50 IU) and 13 had elevated levels of both liver enzymes. When the patients with hematologic diseases (six patients) were excluded, 23 (33.8%) had leukocytosis, four (5.9%) had leukopenia and 29 (42%) had anemia according to the normal age standards¹⁰.

Complications included meningitis (three patients), hemolytic anemia (one patient) and subdural effusion (one patient).

Of 74 patients with *S.typhimurium* septicemia, 39 (52.7%) died. Among 39 deaths, nine (23.1%) were newborns, 25 (64.1%) were between one and 12 months of age, three (7.7%) were between 13 and 24 months and two (5.1%) were more than two years old.

There was a striking difference between the fatality rates of each age group (Table III). In the newborn period, none of the blood isolates survived, but the fatality rate in the group older than two years of age was 9.5%. The fatality rate was also found to be significantly higher in patients with an associated disease than in those without (64.2% versus 23.1%, $p < 0.01$). When hematologic parameters were evaluated, neither hemoglobin (41.4% versus 65.0%, $p > 0.05$) nor leukocyte counts had a statistically significant effect on prognosis. Patients with leukocytosis, leukopenia and normal leukocyte counts had similar fatality rates (58.5%, 50.0% and 56.5% respectively, $p > 0.05$, Table IV).

Table III: Age Versus Fatality Rates of *S.typhimurium* Septicemia

Age (months)	No. of Patients		Fatality Rate (%)
	Total	Deaths	
0-1	9	9	100.0
1-6	23	15	65.2
7-12	12	10	83.3
13-24	9	3	33.3
> 24	21	2	9.5
Total	74	39	52.7

Table IV: White Blood Cell (WBC) and Hemoglobin (Hb) Counts Versus Fatality Rates in *S.typhimurium* Septicemia

Hematologic Parameters*	Total	Deaths
Normal WBC	41 (60.3%)	25 (58.5%)
Leukocytosis	23 (33.8%)	19 (56.5%)
Leukopenia	4 (5.9%)	2 (50.0%)
Anemia	29 (42%)	12 (41.4%)
Normal Hb	40 (58%)	26 (65.0%)

* Patients with hematologic disease (six patients for WBC and five for Hb counts) were excluded.

Discussion

Recently, it has been reported that *S.typhimurium* is the most common blood isolate among the other strains of salmonellae^{2,8,9,11}, as confirmed (70.5%) in this study. Thus, it is important to determine the clinical and laboratory properties and the prognostic factors of *S.typhimurium* septicemia for better management.

In this study, 50.5 percent of *S.typhimurium* septicemia cases had an associated disease, most commonly malnutrition, followed by congenital heart disease. We could not find any report in the literature on the association between congenital heart disease *Salmonella* septicemia. However, it has been shown that the total T cell percentage, T helper cells, Immunoglobulins A and G, complement C3 and C4 levels were low and there was a high frequency of infections in the clinical records of patients with congenital heart disease^{12,13}. Although there were no laboratory data regarding the immunologic status of our patients with congenital heart disease, the high frequency of *Salmonella* septicemia may be attributed to underlying immunodeficiency.

It has also been shown that patients with an associated disease had a higher fatality rate than those without (64.2% versus 23.1%, $p < 0.01$).

In *S.typhimurium* septicemia, age is another important determinant for the prognosis^{2,3,9}. In this study, the fatality rate was 100% in the newborn period, decreasing to 9.5% in the above-two age group.

On the other hand, hemoglobin and leukocyte counts were not significant factors for the fatality rate in *S.typhimurium* septicemia ($p > 0.05$). It is well known that leukopenia is a poor prognostic factor in patients with septicemia¹⁴, which was contrary to our findings.

In conclusion, *S.typhimurium* was the most common strain causing *Salmonella* septicemia, which is more fatal in the newborn period and in the presence of an associated disease, while hemoglobin and/or leukocyte counts do not play an important role in the prognosis. Furthermore, *S.typhimurium* septicemia is commonly encountered in patients with congenital heart disease.

REFERENCES

1. Sirinavin S, Jayanetra P, Lolekha S, Layangkul T. Predictors for extraintestinal infection in *Salmonella* enteritis in Thailand. *Pediatr Infect Dis J* 1988; 7: 44-48.
2. Cherubin CE, Neu HC, Imperato PJ, Harvey RP, Bellen N. Septicemia with non-typhoid salmonella. *Medicine* 1974; 53: 365-377.
3. Clyde WA Jr. Salmonellosis in infants and children: a study of 100 cases. *Pediatrics* 1957; 19: 175-183.
4. Heineman HS, Jensen WN, Cooper WM, Braud AI. Hodgkin's disease and salmonella typhimurium infection. *JAMA* 1964; 188: 632-634.
5. Hann T, Sokal JE, Neter E. Salmonellosis in disseminated malignant diseases. A seven-year review (1959-1965). *N Engl J Med* 1967; 276: 1045-1052.
6. Mussche MM, Lameire NH, Ringoir SMG. *Salmonella typhimurium* infections in renal transplant patients. *Nephron* 1975; 15: 143-150.
7. Smith PD, Macher AM, Bookman MA, et al. *Salmonella typhimurium* enteritis and bacteremia in the acquired immunodeficiency syndrome. *Ann Int Med* 1985; 102: 207-208.
8. Wolfe MS, Armstrong D, Louria DB, Blevins A. Salmonellosis in patients with neoplastic disease. *Arch Intern Med* 1971; 128: 546-554.
9. Tuncer M, Ceyhan M, Erdem G, Oran O, Erdoğan S. Yenidoğan döneminde *Salmonella* enfeksiyonu. *Çocuk Sağlığı ve Hastalıkları Dergisi* 1985; 28: 103-110.
10. Nathan DG, Oski FA. *Hematology of Infancy and Childhood* (3rd ed.). Philadelphia: WB Saunders; 1987: 1680-1688.
11. Cherubin CE, Fodor T, Denmark LI, Master CS, Fuerst HT, Winterr JW. Symptoms, septicemia and death in salmonellosis. *Am J Epidemiol* 1969; 90: 285-291.
12. Radford DJ, Lachman R, Thong YH. The immunocompetence of children with congenital heart disease. *Int Archs Allergy Appl Immunol* 1986; 81: 331-336.
13. Thong YH. Clinical value of IgG subclass investigations in pediatric practice. *Pediatr Infect Dis J* 1990; 9 (8 suppl): S36-S40.
14. Behrman RE, Kliegman RM, Nelson WE, Vaughan III VC. *Nelson Textbook of Pediatrics* (14th ed.). Philadelphia: WB Saunders; 1992: 681-682.