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Brief Original Article

Salmonella gastroenteritis in children: six-year experience in İstanbul, Turkey

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Abstract

Introduction: The aim of this study was to evaluate the demographic and clinical characteristics and treatment outcomes of children with *Salmonella* gastroenteritis.

Methodology: We retrospectively reviewed the medical records of pediatric patients aged between 1 month and 18 years with the diagnosis of *Salmonella* gastroenteritis between May 2015 and December 2021.

Results: A total of 172 children diagnosed with *Salmonella* gastroenteritis, including 113 outpatients and 59 hospitalized children, were included in this study. There were 95 (55.2%) males and 77 (44.8%) females with a median age of 59.5 months (interquartile range [IQR]: 33.5–96 months, min–max: 1–205 months). The most common clinical symptoms were diarrhea (n = 166, 96.5%), fever (n = 113, 65.7%) and abdominal pain (n = 73, 42.4%). Bloody diarrhea was seen in 19.2% of patients. Fifty (29.1%) of the *Salmonella* species could not be typed. Serogroup D (n = 106, 61.6%) was the predominant serogroup isolated from stool cultures, followed by serogroup B (n = 16, 9.3%). 62.2% of the isolates were susceptible to ampicillin, 97.7% to ciprofloxacin, 98.8% to trimethoprim-sulfamethoxazole, and 98.8% to ceftriaxone. Fever, vomiting, and underlying disease occurred more frequently in hospitalized patients than in outpatients (p: 0.005, p: 0.000, p: 0.000, respectively). C-reactive protein value was found to be higher in hospitalized patients (p: 0.000).

Conclusions: *Salmonella* should be considered as a causative agent in pediatric patients with abdominal pain, fever, and bloody-mucous diarrhea, and patients with severe clinical conditions should be hospitalized and antibiotic therapy initiated if indicated.

Key words: *Salmonella*; gastroenteritis; children.

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Introduction

Salmonella, a member of the Enterobacteriaceae family, is a facultative anaerobic, motile, and Gram-negative bacillus that causes a wide variety of infections such as gastroenteritis, enteric fever, bacteremia, osteomyelitis, and abscess. The most common among these diseases is gastroenteritis, which is the fifth most common cause of death in children worldwide, accounting for approximately 2.5 million deaths [1].

Salmonella usually causes self-limited infections; however, it can cause more serious diseases, especially in children who are < 3 years old, those with malignant diseases, patients using corticosteroids over an extended period, and who have immunodeficiency such as human immunodeficiency virus infection [2]. While patients respond well to antibiotic treatment, serious and fatal outcomes may also happen [3].

There are many types of *Salmonella*, and we can broadly divide the *Salmonella* species into two broad categories: Typhoidal *Salmonella* and non-typhoidal *Salmonella*. According to the present classification system, the genus *Salmonella* has two species, *Salmonellabongori* and *Salmonellaenterica*. *Salmonellaenterica* has more than 2500 serovars. Typhoid *Salmonella* serotypes, such as *Salmonella typhi* or *Salmonella paratyphi*, primarily colonize humans, are mostly transmitted through the consumption of fecally contaminated food or water, and cause clinical infection, usually with very mild diarrhea. The non-typhoidal *Salmonella* group, which are a much larger group of species, usually originates from food contaminated with animal or human fecal material. Non-typhoidal *Salmonella* can also be acquired directly from humans or animals through the fecal-oral route [4,5].

In this study, we aimed to present the general characteristics and treatment regimen of patients hospitalized with the diagnosis of

*Salmonella*gastroenteritis. In addition, we aimed to add to the existing data on *Salmonella* infections in Turkey by determining the detected *Salmonella* types and their resistance status.

Methodology

The study was performed in a tertiary city hospital in Istanbul which has a capacity of 1000 beds, including a 100-bed pediatric unit. Electronic medical records from May 2015 to December 2021 were retrospectively reviewed to identify patients aged between 1 month and 18 years who were treated in the pediatric ward with the diagnosis of *Salmonella* gastroenteritis.

Acute diarrhea was defined according to the World Health Organization (WHO) guidelines as three or more watery or loose stools in 24 h or more frequent stools than normal [6]. Stool culture is routinely obtained from children presenting with the diagnosis of acute diarrhea in the pediatric department of our hospital, especially if accompanied by fever and/or abdominal pain. Records of patients with stool cultures that were positive for *Salmonella* were identified and further analyzed.

Participants were identified through the department's archived patient files, and patients' information including age, sex, clinical findings, laboratory findings [(white blood cell; WBC), absolute neutrophil count (ANC), C-reactive protein (CRP)], microbiological findings (blood culture, stool culture, antimicrobial susceptibility of the isolated *Salmonella* serogroups), treatment during the hospital stay, and duration of hospital stay were collected.

Stool specimens were streaked onto Hektoen Enteric Agar (bioMérieux, Marcy-l'Étoile, France), and the plates were incubated at 35–37°C for 18–24 h. After the incubation period, transparent, green colonies with or without black centers (lactose negative and H2S positive or negative) were considered as possible *Salmonella* colonies. Suspected colonies were identified by Vitek-2 compact or MALDI-TOF VITEK® MS systems (bioMérieux, Marcy-l'Étoile, France). *Salmonella* strains that were identified were serotyped by Difco™ *Salmonella* Antisera (Becton, Dickinson and Company, Sparks, MD, USA) and classified into serogroups by using the Kauffmann-White scheme. Antimicrobial susceptibility testing was done by the Kirby–Bauer disk diffusion method and interpreted in accordance with the current EUCAST breakpoints [7].

This study was approved by the Medical Research Ethics Committee of our institution (Report Number: 2022/514/220/4).

Statistical analysis

Normally distributed quantitative variables were expressed as mean ± standard deviation, whereas non-normally distributed quantitative variables were expressed as median with interquartile ranges (IQR). Chi square test was used for comparing categorical variables. Mann–Whitney U test was used to compare two groups of non-normally distributed data. Student t-test was used to compare two groups of normally distributed data. All analyses were conducted using SPSS 25 software (IBM SPSS Statistics, New York), and $p< 0.05$ indicated a statistically significant difference.

Results

A total of 172 children aged between 1 month and 18 years, including 113 outpatients and 59 hospitalized children, diagnosed with *Salmonella* gastroenteritis, were included in this study. There were 95 (55.2%) males and 77 (44.8%) females with a median age of 59.5 months (IQR: 33.5–96 months, min–max: 1–205 months).

Among these 172 patients, 57.6% were ≤ 5 years old, 30.8% 6 -10 years old, and 11.6% were 11-18 years old.

The clinical symptoms were: diarrhea (n = 166, 96.5%), fever (n = 113, 65.7%), abdominal pain (n = 73, 42.4%), vomiting (n = 71, 41.3%), nausea (n = 34, 19.8%), bloody diarrhea (n = 33, 19.2%), and seizure (n = 5, 2.9%).

The mean WBC count was 10364 ± 4557.04/mm^3 (min-max 2900–25300), the mean ANC was 7296.6 ± 4118.6/mm^3 (min-max: 720-19800), the mean platelet count was 266652.08 ± 87529.8/mm^3 (min–max: 23500–562000), and the median CRP was 52.5 mg/dL (IQR: 19.7–105.5, min–max: 3–395).

Fifty (29.1%) of the *Salmonella* species could not be typed. Serogroup D (n = 106, 61.6%) was the predominant serogroup isolated from stool cultures, followed by serotype B (n = 16, 9.3%). The laboratory classified 103 isolates into *Salmonella enteritidis*, 16 isolates into *Salmonella typhimurium*, and 3 isolates into *Salmonella typhi*. All isolates were tested for antimicrobial susceptibility; 62.2% of the isolates were susceptible to ampicillin, 97.7% to ciprofloxacin, 98.8% to trimethoprim-sulfamethoxazole, and 98.8% to ceftriaxone. 107 (62.2%) isolates were susceptible to ampicillin. The ampicillin susceptibility rates of *Salmonella typhimurium*, non-typeable *Salmonella* isolates, *Salmonella typhi* and *Salmonella enteritidis* were 100%, 92%, 66.6%, and 41.7%, respectively.

Salmonella gastroenteritis occurred throughout the year; however, it peaked during the autumn months of October (13.4%) and November (11.6%). Suspicious eggs and egg products history was detected only in 10.2% (n = 6) of the hospitalized patients.

We also recorded the antibiotics used by the hospitalized patients. Intravenous ceftriaxone was administered to 48 (81.3%) patients and intravenous trimethoprim-sulfamethoxazole to 11 (18.6%) patients. Blood cultures were taken simultaneously with stool culture in all patients at the time of hospitalization, and all remained sterile. The mean hospitalization duration was 8.69 + 2.8 days (min–max: 4–20 days). None of the patients died, and clinical cure was achieved in all patients.

The comparison of clinical and laboratory characteristics of the outpatients and the hospitalized patients are presented in Table 1.

Discussion

Our study was conducted in Istanbul and we showed that *Salmonella* gastroenteritis continues to be an important health problem with a 34% hospitalization rate for culture-positive cases. There are very few studies examining pediatric patients hospitalized with a diagnosis of *Salmonella* gastroenteritis in our country. Since it is not a very common disease in developed countries, there is limited information available in literature. Therefore, we think that our study will contribute to the overall understanding of this disease.

Salmonella gastroenteritis usually occurs in the first 5 years of life, and its frequency decreases later on in childhood [5]. Hung *et al.* conducted a study over a 9 year period in Taiwan and showed that 86% of the children diagnosed with *Salmonella* gastroenteritis were less than 5 years old [8]. A study conducted in Turkey spanning a period of 10 years and including 136 patients, showed that 62.5% of the cases were under the age of five years [9]. We examined the cases diagnosed with *Salmonella* gastroenteritis over a 6.5 year period and found that the majority cases were in < 5 years old children.

Salmonella infections are mostly food-borne. Reptiles such as turtles, snakes, and lizards carry certain *Salmonella* serotypes in their intestines and may cause symptoms associated with *Salmonella* infection attacks [5]. It is known that the main sources of *Salmonella* which cause *Salmonella* gastroenteritis in humans are eggs and egg products [10]. Although data were insufficient due to the retrospective nature of the study, we found the rate of suspicious egg and egg products intake to be 10.2% among hospitalized patients.

In previous studies, it has been shown that patients with *Salmonella* gastroenteritis mostly present with fever, abdominal pain, and diarrhea symptoms during the warm seasons [9,11,12]. Similarly, in our study, patients presented with diarrhea (96.5%), fever (65.7%), and abdominal pain (42.4%). In our study, the peak time of infection coincided with autumn. Similarly, in a study in Taiwan which included 157

Table 1. Comparison of clinical and laboratory characteristics of outpatients and hospitalized patients.

Characteristics	Outpatients (n = 113)	Hospitalized patients (n = 59)	*p value*
Age: Median (IQR) months	58 (38-84)	61 (13-104)	0.911
Gender			
Female	61 (54)	34 (57.6)	0.648
Male	52 (46)	25 (42.4)	-
Clinical findings			
Diarrhea	108 (95.6)	58 (98.3)	0.354
Fever	66 (58.4)	47 (79.7)	0.005
Abdominal pain	45 (39.8)	28 (47.5)	0.336
Vomiting	31 (27.4)	40 (67.8)	0.000
Bloody diarrhea	21 (18.6)	12 (20.3)	0.781
Nausea	18 (15.9)	16 (27.1)	0.080
Seizure	2 (1.8)	3 (5.1)	0.219
Underlying disease	4 (3.5)	12 (20.3)	0.000
WBC (Mean) (/mm^3)	10,768.24 ± 4,412.6	9,783.05 ± 4,734.6	0.203
ANC (Mean) (/mm^3)	7,612.9 ± 4,063.9	6,841.02 ± 4,188.9	0.270
Platelet (Mean) (/mm^3)	267,998 ± 79,357	264,711.86 ± 98,804.23	0.826
CRP (Median) (IQR)	41 (15-68)	81 (29-167)	0.000
Serovars of *Salmonella* isolated in stool specimens			
Non-typeable *Salmonella* spp.	30 (26.5)	20 (33.9)	0.796
Salmonella enteritidis	70 (61,9)	33 (55.9)	
Salmonella typhimurium	11 (9.7)	5 (8.5)	
Salmonella typhi	2 (1.8)	1 (1,7)	

children with *Salmonella* enterocolitis, the peak time of infection was determined as August and September [13]. We attributed this to the fact that our country has a temperate climate, and the autumn months are mostly hot.

In a study conducted with pediatric patients in Turkey, it was observed that 67.6% of 136 *Salmonella* isolates could not be typed. In the same study, serogroup A was the most commonly identified type among *Salmonella* isolates [9]. In a multicenter study conducted in 10 provinces in Turkey involving children and adults, 620 *Salmonella* strains were serotyped, and the most common ones were determined as *Salmonella enteritidis* and *Salmonella typhimurium*, respectively [14]. In another multicenter study involving seven countries in South Asia and Africa, isolates of cases with *Salmonella* gastroenteritis under 5 years of age were examined, and 361 of 370 isolates were reported as nontyphoidal *Salmonella* and the most frequently detected isolates were *Salmonella typhimurium*, serogroup O:8 (C2-C3), serogroup O:6.7 (C1), *Salmonella paratyphiB Java*, and serogroup O:4 (B) [15]. In our study, serogroup D followed by serogroup B were the most common types among the *Salmonella* isolates.

Antibiotic treatment is generally not recommended for people with a healthy immune system for over 12 months due to increasing antibiotic resistance and *Salmonella* carriage [16]. However, antibiotic therapy is recommended in patients at risk of developing invasive disease, infants under 3 months of age, patients with persistent high fever, severe diarrhea requiring hospitalization, and patients with immunodeficiency [17]. Therefore, it is important to know the antibiotic susceptibility pattern among the isolates. In a study conducted in Turkey, resistance rates to ampicillin, trimethoprim/sulfamethoxazole, nalidixic acid, and ciprofloxacin were found to be 12%, 6%, 17%, and 4%, respectively [18]. In another study conducted among pediatric patients in our country, the resistances to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, cefotaxime, ceftriaxone, ciprofloxacin, and levofloxacin among isolated *Salmonella* species were determined as 15.4%, 2.9%, 5.1%, 2.2%, 1.5%, 3.7%, and 0.7%, respectively [9]. The resistance rates of *Salmonella* species to third generation cephalosporins were reported as 3.5% in the United States, while it was reported as 1.8% in Europe [19,20]. Antibiotic resistance of *Salmonella* spp in our study were as follows: ampicillin (37.8%), ciprofloxacin (2.3%), trimethoprim-sulfamethoxazole (1.2%), and ceftriaxone (1.2%). All hospitalized patients in our study received antibiotic treatment and ceftriaxone (81.3%) was the most commonly used antibiotic, followed by trimethoprim-sulfamethoxazole (18.6%). We think that the reason for the use of antibiotics by all hospitalized patients in our study may be because our hospital is a third level reference hospital and many clinically serious patients are referred to this hospital from the surrounding regions. A study in China which included 142 pediatric patients diagnosed with *Salmonella* gastroenteritis reported very high antibiotic use rates for similar reasons [21]. All our patients showed clinical improvement with appropriate antibiotic therapy and supportive care and no complications developed.

Conclusions

Salmonella gastroenteritis continues to pose a serious problem in developing countries, especially among children under 5 years of age. In developing countries, when pediatric patients present with abdominal pain, fever, and bloody-mucous diarrhea, *Salmonella* should be considered as a causative agent. Patients with severe clinical conditions should be hospitalized and antibiotic therapy initiated if indicated.

Authors' Contributions

All the authors have participated in drafting of the manuscript and/or critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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