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REVIEW PAPER

Salmonella enterica infection in children

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SUMMARY

The aim of the study was to analyze the sources of infection, taking into account the behavior of parents and their knowledge of the routes of bacterial transmission, the clinical course and the descent symptoms of zoonotic salmonellosis in children from the Wielkopolska region in connection with an endemic outbreak of the disease in the region. The records of 35 patients attending two infectious wards in Wielkopolska from May 2016 to April 2017 were analyzed retrospectively. *Salmonella enterica* infection was diagnosed in children aged 3 months to 15 years, the vast majority (33 patients) previously healthy. Thirty percent of patients had a history of direct contact (ingestion, play) with raw animal products, and parents were unaware of the risk of *Salmonella* infection. In 6 cases, the disease was familial. Generalized inflammatory reaction syndrome was observed in 11 patients. Salmonellosis meningitis was diagnosed in 1 child. The predominant symptoms of infection were loose stools, which occurred in all patients and lasted from 1 to 13 days before hospitalization. Laboratory tests on all patients showed a significant increase in C-reactive protein levels, while significant segmental leukocytosis was observed in children under 5 years of age.

Conclusions: *Salmonella* infection remains an important pediatric problem because of its potential to occur in any age group and the risk of serious complications. An important element of prevention is to educate parents about the routes of transmission.

KEYWORDS:

***Salmonella*, children, complications.**

ABSTRACT

The aim of the study was to evaluate the sources of infection, taking into account the parents' behavior and their knowledge about the pathways of bacteria, and the clinical course and symptoms of salmonellosis in children from Wielkopolska, in connection with the occurrence of outbreaks in endemic disease We retrospectively analyzed the medical documentation of 35 children hospitalized in two infectious diseases wards in Wielkopolska from May 2016 to April 2017.

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Salmonella enterica infection was confirmed in patients aged three months to 15 years, the majority of whom (33 people) were previously healthy. 30% of children had a history of direct contact with raw animal products, and their parents were not aware of the *Salmonella* infection risk. Six patients had a positive family history. Sys- temic Inflammatory Reaction Syndrome was observed in 11 patients. One child developed *Salmonella enterica* meningitis. The predominant symptoms of infection were watery stools, which had occurred in all patients, and lasted from one to 13 days before hospitalization. In laboratory tests we found a significant increase of C-reactive protein in all groups of patients.

Conclusions: *Salmonella enterica* infection is still a significant problem due to the possibility of its occurrence in every age group, and its serious complications. A very important element of the disease prevention is to educate parents about ways of transmission.

KEY WORDS:

***Salmonella*, children, complications.**

INTRODUCTION

Salmonelloses are diseases caused by Gram-negative bacilli of the *Enterobacteriacae* family from two species: *Salmonella* (*S.*) *enterica* and *bongori*. Differentiation of somatic antigens
(O) and ciliary (H) occurring among the protists of *S. enterica* has made it possible to distinguish more than 2,500 serological types with different an- tygenic structure and varied pathogenicity for humans and animals [1]. The somatic antigen of *Salmonella* is in the nature of a polysaccharide chain included in the lipopolysaccharide of the cell wall. The he- terogeneity of the O antigen is the basis for the division of the bacc-tories into serogroups, which were initially defined by successive capital letters of the alphabet. As the number of serogroups discovered increased, letter notations were abandoned in favor of digital designations, based on so-called partial somatic antigens characteristic of the group. *Salmonella* strains with a common partial somatic antigen are further differentiated into individual serogroup subtypes based on the presence of specific ciliary antigens, which are structural proteins of the fiber (filament) of the bacterial cilia [1, 2].

The main serotypes include:

- *S. enteritidis*, *S. typhimurim*, S. *virchow*, *S. hadar* - usually causing inflammation of the small intestine and gastrointestinal tract,
- *S. typhi* - responsible for cases of typhoid fever,
- *S. paratyphi* - causing typhoid fever [2].

COURSE OF DISEASE

In the gastrointestinal form of the infection, symptoms develop within 8-36 hours and usually persist for several days. Patients complain of spasmodic abdominal pain, vomiting, watery stools with an admixture of blood and mucus, and fever. In immunocompromised patients, young children and the elderly, the disease can cross the intestinal barrier and lead to na-
internal governments, resulting in inflammation of the bile ducts, pancreas, lungs, heart muscle, meninges, brain, bones, among others. In the generalized form, *Salmonella* causes septicemia with a very severe course [1]. The infection can take a chronic form, in which dyspeptic complaints and abnormal bowel movements persist for several months [3].

Salmonella infection occurs through the oral route by drinking water or ingesting produce contaminated with animal feces, most often eggs and poultry meat. Many animals are involved in the transmission of the infection: domestic birds (chickens, ducks, turkeys, geese) and wild birds (pigeons), mammals (dogs, cats), farm animals (horses, cows, pigs), fur animals, domestic rodents and reptiles and amphibians kept at home. The source of human infection can also be another person who is a carrier of the bacteria. In special conditions (hospitals, nursing homes), the infection can spread by contact or airborne routes [1].

Widespread in the environment, *Salmonella* is the most common (82%) bacterial cause of gastrointestinal infections in Poland. In 2014, a total of 8392 cases of zoonotic salmonellosis were registered in Poland, including 8197 cases of intestinal sal- monellosis and 195 of extraintestinal salmonellosis, giving an incidence of 21.8/100,000 population [2]. As in previous years, salmonellosis was most common in children under the age of 5, with the highest incidence of 227/100,000 occurring in children in their 2nd year. Parenteral salmonellosis was most often diagnosed in children in the 1st year of life (incidence of 2.77/100,000; at the same time in adults: 0.51/100,000) [4]. In the year 2014 described above, 13 deaths were confirmed to be spi-dicted by *Salmonella* infection [4].

The aim of the study is to analyze the sources of infection, clinical course and descent symptoms of od-animal salmonellosis in children in connection with the currently observed increase in the number of cases. An additional argument prompting the study was the occurrence of an endemic outbreak of infection in the Greater Poland region and the associated increased morbidity.

MATERIAL AND METHODS

We retrospectively analyzed the records of 35 children hospitalized for salmonellosis at the Department of Infectious Diseases and Pediatric Neurology in Poznań and at the Observational-Infectious Disease Unit with Pediatric Infectious Disease Subdivision in Konin between May 2016 and April 2017. The age of the patients ranged from 2 months to 15 years (average 4.29 years). There were 16 girls and 19 boys in the study group. The majority of patients (33 patients) did not have a chronic disease before hospitalization. In 2 children the personal history was burdened with chronic disease: diabetes mellitus (1 child) and hypogammaglobulinemia (1 child).

RESULTS

INTERVIEW ANALYSIS

On the basis of an interview with the parents, it was determined that 9 children (30%) had indirect contact with raw eggs before the disease. Most often, it resulted from helping their parents prepare meals (beating and/or eating raw dough, pairing cutlets). In 6 cases (17%), the illness was familial, with other eaters in the same household (siblings, grandparents) getting sick at the same time.

CLINICAL SIGNS

The most common clinical symptom reported by patients was loose stools ranging from 5 to 20 stools per day. The average duration of acute stool symptoms was 5 days (1 to 13 days). In 2 children, longer episodes of loose stools were observed, lasting from several weeks to 3 months; in one case, diarrhea alternated with constipation. Vomiting was observed in more than half of the patients (54.29%), lasting an average of 3 days (3.08 days), the longest being 7 days, the shortest being 1 day. Fever was noted in 88.57% of cases, its average duration was 4 days (3.64 days), maximum 7 days, minimum 1 day. There was a history of 1 child with febrile conditions lasting about 3 weeks before hospitalization. 20% of patients complained of abdominal pain. Of the less typical symptoms, cough was reported in 2 cases (5.7%), poor weight gain, osteoarticular pain, headache, cervical lymph node enlargement were observed in individual patients.

In 11 children with salmonellosis, there were general symptoms of infection, typical of the acute systemic inflammatory response syndrome (SIRS): tachycardia, tachypnoe, fever and high leukocytosis. Despite the dynamic course, microbiological blood cultures performed did not confirm bacteremia. One child (a two-month-old infant) developed purulent meningitis. -spinal fluid. The microbiological examination of the cerebrospinal fluid performed confirmed the presence of bacteria
S. enteritidis.

Increased leukocyte count (> 12 g/l) was found in 28.74% of children and averaged 18.42 g/l. Elevated levels of C-reactive protein (CRP > 5 mg/L) were noted in all patients. The mean CRP value was 59.59 mg/L. At least a 10-fold increase in CRP was found in 16 patients (45.71%). The mean age in this group was 5.72 years. Microbiological examination of stools performed in all patients showed the presence of *S. enteritidis* bacilli in 100% of the subjects, which became the basis for the diagnosis. In addition, *Clostridium difficile* toxin A was detected in 1 patient.

In addition, peripheral blood cultures were performed in 3 patients (9.4%), all of whom were sterile, while urine cultures in 3 (8.6%) were positive for *E. coli*. In 1 case, cerebrospinal fluid was collected, yielding a positive result.

For a more detailed analysis, patients were divided into age groups: 0-24 months, 25 months-5 years, over 5 years. The youngest group included 16 pa- tients. Diarrhea lasted in them for almost 5 days (4.98 days), vomiting occurred in almost a third of patients (5 patients) and lasted for less than 3 days (2.6 days). Fever was found in 81.25% of patients (13), and lasted an average of 3 days (3.4 days). Leukocytosis was found in one-third of the patients (31.25%), the average level of white blood cells in the blood was 18.22 g/l, while the average CRP value was 40.13 mg/l. Half of the children required antibiotic administration. The average hospitalization time was less than a week.

The second group included 7 children. Diarrhea lasted 5.6 days in them, vomiting was present in 57% of patients and lasted 3.75 days. Fever was observed in 90% of the patients and lasted for 4.44 days. Leukocytosis was found in 28.6% of patients, the average level was 19.35 g/L, while the average CRP value was 62.6 mg/l. An antibiotic was included in 85.7% of cases. Hospitalization lasted an average of 6 days.

The group of the oldest children included 12 patients. Diarrhea lasted 4.45 days in them, 83.3% of patients complained of vomiting for an average of 2.5 days. Fever was present in 91.67 patients and lasted an average of 3.1 days. Leukocytosis was found in only 1 patient (8.33%) and was 12.8 g/l, the average CRP was 79.81 mg/l. Antibiotic therapy was administered in 83.33% of patients. The average duration of hospitalization was one week (Table 1).

TREATMENT

Twenty-four patients (68.57%) received antibiotic therapy during hospitalization: cefuroxime (12 children treated at the Koni- no infectious diseases unit), cefotaxime (6 children) and ceftriaxone (3 children). In 1 patient diagnosed with coexisting symptomatic *Clostridium difficile* infection, therapy was administered

with

Combination: cefotaxime and vancomycin. The most common indication for antibiotic therapy was the child's severe general condition, high fever and at least 10-fold elevated CRP levels.

The average length of hospitalization was about 7 days (6.95), the longest 18 days for *C. difficile* co-infection, the shortest 3 days.

REVIEW

Salmonella are the most common cause of bacterial gastroenteritis in Poland [2]. The majority of these infections are caused by *Sal- monella enteritidis* - they account for as many as 76% of cases, second only to *Salmonella typhimurium* [4]. In order to minimize the risk of infection, the Rapid Alert System for Unsafe Food and Feed (RASFF) was created within the European Union, which covers 28 countries and allows for ongoing monitoring of food contamination in Poland with *Salmonel- la* bacteria. It was found that in 2015, Polish poultry meat and related products accounted for as much as 19.6% of all notifications [2]. These products (poultry meat and eggs) are the most common, although not the only source of infection. Other reported sources include chocolate pralines, snacks made of dried salami or roasted corn, ready-made cheese sandwiches or hamburgers [5, 6]. Infection occurs both through ingestion of contaminated food products, as well as direct contact with contaminated objects (boards, kitchen countertops, cutlery, household dust). This contact is particularly important in the spread of infection in younger children, who are often eager to place various objects in their mouths in order to become more familiar with them.

An interesting route of infection transmission was described in Ka- hope in 1999, when many cases of salmonellosis among the youngest children occurred. The source turned out to be a bacilli-contaminated dog treat in the form of dried pig's ears, which the animal played with on the floor [5]. In the group of children we analyzed, the most common source of infection was raw chicken eggs. Direct contact with the eggshell by helping with kitchen work seems to be of particular importance in the transmission of the disease. This may reflect caregivers' neglect of food hygiene rules involving washing the surface of the egg before use. At the time of interview collection, many parents marginalized the importance of such a mode of infection, or were surprised by the need to perform proper procedures when handling eggs. For many, the purchase of so-called organic eggs or those obtained directly from the people producing them (e.g., their grandmother) was a guarantee of their safety. 17% of the analyzed pa- cients had documented contact with a sick person, and salmonellosis was a family illness. In many children, especially the youngest, it was not possible on the basis of-

TABLE 1. Analysis of clinical manifestations, laboratory findings, and length of hospitalization of patients with *Salmonella ente- ritidis* infection according to child age

	Children aged 0-24 months	Children aged 25 months-5 years	Children over 5 years of age	Total
Clinical manifestations				
Loose stools: incidence (%) mean time (days)	100 4,98	100 5,6	100 4,45	100 5
vomiting: incidence (%) mean time (days)	31,3 2,6	57 3,8	83,3 2,5	54,3 3,1
fever: incidence (%) mean time (days)	81,3 3	90 4,4	91,7 3,1	88,6 3,6
laboratory test results				
leukocytosis (> 12 g/l): incidence (%) mean value (g/l)	31,3 18,2	28,6 19,4	8,3 12,8	28,7 18,4
CRP > 5 mg/dL: prevalence (%) mean value (mg/l)	100 40,1	100 62,6	100 79,8	100 59,6
Antibiotic therapy: frequency of use (%)	50	85,7	83,3	68,6
Average length of hospitalization (days)	7	6	7	7

know history to determine the source of the infection, which may have been due to both the "less typical route of infection" and the reluctance of caregivers, especially mothers, to reveal their mistakes in handling food products.

According to data presented by the National Institute of Hygiene, salmonellosis is most often diagnosed in children under the age of 5, which is confirmed by our results [4]. Patients mostly presented typical symptoms of gastroenteritis in the form of diarrhea, vomiting (55%), almost always coexisting with elevated body temperature (nearly 90% of cases) and abdominal pain (20%). The data obtained are consistent with the literature, which reports the frequency of diarrhea in nearly 100% of cases, fever in 61% to 100%, vomiting in about 34-76%, abdominal pain in about 33-100% [7-9]. In the study group, diarrhea lasted for an average of 5 days, vomiting for 3, and fever for 4 days. Studies in other countries have shown similar persistence lengths for diarrhea and fever, averaging 6 and 3 days, respectively, while vomiting was shorter, at less than 1 day [6, 10]. These symptoms in our study population lasted similarly regardless of age, only the frequency of vomiting increased with age (the youngest children 33%, the oldest 83%). According to the Lodz researchers, there is a difference in the clinical manifestation of salmonellosis depending on age. In younger children under

At age 4, diarrhea occurred in about 35%, in older patients in 50%, vomiting in about 25% and 60%, respectively, and fever in about 15% and 60% of cases [1]. In studies involving adult patients, the incidence of vomiting was about 18-35%, which would indicate a reversal of the trend in the elderly population [9, 10]. In the study group, individual patients complained of cough, osteoarticular pain, and headache. Symptoms of respiratory tract infections are not typical of salmonellosis, which may argue for co-infection [6]. According to French authors, headache and myalgia occur in 74% and 62% of children, respectively, which is more common than in the patients studied [9].

In the study group, one 9-year-old child complained of constipation alternating with diarrhea for 3 months. It has been proven that intestinal infection can be a cause of functional disorders of the gastrointestinal tract of a chronic nature, and 4-32% of people who have experienced a bacterial infection of the gastrointestinal tract will develop irritable bowel syndrome as a consequence [12]. In addition, Lodz researchers have shown that in children the risk of long-term persistence of gastrointestinal discomfort after *Salmonella* infection increases with age. In a group of children over the age of 4, the duration of abdominal pain was longer at about 94 days. In addition, about 54% of older patients reported abdominal pain for longer than 3 months, and about 35% had diarrhea lasting longer than 14 days [4].

Analysis of the laboratory tests performed showed that an elevated leukocyte count was present in 28.57% of the children; in the first and second age groups, the percentage was

was very similar, while among the oldest patients it was 8.3%. These values are confirmed by lite- ratur studies, in which leukocytosis is found in 14.8-21.6% of patients [8, 11]. The mean CRP value was 59.59 mg/dL and increased in proportion to age. In contrast, the mean CRP value was higher: 64-75% [6, 8, 11]. Nearly 69% of the patients were treated with an antibiotic. In studies by other authors, this percentage ranges from 11.2% to 38.8% [8, 11], with infants being treated more often (61.1% vs. 31.3% of older children), and among them children younger than 12 weeks (83.3% *vs.* 33.3% of children older than 12 weeks) [13]. Current guidelines for indications for antibiotic therapy according to the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) include high-risk patients, i.e. newborns and infants up to 3. months of age, children with immunodeficiency, anatomical or functional asplenia, treated with glucocorticosteroids or immunosuppressive drugs, and with a history of inflammatory bowel disease or achlorhydria [14, 15]. Among our patients, the most common indication for the inclusion of antibiotic therapy was the pa- tient's low age, severe general condition combined with high fever. In individual cases, hypogammaglubilinemia and newly diagnosed diabetes mellitus were such indications. Among the children studied, the average duration of hospitalization was 7 days. In the works of other authors, this time ranged from 3.3 to 5.7 days [6-8, 16].

CONCLUSIONS

Salmonella enterica infection remains a significant pediatric problem due to its potential to occur in any age group and the risk of serious complications. An important element of prevention is educating parents about the routes of transmission.

STATEMENT

The authors declare no conflict of interest.

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