Case Report: *Salmonella Enterica* Serovar Paratyphi B Infection in a Febrile Ill Child during Enhanced Passive Surveillance in an Urban Slum in Mirpur, Dhaka

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Abstract. Paratyphoid fever is one of the major causes of morbidity of febrile illnesses in endemic regions. We report a case of high-grade fever in an infant who was positive for *Salmonella enterica* serovar Paratyphi B (*S.* Paratyphi B) both in blood and stool cultures. The baby was enrolled in the passive surveillance of multicenter, multicomponent epidemiological study of enteric fever (Strategic Typhoid alliance across Africa and Asia; STRATAA) conducted in a population of 110,000 residents over 2 years in an urban slum, Dhaka, Bangladesh. This is the only patient who was positive for *S.* Paratyphi B in blood and stool among more than 6,000 febrile ill patients enrolled in the passive surveillance. The report shows the significance of surveillance to identify changes in the epidemiology of enteric fever.

INTRODUCTION

Typhoid and paratyphoid fever are collectively known as enteric fever, and the greatest burden of enteric fever is seen among impoverished populations who do not have access to clean drinking water and proper sanitation.[1,2] *Salmonella enterica* serovar Typhi (*S.* Typhi) and serovar Paratyphi (*S.* Paratyphi A, B, and C) are the etiologies of enteric fever. In recent decades, *S.* Paratyphi A has been the dominant cause of paratyphoid fever in South Asia,[3] and sporadic reports for *S.* Paratyphi B and C are available.[1,4,5]

A multicenter, multicomponent epidemiological study was carried out to determine the age-stratified burden of enteric fever (Strategic Typhoid alliance across Africa and Asia; STRATAA) conducted in field sites in Bangladesh, Nepal, and Malawi from August 2016 to January 2019.[6] More than 6,000 febrile ill patients were enrolled in the STRATAA passive surveillance study in Bangladesh in Mirpur, Dhaka, and microbiological culture of blood and stool from patients was carried out to allow assessment of the enteric fever disease burden. A high burden of typhoid and paratyphoid fever was found in both children and adults. In Bangladesh, the overall crude incidence rate of blood culture–confirmed *S.* Typhi was 161 per 100,000 person-years of observation (pyo). For *S.* Paratyphi A, the rates in Bangladesh and Nepal were 117 and 37 per 100,000 pyo in the 5- to 9-year age-group, respectively. In Malawi, there were no cases of *S.* Paratyphi A and *S.* Paratyphi B (unpublished observations). We report here a case of an 11-month-old female infant from whom *S.* Paratyphi B was isolated from both blood and stool at enrollment in a health facility. This is the only case of *S.* Paratyphi B infection for febrile illness surveillance of three study sites.

CASE PRESENTATION

A febrile female infant, aged 11 months, was brought by her parents to a passive surveillance facility, which was part of the STRATAA surveillance study (Mirpur Field Clinic; MFC) in June 2018 with a history of fever for the past 3 days. The baby was previously healthy. She did not have any significant past medical history, and she was not taking any medication.

Her parents gave a history of vomiting and diarrhea. On examination, the infant was found to be lethargic and irritable, and was crying persistently; she showed signs of some dehydration. The axillary temperature was 39.5°C (103.1°F). There was no evidence of hepatosplenomegaly, and the pulse rate was 110 beats/minutes. The parents of the patient did not give a history of ingestion of street food during the 2 weeks before the onset of symptoms. The mother of the baby explained that they consume boiled water for drinking and use boiled water for preparing food for the infant.

There was no history of antibiotic intake before blood collection. Blood culture was undertaken (BacT/Alert, bioMérieux, Durham, NC) using 3 mL of blood, and stool culture was also performed. Biochemical and serological testing of the bacterial isolates from blood and stool confirmed the diagnosis.[7–9] *Salmonella enterica* serovar Paratyphi B (*S.* Paratyphi B) was identified, and disk diffusion was used to assess antimicrobial sensitivity using Clinical and Laboratories Standards Institute guidelines.[10] Strains isolated from blood and stool were both sensitive to all of the tested antibiotics (amoxiclav, ampicillin, cotrimoxazole, ciprofloxacin, chloramphenicol, azithromycin, cefixime, and ceftriaxone). The minimum inhibitory concentration value was determined by the E test for the tested antibiotics (Bio Merieux, Craponne, France). Other laboratory investigation of the patient showed raised C-reactive protein (2.26 mg/dL; reference range: 0.01–0.50 mg/dL).

Treatment of the patient was initiated empirically with azithromycin (10 mg/kg/day) after the collection of blood and stool specimens. Oral rehydration solution, zinc, and paracetamol were also given on the day of enrollment. The patient did not respond for 3 days to treatment and came back to the MFC with a history of high-grade fever. On examination, the axillary temperature was 37.5°C (99.5°F), and the patient was toxic. Azithromycin treatment was replaced with cefixime (20 mg/kg/day) once the results of the antibiotic susceptibility testing were available. Because the fever had not subsided after 3 days of azithromycin treatment and there is no validated guideline for azithromycin susceptibility for *S.* Paratyphi B,[11] a switch to cefixime was made empirically at the discretion of the attending physician. The patient was followed up,

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and physical examination was carried out regularly. No other focus of infection was found. The patient's condition improved gradually with the treatment of cefixime. Temperature subsided after 9 days of antibiotic treatment, and the patient had fully recovered on day 11 of follow-up.

Follow-up of the patient was carried out at 1 and 6 months following presentation at enrollment, and two stool specimens were collected from the patient, but all cultures were negative. To investigate possible transmission links, stool specimens were collected for microbiological culturing from the household members of the patient.[6] None of them were positive for S. Typhi or for S. Paratyphi A/B.

DISCUSSION

Several studies incorporating existing burden data and modeling approaches at different geographical locations have contributed to the understanding of the global burden of typhoid fever.[3,12–14] Although few data exist on the global burden of S. Paratyphi infection,[1,5,13,15] S. Paratyphi B has an epidemiologic significance and causes outbreaks.[16]

The case report describes the detection of S. Paratyphi B infection in one patient who was enrolled in the passive surveillance conducted in a population of 110,000 residents over 2 years in Bangladesh. The patient presented to the healthcare facility with a high-grade fever and was enrolled in the study as a suspected case of typhoid fever, as clinically paratyphoid fever is indistinguishable from typhoid fever and laboratory confirmation is required for accurate diagnosis of the disease.[17,18] Salmonella enterica serovar Paratyphi B was isolated from both blood and stool of the patient. During the acute stage of Salmonella infection, patients excrete the organism in their stool, and convalescent and chronic carriers may continue shedding of organism in stool specimens after the resolution of symptoms.[19–24] However, stool culture was negative in our patient on follow-up at 1 and 6 months after presentation, and negative stool cultures were also obtained from her family members.

The household members of the child patient had no complaints of enteric fever, and their stool culture results did not show any evidence of being asymptomatic carrier of S. Paratyphi B. The infant also did not have any history of contact with animals. Hence, the patient could have acquired the infection from the environment while playing in surroundings around the household. Recent studies have suggested that children are more likely to be infected by fecal contamination from the environment in slum settings with contaminated water bodies and open sewers.[25–28] Improvement of sanitation system will be beneficial for the children who are at risk for acquisition of enteric fever from the environment.[29]

Resistance to first-line antibiotics (chloramphenicol, ampicillin, and cotrimoxazole) has complicated antibiotic choice to treat the patients with typhoid and paratyphoid fever.[30,31] Third-generation cephalosporins, fluoroquinolones, and azithromycin are widely used to treat enteric fever.[30,31] Delayed defervescence has been reported for the currently used antibiotics, except fluoroquinolones (ofloxacin and gatifloxacin).[32–34] Fluoroquinolones are now not recommended for the treatment of enteric fever patients empirically in South Asia as a result of the spread of antimicrobial resistance.[34–36] Although antibiotic susceptibility testing indicated that the strain isolated from both blood and stool was sensitive to azithromycin,

the patient did not respond despite 3 days of treatment. The breakpoints for azithromycin in the treatment of typhoidal Salmonellae are uncertain,[37] and there are few clinical data on response to treatment in S. Paratyphi A infection.[38] In addition, there are no validated guidelines for azithromycin susceptibility in S. Paratyphi A/B[37]; hence, further studies are needed to define optimal management for treatment of S. Paratyphi B infection. Good responses are expected with the use of third-generation cephalosporin,[34] and, therefore, the antibiotic was switched to cefixime. However, after initiation of appropriate treatment, it generally takes long time (96–145 hours) for defervescence from enteric fever,[39,40] as was seen in our patient.

This report shows the presence of S. Paratyphi B in South Asia, where S. Paratyphi A is considered as the main cause of paratyphoid fever,[41,42] and highlights the importance of surveillance to identify changes in the epidemiology of enteric fever, particularly in the context of introduction of new typhoid conjugate vaccines to control typhoid, which may promote emergence of paratyphoid as a more significant cause of enteric fever.

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