

Invasive Non-typhoidal *Salmonella* Sepsis in Top-up Fed Five-Month-Old Infant: Case Report

SHAZIA NAAZ¹, VIVEK HADA², SWATHI SURAVARAM³, LAKSHMI JYOTHI TADI⁴, MOHAMMAD WAJID⁵



ABSTRACT

Non-typhoidal *Salmonella* (NTS) are generally associated with self-limiting gastrointestinal disease, often acquired through the ingestion of contaminated food and it seldom requires antimicrobial therapy for treatment. Extra-intestinal manifestations could be localised infection leading to septic arthritis, osteomyelitis. In complicated invasive disease, there could be bronchopneumonia with or without bacteraemia leading to mortality. Invasive NTS infections are infrequently reported in India. The *S. Typhimurium* is one of the common serovars associated with invasive disease and its virulence factors are responsible for causing the disease. *S. enteritidis*, *S. Dublin* are the other serovars which are commonly responsible for invasive NTS infection. It is difficult to diagnose invasive disease without appropriate bacteriological culture based method. With emergence to resistance to antimicrobials the treatment of this condition is also becoming challenging. In this case report, a five-month-old infant presented with cough fever, stuffed nose dyspnoea and was diagnosed as bronchopneumonia. Mechanical ventilation was required for five days along with admission to intensive care unit. Invasive NTS infection was diagnosed using automated blood culture and the child responded to intravenous antimicrobial chemotherapy.

Keywords: Blood culture, Bronchopneumonia, Food borne infection, *Salmonella typhimurium*

CASE REPORT

A five-month-old male child was brought to the Paediatrics OPD by his parents. They complained that the child had cough along with nasal stuffiness for past six days which was followed by onset of fever and rapid breathing in last three days. The child was admitted with a high-grade intermittent fever of 102°F, dyspnoea (74 breaths/min), tachypnoea (152 beats/min). The child had received syrup containing amoxicillin clavulanic acid for three days prior to admission.

The baby was born at term via normal vaginal delivery. The APGAR score was normal after birth and there was no untoward complications prior to or at the time of delivery. The mother was feeding the child with diluted cow's milk for past one month.

On examination, the child was fully alert but irritable with weight 5.6 kg, length 58 cm and was having cough with grunting. During auscultation of chest, bronchial breathing with decreased breath sounds was observed. There was presence of crepitation over the middle and lower lobes of both lung fields. The abdomen was soft with liver margin palpable 2 cm below the right costal margin. The neurological examination was otherwise unremarkable. Pulse oxymeter showed SpO₂ of 84% while breathing room air. A presumptive diagnosis of acute bronchopneumonia with severe respiratory distress was made based on acute onset dyspnoea, decreased breath sound and chest x-ray [Table/Fig-1]. Parental consent was obtained.

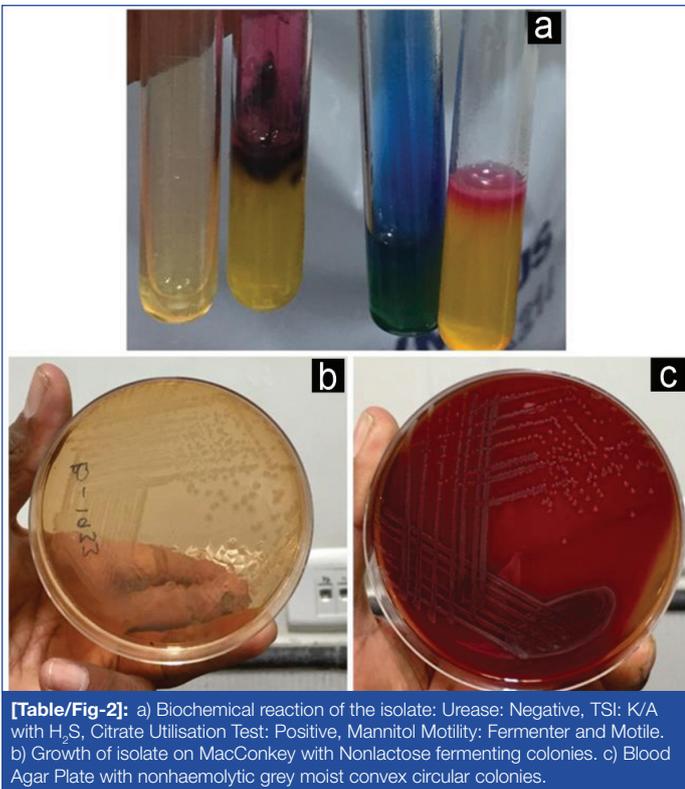
On laboratory examination, white blood cell count was 10,000/mm³ with neutrophils 75% and marked lymphocytopenia. The serum electrolytes were well-maintained. C-Reactive Protein (CRP) levels were 4.8 mg/dL. The child was empirically started on parenteral antimicrobial chemotherapy. Inj ceftriaxone 250 mg i.v., twice daily and syrup azithromycin (200 mg/5 mL), 1.5 mL once orally, were administered along with Nebulisation with 3% normal saline every six hourly and 0.6 mL Salbutamol every 4-6 hourly for bronchodilation.

Blood culture sample was taken in BACTEC blood culture bottles on admission which flagged positive following 24 hours



[Table/Fig-1]: The Chest X-ray of child at the time of admission showing bilateral patchy appearance with peri-bronchial thickening and poorly defined air-space opacities suggestive of bronchopneumonia.

of incubation. The sample was processed according to standard Microbiological techniques on Blood agar and Mac-Conkey agar which yielded Gram-negative aerobic bacilli which was identified as *Salmonella* species using biochemical tests [Table/Fig-2] and VITEK 2 Gram Negative (GN) panel. On basis of phenotypic tests (i.e., citrate utilisation, gas production during glucose fermentation, adequate H₂S in Triple Sugar Iron, both Lysine and ornithine decarboxylation) along with slide agglutination using polyvalent anti-sera; the isolate was reported as probable *Salmonella enterica* serovar Typhimurium. Any past history of diarrhoea was reconfirmed from the parents, but no history of loose stool was present. Stool culture was also done using Xyline Lysine Deoxycholate agar, MacConkey Agar and Selenite F broth, but no pathogen was isolated.



Antimicrobial susceptibility testing was performed by the Kirby Bauer disk diffusion method and Vitek 2 AST cards. The zone diameter breakpoints available in Clinical Laboratory Standards Institute Supplement M-100, 29th edition were used for interpretation of the results [1]. The isolates were sensitive to commonly used antibiotics, such as ceftriaxone (MIC <0.125 µg/mL), cefuroxime (MIC ≤4 µg/mL), and trimethoprim-sulfamethoxazole (MIC <20 µg/mL), cefepime (MIC ≤1 µg/mL), meropenem (MIC ≤0.25 µg/mL), chloramphenicol (MIC ≤8 µg/mL). Resistance was observed against ampicillin (MIC ≥32 µg/mL), ciprofloxacin (MIC ≥1 µg/mL) and nalidixic acid (MIC ≥1 µg/mL).

Initially, during the first two days after admission, the child developed worsening of respiratory function (severe dyspnoea, tachypnoea, and SpO₂ at room air of 82%). The patient was treated with non-invasive Continuous Positive Airway Pressure (CPAP) ventilation. Third day suprasternal retractions and stridor were also observed. The child was continued on CPAP ventilation for the next two days. Nebulisation with adrenaline (0.1 mL/kg/dose in 1 in 10,000 solution of adrenaline mixed in normal saline to make a total volume of 3 mL) using oxygen flow of 8 L/min was done intermittently to relieve bronchoconstriction [2].

Five days after his admission to the hospital the patient's condition started improving and the child became afebrile with reduced cough and respiratory distress. Nebulisation with adrenaline was stopped and CPAP was withdrawn. C-Reactive Protein (CRP) also became negative. Syrup azithromycin was stopped on Day 5.

The clinical course of illness improved and the child was continued on injection ceftriaxone. The repeat blood culture sent after completion of 14 days of ceftriaxone therapy was sterile. The child was discharged after proper counselling of the parents.

DISCUSSION

The NTS consist of the members of genus *Salmonella* which are not associated with typhoid fever. They are important food borne pathogens generally associated with self-limiting diarrhoea with low case fatality. Although in some cases especially those with risk factors i.e., malnourished infants, elderly, sickle cell disease, Human Immunodeficiency Virus (HIV) and recent attack of malaria; there could be bacteremia followed by focal infections in extra-intestinal

sites such as meninges, joints, bones etc., [3-5]. The mode of transmission in most of these cases is consumption of contaminated food of animal origin (e.g., poultry, milk, egg etc.). The most common serovars associated with invasive infection are *S. Enteridis*, *S. Typhimurium* and *S. Dublin* [6]. Here authors' report a case of invasive NTS in an infant aged less than six months of age.

Invasive NTS (iNTS) diseases are increasing worldwide and have higher case fatality of 13.4% among under five years population [4]. The data on NTS invasive disease remain limited from developing countries of south-east Asia. One of the reasons for this low reporting could be failure of clinic-based surveillance to capture individual with NTS invasive disease and other could be non-availability of bacteriology culture based diagnostic services [4]. Isolation of NTS from extra-intestinal samples is still infrequently reported from India. Sudhaharan S, reported isolation of 27 NTS in extra-intestinal samples in the three years and *S. Typhimurium* was the most common isolate to be recovered during their study period [7]. There have been few reports regarding bronchopneumonia caused by NTS in the past [8,9]. In these most of these cases *S. Typhimurium* was found to be the most common NTS isolated in children and adults. In case of children, most of the cases were above six months of age. Infection under six months will be difficult in exclusively breast-fed children due to food borne nature of the illness [9]. In most cases of invasive NTS disease, organism gains entry through gastrointestinal tract and subsequently moves to extra-intestinal sites via blood with absence of any diarrhoeal illness during the course of disease [10]. In this case also, there was no history of diarrhoea. Even in patients with gastrointestinal illness almost 5% of individuals will develop bacteremia, or serious potential problem. The cautious clinical assessment for septic foci, additional blood cultures, and antimicrobial therapy for all children with bacteremia caused by NTS should be done to prevent any mortality [3]. The mode of transmission is ingestion of animal origin food, thus infection in below 6-month infants, who are exclusively breast-fed is very rare. In this case, ingestion of cow milk by the child could be one possible source that leads to infection in the child, and progressing to severe pneumonia in the infant. The gastrointestinal illness caused by these organisms is self-limiting which seldom requires antimicrobial chemotherapy, third generation cephalosporin viz., ceftriaxone is considered as the drug of choice in most of the cases of iNTS disease [3]. There, an increase in antibiotic resistance among NTS isolated in various clinical samples. In a study carried out in Southern India, it was observed that resistance to ceftriaxone was showing increasing trend among NTS over the last 10 years [11]. In a recently published report from Southern India, it was observed that *S. Typhimurium* was most prevalent serotype with 393 isolates (27.3%) recovered during the 19 years period with a consistent and stable distribution during the study period. It also showed that multidrug resistance has increased among NTS and there is major increase in last decade [12].

Antimicrobial resistance in NTS an important risk factor for hospitalisation and bacteraemia. In analysis of five years data from two surveillance systems in United States, Foodborne Diseases Active Surveillance Network (FoodNet) and National Antimicrobial Resistance Monitoring System (NARMS), it was observed that occurrence of hospital admission and bloodstream infection was more, after infection with drug resistant NTS. This finding was strongly associated in case of drug resistant *Salmonella* Typhimurium, which was the most common NTS serotype isolated in the study period [13]. The isolate recovered in present case was also resistant to ampicillin and fluoroquinolones. The rampant use of antimicrobial in agriculture and poultry farms is considered as one of the important drivers for upsurge of antimicrobial resistance [14].

CONCLUSION(S)

The NTS are emerging food borne infection worldwide. Invasive disease with unusual manifestations can lead to severe disease.

It should be suspected in cases of febrile illnesses with history of consumption of contaminated food of animal origin (mainly eggs, meat, poultry, and milk). Parents need to be educated and counselled regarding the importance of boiling of milk, proper cooking of food and using safe water especially in case of top-up fed young infants to prevent this disease. The invasive NTS will not be necessarily preceded by diarrhoea. Thus, timely blood culture in case of febrile illness in top-up fed young infant is essential to correctly diagnose invasive NTS infection to prevent mortality.

REFERENCES

- [1] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests. CLSI supplement M100. 29th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
- [2] Verma N, Lodha R, Kabra SK. Recent advances in management of bronchiolitis. *Indian Pediatr*. 2013;50(10):939-49.
- [3] Acheson D, Hohmann EL. Nontyphoidal salmonellosis. *Clinical Infectious Diseases*. 2001;32(2):263-69.
- [4] Stanaway JD, Parisi A, Sarkar K, Blacker BF, Reiner RC, Hay SI, et al. The global burden of non-typhoidal salmonella invasive disease: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Infectious Diseases*. 2019;19(12):1312-24.
- [5] Ao TT, Feasey NA, Gordon MA, Keddy KH, Angulo FJ, Crump JA. Global burden of invasive nontyphoidal salmonella disease, 2010. *Emerging Infectious Diseases*. 2015;21(6):941-49.
- [6] Haselbeck AH, Panzner U, Im J, Baker S, Meyer CG, Marks F. Current perspectives on invasive nontyphoidal *Salmonella* disease. *Current Opinion in Infectious Diseases*. 2017;30(5):498-503.
- [7] Sudhakaran S, Kanne P, Vemu L, Bhaskara A. Extraintestinal infections caused by nontyphoidal *Salmonella* from a tertiary care center in India. *Journal of Laboratory Physicians*. 2018;10(04):401-05.
- [8] Khan S, Kumar VA, Sidharthan N, Mehta A, Backer B, Dinesh KR. *Salmonella* Typhimurium pneumonia in a patient with multiple myeloma. *Tropical Doctor*. 2015;45(2):135-36.
- [9] Saeed NK. *Salmonella* pneumonia complicated with encysted empyema in an immunocompromised youth: Case report and literature review. *J Infect Dev Ctries*. 2016;10(4):437-44.
- [10] Feasey NA, Dougan G, Kingsley RA, Heyderman RS, Gordon MA. Invasive nontyphoidal salmonella disease: An emerging and neglected tropical disease in Africa. *Lancet*. 2012;379(9835):2489-99.
- [11] Pragasam AK, Anandan S, John J, Neeravi A, Narasimman V, Muthurilandi Sethuvel DP, et al. An emerging threat of ceftriaxone-resistant non-typhoidal salmonella in South India: Incidence and molecular profile. *Indian J Med Microbiol*. 2019;37(2):198-202.
- [12] Jacob JJ, Solaimalai D, Muthurilandi Sethuvel DP, Rachel T, Jeslin P, Anandan S, et al. A nineteen-year report of serotype and antimicrobial susceptibility of enteric nontyphoidal *Salmonella* from humans in Southern India: Changing facades of taxonomy and resistance trend. *Gut Pathog*. 2020;12:49.
- [13] Varma JK, Molbak K, Barrett TJ, Beebe JL, Jones TF, Rabatsky-Ehr T, et al. Antimicrobial-resistant nontyphoidal *Salmonella* is associated with excess bloodstream infections and hospitalisations. *J Infect Dis*. 2005;191(4):554-61.
- [14] Taneja N, Sharma M. Antimicrobial resistance in the environment: The Indian scenario. *Indian J Med Res*. 2019;149(2):119-28. doi:10.4103/ijmr.IJMR_331_18.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Microbiology, ESIC Medical College and Hospital, Sanathnagar, Hyderabad, Telangana, India.
2. Assistant Professor, Department of Microbiology, All India Institute of Medical Sciences, Gorakhpur, Uttar Pradesh, India.
3. Assistant Professor, Department of Microbiology, ESIC Medical College and Hospital, Sanathnagar, Hyderabad, Telangana, India.
4. Professor, Department of Microbiology, ESIC Medical College and Hospital, Sanathnagar, Hyderabad, Telangana, India.
5. Associate Professor, Department of Microbiology, ESIC Medical College and Hospital, Sanathnagar, Hyderabad, Telangana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Vivek Hada,
Assistant Professor, Department of Microbiology, All India Institute of Medical Sciences,
Kunraghat, Gorakhpur-273008, Uttar Pradesh, India.
E-mail: vivekhada7285@gmail.com

PLAGIARISM CHECKING METHODS: [Jan H et al.]

- Plagiarism X-checker: Dec 24, 2020
- Manual Googling: Jan 10, 2021
- iThenticate Software: Jan 20, 2021 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes (Parental consent)
- For any images presented appropriate consent has been obtained from the subjects. Yes (Parental consent)

Date of Submission: **Dec 17, 2020**

Date of Peer Review: **Jan 05, 2021**

Date of Acceptance: **Jan 13, 2021**

Date of Publishing: **Feb 01, 2021**