

ENTERIC DISEASES

Multi-facility healthcare-associated outbreak of *Salmonella enterica* serovar Isangi, Eastern Cape province

Healthcare-associated infections and outbreaks of nontyphoidal *Salmonella* (NTS) are uncommon but well described. Owing to the mode of spread and specific healthcare-population characteristics, the majority of NTS healthcare-associated outbreaks have been reported in paediatric- and neonatal-care settings.

An outbreak caused by a unique 'strain' of *Salmonella enterica* serovar Isangi (*Salmonella Isangi*) has been identified in the Nelson Mandela Bay Metropolitan Municipality (NMBMM), Eastern Cape province. From April through July 2022 the NHLS laboratory noted an increase in the number of cases of extended β -lactamase producing (ESBL) NTS diagnosed on culture; the case numbers peaked in May and decreased steadily thereafter. To date, the total number of cases is 43, of which 36 case patients had symptoms or evidence of an illness from infection, and 7 case patients were asymptomatic (i.e. they had no symptoms or evidence of illness; 6 were detected when all patients in the affected hospital wards were tested, and one case of carriage was detected incidentally). The cases included children and adults, and most were patients at the three largest public hospitals in NMBMM (Dora Nginza, Livingstone and Uitenhage provincial hospitals).

Available isolates which were submitted to the Centre for Enteric Diseases at the National Institute for Communicable Diseases, from patients diagnosed with nontyphoidal salmonellosis in Eastern Cape province from 2020 through 2022, underwent further investigation including whole-genome sequencing (WGS). Phenotypic serotyping identified the isolates as *Salmonella* Isangi and antimicrobial resistance testing confirmed their antimicrobial susceptibility profile as reported by the NHLS laboratory (multi-drug resistant, resistant to ciprofloxacin, ESBL-producing). Core genome multi-locus sequence typing analysis of WGS results identified a cluster of highly related *Salmonella* Isangi isolates, and revealed that the first two cases due to this unique 'strain' occurred in late 2021.

Following an outbreak investigation, including a review of patients' laboratory and medical records, it was determined that this prolonged outbreak was a multi-facility healthcare-associated outbreak. Records showed that the majority of patients were tested for and diagnosed with NTS infections at least 48 hours after admission. The few patients who tested positive for *Salmonella* Isangi on admission had recent exposure to one of the three hospitals. Transfer of patients between these facilities is common practice and likely facilitated transmission of the strain from patients in one hospital to the next.

Following the implementation of targeted and enhanced infection prevention and control measures in these hospitals, the number of cases decreased and only one probable case has been identified since the end of July 2022.

The predominant mode of transmission in NTS healthcare-associated outbreaks has been reported as person-to-person transmission, usually as a result of NTS contamination of healthcare workers' hands. In such cases, the initial source of infection is usually a symptomatic patient who is shedding NTS bacilli. Other important sources for ongoing transmission of NTS in an established outbreak include environmental and fomite contamination. NTS has been isolated from a range of environmental sources during outbreaks, including cots, mattresses, washbasins, bedpans, bedpan washers, rectal thermometers, thermometer holders, gastroscopes, suction apparatus, and soiled linen. Contaminated food served to patients (being inherently contaminated or contaminated during handling/processing by infected food-handlers) has also been documented as a source of infection during outbreaks amongst adolescent/adult patients, as has contaminated milk formula feeds amongst young children (again, either inherently contaminated or contaminated during handling/processing by infected milk kitchen staff). Transmission of NTS via pooled breast milk resulted in an outbreak in a neonatal ward, ward. This outbreak was shown to be as a result of an infected mother excreting NTS in breast milk.

Within outbreak settings, persons with underlying medical conditions or immunosuppression (including HIV) are most at risk of developing symptomatic disease and complications. Young children in particular are at considerable risk of morbidity if infected, with other underlying medical conditions or predisposing factors (e.g. prematurity) compounding this risk. As a consequence, NTS outbreaks in paediatric- or neonatal-care settings often have high attack rates (as high as 43% in some reported outbreaks) and high case fatality rates (12-41% in published studies). In an outbreak of *Salmonella* Isangi in the paediatric wards at Chris Hani Baragwanath Hospital in 2001, a case fatality rate of 22% (9/41) was recorded, with 78% (7/9) of fatal cases being HIV co-infected.

The duration of NTS outbreaks in paediatric/neonatal wards may also be prolonged, and outbreaks lasting >1 year have been described. Asymptomatic patients, asymptomatic healthcare workers, and asymptomatic mothers of hospitalised children may shed NTS bacilli for many weeks (even months) and serve as an invaluable source of ongoing transmission to susceptible patients. Symptomatic NTS-infected patients may shed NTS for prolonged periods (many months), particularly

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very young children, children with HIV co-infection, and children on antibiotic therapy. Children with symptomatic NTS infection who are treated with antibiotics and show clinical response to treatment and resolution of symptoms can still have NTS for many weeks or months thereafter.

The incubation period of NTS in healthcare-associated outbreaks is variable, and depends on the patient characteristics as well as the serotype of NTS. *Salmonella Typhimurium* has been documented as having incubation periods from ± 24 hours to 14 days in hospital outbreaks. As a result, patients may develop symptomatic disease after being discharged from the hospital. If such patients are readmitted (which frequently happens, particularly if they have other underlying medical conditions etc), they may serve as additional propagators of NTS transmission. A feature of many published NTS outbreaks in paediatric/neonatal wards is that many weeks may pass with

no new cases detected, but due to asymptomatic shedders and readmission of previously infected patients who have since become symptomatic, ongoing cases occur.

Factors shown to contribute to the persistence of the organism and ongoing transmission during outbreaks include suboptimal infection prevention and control practice (particularly hand hygiene and contact precautions), inadequate cleaning and disinfection of the environment and medical equipment, understaffing, and overcrowding. Review, inspection and audit of these practices and institutional factors facilitate corrective actions and intervention measures to reduce transmission and stop the outbreak. Screening of all patients in affected wards to identify those who may have asymptomatic carriage is also recommended; isolation or cohorting of patients with NTS infection (whether symptomatic or asymptomatic) may reduce the risk of onward patient-to-patient transmission.