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Enteric Fever Surveillance Report, South Africa, 2020-2023

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Summary

South Africa is endemic to enteric fever caused by *Salmonella* Typhi. Sporadic cases occur in most or all provinces annually. Clusters and larger outbreaks occasionally occur. Enteric fever is a category 1 notifiable medical condition in South Africa. Following the last large outbreak in Delmas in 2005, the number of laboratory-confirmed enteric fever cases in South Africa remained stable at less than 150 cases per year until 2022, when 205 cases occurred nationally. In 2023, national case numbers returned to below 150 cases (141 cases). At provincial level, an increased number of cases occurred in the Western Cape and North West provinces in 2021, with a concurrent decrease in the number of cases reported from Gauteng Province. However, in 2022, the number of cases identified in Gauteng Province increased notably. Core-genome multilocus sequence typing (cgMLST) analysis of whole genome sequencing (WGS) data from *Salmonella* Typhi isolates submitted to the National Institute for Communicable Diseases (NICD) showed that the increased number of cases in the Western Cape and North West provinces was driven by specific clusters (outbreaks) as defined by the genetic relatedness of isolates. Similarly, several enteric fever clusters were identified in Gauteng Province using core-genome multilocus sequence typing (cgMLST) analysis. Cases of enteric fever caused by the strain identified in North West Province were subsequently also identified in other provinces. The ongoing challenge of identifying the source(s) of infection in some provinces attests to the complex epidemiology and range of transmission pathways for this pathogen. Recommendations for the prevention and control of enteric fever in South Africa include raising healthcare worker awareness for identification and appropriate treatment of cases; follow-up and management of chronic carriers to reduce transmission; and community health education on general preventative measures such as hand hygiene, water treatment, and food safety practices.

Introduction

Enteric fever, including typhoid and paratyphoid fever, is caused by systemic infection with *Salmonella enterica* subspecies enterica serotype Typhi (*Salmonella* Typhi) and *Salmonella enterica* subspecies enterica serotypes Paratyphi (*Salmonella* Paratyphi) A, B, or rarely, C, respectively[1]. The World Health Organization estimates that, globally, nine million cases of typhoid fever occur annually, resulting in approximately 110 000 deaths per year.[2] South Asia, Southeast Asia, and sub-Saharan Africa bear the highest burden of enteric fever disease, with marked inter- and intra-country heterogeneity. There is a disproportionate effect on children, i.e., the highest incidence typically occurs in the 5–15 age group, but recent studies from Africa and Asia have highlighted the substantial burden of disease among children less than 5 years of age and in infants.[1, 3]

South Africa is endemic to enteric fever caused by *Salmonella* Typhi, although the disease prevalence is much lower than in most other countries in sub-Saharan Africa.[4] Sporadic cases occur in most or all provinces annually, with occasional clusters or larger outbreaks. The last large outbreak of enteric fever in South Africa occurred in Delmas, Mpumalanga Province, in 2005, with over 600 clinically diagnosed cases.[5] Paratyphoid fever remains uncommon in South Africa.[4] Typhoid fever has been

largely eliminated in higher-income countries through the provision of modern sanitary facilities and safe drinking water.[1]

Salmonella Typhi and *Salmonella* Paratyphi only infect humans. The bacteria are shed in the faeces of an infected person, and transmission occurs through the consumption of contaminated food or water.[6] Clusters usually result from secondary transmission to close contacts in household-type settings, or because of contamination of food by a person who is a carrier. Faecal contamination of water sources is usually associated with larger outbreaks. The incubation period is typically 7–14 days on average (range 3–60 days).[7] Prolonged fever is the cardinal symptom of enteric fever, and other symptoms may include fatigue, abdominal pain, diarrhea, and constipation. The clinical presentation of enteric fever ranges from mild, non-specific illness to severe life-threatening systemic illness with complications such as intestinal perforation, haemorrhage, or encephalopathy. Case fatality rates in patients who receive adequate therapy are estimated to be 1– 4%.[6]

Without effective treatment, approximately 1–5% of patients with acute typhoid infection will become chronic carriers,[7] i.e., continue to shed *Salmonella* Typhi in the stool or urine for at least 12 months after finishing an appropriate course of antimicrobial treatment and the resolution of symptoms following a laboratory-confirmed episode of acute disease. Asymptomatic carriers serve as biological reservoirs and have important implications for public health, with unsafe water, unimproved sanitation facilities, and poor hygiene driving ongoing transmission.

The definitive diagnosis of typhoid fever requires the isolation of *Salmonella* Typhi from blood, bone marrow, or a specific anatomical lesion.[8] Stool cultures are useful for monitoring carriage in persons who have recovered from enteric fever, as well as for screening for carriage in close contacts.

The emergence and spread of multidrug-resistant (MDR) *Salmonella* Typhi (resistant to ampicillin, chloramphenicol, and cotrimoxazole) and MDR plus fluoroquinolone-resistant strains of *Salmonella* Typhi over the last two decades highlights the need for ongoing surveillance and antimicrobial stewardship.[6] There is wide variation in the rates of antimicrobial resistance across regions and even across countries or areas within regions. An outbreak of extensively drug-resistant (XDR) *Salmonella* Typhi, resistant to the first-line antibiotics, a fluoroquinolone and a third-generation cephalosporin but susceptible to azithromycin and carbapenems, was described in Pakistan in 2016.[9] Subsequent travel-associated cases of the Pakistan XDR strain have been described.[10]

In 2017, the World Health Organization prequalified a Vi-tetanus toxoid typhoid conjugate vaccine now recommended for programmatic use from six months of age in typhoid-endemic countries, prioritising countries with a high burden of typhoid fever or high rates of antimicrobial resistance.[6, 11, 12]

The aim of the national laboratory surveillance is to systematically collect, collate, and analyse data on pathogens of public health importance in South Africa. This includes reporting trends in enteric

fever case incidence over time, detecting outbreaks, monitoring for existing and emerging antimicrobial resistance, and describing the molecular epidemiology of the isolates.

Methods

The Centre for Enteric Diseases (CED) of the National Institute for Communicable Diseases (NICD) provides reference microbiology testing, surveillance, epidemiological, and technical support to the South African National Department of Health's response to enteric diseases. The NICD, a division of the National Health Laboratory Service (NHLS), participates in national laboratory-based surveillance for organisms of public health importance, including *Salmonella* spp, through the NICD GERMS-SA surveillance platform.[13] Following identification of *Salmonella* Typhi at any public or private laboratory, isolates are submitted to the CED for further testing, including phenotypic characterisation, antimicrobial susceptibility testing, and whole genome sequencing (WGS). Laboratory request forms accompanying the isolates provide basic demographic data of varying completeness, including patient age, place of residence, referring health facility, and date of specimen collection. Following WGS, all isolates are investigated using core-genome multilocus sequence typing (cgMLST) analysis to identify clusters of cases and complement epidemiological investigations of outbreaks. cgMLST includes the analysis of 3002 genes to assess genetic relatedness. The definition of a cluster is a group of *Salmonella* Typhi isolates that, on cgMLST analysis, differ from each other by ≤5 alleles, meaning that they are highly genetically related. Unfortunately, not all isolates are received, so cases with missing isolates cannot be definitively linked to or excluded from clusters. All laboratory-confirmed diagnoses from NHLS laboratories nationally are automatically downloaded to the Notifiable Medical Conditions (NMC) system, enabling audits for isolates not received. Similar processes for downloading private laboratory results are in progress.

Enteric fever is a category 1 NMC in South Africa, and notification is required within 24 hours based on clinical suspicion or laboratory confirmation, in keeping with standard case definitions. Standard guidelines for case investigation and management are available.[8]

Results

Following the outbreak in Delmas in 2005, the number of enteric fever cases in South Africa remained stable, with less than 150 cases per year (an average of 102 cases annually) until 2021 (Figure 1).

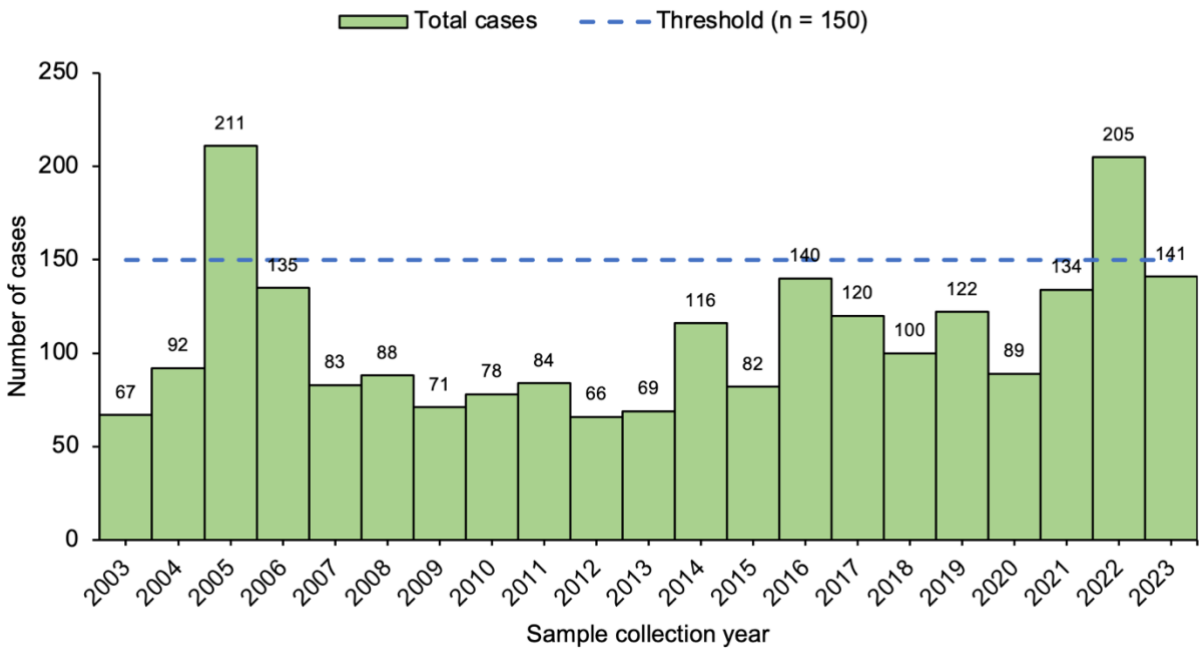

Figure 1. Laboratory-confirmed enteric fever cases by year, South Africa, 1 January 2003 to 31 December 2023.

From 2020 through 2023, the public sector reported the majority of cases (495/569, 87%). A diagnosis of 80% (456/569) was on blood culture and 12% (70/569) on stool culture. *Salmonella* Typhi accounted for 98% (558/569) of the total cases, while *S.* Paratyphi accounted for 2% (11/569). The age groups most commonly affected were 15-49 years (50%, 274/547), followed by persons aged below 15 years (42%, 232/547) followed by those of 50-64 years (6%, 33/547). Males accounted for 62% (345/558) of the cases. Isolates received were for 89% (79/89) of the cases in 2020, 95% (127/134) of cases in 2021, 88% (180/205) of cases in 2022, and 87% (123/141) of cases in 2023.

Reference laboratory antimicrobial susceptibility testing includes ciprofloxacin, azithromycin, chloramphenicol, and imipenem. Data from 2003 to date show a steady decrease in susceptibility to chloramphenicol, a former first-line antibiotic for treating typhoid fever, from 97% in 2005 to 16% in 2021. Susceptibility to ciprofloxacin has fluctuated from 94% in 2003, 73% in 2012 and 2019, to 88% in 2023. All isolates tested to date have been susceptible to imipenem, and susceptibility to azithromycin is consistently above 98% (Figure 2). Currently, recommended as the treatment of choice for uncomplicated enteric fever is ciprofloxacin, but ongoing monitoring of susceptibility is essential.

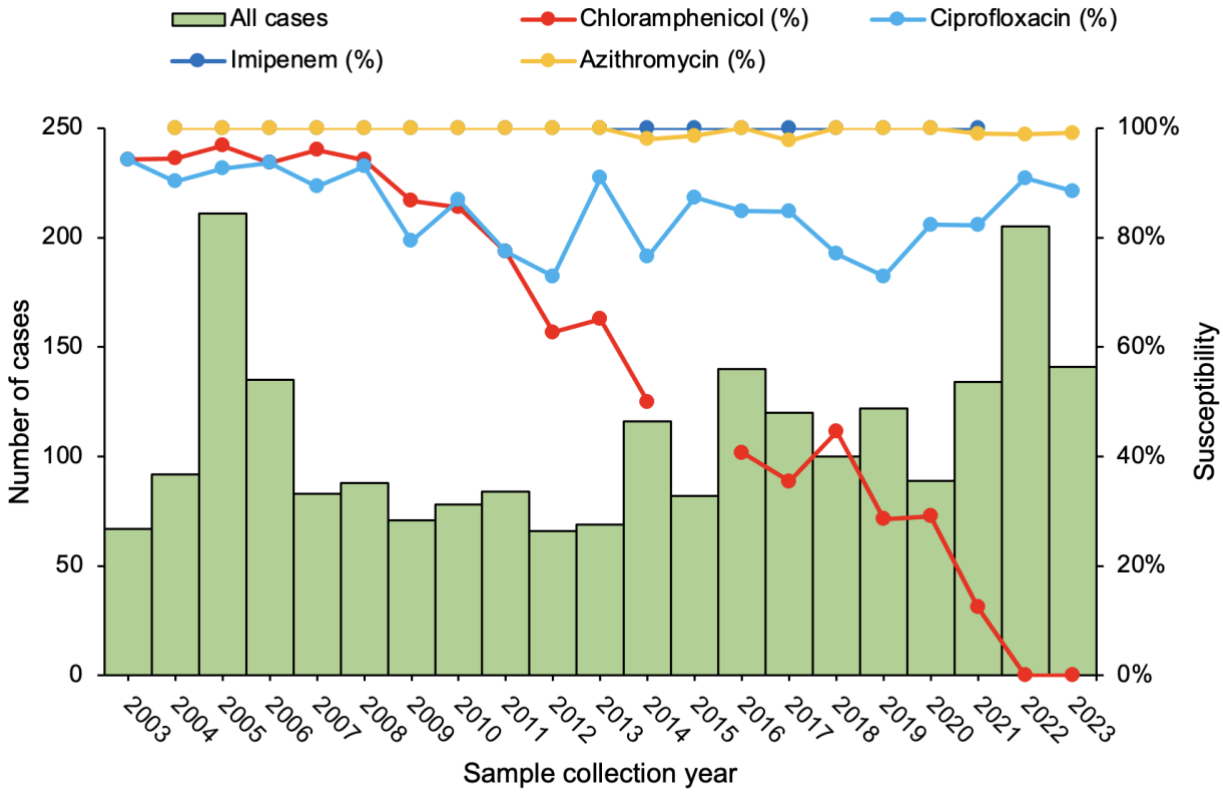

Figure 2. Trends in antimicrobial susceptibility of *Salmonella* Typhi isolates to ciprofloxacin, chloramphenicol, azithromycin, and imipenem, South Africa, 2003 – 2023.

Enteric fever cases by province, 2020-2023

From 2009 to 2019, Gauteng Province usually reported the most cases per year, followed by the Western Cape, Mpumalanga, and KwaZulu-Natal provinces (Figure 3; Table 1).

Table 1. Enteric fever cases by province and year, South Africa, January 2020 – December 2023.

Province	2020	2021	2022	2023	Total
Gauteng	27	39	103	73	242
Western Cape	36	52	40	32	160
North West	3	16	27	7	53
KwaZulu-Natal	7	8	12	12	39
Eastern Cape	5	6	4	8	23
Mpumalanga	3	10	5	4	22
Free State	3	3	7	3	16
Limpopo	5		7		12
Northern Cape				2	2
Total	**89**	**134**	**205**	**141**	**569**

During 2020 and 2021, the total number of enteric fever cases across the country (89 cases in 2020 and 134 cases in 2021) was similar to previous years. There was, however, an increase in the number of cases reported from the Western Cape and North West provinces in 2021, with a concurrent

decrease in the number of cases reported from Gauteng Province (Figure 3; Table 1). In 2022, the number of laboratory-confirmed enteric fever cases increased dramatically, with 205 cases reported across eight provinces. The number of cases from Gauteng Province increased notably, accounting for half of the cases (50%, 103/205), followed by the Western Cape (20%, 40/205) and North West (13%, 27/205) provinces (Figure 3). In 2023, 141 cases were reported from eight provinces, with Gauteng Province accounting for the most (52%, 73/141), followed by the Western Cape (23%, 32/141) and KwaZulu-Natal (9%, 12/141) provinces.

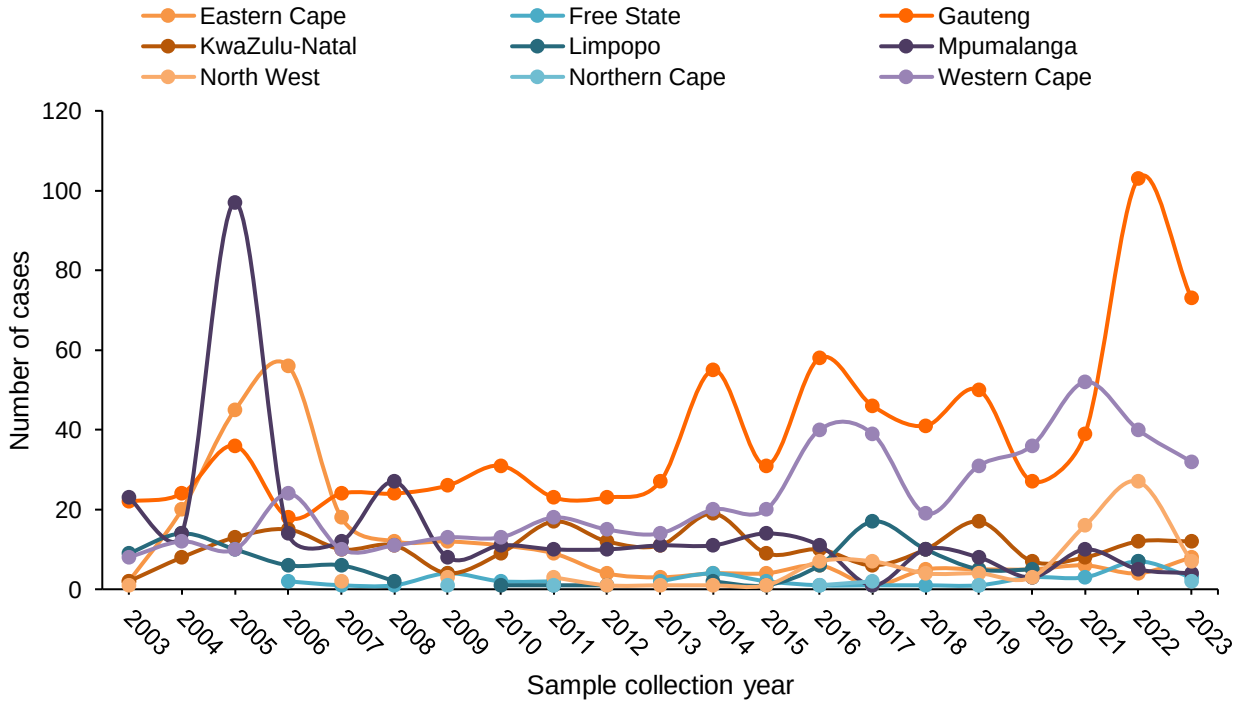

Figure 3. Enteric fever cases by province, South Africa, 1 January 2003 – 31 December 2023.

For the Western Cape Province, the increase in cases for 2021 was attributable to increased numbers of cases in only three districts (City of Cape Town Metro, Cape Winelands, and Garden Route), and in the North West Province, the increase in 2021/2022 was solely due to cases in a single district (Dr Kenneth Kaunda District). For Gauteng Province, the increase in cases in 2022/2023 affected all districts, with the most cases coming from the City of Johannesburg, followed by the City of Tshwane and West Rand districts.

Clusters of enteric fever cases by province, 2020-2023

Specific clusters (outbreaks), as defined by core-genome multilocus sequence typing (cgMLST) analysis of WGS data, drove the increase in cases in the Western Cape and North West provinces since 2020. The first identified case in all clusters occurred in 2020. Similarly, there were several enteric fever clusters in Gauteng Province, as shown using cgMLST analysis (Figure 4).

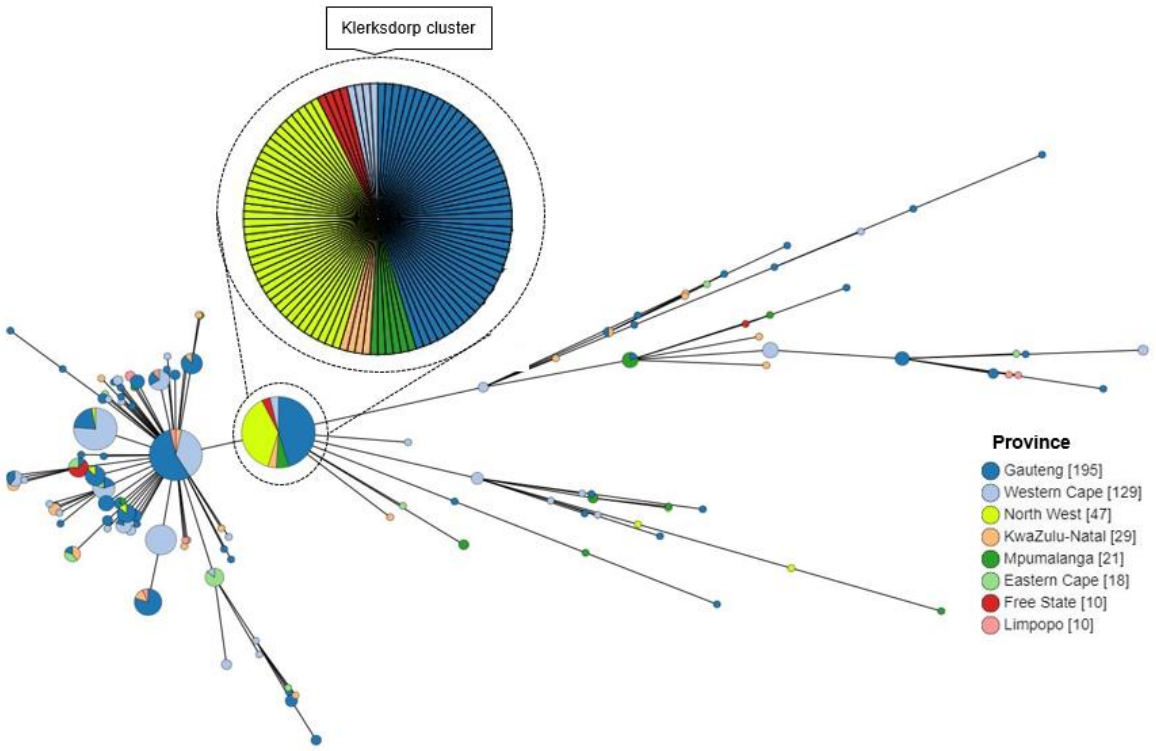

Figure 4. Minimum spanning tree drawn using cgMLST data from *Salmonella* Typhi isolates sourced from South Africa, 2020–2023. The circular nodes represent isolate(s). Isolates showing ≤5 allelic differences are collapsed together into a single circular node. The larger the circular node, the more isolates that are reflected.

Enteric fever clusters in the Western Cape Province

Western Cape Province reported its highest number of annual cases in 2021, most of which were attributed to three separate clusters, designated the Cape Winelands (n = 11), Garden Route (n = 15) and City of Cape Town (n = 23) clusters.[14] The Winelands cluster comprised 11 cases, identified from October 2020 through May 2021. The majority of case patients (8/11; 73%) were 15 years of age or younger, and males predominated (8/11; 73%). The Garden Route cluster comprised 15 cases. The first case occurred in August 2020, followed by an 8-month hiatus, after which there were 14 cases from April 2021 through February 2022. The majority of case patients (13/15; 87%) were 15 years of age or younger, and males predominated (10/15; 67%). The City of Cape Town cluster comprised 23 cases. The first case occurred in July 2020, after which there were 22 cases from October 2020 through to September 2022. Among case patients, males predominated (14/23; 61%), and the age of patients ranged from 5 to 54 years (median age of 24 years), with eight cases (35%; 8/23) aged 15 years or younger. Since February 2022, no new cases belonging to any of the three clusters have been reported, suggesting that these clusters are no longer active.

Enteric fever clusters in the North West Province

North West Province reported the highest number of annual cases on record in 2022 (n = 27). Analysis

of the *Salmonella* Typhi isolates using cgMLST showed that the majority of isolates were part of a highly genetically related cluster designated the Klerksdorp cluster.[15] The first case of enteric fever caused by the Klerksdorp strain occurred in November 2020. By 31 December 2023, there were 92 cases belonging to the Klerksdorp cluster strain in six different provinces. Cases belonging to the Klerksdorp cluster were identified in Gauteng (n = 42), North West (n = 37), Mpumalanga (n = 6), KwaZulu-Natal (n = 3), Western Cape (n=2) and Free State (n=2) provinces. The commonest age group affected was 15–49 years (61%, 54/89) and males predominated (69%, 63/91; Figure 5). The last case identified in the North West Province occurred in February 2023, and cases identified from October 2022 to date are mostly from Gauteng Province. The outbreak was still active at the time of this writing.

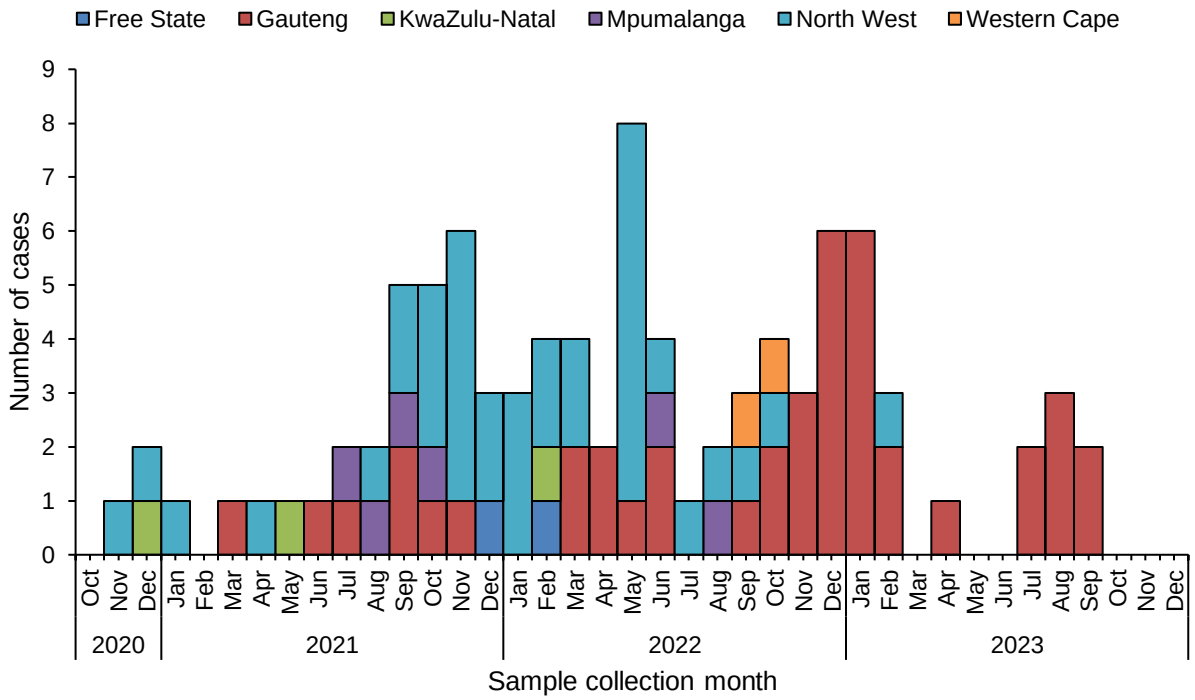

Figure 5. Number of laboratory-confirmed enteric fever cases in the Klerksdorp cluster by month of sample collection and province of residence, 1 November 2020–31 December 2023, South Africa (n = 92).

Enteric fever clusters in Gauteng Province

Gauteng Province accounted for over 50% of the cases reported nationally in 2022 and 2023. In 2022, most cases were from the City of Tshwane Metro, but in 2023, the majority of cases were from the West Rand District. On cgMLST analysis of WGS data, two closely related but distinct slow-growing clusters occurred in Gauteng Province. The first Gauteng Province cluster consisted of 32 cases, detected from January 2020 through October 2022. Most cases in this cluster were reported from the City of Tshwane Metro (78%, 25/32), with half (55%, 17/31) of the cases aged ≤15 years and males comprising 60% (18/30). The second Gauteng Province cluster consists of 12 cases detected from June 2020 through April 2022. Unlike the clusters in the Western Cape and North West provinces, the cases in this cluster were not localised to a single district. A case diagnosed in Rustenburg, North West Province, is linked to this cluster. The cases spanned a range of age groups between 8 and 39 years, with a median age of 26 years. Half were male. No new cases belonging to either cluster have occurred since October

2022 and April 2022, respectively.

By 31 December 2023, 42 cases belonging to the Klerksdorp cluster strain occurred in Gauteng Province, predominantly from the West Rand District (52%, 22/42) that borders the North West's Dr Kenneth Kaunda District. The majority were aged between 15–49 years (63%, 25/40) and 76% (31/41) were male.

Discussion

The relevant provincial and district departments of health were aware of the above-mentioned clusters, which led to outbreak investigations. To date, no confirmed source(s) of infection were identified for the Gauteng or Western Cape clusters.[14] Other studies have reported similar challenges in identifying the sources of strains.[16, 17] Despite this, public health responses and outbreak investigations can also serve to raise awareness among healthcare workers and communities and provide opportunities for health education.

On epidemiological investigation, a subset of the early Klerksdorp cluster cases was associated with consumption of contaminated water in illicit gold mines in the City of Matlosana.[15] However, different concurrent patterns of transmission were likely occurring in the Klerksdorp cluster, including the initial probable ongoing exposure of miners working underground through persistent contamination of underground source(s) of drinking water and/or food by acutely infected persons or asymptomatic carriers of *Salmonella* Typhi. There was likely also transmission from infected persons to household contacts, possibly leading to community transmission. Infected persons or household contacts may then seed the Klerksdorp cluster strain to other provinces through travel.

Contamination of municipal water was unlikely to be the source of infection in any of these clusters, based on the demographics of the cases (including their age profiles, places of residence, source(s) of drinking water and access, to improved sanitation) and, in particular, the scale of the clusters and the slow accumulation of cases over several months. It is likely that unrecognised cases and carriers who serve as reservoirs of infection contribute to ongoing transmission within communities, making it challenging to investigate and identify definite sources(s) of infection.

There were several limitations to this study. Although enteric fever is a notifiable medical condition in South Africa, reported cases significantly underrepresent the true number of cases. The likelihood of enteric fever case diagnoses and notifications depends on many factors, including the severity of illness, health-seeking behaviour, health-worker awareness, and testing practices, as well as laboratory capacity and availability. Furthermore, WGS data is only available on isolates submitted by diagnostic laboratories to the reference laboratory at the CED, NICD/NHLS.

Owing to technological advances and decreasing costs, many reference laboratories in public health institutions globally have transitioned to WGS as the primary method for assessing relatedness of

bacterial isolates for surveillance activities, cluster searches and outbreak investigations.[18, 19] The implementation of routine WGS analyses of all outbreak-prone enteric bacterial pathogens (including *Salmonella* species) into a laboratory-based surveillance system[20] has enabled detection of clusters indicative of possible outbreaks, facilitating targeted epidemiological investigations. In addition, information on antimicrobial susceptibility and molecular epidemiology of bacterial infections obtained through laboratory surveillance can also be used to inform decisions on antimicrobial treatment and vaccine interventions.[21]

Conclusion

This report underlines the importance of ongoing surveillance of enteric fever in South Africa and demonstrates the value of routine WGS of isolates to detect clusters and guide epidemiological investigation. The ongoing challenge of identifying the source(s) of infection in some provinces attests to the complex epidemiology and range of transmission pathways for this pathogen.

Recommendations

Raising awareness of enteric fever among healthcare workers nationally is critical for the detection and appropriate treatment of enteric fever cases. It is essential that all cases are followed up to ensure clearance of the organism and to screen household/close contacts for *Salmonella* Typhi. There is a need to identify chronic carriers and manage them appropriately to prevent ongoing transmission. The national and provincial Departments of Health should provide ongoing education to healthcare workers.

Recommendations for diagnosis, management, and public health response to enteric fever, as well as the enteric fever case investigation form, are available on the NICD website.

We recommend that healthcare workers provide ongoing health education in communities and raise awareness of general preventative measures for the public, including:

- Hand hygiene. Wash hands with soap and safe water before eating or preparing food, and after using the toilet or changing a baby's nappy.
- Food safety practices. Follow the World Health Organization's five keys to safer food: keep clean; separate raw and cooked food; cook food thoroughly; keep food at safe temperatures; use safe water and raw materials.[22]
- Using safe water. If people are concerned about the quality of water they use for drinking and cooking, then it is recommended that they treat the water first by boiling it, i.e., place water in a clean container and bring to a boil for 1 minute, or treat it with household bleach (add 1 teaspoon of household bleach containing 5% chlorine to 20–25 litres of water, mix well, and leave it to stand for at least 30 minutes before use).
- Provision of safe water. Provincial Departments of Health and other stakeholders must continue to advocate for the provision of safe water and improved sanitation for all South Africans, as well as the implementation of food safety regulations.

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Ethical considerations

Ethical approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (protocol reference number M1 809 107) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Kim CL, Cruz Espinoza LM, Vannice KS, Tadesse BT, Owusu-Dabo E, Rakotozandrindrainy R, et al. The burden of typhoid fever in sub-Saharan Africa: a perspective. *Research and Reports in Tropical Medicine*. 2022:1-9.

2. Stanaway JD, Reiner RC, Blacker BF, Goldberg EM, Khalil IA, Troeger CE, et al. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Infectious Diseases*. 2019; 19(4):369-81.

3. Marks F, von Kalckreuth V, Aaby P, Adu-Sarkodie Y, El Tayeb MA, Ali M, et al. Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicentre population-based surveillance study. *The Lancet Global Health*. 2017; 5(3):e310-e23.

4. Keddy KH, Smith AM, Sooka A, Tau NP, Ngomane HM, Radhakrishnan A, et al. The burden of typhoid fever in South Africa: the potential impact of selected interventions. *The American Journal of Tropical Medicine and Hygiene*. 2018; 99(3 Suppl):55.

5. Keddy KH, Sooka A, Ismail H, Smith AM, Weber I, Letsoalo M, et al. Molecular epidemiological investigation of a typhoid fever outbreak in South Africa, 2005: the relationship to a previous epidemic in 1993. *Epidemiology & Infection*. 2011; 139(8):1239-45.

6. WHO [Internet]. Typhoid vaccines: WHO position paper - March 2018. 2018 [updated 2018 March 30; cited 2024 February 8]. Available from: https://www.who.int/publications/i/item/whio-wer9313.

7. Gibani MM, Britto C, Pollard AJ. Typhoid and paratyphoid fever: a call to action. *Current Opinion in Infectious Diseases*. 2018; 31(5):440.

8. NICD [Internet]. Enteric fever (typhoid and paratyphoid fever): Recommendations for diagnosis, management and public health response. 2022 [updated 2022; cited 2024 February 8]. Available from: https://www.nicd.ac.za/wp-content/uploads/2022/06/Enteric-Fever_NICD-recommendations_June-2022_final.pdf.

9. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al. Extensively drug-resistant (XDR) typhoid: evolution, prevention, and its management. *BioMed Research International*. 2020; 2020

10. Posen HJ, Wong W, Farrar DS, Campigotto A, Chan T, Barker KR, et al. Travel-associated extensively drug-resistant typhoid fever: a case series to inform management in non-endemic regions. *Journal of Travel Medicine*. 2023; 30(1):taac086.

11. Patel PD, Patel P, Liang Y, Meiring JE, Misiri T, Mwakiseghile F, et al. Safety and efficacy of a typhoid conjugate vaccine in Malawian children. *New England Journal of Medicine*. 2021; 385(12):1104-15.

12. Thilliez G, Mashe T, Chaibva BV, Robertson V, Bawn M, Tarupiwa A, et al. Population structure of *Salmonella enterica* Typhi in Harare, Zimbabwe (2012–19) before typhoid conjugate vaccine roll-out: a genomic epidemiology study. *The Lancet Microbe*. 2023; 4(12):e1005-e14.

13. NICD [Internet]. GERMS-SA Annual Surveillance Review. 2021 [updated 2021; cited 2024 February 8]. Available from: https://www.nicd.ac.za/wp-content/uploads/2022/12/2021-GERMS-SA-Annual-Review.pdf.

14. Smith AM, Erasmus LK, Tau NP, Smouse SL, Ngomane HM, Disenyeng B, et al. Enteric fever cluster identification in South Africa using genomic surveillance of *Salmonella enterica* serovar Typhi. *Microbial Genomics*. 2023; 9(6):001044.

15. Sekwadi P, Smith AM, Maruma W, Mongologa G, Tsele G, Ngomane M, et al. A prolonged outbreak of enteric fever associated with illegal miners in the City of Matlosana, South Africa, November 2020 – September 2022. *Open Forum Infectious Diseases.* 2024; doi:10.1093/ofid/ofae118

16. Purighalla S, Esakimuthu S, Reddy M, Seth T, Patil SD, Varghese GK, et al. Investigation into a community outbreak of *Salmonella* Typhi in Bengaluru, India. *The Indian Journal of Medical Research*. 2017; 146(Suppl 1):S15.

17. Tiba-Casas MR, Sacchi CT, Gonçalves CR, Almeida EA, Soares FB, de Jesus Bertani AM, et al. Molecular analysis of clonally related *Salmonella Typhi* recovered from epidemiologically unrelated cases of typhoid fever, Brazil. *International Journal of Infectious Diseases*. 2019; 81:191-5.

18. Chattaway MA, Dallman TJ, Larkin L, Nair S, McCormick J, Mikhail A, et al. The transformation of reference microbiology methods and surveillance for Salmonella with the use of whole genome sequencing in England and Wales. *Frontiers in Public Health*. 2019; 7:317.

19. Gwinn M, MacCannell DR, Khabbaz RF. Integrating advanced molecular technologies into public health. *Journal of Clinical Microbiology*. 2017; 55(3):703-14.

20. Smith AM, Tau NP, Ngomane HM, Sekwadi P, Ramalwa N, Moodley K, et al. Whole-genome sequencing to investigate two concurrent outbreaks of salmonella enteritidis in South Africa, 2018. *Journal of Medical Microbiology*. 2020; 69(11):1303-7.

21. Smith AM. Review of molecular subtyping methodologies used to investigate outbreaks due to multidrug-resistant enteric bacterial pathogens in sub-Saharan Africa. *African Journal of Laboratory Medicine*. 2019; 8(1):1-10.

22. WHO [Internet]. Five keys to safer food manual. 2006 [updated 2006 May 16; cited 2024 February 8]. Available from: https://www.who.int/publications/i/item/9789241594639.