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Salmonella Typhi From Blood Cultures in the Democratic Republic of the Congo: A 10-Year Surveillance

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Background. This study gives an overview of a decade (2007–2017) of hospital-based *Salmonella* Typhi bloodstream infection (BSI) surveillance in the Democratic Republic of the Congo (DRC), at 4 main sampling sites.

Methods. Blood cultures were sampled in hospital-admitted patients with suspected BSI, according to standardized clinical indications. The results of the surveillance period 2015–2017 were compiled with those of previous surveillance periods (2007–2010 and 2011–2014). Whole genome sequencing of isolates with decreased ciprofloxacin susceptibility (DCS) was performed.

Results. *Salmonella* Typhi was isolated in 1.4% (531/37 388) and 10.3% (531/5177) of suspected and culture-confirmed BSI episodes, respectively. *Salmonella* Typhi ranked first among the BSI pathogens in adults (n = 220), but was mostly (n = 301 [56.7%]) isolated from children, of which 72.1% (217/301) and 31.6% (95/301) were <10 years and <5 years old, respectively. Multidrug resistance (MDR), DCS, and combined MDR/DCS were found in 38.3% (n = 180), 24.5% (n = 115), and 11.9% (n = 56) of 470 first isolates, respectively. MDR and DCS rates had increased since 2007, but remained stable during 2015–2017 with no geographical clustering at the province level. Most (91/93 [97.8%]) DCS isolates sequenced belonged to Genotyphi genotype 2.5.1, and gyr S83 was the most frequent DCS mutation (76/93 [81.7%]). Infections occurred perennially, but increased during the rainy season.

Conclusions. *Salmonella* Typhi was a frequent cause of BSI in adults and children in DRC, with high rates of antibiotic resistance. Sustainable surveillance and implementation of vaccination are compelling.

Keywords. typhoid fever; *Salmonella* Typhi; Democratic Republic of the Congo; surveillance.

Typhoid fever is a poverty-related disease with a high disease burden in low- and middle-income countries [1, 2]. Its causative organism—*Salmonella enterica* subspecies *enterica* serovar Typhi—has been listed on the World Health Organization (WHO) priority list of antibiotic-resistant bacteria [3]. Recent studies have confirmed high incidence rates of typhoid fever in sub-Saharan Africa, which have incited vaccination efforts [4–6]. Central Africa has been estimated to face the worldwide highest incidence of typhoid fever [7]. As to the Democratic Republic of the Congo (DRC), the country's poor infrastructure and health services (Supplementary Table 1) make it vulnerable to typhoid fever, and clinical and epidemiological observations have confirmed its frequency and impact [8, 9]. In the aftermath of the typhoid fever peritonitis outbreak in 2005 [8], the National Institute of Biomedical Research (INRB) in Kinshasa

started, in collaboration with the Institute of Tropical Medicine (ITM) in Antwerp, Belgium, a microbiological surveillance in sentinel hospitals around the country with the initial objectives to investigate and confirm epidemic alerts of typhoid fever and to assess the antibiotic resistance of *Salmonella* Typhi [10, 11].

The present study reports, for the period 2007–2017 in DRC, the cumulative temporal, spatial, and age distributions of *Salmonella* Typhi blood culture isolates, their antimicrobial resistance patterns, and their genetic relatedness to the global *Salmonella* Typhi population.

METHODS

Microbiology Surveillance Network in DRC

Blood cultures were collected and processed free of charge in healthcare facilities in the capital, Kinshasa, and the Bas-Congo province (referral hospital of Kisantu) and later extended to sentinel hospitals in the Oriental Province (University Hospital Kisangani with affiliated hospitals and health centers) and the Equateur Province (referral hospital of Bwamanda). Over the years, this network was extended with other partners, and blood cultures were also added to the diagnostic tools of the outbreak investigation teams of INRB in collaboration with the

Ministry of Health. Indications of blood culture sampling were, outside the neonatal period, a body temperature of ≥38.0°C or ≤35.5°C (axillary) or history of fever during the last 48 hours and/or (1) signs of severity such as hypotension, confusion, or increased respiratory rate; (2) suspicion of severe localized infections (pneumonia, meningitis, complicated urinary tract infection, osteomyelitis and arthritis, severe skin and soft tissue infections, gynecological and abdominal infections/peritonitis); or (3) suspicion of other severe infection: sepsis, typhoid fever, and severe malaria. Basic demographic and clinical data were recorded. In adults, blood cultures consisted of 2 × 10 mL of blood sampled in aerobic BACT/ALERT bottles (bioMérieux, Marcy-L'Etoile, France); for children (defined as ≤14 years old), 1–4 mL was sampled in pediatric BACT/ALERT bottles. Grown blood cultures were worked up for identification according to conventional biochemical methods and serotyping (for antibiotic susceptibility testing, see below). For reasons of integration in clinical care and capacity building, blood cultures were preferentially worked up in the participating referral hospitals. However, when no competent laboratory services were available, samples were transported to INRB for workup. Isolates were stored for in-depth reference testing, and the results of the blood culture isolates and their resistance patterns were registered. Coagulase-negative *Staphylococcus*, *Corynebacterium* species, *Micrococcus* species, *Cutibacterium* species, and *Lactobacillus* species were considered as environmental or skin contaminants; the other bacteria were classified as pathogens. The term "suspected bloodstream infection (BSI) episode" was used to indicate all blood cultures in a single patient sampled within a 2-week period according to the indications mentioned above. A BSI episode was considered as culture confirmed when a pathogen was isolated in at least 1 of the bottles. Supplementary Document 1 provides a detailed overview of the workflow, criteria, and definitions used in the sampling, and the processing and reporting of the blood cultures.

Design of the Present Study

The blood culture isolates from the period January 2015–October 2017 were retrieved from storage at –80°C and batch-tested for identification and antibiotic susceptibility. To allow a complete 10-year retrospective view, a comprehensive database was compiled using the most recent data from 2015–2017 and 2 databases used for 2 previous *Salmonella* Typhi reports, comprising the periods April 2007–January 2011 (further referred to as "2007–2010") [10] and January 2011–December 2014 (referred to as "2010–2014"), respectively [11]. The resulting database contained all BSI episodes and isolates obtained from a 10-year period between April 2007 and October 2017. Part of the data were presented in the 2 aforementioned survey reports [10, 11], as well as in reports of outbreak publications [10–15]. In addition to the methods described in Supplementary Box 1, detailed data of rainfall were retrieved for the entire study

period, and additional molecular analysis of the DCS-associated factors and genetic typing of the isolates was performed (see "Molecular Analysis" below).

Antibiotic Susceptibility Testing

Antibiotic susceptibility testing was carried out on the 2015–2017 isolates as described in Supplementary Document 1 with slight modifications. In brief, disk diffusion was performed with the exception of minimum inhibitory concentration (MIC) values testing for ciprofloxacin and azithromycin, for which the E-test macromethod (bioMérieux) was used [16]. Intermediate-susceptible isolates are grouped together with the resistant ones [17]. Where applicable, the databases of previous reports [10, 11] were reinterpreted according to the current guidelines of the Clinical and Laboratory Standards Institute (document M100-S28) [16]. Multidrug resistance (MDR) refers to the combined resistance to amoxicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, and decreased ciprofloxacin susceptibility (DCS) refers to ciprofloxacin MIC values >0.06 mg/L and <1 mg/L. The term "full ciprofloxacin resistance" was reserved for MIC values ≥1 mg/mL [1, 16] and resistance to azithromycin was defined at MIC values >16 mg/L [16].

Geographic Data and Data About Rainfall

In 2015, the 11 DRC provinces were split into the actual 26 provinces; for convenience of data display and comparison with previous publications, the former provinces were still used as the reference.

Satellite-based remote sensing techniques (Tropical Rainfall Measuring Mission [TRMM] data used for TRMM multisatellite precipitation analysis, Near Real-Time product version 7) were used to estimate the average accumulated monthly rainfall in millimeters per month [18]. Datasets can be accessed at https://disc-beta.gsfc.nasa.gov/. Calculations were performed using the R open source software (release 3.3.2) and linked to the actual provinces based on spatial data from the Royal Museum for Central Africa (Tervuren, Belgium). To obtain the monthly rainfall for the former provinces Equateur and Orientale, the average of the involved actual provinces was used.

Molecular Analysis

DNA was extracted from the *Salmonella* Typhi isolates showing DCS and listed in Supplementary Table 2, using the Gentra PureGene Yeast/Bact Kit (Qiagen, Hilden, Germany) following the manufacturer's guidelines, and whole genome sequencing was performed on an Illumina HiSeq platform (Illumina, San Diego, California). The sequencing data generated in this study (89 isolates) are available at the European Nucleotide Archive under the study accession number ERP109963. Four *Salmonella* Typhi had been sequenced in previous studies and the sequencing data are available under the sample accession numbers ERR349525, ERR352599, ERR357591 and PRJEB19771 [12, 19]. Molecular resistance mechanisms were determined from the raw Illumina sequencing data using ARIBA

version 2.11.1 [20] with the Comprehensive Antibiotic Resistance Database version 2.0.2 [21]. Both known and novel variants of *gyr* and *par* genes conferring DCS were determined. Genome assemblies, constructed using de novo assembly [22], were used to determine the *Salmonella* Typhi Genotyphi genotype. Hereto, the Genotyphi implementation [23] or Pathogenwatch (https://pathogen.watch; Wellcome Trust Sanger Institute, Hinxton, Cambridge, United Kingdom) was used.

Statistical Analysis

Unless otherwise stated, analysis and reporting were done for the first isolate per BSI episode and for those isolates that were available for reference testing at INRB/ITM. Statistical analysis was done with Stata software, version 12 (Stata Corp, College Station, Texas). Proportions were tested for significance using the χ^2 test and differences in age distribution by the Wilcoxon-Mann-Whitney nonparametric test and the median test.

Ethical Considerations

Ethical approval for the microbiological surveillance study was granted by the Institutional Review Board of ITM, the Ethics Committee of Antwerp University, and the Ministry of Health of the DRC.

RESULTS

Overview of Sampling

For the entire period (2007–2017), blood cultures sampled in 37 388 BSI episodes yielded 13.9% pathogens; for the period 2015–2017, the corresponding data were 13 657 and 12.0% (Figure 1). Yields of pathogens over time and sampling site were mostly between 10.0% and 15.0%. The highest yield (24.3%, Equateur 2011–2014) was associated with an outbreak of non-Typhi *Salmonella* infection [13]. The overall contamination rate was 9.2%; for the period 2015–2017, it was 7.17% with the lowest and highest rates at the sampling site Kisantu Hospital (Bas-Congo, 6.2%) and the surveillance network in Kinshasa (16.4%), respectively. Figure 2 shows the provinces of DRC with the main sampling sites and total numbers of *Salmonella* Typhi and non-Typhi isolates.

Overall, 4 of 5 suspected BSI episodes occurred in children (80.6% among 36.643 episodes for which data about age and year of sampling were available). The proportion of BSI episodes in children increased over time from 60.5% (5684/9398) in 2007–2010 to 90.2% (12 188/13 519) in 2015–2017, mainly by higher numbers of children sampled but—to a lesser extent—also due to lower numbers of adults sampled (1331 in 2015–2017 vs 2045 and 3714 in 2011–2014 and 2007–2010, respectively).

Proportions of *Salmonella* Typhi Among Grown Blood Cultures

Overall, *Salmonella* Typhi accounted for 1.4% (531/37 388) and 10.3% (531/5177) of suspected and confirmed BSI, respectively (Figure 1). Among adults, *Salmonella* Typhi consistently ranked first among the pathogens recovered, representing 24.6% (110/447), 22.9% (67/293), and 24.3% (42/173) for the successive surveillance periods. Among the pathogens isolated

| Total blood cultures sampled | n=42.218 |
| Total suspected bloodstream infection (BSI) episodes | n=37.388 |

No growth in 32.762/42.218 samples (77.6%)

Contaminants in 3895/42.218 samples (9.2%)
Coagulase-negative *Staphylococcus* n = 2712
Bacillus spp. n = 1064
Other n = 121

All pathogens
grown in 5561/42.218 samples (13.2%)
grown in 5177/37.388 BSI episodes (13.9%)
from which 93 polymicrobial (1.8% of BSI episodes)

103 confirmed BSI episodes where no age available

Pathogens in children (≤14y) n = 4160 (80.4%)

1. *Salmonella* non-Typhi n = 1931 (46.4%)
2. *Klebsiella* spp. n = 431 (10.4%)
3. *Enterobacter* spp. n = 330 (7.9%)
4. *Salmonella* Typhi n = 301 (7.2%)
5. *Staphylococcus aureus* n =262 (6.3%)

Pathogens in adults n = 914 (17.7%)

1. *Salmonella* Typhi n = 220 (24.1%)
2. *Salmonella* non-Typhi n = 150 (16.4%)
3. *Escherichia coli* n = 148 (16.2%)
4. *Klebsiella* spp. n = 115 (12.6%)
5. *Staphylococcus aureus* n = 81 (8.9%)

	BSI episodes	% of all pathogens	% of all suspected BSI episodes	available for analysis (% of BSI episodes)
Salmonella Typhi	531	10.3%	1.4%	472 (88.9%)
Salmonella non-Typhi	2099	40.5%	5.6%	1951 (92.9%)
All *Salmonella*	2630	50.8%	7.0%	2423 (92.1%)

Figure 1. Breakdown of blood cultures sampled as part of the surveillance network, 2007–2017; unless otherwise stated, data are presented as first isolates per bloodstream infection episode (all blood cultures in a single patient within a 2-week period). In the top 5 of pathogens, the percentages represent the proportion of all pathogens in children or adults for whom information about age was available (n = 4160 and 914, respectively). Abbreviation: BSI, bloodstream infection.

Figure 2. Map of the Democratic Republic of the Congo, with its (former) provinces, the main participating sampling sites in the microbiological surveillance network (call-outs), and the total numbers of *Salmonella* Typhi and *Salmonella* non-Typhi isolates. Additional numbers of isolates were 11 and 0, respectively, in Kasai-Occidental, 9 and 1 in Bandundu, 3 and 2 in Kasai Oriental, and 0 and 2 in Maniema. The new provinces are identified by numbers: 1, Nord-Ubangi; 2, Sud-Ubangi; 3, Mongala; 4, Bas-Uele; 5, Haut-Uele; 6, Equateur; 7, Tshuapa; 8, Tshopo; 9, Ituri; 10, Nord-Kivu; 11, Mai-Ndombe; 12, Kasai; 13, Sankuru; 14, Maniema; 15, Sud-Kivu; 16, Kinshasa; 17, Kwilu; 18, Kasai-Central; 19, Kasai-Oriental; 20, Lomami; 21, Tanganyika; 22, Kongo-Central; 23, Kwango; 24, Lualaba; 25, Haut-Lomami; 26, Haut-Katanga.

from children, the proportion of *Salmonella* Typhi was lower—that is, 7.2% overall (Figure 1) and 11.4% (107/943), 7.1% (126/1774), and 4.7% (68/1442) for the successive surveillance periods. When subtracting neonates, the overall proportion of *Salmonella* Typhi among the pathogens increased to 7.8% (300/3831). *Salmonella* Typhi ranked third and second in frequency among pathogens isolated from children in Bas-Congo

and Equateur, respectively. Non-Typhi *Salmonella* ranked first at all but 1 (Kinshasa) sampling site.

Absolute numbers of *Salmonella* Typhi BSI were higher in children compared to adults. A total of 531 single isolates of *Salmonella* Typhi were obtained (301 [56.7%] from children vs 220 [41.4%] from adults; for 10 isolates no age was available [for details about age, see the next section]). Three recurrent BSI episodes were identified, occurring in children aged 12, 15, and 10 years old, respectively, with the recurrent episode occurring 3 weeks, 9 weeks, and 3 years after the initial BSI episode. A total of 472 (88.9%) of the isolates were available for further analysis (with missing isolates randomly distributed over time and sampling site). The numbers of *Salmonella* Typhi in adults showed little variation over time (Figure 3A), apart from small peaks in 2012 and 2015, which were randomly distributed over the sampling sites. The same observation was made for children; however, the rate of *Salmonella* Typhi vs non-Typhi *Salmonella* decreased sharply, in particular during the 2015–2017 surveillance period and mainly at the account of an increase of the non-Typhi *Salmonella* (Figure 3B).

Age and Sex of Patients With *Salmonella* Typhi

Figure 4 and Supplementary Figure 1 show the detailed age distribution. Absolute numbers of isolates in children were concentrated between 2 and 10 years of age and peaked around the age of 5. As a proportion of all isolates from BSI episodes, the highest rates were observed among children between 5 and 14 years old (19.9%–47.2%); 72.1% (217/301) and 31.6% (95/301) of *Salmonella* Typhi isolates were obtained in children <10 years and <5 years old, respectively, with 10 children <1 year old and the youngest 10 days old. The median age (interquartile range [IQR]) of patients with *Salmonella* Typhi BSI was 12 (IQR, 6–24) years, which was significantly higher than the corresponding data for the non-Typhi *Salmonella* (20 [IQR, 11–36] months) and all other BSI pathogens
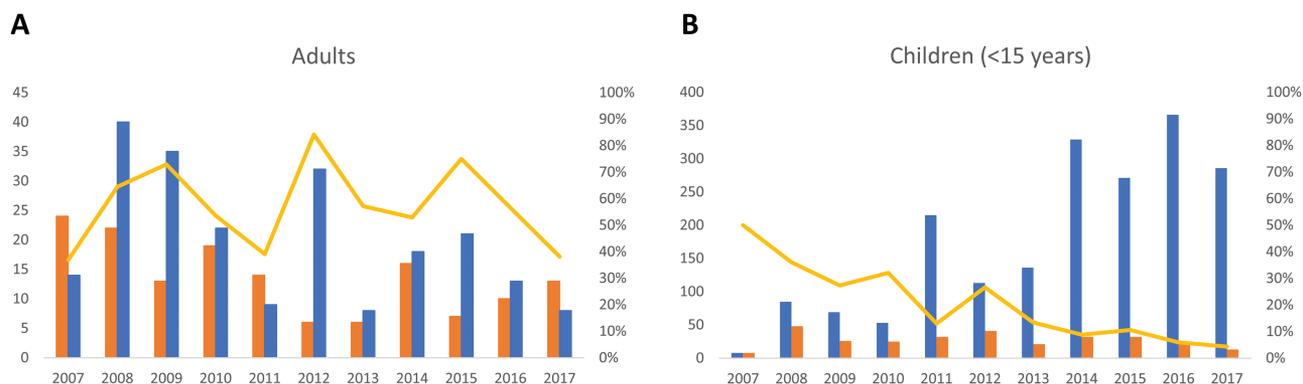
Figure 3. Over-time evolution of the frequency of *Salmonella* Typhi compared to non-Typhi *Salmonella* for adults (*A*) and children aged <15 years (*B*). The absolute numbers of *Salmonella* Typhi and non-Typhi *Salmonella* are shown by the blue and orange bars, respectively, and can be read on the left y-axis (note that the y-axis has a different scale for adults vs children). The yellow line represents the percentage of *Salmonella* Typhi vs all *Salmonella* isolates (Typhi and non-Typhi combined), reflected on the right y-axis.
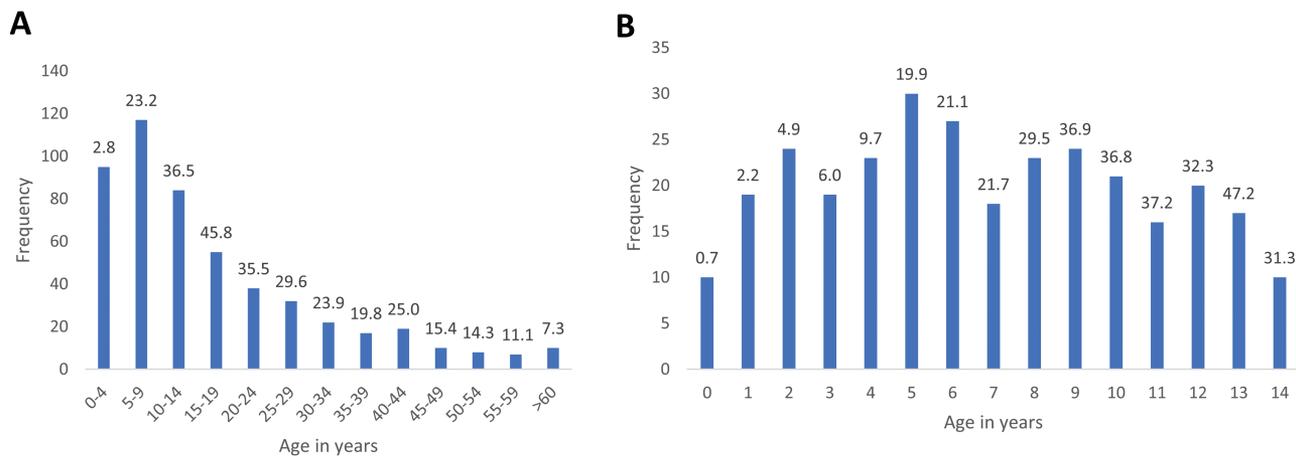
Figure 4. Distribution of *Salmonella* Typhi bloodstream infection episodes per age category (*A*) and per year of age for children (*B*), in absolute numbers (bars) and as a percentage of the total number of pathogens from patients with the same age (shown at top of bars). Data were generated for a total of 519 of 531 episodes for which data on age were recorded.

compiled (24 [IQR, 0–132] months) (*P* < .001). Median ages for *Salmonella* Typhi BSI were similar for the successive surveillance periods: 15 (IQR, 8–25), 10 (IQR, 5–21), and 10 (IQR, 5–21) years, respectively.

Seasonality and Rainfall

The rainy season of Kinshasa and Bas-Congo (south of the equator) lasted from October through May and from March through November for Equateur and Orientale (north of the equator), respectively, although for the latter the difference between the rainy and dry season was less pronounced (Figure 5). In all provinces, *Salmonella* Typhi BSI was more frequent at the beginning and during the rainy season. In contrast to the nonfluctuating background of all-cause BSI in Kinshasa, Orientale, and Equateur, the all-cause BSI in Bas-Congo followed a seasonal pattern comparable to that of *Salmonella* Typhi.

Antibiotic Resistance

As a percentage of *Salmonella* Typhi isolates for which antibiotic susceptibility was assessed, MDR was seen in 38.4% (n = 180), DCS in 24.5% (n = 115), and MDR combined with DCS in 11.9% (n = 56) of isolates, and azithromycin resistance was observed in 1 isolate (Table 1). One *Salmonella* Typhi isolate showing resistance to third-generation cephalosporins was found during an outbreak investigation in the province of Bandundu [12]. MDR rates over the successive surveillance periods were 39.9% (77/193), 36.9% (62/168), and 38.0% (41/108); corresponding DCS rates were 14.0% (27/193), 36.3% (61/168), and 25.0% (27/108), respectively. There was no apparent geographical concentration of MDR or DCS isolates. Overall, in almost half (204/422 [48.3%]) of the *Salmonella* Typhi BSI episodes, antibiotics had been given prior to admission (93/159 [58.5%], 71/153 [46.4%], and 40/110 [36.4%] for the successive

surveillance periods). No statistically significant increased rate of MDR was observed when prehospital antibiotics were given (2015–2017: 38.5% MDR with and 37.7% MDR without prehospital antibiotic use; *P* = .936, χ² test). There was a trend toward an increased rate of DCS if prehospital antibiotics had been given (2015–2017: 35.0% vs 18.6%; *P* = .054, χ² test).

Decreased Ciprofloxacin Susceptibility and Genotyphi Genotype

Figure 6A shows the ciprofloxacin MIC value distribution of the *Salmonella* Typhi isolates from the entire surveillance period. No full resistance was noted. A nonsynonymous mutation in the *gyrA* or *gyrB* genes was identified for all 93 confirmed DCS *Salmonella* Typhi isolates (Supplementary Table 2), with 1 isolate showing 2 nonsynonymous mutations in *gyrA*. A substitution of gyrA S83 was seen in 91.7% of isolates (n = 76, of which 72 were S83F and 4 were S83Y); another 15.1% had a substitution of D87 in gyrA (n = 14, of which 13 were D87G and 1 was D87Y) and 1.1% showed a novel gyrA A119E substitution. A substitution of gyrB E466D and S464Y was each observed in 1.1% (n = 1). Strikingly, the gyrA S83F substitution resulted in higher MIC values (clustering around 0.25 and 0.38 mg/L compared with the substitution at gyrA D87G, which clustered at 0.094 and 0.125 mg/L; Figure 6B). The majority (97.8 %) of the sequenced DCS isolates belonged to Genotyphi genotype 2.5.1, whereas 1.1% (n = 1) had genotype 4.3.1 and 1.1% (n = 1) had genotype 2.1, also known as lineage H58.

DISCUSSION

This study gives an overview of *Salmonella* Typhi BSI in the light of a decade of microbiological surveillance in DRC, a country where diagnostic microbiological facilities are almost nonexistent [24]. The embedment in the routine patient management in a low-resource setting faced the well-known technical,
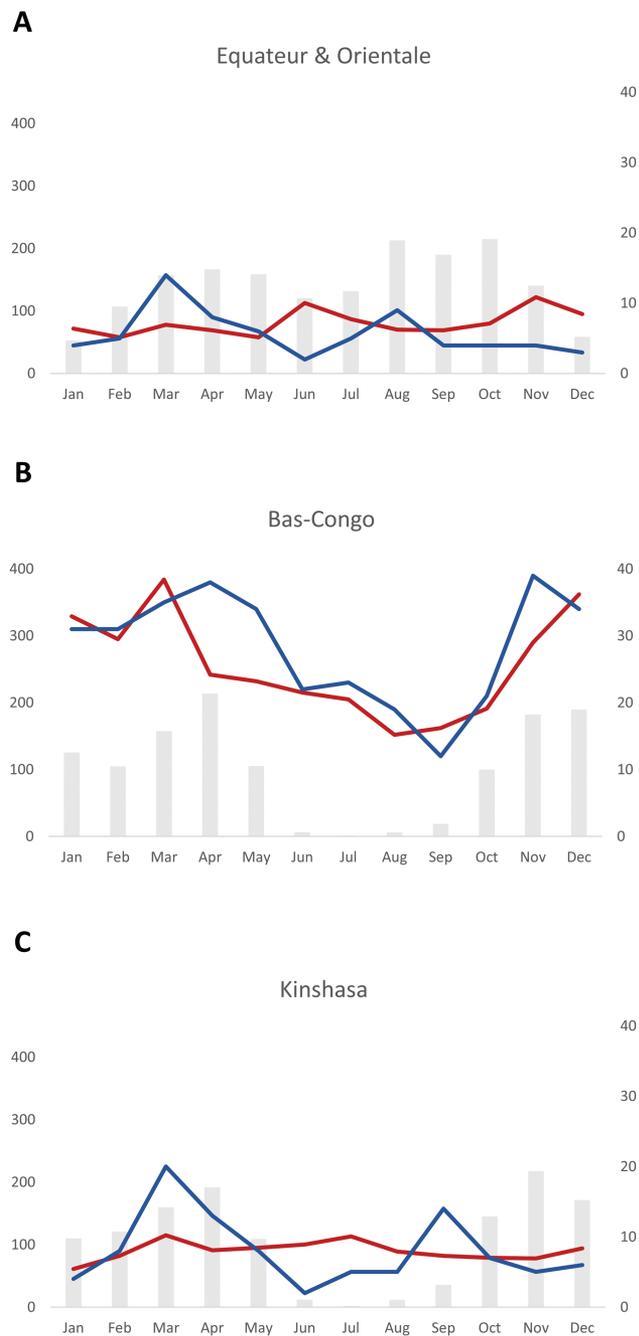
Figure 5. Relation between rainfall and frequency of *Salmonella* Typhi bloodstream infection in a rural area north (Orientale and Equateur, *A*) and south (Bas-Congo, *B*) of the equator, and an urban area (Kinshasa, *C*). The average rainfall for the 10-year surveillance period is displayed as gray bars and expressed in millimeters per month (left y-axis), the average numbers of *Salmonella* Typhi isolates (blue line), and bloodstream infection episodes caused by all pathogens (red line) per month, corresponding to the right y-axis.

logistical, and human resource problems [25, 26]. Furthermore, accessibility, local needs of patient care, and security concerns directed the selection of the healthcare facilities. Besides representativeness and coverage, the healthcare facility–based approach had other limitations. Most important, it was not

possible to calculate and monitor population-based incidence in the absence of solid demographic data (census, health utilization data) [4, 6]. Second, sampling and laboratory workup were done by local staff and may have accounted for higher rates of contaminants and more missing data compared to a research setting. Finally, the health facility–based approach was dependent on the health-seeking behavior and the referral itinerary of patients with a consequently low spatial resolution (presently limited to the health center or village level).

As to its strengths, the healthcare facility surveillance approach was free of charge for patients and integrated in clinical care. This allowed us to reach many patients in a clinical context and was a most cost-effective strategy to obtain a consistently large number of isolates—among them also those of other bacterial species. The INRB team managed to maintain the network over a long time period, with a high proportion of isolates available for reference testing. Despite a too high contamination rate (9%), the pathogen rate remained high and within the expected ranges over time and site.

Salmonella Typhi consistently ranked first as the cause of BSI in adults, indicative of its frequent occurrence of typhoid fever in the population, as laboratory-confirmed *Salmonella Typhi* in hospital admitted patients represent only a small fraction of all cases [27]. Despite the overrepresentation of children sampled, *Salmonella* Typhi accounted for 7.2% of BSIs in children, most of them in the first decade of life, comparable to recent observations in East and West Africa [5, 28]. The predominance of *Salmonella* Typhi in young children highlights the importance of identifying the most effective vaccination strategy. Since March 2018, the WHO has recommended the new typhoid conjugate vaccine for single-dose immunization of children from 6 months of age onward [29]. Although typhoid fever occurred perennially, there was a seasonal trend with a moderate increase in the rainy season as previously described in other African countries [30, 31]. The contamination of surface and drinking water is the most plausible explanation, although the component of malnutrition, which in DRC occurs mainly during the rainy season [32], might play a role.

MDR and DCS were found in approximately 1 of 3 and 4 isolates, respectively; 1 in 8 isolates showed combined DCS and MDR. After an increase of DCS in 2011–2014 compared to 2007–2010, the rate of DCS slightly decreased (24.6%). The rate of MDR remained stable in 2015–2017 (37.9%). The observed MIC values for gyrA substitutions are comparable to those previously published from Asia [33, 34]. The frequency of antimicrobial resistance was high and widespread, with no geographical clustering on province level. Of note, the *Salmonella* Typhi with MDR and cephalosporin resistance previously reported from the DRC belonged to the same clade (genotype 2.5.1) as the majority of the presently assessed DCS isolates, which highlights the relevance of ongoing surveillance and the implementation of vaccination [12].

Table 1. Antibiotic Resistance Profile of *Salmonella* Typhi Isolates Recovered From Blood Cultures and for Which Antimicrobial Susceptibility Testing Was Done

Antibiotic	No. of Resistant Isolates	Percentage of Resistant Isolates
Ampicillin	329	70.0%
Trimethoprim-sulfamethoxazole	303	64.5%
Chloramphenicol	258	54.9%
Multidrug resistance	180	38.3%
DCS	115	24.5%
Azithromycin	2	0.4%
Third-generation cephalosporins	1	0.2%
Gentamicin	0	0%
Multidrug resistance + DCS	56	11.9%
DCS + azithromycin	1	0.2%
DCS + third-generation cephalosporins	1	0.2%

The total number of isolates available for reference testing was 470.

Abbreviation: DCS, decreased ciprofloxacin susceptibility.

In conclusion, the established microbiological surveillance network and the high numbers of *Salmonella* Typhi BSI episodes in children elicit the DRC as a candidate to study the efficacy of the introduction of the typhoid conjugate vaccine [4]. MDR and DCS remained a major threat over the whole decade and warrant sustainable surveillance efforts [35].

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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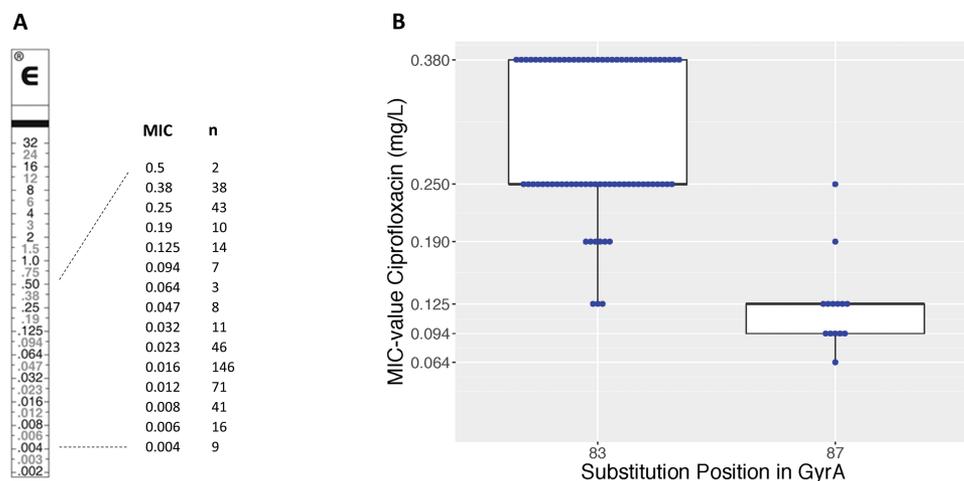
Figure 6. *A*, Minimum inhibitory concentration (MIC) values of ciprofloxacin for 465 isolates of *Salmonella* Typhi with decreased ciprofloxacin susceptibility, along an E-test macromethod strip. *B*, Box plot with ciprofloxacin MIC values for S83F and D87G amino acid substitutions in gyrA. Abbreviation: MIC, minimum inhibitory concentration.

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