SURVEILLANCE FOR BLOODSTREAM INFECTIONS CAUSED BY CARBAPENEM-RESISTANT ENTEROBACTERALES IN SOUTH AFRICA, 2019 AND 2020

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Summary

The World Health Organization has recently urged all countries to prioritize antimicrobial resistance surveillance for selected organisms including carbapenem-resistant Enterobacterales (CRE). We conducted a mixed-methods cross-sectional study with both quantitative and qualitative components using GERMS-SA enhanced CRE national surveillance at four sentinel sites in Gauteng Province (Steve Biko academic, Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani Baragwanath, and Dr. George Mukhari), South Africa, from 1 January 2019 to 31 December 2020. A case was defined as any person from whom Enterobacterales was isolated from blood culture and was resistant to ertapenem or any other carbapenem if ertapenem susceptibility testing was not done (doripenem, imipenem, meropenem).

Laboratory-based surveillance for CRE from bloodstream infections was performed at the National Institute for Communicable Diseases (Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM), South Africa. Sentinel laboratories submitted case report forms together with isolates to CHARM for phenotypic and genotypic characterization, as well as antimicrobial susceptibility testing. A surveillance audit comprising demographic and laboratory characteristics was conducted using data extracted from the National Institute for Communicable Diseases surveillance data warehouse. CRE bloodstream infection cases were described epidemiologically and surveillance attributes pertaining to simplicity, acceptability, usefulness, and timeliness were evaluated. Qualitative data were

collected through a Google Forms online survey, distributed to participants by email. During this surveillance evaluation, a total of 1 266 case-patients was detected from the four enhanced sentinel sites. The median age of the cases was 35 years (Interquartile range (IQR), 17–52 years) and males accounted for 53% (n=673). Among CRE case patients, outcomes were known for 64% (n=810) and 38% (310/810) were known to have died. Of the total cases, 43% (n=556/1 265) were audit (only demographic and laboratory data, no isolates sent to CHARM). CHARM received 709 isolates from the sentinel laboratories. Of those, 86% (609/709) were viable and tested positive for genes present in carbapenemase-producing Enterobacterales. Online questionnaires were distributed to forty surveillance system stakeholders, of which 65% (n=26) consented to participate. Ninety-two percent (22/24) of participants reported that the role they played in this CRE surveillance system was their responsibility and 63% (15/24) of those reported that their roles did not require a lot of effort. The system evaluation reported longer durations between the steps of the surveillance system; the median time taken from CRE diagnosis to receipt of specimen at the surveillance laboratory was 9 days (IQR 5–14 days), and the median time from when isolates were received by the surveillance laboratory to phenotypic characterization was 15 days (IQR 7–53 days). About 76% (19/25) were not aware of the purpose of the data collected by the CRE surveillance system and 50% (13/26) reported never receiving any feedback on data collected by the surveillance system. The sub-optimal survey response rate and participants not knowing about surveillance reports suggest that the GERMS—SA surveillance system was not operating as effectively. To improve usefulness, the GERMS-SA CRE surveillance implementers should facilitate ongoing training and non-electronic dissemination of surveillance findings to stakeholders.

Background

Enterobacterales are a large group of Gram-negative bacteria that are found in humans, animals, and the environment. These include the highly adaptable *Escherichia coli, Serratia* spp*, Klebsiella pneumoniae* spp, and *Enterobacter* spp.[1] Enterobacterales have developed resistance to various antibiotics including the carbapenems.[1] Carbapenems are a class of broad-spectrum beta-lactam antibiotics that include imipenem, meropenem, ertapenem, and doripenem.[2] In the treatment of multidrug-resistant bacterial infections, carbapenems are considered the last line of antimicrobials.[2]

Carbapenem-resistant Enterobacterales (CRE) possess multiple antibiotic resistance mechanisms including producing carbapenemases (carbapenemase-producing Enterobacterales [CPE]).[3] Examples

include *Klebsiella pneumoniae* carbapenemase (KPC), oxacillinase-48 (OXA-48) types, and class B Metallo-β-lactamases (MBLs), veronica integron Metallo-beta-lactamases (VIM), imipenemase (IMP) and New Delhi Metallo-β-lactamase-1 (NDM-1).[3] Antimicrobials are broken down by these carbapenemase enzymes, which prevent them from killing bacteria.[3] Carbapenemase genes are carried on plasmids (mobile genetic components) that facilitate resistance mechanisms between organisms against various antibiotics such as fluoroquinolones, cephalosporins, aminoglycosides, polymyxins, tetracyclines, and others.[4] It is therefore difficult to treat CREs since there are very few antimicrobial options available to which these organisms may be susceptible.[4]

Infections caused by CRE are increasing in South Africa (SA), causing substantial morbidity and mortality.[5] An in-hospital crude mortality ratio associated with CRE bloodstream infection is 38%, and the case fatality ratio is as high as 52% among children.[6-7]

Antimicrobial resistance surveillance in South Africa

The NICD conducts national GERMS-SA surveillance for laboratory-based, healthcare-associated antimicrobial resistance (AMR) pathogens. GERMS-SA surveillance data provides an accurate baseline from which appropriate prioritization, planning of programs, and actions can be taken to protect and promote the health of the public. This surveillance system aims to monitor AMR trends, phenotypically and genotypically characterize pathogens, perform antimicrobial susceptibility testing, and detect and manage outbreaks caused by healthcare-associated infections (HAI) pathogens.

Carbapenem-resistant Enterobacterales surveillance system

CHARM conducts CRE bloodstream infection surveillance in 13 public and private enhanced surveillance sites (ESS) across five South African provinces. This surveillance was previously evaluated after its conception in 2016.[8] The system was reported to be simple, useful, timely, and acceptable although areas of improvement were recommended.[8]

GERMS-SA CRE bloodstream infection enhanced surveillance system description

The sentinel site laboratories (National Health Laboratory Service (NHLS)), GERMS-SA, and CHARM are all stakeholders of the CRE surveillance system. The clinicians and laboratory staff, medical technologists, microbiologists, pathologists at the sentinel sites, GERMS-SA surveillance officers (SOs), programme

coordinators, administrators, epidemiologists, data managers, medical technologists, medical scientists, and pathologists all play important roles in ensuring that CRE cases are identified, captured, and reported by the surveillance system.

Case definition

A CRE case was classified as any hospitalised patient with an Enterobacteriaceae isolate from a blood culture specimen that is resistant to any of the carbapenems. Only the first episode was considered as a case defined as the first CRE-positive specimen within 21 days. When the same CRE was isolated from the same patient after 21 days, it was considered a new case. Patients with isolated distinct CRE species within 21 days of the first positive specimen were considered different cases.

Case identification and reporting

Clinicians request the collection of blood culture specimens from a patient suspected of having a CRE bloodstream infection and send them for culture at the NHLS laboratory. If a pathogen is isolated, the NHLS laboratory sends the isolate on Dorset transport media to CHARM at the NICD.[9] After isolation of CRE, a notification is sent to the SO who locates the patient and completes an electronic case report form (CRF) using a web-based application (MOBENZI) through patient interviews. If the patient has died or has already been discharged, the SO completes the CRF through medical record review. Field project coordinators (FPCs) ensure CRF data quality by checking the completeness of data on the CRF and liaising with SO's for any queries. Both CRF and laboratory data are stored on a GERMS-SA password-protected Microsoft Access database.

Upon receipt of isolates to CHARM, they are checked for eligibility. Duplicate isolates, incorrect specimens, and those that do not meet the case definition are discarded. All eligible isolates are phenotypically characterized, subsequently, carbapenemase genes are identified using genotypically characterization. Isolates are kept for a maximum of three months for further analysis when the need arises. Laboratory results are recorded and stored in a dedicated Microsoft Access database on a dedicated server (Figure 1).

Every quarter (three months), CRE data extracts are requested from the surveillance data warehouse (SDW), a data repository containing laboratory results from all NHLS laboratories. This is a way of identifying audit cases, whereby CRFs were not completed or isolates were not submitted to CHARM.

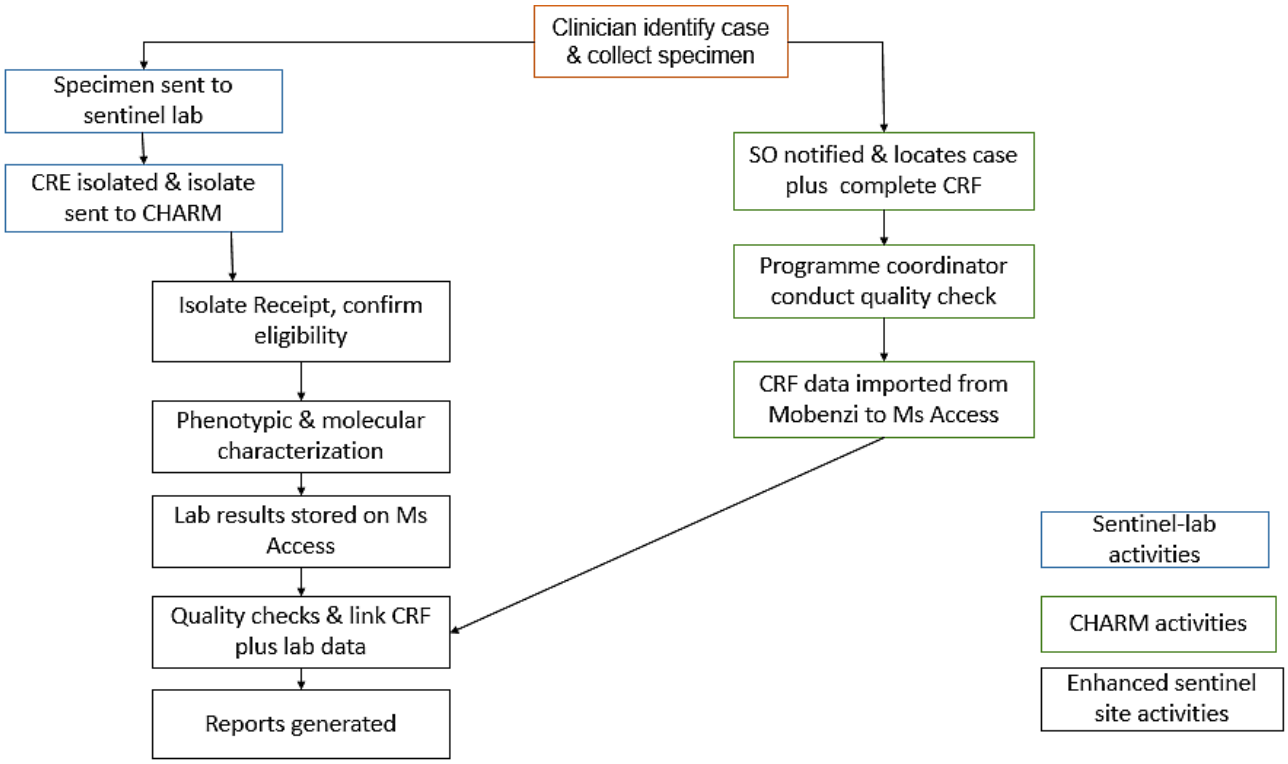

Figure 1. GERMS-SA carbapenem-resistant Enterobacterales bloodstream infection surveillance system flow chart.

Lab: NHLS laboratory. MS: Microsoft. CRF: Case report form. SO: Surveillance officer. CRE: carbapenem-resistant Enterobacterales. CHARM: Centre for Healthcare-Associated infections, Antimicrobial Resistance and Mycoses.

Aim and objectives of the GERMS-SA CRE surveillance system evaluation

This project aimed to evaluate the GERMS-SA CRE surveillance system and compare the findings to those from the baseline 2016 surveillance system evaluation, thereby assessing the need to continue with ongoing CRE enhanced surveillance. The primary objectives were:

1. To describe the clinical and epidemiological characteristics of cases with CRE bloodstream infection at four GERMS-SA enhanced surveillance sites (ESSs) in Gauteng Province from 1 January 2019 to 31 December 2020.
2. To evaluate the GERMS-SA CRE surveillance system attributes as specified in the updated Centers for Disease Control and Prevention (CDC) guidelines: simplicity, timeliness, acceptability,

sensitivity, data quality, and usefulness at these four GERMS-SA ESSs in Gauteng Province from 1 January 2019 to 31 December 2020.

Methods

Study design

This was a mixed-methods cross-sectional study with both quantitative and qualitative components. Qualitative data were collected through a Google Forms online survey that was distributed to participants by email. Participants who did not respond to the email were contacted to complete an alternative paper-based or telephonic interview. The following attributes were evaluated: simplicity, acceptability and timeliness. Stakeholders invited to participate include those who took part in the CRE surveillance system from both surveillance sites and at the NICD: laboratory staff, site investigators, data management team members, SOs, FPCs, medical technologists, medical scientists, clinicians, epidemiologists and pathologists. The quantitative component entailed the extraction of secondary data (1 January 2019–31 December 2020) from the GERMS-SA CRE database. Cases of CRE bloodstream infection were described epidemiologically and data quality, timeliness and usefulness of the surveillance system were evaluated.

Operational case definition

A CRE case was defined as any patient from whom Enterobacterales was cultured from blood and was resistant to ertapenem or any other carbapenem if ertapenem susceptibility testing was not done. If the same organism was isolated from blood in the same patient within 21 days, it was considered a duplicate isolate and excluded.

Study setting

Among the 13 participating NHLS microbiology laboratories and institutions that conducted GERMS-SA CRE surveillance, our study included four ESSs: Chris Hani Baragwanath Academic Hospital, Charlotte Maxeke Johannesburg Academic Hospital, Steve Biko Academic Hospital and Dr. George Mukhari Hospital (Figure 2).

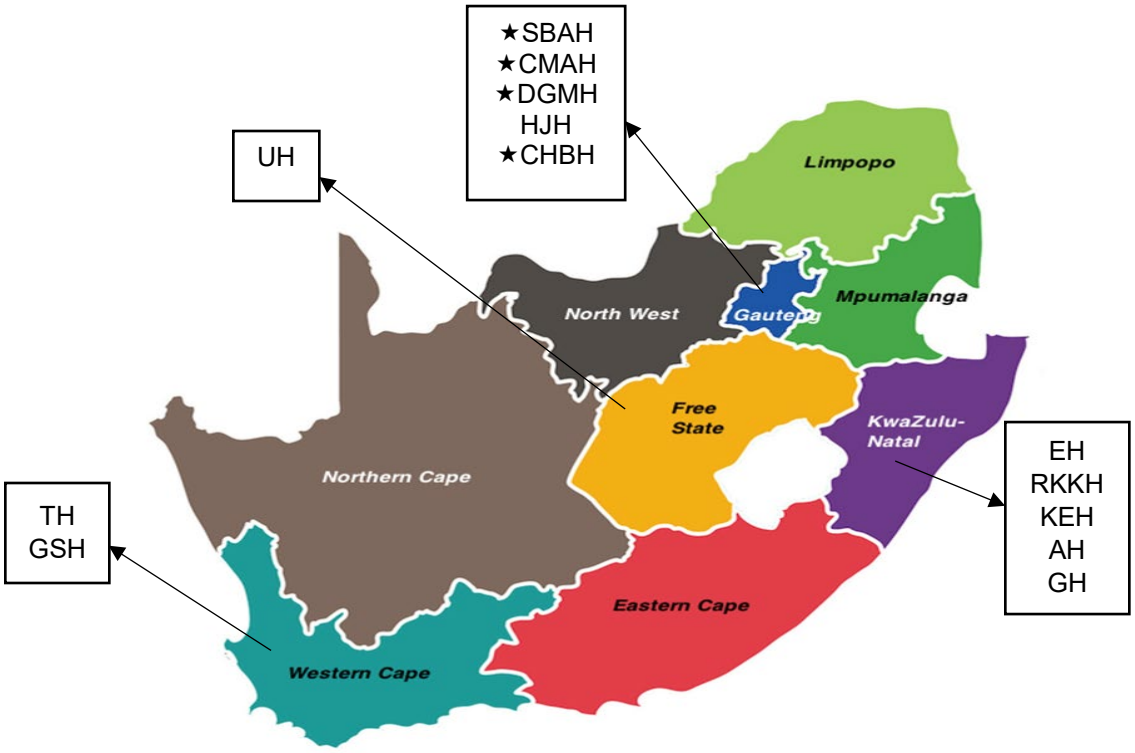

Figure 2. GERMS-SA carbapenem-resistant Enterobacterales surveillance sentinel sites by province, South Africa.

SBAH: Steve Biko Academic Hospital. CMAH: Charlotte Maxeke Johannesburg Academic Hospital. CHBH: Chris Hani Baragwanath Hospital. HJ: Hellen Joseph Hospital. UH: Universitas hospital. DGMH: Dr.George Mukhari. TH: Tygerberg Hospital. GSH: Groote Schuur Hospital. EH: Edendale. RKKH: RK Khan Hospital. KEH: King Edwards Hospital. AH: Addington. GH: Grey Hospital.

★ Enhanced surveillance site under evaluation

Data management

Questionnaire responses were extracted from the Google Forms database and imported into MS Excel (Microsoft Corporation, USA). In addition, we extracted data from January 2019 to December 2020 from the GERMS-SA MS Access database (Microsoft Corporation, USA) and imported it into MS Excel. Data cleaning and analysis were carried out using Stata Corp LLC version 17.

Data analysis

For the quantitative analysis, cases of CRE bloodstream infections were described using frequency distributions, percentages, and graphs. Surveillance system attributes defined in Table 1.

Table 1. Definitions and assessment criteria for GERMS-SA surveillance system attributes, South Africa 2019 – 2020.

Attribute	Definition of attribute	Type of assessment and analysis conducted
Simplicity	The structure and ease of GERMS-SA CRE surveillance operation.	Measured the amount of time required to identify a case, collect and manage data. Among trained participants, we assessed the need for further training required and the simplicity of the case definition.
Timeliness	The delay between the steps in the system and the availability of data for action.	Timelines and turnaround times between the following surveillance activities were assessed. **CRE diagnosis to isolate receipt at CHARM:** Date at which the CRE isolate was received at CHARM minus date of CRE result at the NHLS laboratory**.** **Isolate receipt at CHARM to phenotypic characterization**: Date the which minimum inhibitory concentration (MIC) test was done at CHARM minus the date at which the isolate was received at CHARM. **CRE diagnosis to CRF completion:** Date of CRF completion minus date of CRE result at NHLS laboratory. Median days and corresponding interquartile range (IQR) were assessed.
Acceptability	The willingness of the CRE surveillance stakeholders to participate in the system.	We assessed the participants' knowledge and attitudes towards participating in the surveillance system. We asked participants to describe how difficult it was to complete the CRF by using a scale of one to five, one being the least difficult and five being very difficult.
Data quality	A reflection of the completeness and validity of the data in the surveillance system.	We assessed the percentage (%) of missing data among important variables including clinical, demographic data and laboratory data
Usefulness	Whether or not the system contributes to the prevention and control of CRE infections. Whether the system provides estimates of morbidity and mortality, identifies disease risk factors, and stimulates research.	We conducted an internet search of any CRE NICD published guidelines, policy documents, communique, bulletins, or reports published. We also asked participants if they had ever received any reports with analyzed data.

Ethical considerations

Ethical approval to conduct this study was obtained from the Faculty of Health Sciences Research Ethics Committee, University of Pretoria (118/2021). Further permission to use data was obtained from data gatekeepers at GERMS-SA and CHARM/NICD. The participants that consented to be part of the study were enrolled anonymously using unique identifiers during data analysis.

Results

Using the operational case definition, 1 266 CRE cases were identified from the four selected ESSs in Gauteng Province during the period 1 January 2019 to 31 December 2020 (Figure 3).

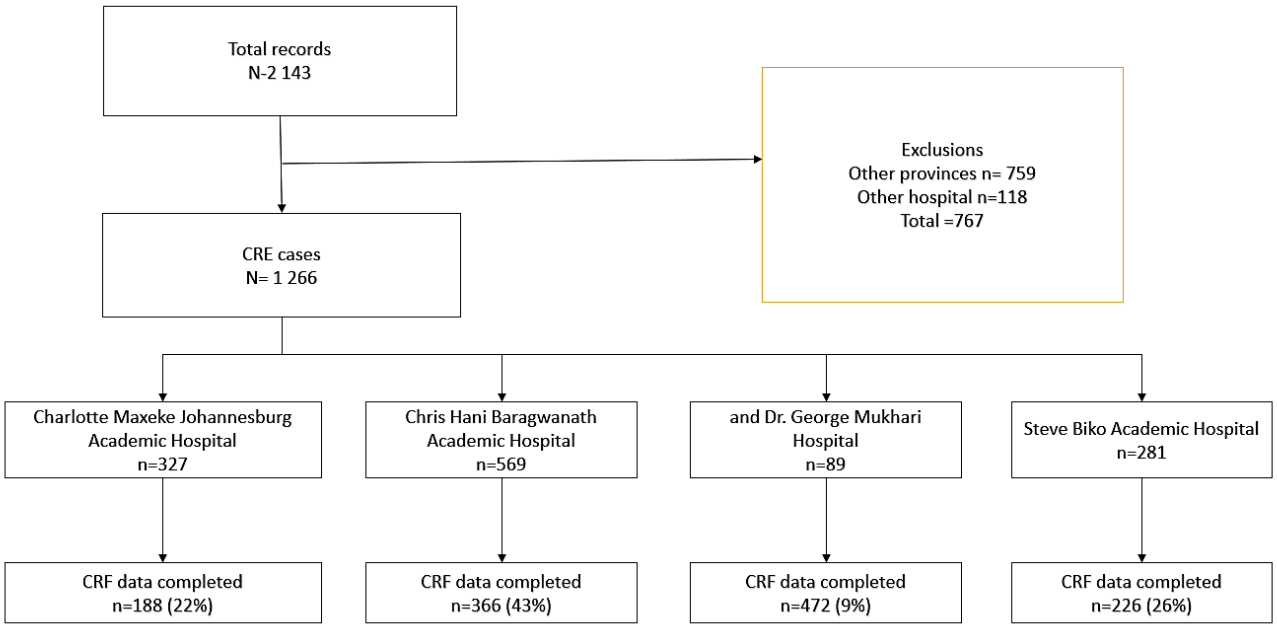

Figure 3. Carbapenem-resistant Enterobacterales surveillance cases from four GERMS-SA sentinel sites, Gauteng Province, January 2019–December 2020.

Other hospitals: Helen joseph / Coronation / Rahima Moosa Mother and Child Hospital, Tshwane District Hospital, Zola-Jabulani District Hospital, Nelson Mandela Children Hospital. Other provinces: Free State, Western Cape, KwaZulu-Natal.

Of the 1 266 CRE cases, 31% (n=389) were older than 50 years and males accounted for 53% (n=673). Forty-six percent (n=569) of cases were reported from Chris Hani Baragwanath Academic Hospital followed by 26% (n=327) from Charlotte Maxeke Johannesburg Academic Hospital. Twenty-six percent (n=334) had an intravenous line inserted at diagnosis. Cases that underwent surgery before a positive blood culture accounted for 15% (n=194), and 21% (n=264) of cases were mechanically ventilated at the time of blood culture. Five percent (n=64) of cases had a known history of previous hospital admission and 28% (n=365) of cases received antibiotics in the last six months of admission. Hospital outcome was known for 64% (n=810), of whom 38% (n=310) died (Table 3).

Table 2. Demographic and clinical characteristics of 1 266 cases of carbapenem-resistant Enterobacterales infection at 4 GERMS-SA sentinel sites, Gauteng Province, January 2019–December 2020.

Characteristics	**Frequency (N=1266)**	
Demographic characteristics	**n**	**%**
Age		
Median (IQR)	35 years (IQR 17–52 years)	
Sex		
Female	583	46
Male	673	53
Unknown	10	1
Clinical characteristics		
Medical device at the time of positive blood culture		
Intravenous line	334	26
Urinary catheter	135	11
Intra-arterial line	52	4
Drainage port	22	2
Central venous line	3	0.2
Other medical devices	141	11
Unknown	579	45
Received antibiotics in the past 6 months of current admission		
No	359	28
Yes	365	28
Unknown	542	42
Comorbidities		
HIV-infected	155	12
Malignancy	93	7

Diabetes	44	3
Renal disease	40	3
Cardiovascular disease	9	1
Unknown	925	73
Mechanical ventilation at the time of positive blood culture		
No	491	39
Yes	264	21
Unknown	414	40
Source of infection		
Skin/ soft tissue infection	142	22
Lower respiratory tract infection	122	19
Abscess	15	2
Central nervous system	20	3
Bone/ joint infection	4	1
Other	63	10
Unknown	275	43
Previous hospital admission in the last year		
No	623	49
Yes	64	5
Unknown	579	46
Hospital of diagnosis		
Charlotte Maxeke Johannesburg Academic	327	26
Chris Hani Baragwanath	569	46
Steve Biko Pretoria Academic	281	22
Dr. George Mukhari	89	8
In-hospital outcome		
Alive[a]	500	39
Dead	310	24
Unknown	456	36

[a] refused hospital admission, recovered, discharged, still admitted, transferred.

CHARM received 709 isolates from the sentinel laboratories (NHLS). Of those, 86% (609/709) were viable. Of the 609 organisms identified, *Klebsiella pneumoniae* accounted for the majority of organisms (80%, n=491) followed by *Enterobacter cloacae* (5%, n=38), and the least common organisms were *Enterobacter aerogenes* and *Proteus* species (<1%, n=1) (Table 4).

Table 3. Carbapenem-resistant Enterobacterales organisms identified by the GERMS-SA CRE surveillance system, Gauteng Province sentinel sites, January 2019–December 2020.

Organism	**n**	**%**
Klebsiella pneumoniae	491	81
Enterobacter cloacae	38	6
Serratia marcescens	25	4
Escherichia coli	23	4
Klebsiella pneumoniae species	22	4
Enterobacter species	8	1
Citrobacter freundii	1	0.2
Providencia rettgeri	1	0.2
Total	**609**	**100**

Klebsiella pneumoniae: Klebsiella pneumoniae ESBL, Klebsiella pneumoniae sssp, pneumoniae; Klebsiella pneumoniae species*: Klebsiella pneumoniae variicola, Klebsiella pneumoniae aerogenes, Klebsiella pneumoniae ozaenae, Klebsiella pneumoniae oxytoca; Enterobacter* species*: Enterobacter kobei, Enterobacter asburiae.*

Of the cases identified by the CRE bloodstream infection surveillance at the four Gauteng sentinel sites, 43% (n=556/1 266 were reported as audit (no isolates sent to CHARM). Of the CPE genes identified in this study, the majority were PCR-positive for OXA-48 & variants (71%, n=434), followed by NDM (11%, n=70). The least common CPE gene identified was KPC at <1% (n=3) (Figure 4).

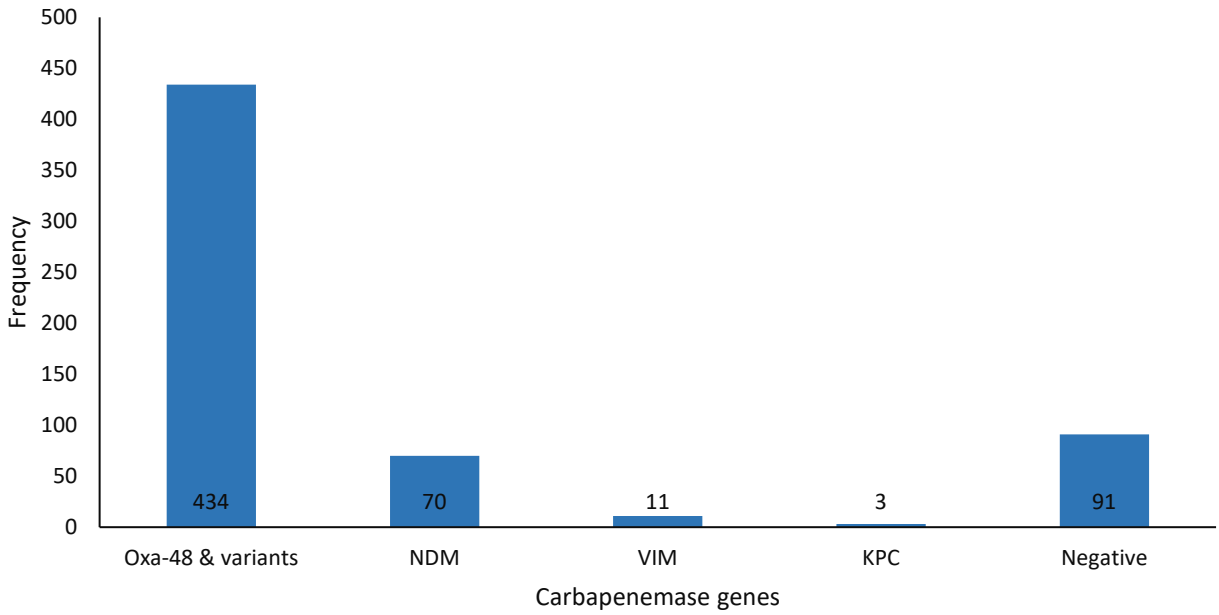

Figure 4. Distribution of carbapenemase genes of 609 carbapenem-resistant Enterobacterales isolates at four GERMS- SA sentinel sites, Gauteng Province, January 2019–December 2020.

OXA: Oxacillinase; NDM: New Delhi metallo-beta-lactamase; VIM: veronica integron Metallo-beta-lactamases type; KPC: *Klebsiella pneumoniae* carbapenemase.

Surveillance system attributes

Simplicity

Of the 40 questionnaires that were distributed to staff, 65% (n=26) consented to participate. Five participants responded to a paper-based and in-person interview, while the remaining 21 participants responded to the online Google Forms survey. The majority of participants were from Chris Hani Baragwanath 36% (n=8), followed by GERMS-SA 32% (n=7) and Charlotte Maxeke Johannesburg Academic Hospital 23% (n=5). Medical technologists from CHARM and surveillance sites comprised the majority of respondents 41% (n=9), followed by surveillance officers 23% (n=5). Most participants were female 86% (n=19).

Of the total participants, 86% (n=16) reported that the case definition was easy to understand, and 14% (n=3) reported that the case definition was difficult to understand but did not specify a reason. Among all participants, 68% (17/26) reported that they had been trained on the system, and this percentage was

higher compared to the previous GERMS-SA CRE 2016 evaluation of 44% (14/32). Among those who were trained, 17% (4/24) reported they would appreciate further training; this percentage was lower than the previous evaluation of 70% (7/10).

Eighty-six percent (18/22) of participants correctly identified blood culture as the specimen used to diagnose CRE according to the case definition, this percentage is higher than the previous evaluation finding of 37% (7/18).

Acceptability

About 87% (21/24) of the participants were familiar with the GERMS-SA CRE surveillance system and this percentage was higher than the previous evaluation (84%, 27/32). The majority of participants (58%, 15/26) reported that CRE infections were a significant cause of morbidity and mortality, but this percentage was lower than the previous evaluation with 84% (27/32).

About 96% (25/26) of the participants correctly identified the route of CRE transmission (person-to-person). This percentage was higher than in the previous evaluation where the mode of transmission was correctly identified by 53% (17/32) of participants.

About 77% (20/26) of participants reported that they played a role in the CRE surveillance system and 92% (22/24) reported that the role they played was their responsibility; this percentage was higher than the previous evaluation of 89% (17/19). Sixty-three percent (15/24) of participants reported that their roles did not require a lot of effort, and this percentage was lower than the previous evaluation of 78% (15/19).

Surveillance officers reported that the time taken to complete a CRF was less than 15 days. Two of the five participants reported that CRFs were difficult to complete. On a scale of one to five, one being easy and five being very difficult, both of the participants chose three (average). The reason for their response was that the dates for invasive devices were often missing from patients' files. Five out of 11 participants agreed that data were readily available, while 27% (3/11) reported that they were not sure if data were readily available. One participant disagreed that data were readily available for public health action.

Timeliness

The median time taken from CRE diagnosis to receipt of isolates at the surveillance laboratory was 9 days (IQR 5–14 days), which was longer than the previous evaluation of 6 days (IQR 3–11 days). The median time from receipt of isolates by the surveillance laboratory to phenotypic characterization was 15 days (IQR 7–53 days) and was longer than the previous evaluation of 5 days (IQR 2–7 days). The duration between a CRE diagnosis at a sentinel laboratory to CRF completion was longer (median of 58 days; IQR 9–158 days) compared to the previous evaluation (median 12 days; IQR 8–16 days) (Figure 4).

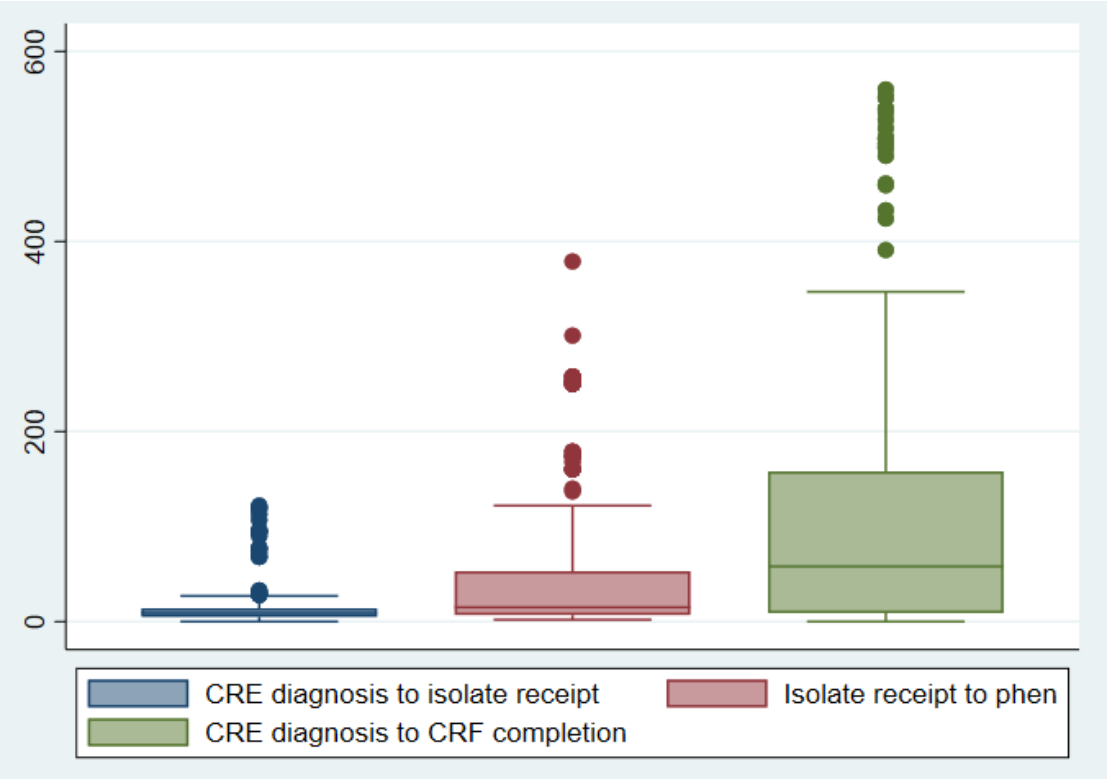

Figure 4. Duration between steps of the carbapenem-resistant Enterobacterales surveillance system in Gauteng Province, January 2019 – December 2020.

CRE: Carbapenem-resistant Enterobacterales: Case report form. Phen: phenotypic characterisation
CRE diagnosis to isolate receipt: 9 days (IQR 5-14). CRE diagnosis to CRF completion: 58 days (IQR 9-158). Isolate receipt to phonotypic characterization 15 days (IQR 7-53).

Data quality

Of the 1 266 cases reported from the four ESS, 67% (n=852) had complete clinical data, this percentage was lower than the previous surveillance where 84% (153/182) of cases had complete clinical data. Among demographic variables, the date of birth was the least completed with 2% (n=17) missing data, followed by age with 1% (n=10) missing data. The remaining demographic variables namely, sex, province and hospital name were complete for all case-patients. During the previous evaluation, patient race was the least completed, 26% (40/153), followed by age 7% (10/153). Sex, province and hospital name were complete for all records. Our evaluation reported the source of infection for clinical data was the least completed with 32% (n=275) followed by admission date with 31% (n=267). The most incomplete clinical variable was patient outcome with 5% (n=42) of patients missing this information. Ward type was complete for all case patients. During the previous evaluation, admission date and outcome were both the most incomplete variables 19% (29/153), followed by the source of infection, 29% (45/153). The least incomplete variable was ward type, 7% (10/153). Specimen collection date was complete for all case-patients.

Among risk factor variables, comorbidity was the least complete variable with 17% (n=145) missing data, followed by previous hospitalization (16%, n=116). The least completed variable was whether or not the patient was referred from another facility (6%, n=470). During the previous evaluation, the least completed variable was a medical device, 30% (46/153), followed by whether the patient was a health care worker, 28% (43/153), and the least incomplete variable was the specified medical device, 1% (1/95). Among laboratory data, organism name was fully completed for viable isolates. The least incomplete risk factor variable was the CRE diagnosis date at 33% (n=245). Previous infections were complete for all the case patients. During the previous evaluation, CRE diagnosis was the most incomplete, 19% (29/153), while the least incomplete was organism name, 4% (6/153). Previous infections and carbapenem genes were complete for all the records (Table 6).

Table 4. Quality of data for the carbapenem-resistant Enterobacterales surveillance system at four GERMS-SA sentinel sites, Gauteng Province, January 2019 – December 2020.

Variable	Cases with missing data	
	n=852	%
Demographic		
Age	10	1
Sex	0	0
Province	0	0
Hospital name	0	0
Date of birth	17	2
Clinical		
Admission date	267	31
Ward type	69	8
Specimen collection date	0	0
Source of infection	275	32
Outcome	42	5
Risk factors		
Comorbidity	145	17
Medical devices	86	11
Mechanical ventilation	97	10
Previous hospital admission	116	16
Previous exposure to antibiotics	128	14
Referred from another facility	63	6
Laboratory		
CRE diagnosis date	245	33
Organism name	0	0
Carbapenem resistance genes	417	45
Previous organism isolated	0	0

Usefulness

Based on the system database analysis, the information collected was enough to fulfill the system's objectives. Sufficient information on demographic, clinical, and other epidemiological characteristics of CRE cases was collected by the system. Publications (n=3), bulletin articles (n=9), and yearly CRE surveillance reports (n=5) were discovered through an online search.

About 76% (19/25) of participants were not aware of what was done with the data collected by the system. This percentage was higher than the last surveillance evaluation at 68% (21/31). Fifty percent (13/26) of the participants reported having never received any feedback or reports presenting data

collected by the CRE surveillance system. This percentage was lower than it was during the initial surveillance evaluation at 74% (23/31). All participants reported that they would welcome reports or publications and this finding was higher than it was during the previous surveillance evaluation at 90% (17/19).

Discussion

CREs remain one of the leading causes of healthcare-associated infections globally, and SA monitors CRE patterns and their implications in the healthcare system as recommended by the WHO[9-11]. The overall performance of various CRE surveillance systems in four Gauteng ESS in comparison with the earlier system evaluation had improved, although some components worsened. The NICD GERMS-SA CRE surveillance system was found to be useful as there were bulletin reports, published articles, and annual GERMS-SA CRE surveillance reports identified through an internet search and on the NICD website.[12-16] However, more than 75% of the participants never knew why the data were collected and none had received any reports.

There was an overall sub-optimal survey response rate from participants and some were not willing to participate during this surveillance system evaluation. This may have negatively impacted the generalizability of the results. The knowledge of the clinical site from which CRE should be isolated for a case to be included in the surveillance system was good. Participants not receiving feedback and reports on the work they do may also affect work morale, productivity, and the enthusiasm of system users. This may also be the reason behind the poor attitude towards participating in this surveillance system evaluation. Another contributing factor is that new employees may have not been trained or orientated on the CRE surveillance system.

Completeness of data particularly on important variables which include demographic, clinical, risk factors, and laboratory variables guides adequate analysis and inference of the study findings to the population of interest. Of the overall cases reported in the four Gauteng ESS, there was a lower proportion of CRF completed than in previous surveillance system evaluations. In our evaluation, there were some missing values among demographic, clinical, laboratory, and risk factors variables but the proportion of missing data was lower compared to the previous evaluation.

The latest annual report published by the NICD showed increasing CRE prevalence and CRE-associated mortality, highlighting the increasing health burden these organisms pose on the public health care system.[17] Timeliness of the surveillance system may assist with identifying and controlling for healthcare-associated outbreaks, and may inform guidelines on CRE prevention measures. The system evaluation reported longer durations between the steps of the surveillance system; the median days from time CRE diagnosis to receipt of isolates at surveillance laboratory, from when isolates were received by the surveillance laboratory to phenotypic characterization as well as from CRE diagnosis at a sentinel laboratory to CRF completion. The poor system timeliness compared to the previous surveillance system evaluation may have been attributed to the COVID-19 pandemic interruptions, particularly during the national lockdown.[18]

Our CRE surveillance system evaluation at Gauteng ESS showed that the most predominant organism causing CRE infections was *K. pneumoniae* followed by *E. cloacae,* which was consistent with a previous report published in SA where *K. pneumoniae* accounted for 80% of isolates followed by *S. marcescens.* The most predominant CPE genes circulating in Gauteng during the evaluation period were OXA-48 & its variants and NDM. This is consistent with a previously published South African CRE report in 2018, which found OXA-48 and its variants & NDM to be the most predominant CPE genes identified.[5]

Findings from the descriptive analysis showed that more than a quarter of the cases died. These findings are consistent with GERMS-SA 2019 annual report that reported a 38% mortality rate.[17] Since our study employed descriptive analysis, we, therefore, report all-cause mortality and there may have been other factors that contributed to these hospital deaths yet we could not account for them. We also described demographic clinical characteristics but could not establish risk factors for CRE bloodstream infections in Gauteng ESS. An analytical study is recommended to explore mortality and risk factors associated with CRE bloodstream infections.

Conclusions

The evaluation study showed that the GERMS-SA CRE surveillance system in the Gauteng Province among four ESS is not operating efficiently. Although some of the system's components have improved from the initial evaluation, the response rate, overall CRF completed and timeliness during this evaluation worsened. The poor survey response rate suggests the need for ongoing training. The majority of sentinel laboratory staff had no access to the online published reports, hence poor knowledge of the usefulness

of surveillance data collected suggests the need for non-electronic dissemination of surveillance system findings. Surveillance for CRE should continue in different formats such as periodic surveillance.

Limitations

Not all public health system evaluation system attributes were evaluated in this study. The poor response rate to the survey may affect the generalizability of the findings.

Recommendations

The evaluation identified areas that could be improved including:

- Regular feedback to stakeholders at the end of every quarter
  - Feedback can be written in the form of a newsletter and orally communicated at all sentinel sites (updates during regular morning staff meetings).
  - Feedback should include the burden and trends of the CREs. Most importantly, the role that the surveillance system plays should be emphasized and reports on the work done should be produced. These should include public health importance and implications for the surveillance system.
- Ongoing, training of stakeholders to mitigate problems caused by regular staff turnover.
- Improved data collection as all risk factor variables, and some demographic and clinical variables were not fully completed, resulting in poor data quality.
- Improved timeliness between surveillance steps to ensure that the enhanced surveillance system operates more efficiently.
- Establishment of periodic surveillance for CRE going forward.

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