NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Volume 18. Issue 1 – June 2020

PUBLIC HEALTH SURVEILLANCE BULLETIN

FOREWORD

This issue includes the measles and rubella surveillance report for 2019. South Africa's measles incidence rate in 2019 was comparable to that of 2018, and the pre-elimination target according to WHO guidelines was again met. We can therefore be optimistic of achieving measles elimination in South Africa by implementing significant improvements in surveillance and vaccine coverage.

The second surveillance report in this issue is an overview of the antimicrobial susceptibility patterns in South Africa of those pathogenic bacterial species against which new antimicrobial agents are urgently needed. Also presented here is an overview of blood culture specimen collection practices at a tertiary hospital in Johannesburg. It was found that blood culture collection guidelines are not consistently adhered to, leading to poor blood culture uptake that can affect decisions on subsequent treatment regimens.

Malaria features prominently in this issue, which includes a report of an Odyssean malaria case that occurred in the City of Tshwane. Odyssean malaria refers to locally acquired malaria in a non-endemic area that occurs because of the inadvertent importation of an infective mosquito from a malarious area by land or air transport. Malaria-affected regions in South Africa primarily include the endemic Limpopo, Mpumalanga and KwaZulu-Natal provinces. The occurrence and distribution of malaria vector mosquito species from routine surveillance conducted in these provinces in 2019 is presented here.

We trust that you will find these diverse reports interesting and informative. All participating laboratories, contributors and reviewers are thanked for their inputs.

Basil Brooke. Editor

ANNUAL MEASLES, RUBELLA AND CONGENITAL RUBELLA SURVEILLANCE REVIEW, SOUTH AFRICA, 2019

Heather Hong[1,2], Lillian Makhathini[1], Mirriam Mashele[1], Sheilagh Smit[1], Susan Malfeld[1], Tshepo Motsamai[1], Dipolelo Tselana[1], Morubula Jack Manamela[1], Nkengafac Villyen Motaze[1, 3], Genevie Ntshoe[4,5], Mercy Kamupira[6], Ester Khosa-Lesola[6], Sibongile Mokoena[6], Thulasizwe Buthelezi[7], Elizabeth Maseti[7], 'Ramokone Maphoto[7], Melinda Suchard[1,8]

[1]Centre for Vaccines and Immunology, NICD
[2]Department of Virology, School of Pathology, University of the Witwatersrand, Johannesburg
[3]Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town
[4]Outbreak Response Unit, Division of Public Health Surveillance and Response, NICD
[5]School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria
[6]World Health Organization, Pretoria, South Africa
[7]Child, Youth and School Health, National Department of Health, Pretoria, South Africa
[8]Department of Chemical Pathology, School of Pathology, University of the Witwatersrand, Johannesburg

Summary

In 2019, 4,608 febrile rash cases were recorded via active national surveillance systems. Of those tested for measles and rubella IgM antibodies, 65 (1.4%) were laboratory-confirmed measles cases, 1,496 (33.2%) were laboratory-confirmed rubella cases, and 44 (1.0%) were dual measles and rubella cases. There were four laboratory confirmed congenital rubella cases.

Overall, the national measles incidence rate was comparable to that of 2018. Use of serology for case determination has limitations in South Africa, where rubella is endemic and rubella vaccine is not in use in public health programmes. Future use of throat swabs in addition to serology is therefore recommended.

Using a narrow case definition (excluding cases dual positive for measles and rubella IgM), South Africa met the pre-elimination target of less than one case per million (0.4 per million population). There is therefore optimism that measles elimination can be achieved in South Africa. To achieve elimination, a target date will need to be set and significant improvements in surveillance and vaccine coverage will be necessary to prevent sporadic cases or outbreaks.

Background

Measles is a highly infectious viral disease.[1] Infants and young children are at greatest risk from measles infections, with potential complications including pneumonia and encephalitis, as well as lifelong disabilities such as permanent brain damage, blindness or hearing loss.[2] In 2011, the World Health Organisation (WHO) African Region set a measles elimination goal for 2020. However, despite effective vaccination that resulted in a global drop in measles deaths between 2000 and 2011[3], recent measles outbreaks have occurred worldwide, particularly in the Democratic Republic of the Congo, Liberia, Madagascar, and Somalia. In 2018, more than 140,000 people died from measles. The WHO estimated that 52,600 of these deaths occurred in Africa.[2]

Measles elimination is defined as the absence of endemic measles virus transmission in a region or other defined geographical area for more than 12 months in the presence of a well-performing surveillance system.[4] To meet this goal, vaccine coverage needs to be 95% or higher, with two doses administered per person. However, over the past decade completion of the primary series of infant vaccines in sub-Saharan Africa has stalled at approximately 72%[5], exposing populations to vaccine-preventable diseases and outbreaks. In South Africa, vaccination coverage also plateaued. Immunisation coverage of children under 1 year averaged 71.7%, whilst measles 2nd dose coverage averaged 68.8% over the period 2012 to 2017.[6] In 2018, the national measles 2nd dose coverage was 76.4%, and at the provincial level only two of nine provinces (Mpumalanga and Northern Cape) exceeded the coverage target of 87% for measles 2nd dose coverage.[6] South Africa has consistently experienced several measles outbreaks over the last decade.[7,8]

In South Africa, the measles vaccine is available in single (Measbio®) or in combination format i.e. measles-mumps-rubella (MMR, Trimovax® or Priorix®) or measles-mumps-rubella-varicella (MMRV, Priorix Tetra®). Currently, the South African Expanded Programme on Immunization (SA-EPI) offers the MeasBio® vaccine to infants within the public health sector at 6 months and again at 12 months of age. A rubella containing vaccine (RCV) is not yet part of the SA-EPI, but can be obtained within the private health sector as MMR administered at 6 months and again at 12 months.

Rubella is generally a mild infection caused by the rubella virus.[9] Complications of rubella are rare and generally occur more often in adults than in children. The most serious complication of rubella infection is congenital rubella syndrome (CRS), which occurs when the virus is transmitted transplacentally during pregnancy.[10,11] Infection within the first trimester is teratogenic and can lead to miscarriage, foetal death, stillbirth, or serious birth defects. Historically, the omission of a rubella vaccine from the SA-EPI was based on the understanding that that natural rubella infection during childhood should render most women of childbearing age immune, thereby preventing CRS. Under conditions of imperfect vaccine coverage, the addition of a RCV could increase the susceptibility of adult women by slowing, not interrupting, rubella transmission.[12] This paradoxical increase has been attributed to the overall decrease in childhood rubella such that the age of primary rubella infection shifts to adolescence or adulthood, thus increasing the number of CRS cases.[12-15]

This report summarises the results of the South African measles and rubella surveillance programme for the period 1 January to 31 December 2019. We review the measles incidence in terms of reaching the African 2020 measles elimination goal of less than one measles confirmed case per million population.

Methods

Measles is a category 1 notifiable medical condition (NMC) in South Africa and, as such, health care workers in the public and private health sectors are required to report any suspected measles case to the National Department of Health (NDoH) within 24 hours. Additionally, suspected cases must have a blood sample taken for confirmatory testing at the Centre for Vaccines and Immunology, National Institute for Communicable Diseases (NICD). Private laboratories that test for measles are therefore requested to send all positive measles samples to the NICD for confirmatory testing and inclusion in the national database.

Unlike measles, rubella is a category 3 NMC, to be notified through a written or electronic notification to the NDoH within 7 days of diagnosis by private and public health laboratories. Rubella does not require confirmatory testing at the NICD. The rubella surveillance data presented here are from samples tested at the NICD only.

Sample collection and laboratory testing

Serum samples were tested using commercial enzyme-linked immunosorbent assay (ELISA) kits for anti-measles and anti-rubella IgM antibodies (Euroimmun, Luebeck, Germany) according to the manufacturer's instructions. A second sample was requested for repeat testing on all those with measles IgM equivocal results. Sera that tested positive and/or equivocal for measles IgM were assayed for the presence of measles virus by real-time reverse transcription (RT)-PCR amplification and, where possible, selected for genotyping. Of note, sera are suboptimal samples for measles detection by RT-PCR. Throat swabs are ideal but are not routine.

Based on the measles serology and/or PCR result, each suspected case was provisionally classified as measles IgM positive, measles PCR positive, measles compatible or epidemiologically linked. Each case was thereafter classified as either discarded, compatible or confirmed (Table 1) on review of case information. The definition of a measles outbreak is considered as three confirmed cases within one district within one month.

Table 1. Final classifications for laboratory-confirmed measles cases in South Africa.

Final measles classification	**Comment**
1. Discarded	Case did not meet the clinical or laboratory definition (IgM negative, vaccine associated, or had vaccine strain present)
2. Compatible	Case met the clinical case definition, was not epidemiologically linked, but no blood specimen was received, or blood specimen was equivocal
3. Confirmed	Case was laboratory-confirmed (IgM positive and/or PCR positive and/or epidemiologically-linked) - Narrow case definition: excludes those with rubella IgM positive result - Wide case definition: regardless of rubella IgM result

IgM: Immunoglobulin M; PCR: polymerase chain reaction)

Congenital rubella syndrome surveillance

Congenital rubella syndrome sentinel-site surveillance was established in 2015 at 28 clinical sites and 6 laboratories.[16] Paediatricians, neonatologists, paediatric infectious disease specialists and the virology departments of the National Health Laboratory Service (NHLS) were

requested to share information on any laboratory-confirmed CRS cases on a monthly basis. The CRS case definition included any positive rubella result in patients aged ≤12 months who presented with cataract, congenital glaucoma, congenital heart disease, hearing impairment, pigmentary retinopathy, purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, or radiolucent bone disease.[16]

Notifiable medical conditions system

In 2017, a web- and mobile-based NMC notification (app) system was launched to provide for the collection, collation, analysis, interpretation and dissemination of health/disease surveillance information in South Africa. For this report NMC cases received over the period 1 January to 31 December 2019 were included in the analysis, with specific attention paid to suspected cases without samples for confirmatory testing.

Data analysis

Descriptive analyses were performed using Excel 2016. Results were reported as frequencies for categorical variables or as median values with ranges for continuous variables. Where date of rash onset was not available, date of sample collection was used.

Results

A total of 4,608 febrile rash-based samples was received between 1 January and 31 December 2019 (Figure 1). A total of 4,500 (97.7%) samples was tested for measles and rubella IgM antibodies, whilst the remaining 108 (2.3%) were rejected either due to insufficient sample volume or inappropriate sample type. For measles, 69 (2.5%) were IgM positive, 4,308 (95.9%) were IgM negative and 114 (2.5%) were IgM equivocal. For rubella, 1,496 (33.2%) were IgM positive, 2,643 (58.7%) were IgM negative and 361 (8.0%) were IgM equivocal. Of note, 44 (0.98%) samples were dual positive for measles and rubella IgM antibodies. Of the samples tested, 95.4% of results were reported within seven days of receipt in the laboratory, exceeding the target of 80% within 7 days.

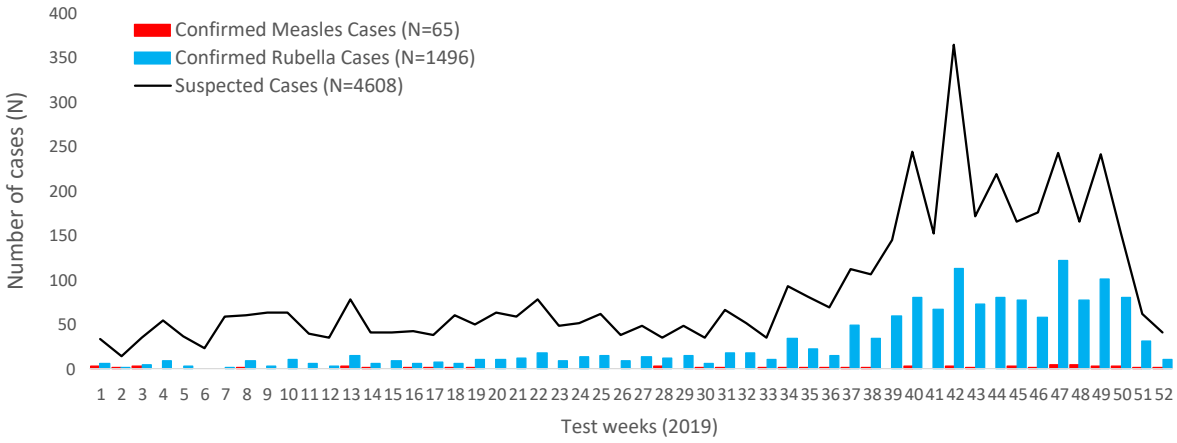

Figure 1. The number of suspected cases (N=4,608) from febrile rash surveillance in South Africa, with corresponding laboratory-confirmed measles (N=65) and rubella cases (N=1,496) for the period 1 January to 31 December, 2019.

Circulating measles

Of those that were measles IgM positive and/or PCR-positive, 65 cases were classified as confirmed, two were denotified, nine were discarded and one was left pending receipt of case investigation reports by the end of 31 January 2020. Of the discarded cases, six (66.7%) were classified as vaccine-associated after epidemiological investigation, and the remaining cases failed to meet the clinically compatible measles case definition. Of the confirmed measles cases, 64.6% (42 of 65) had dual rubella positive IgM results. Although rubella was the more likely diagnosis based on higher incidence, we did not use the rubella IgM result to discard measles IgM positive cases as dual infection is not impossible. For the purposes of this report, we refer to confirmed measles cases as either single positive measles samples (narrow case definition) or single and dual positive rubella samples (wide case definition).

Using the wide case definition, there were 65 laboratory-confirmed measles cases which occurred throughout the year, and were detected in eight of nine provinces (Figure 2), of which the Western Cape (N=14, 21.5%) and Gauteng (N=13, 20.0%) provinces had the highest disease burden. Measles case numbers were higher in females compared to males (60.3% vs. 39.7%, respectively). Measles cases occurred predominantly in the 1 - 4 year old age group, accounting for 30.8% of the total measles cases (Figure 3A). However, when comparing age distribution of laboratory-confirmed measles cases without rubella infection (Figure 3B), both the 1 – 4 and 20 – 44 year old age groups were equally affected (21.7%). When stratifying according to age

group and population figures as defined by Statistics South Africa[17], the 0 - 4 year old age group had the highest measles incidence rate compared to the other age groups (Table 2).

Of the measles IgM-equivocal cases (N=114), five (4.4%) tested positive for measles RNA and were classified as confirmed measles cases, 33 (28.9%) met the clinical case definition and were classified as compatible, and the remaining 76 (52.8%) did not meet the clinical case definition and were discarded. Compatible measles cases were mostly identified in the Western Cape (N=12, 36.4%) and KwaZulu-Natal (N=9, 27.3%) provinces, and were predominant in the 5 - 9 year old age group (N=16, 48.5%). Of note, 19 (57.6%) of the compatible measles cases were also positive for rubella, suggesting that despite best efforts to classify the measles equivocal cases, a proportion were likely not true measles, although that possibility cannot be excluded. Other concomitant rash illnesses may cause elevated IgM antibody levels leading to false positive measles serology.

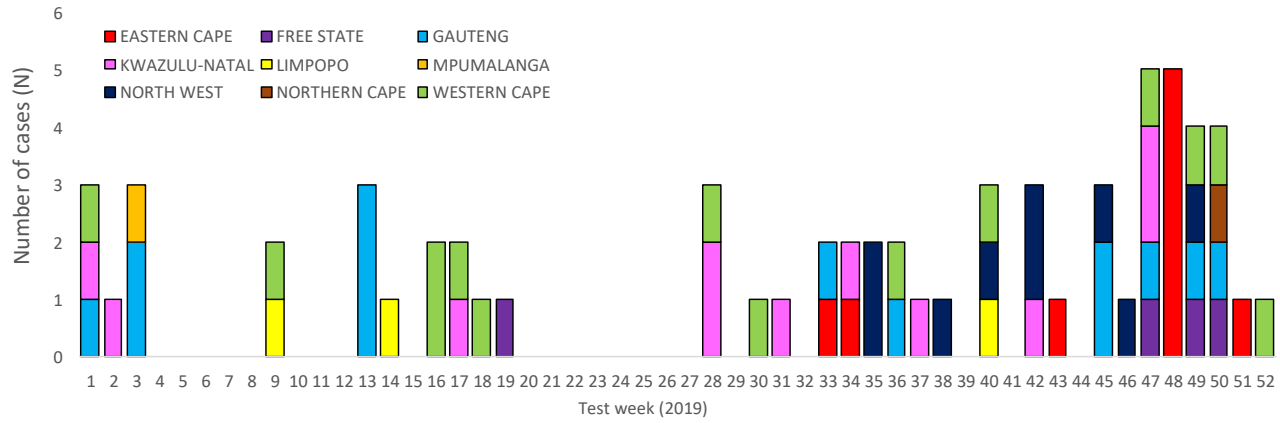

Figure 2. Provincial distribution of laboratory-confirmed measles cases in South Africa for the period 1 January to 31 December 2019 (N=65).

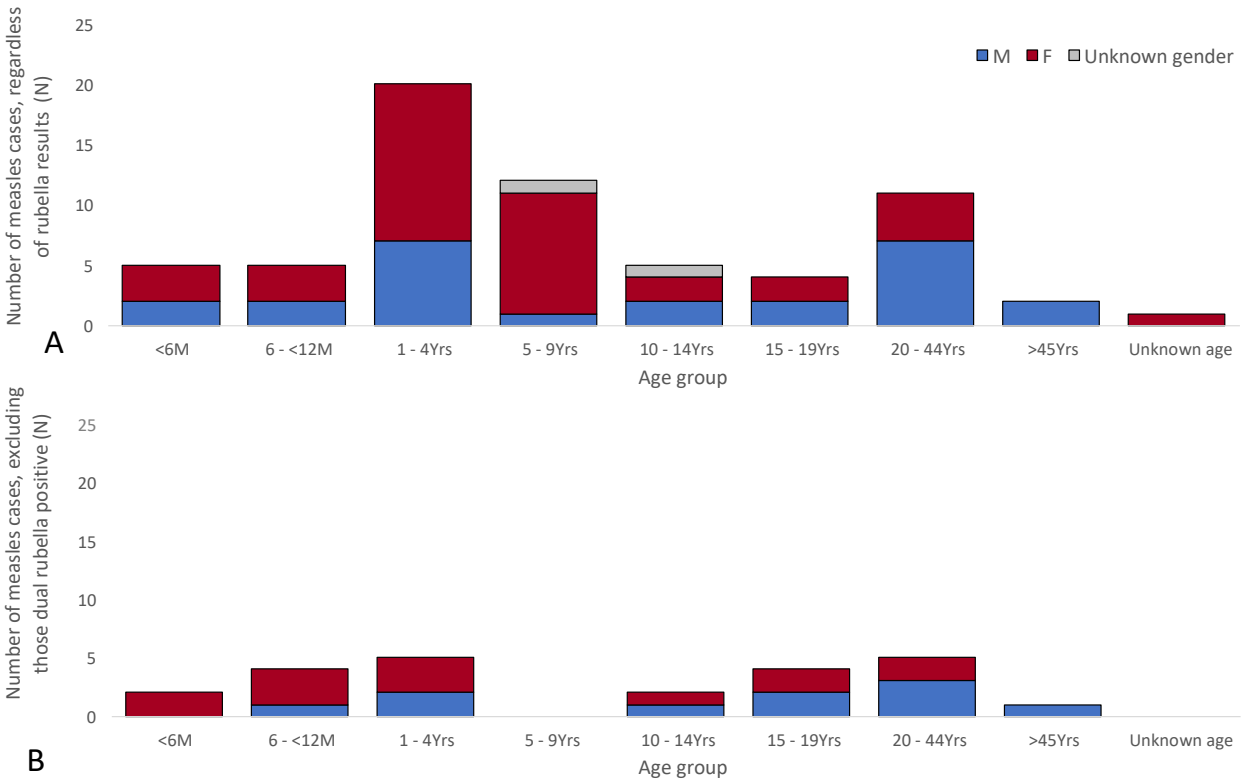

Figure 3A. Age and gender distribution of laboratory-confirmed measles cases, including samples dual-positive for rubella (wide case definition, males N=25; females N=38; unknown gender N=2). **B**. Age and gender distribution of laboratory-confirmed measles cases after the exclusion of dual-positive rubella cases (narrow case definition; males N=10; females N=13) in South Africa for the period 1 January to 31 December 2019.

Table 2. Measles and rubella incidence rate per million by age group in South Africa for the period 1 January to 31 December 2019.

Age group (years)	Confirmed Measles cases (wide case definition)	Confirmed Measles cases (narrow case definition)	Confirmed rubella cases	Total population	Confirmed Measles cases (wide case definition) per 1,000,000	Confirmed Measles cases (narrow case definition) per 1,000,000	Confirmed rubella case incidence per 1,000,000
0 – 4	30	11	594	5,733,946	5.23	1.92	103.59
5 – 9	12	0	718	5,737,439	2.09	0.00	125.14
10 – 14	5	2	102	5,427,902	0.92	0.37	18.79
15 – 19	4	4	15	4,660,002	0.86	0.86	3.22
20 – 44	11	5	39	24,137,303	0.46	0.21	1.62
> 45	2	1	6	13,078,429	0.15	0.08	0.46
unknown	1	0	22	-	-	-	-
Total	**65**	**23**	**1,496**	**58,775,021**	**1.11**	**0.39**	**25.45**

Total population figures by age group are 2019 mid-year population estimates supplied by Statistics South Africa[17]

Measles cases notified through the NMC system

A total of 882 cases was notified through the national NMC system. Of the 796 (90.2%) cases with blood samples that were received for testing at the NICD, 86 (9.8%) were without a blood sample and classified as compatible based on signs and symptoms (N=22, 25.6%), or discarded due to incomplete case information (N=64, 74.4%).

Measles/rubella clusters

Three measles clusters were investigated in 2019. However, on subsequent review two of these were reclassified as rubella clusters, highlighting the complexities of serological measles surveillance in an area with high rubella prevalence.

The first cluster was reported in April in the City of Cape Town, Western Cape Province. Four cases were unvaccinated siblings aged 12, 14, 17 and 19 years who had recently travelled to Georgia. Three tested positive for measles IgM (one also tested measles PCR positive) and one was IgM negative, likely in the incubation period. Outbreak response measures were implemented and contacts were vaccinated. As these cases were related and no additional cases were found in the district, it is likely that these cases were imported.

The second cluster was detected in October in the Bojanala Platinum district, Rustenburg, North West Province (Figure 5). Four cases tested IgM positive for measles infection. The North West Provincial Department of Health initiated localised vaccination response activities. Of note, all four had dual rubella infection, 2 (50%) had received the two doses of measles vaccine, and none had any travel history. On review, this cluster was considered to be due to rubella.

The third cluster occurred in November in the Sarah Baartman district, Eastern Cape Province. Seven cases with febrile rash were investigated for suspected measles infection, of which three tested dual positive for measles and rubella IgM. Two of the three cases were up-to-date with their measles vaccination, and one had unknown vaccination status. The cases were investigated and contacts vaccinated for measles. A local mass vaccination campaign was conducted with 731 children aged <5 years old being vaccinated. On review by the National Advisory Group on Immunisation, this cluster was determined as likely due to rubella.

Circulating rubella

Of 4,500 samples tested for rubella, 1,496 (33.2%) were laboratory-confirmed rubella cases, with North West (N=332, 22.2%) and Western Cape (N=278, 18.6%) provinces having the highest burden of disease (Figure 4A). Rubella was similarly distributed amongst males (N=695, 47.9%) and females (N=757, 52.1%) and was predominant in the 1 – 4 and 5 - 9 year old age groups (Figure 4B). Of females with rubella, 4.2% (32 of 757) were aged between 15 – 44 years old, comparable to the figures reported in 2018 (4.1%, 24 of 579). As rubella vaccination is not part of the expanded programme on immunisation in South Africa, rubella circulates widely and rubella clusters are not routinely investigated unless occurring within a particular institution.

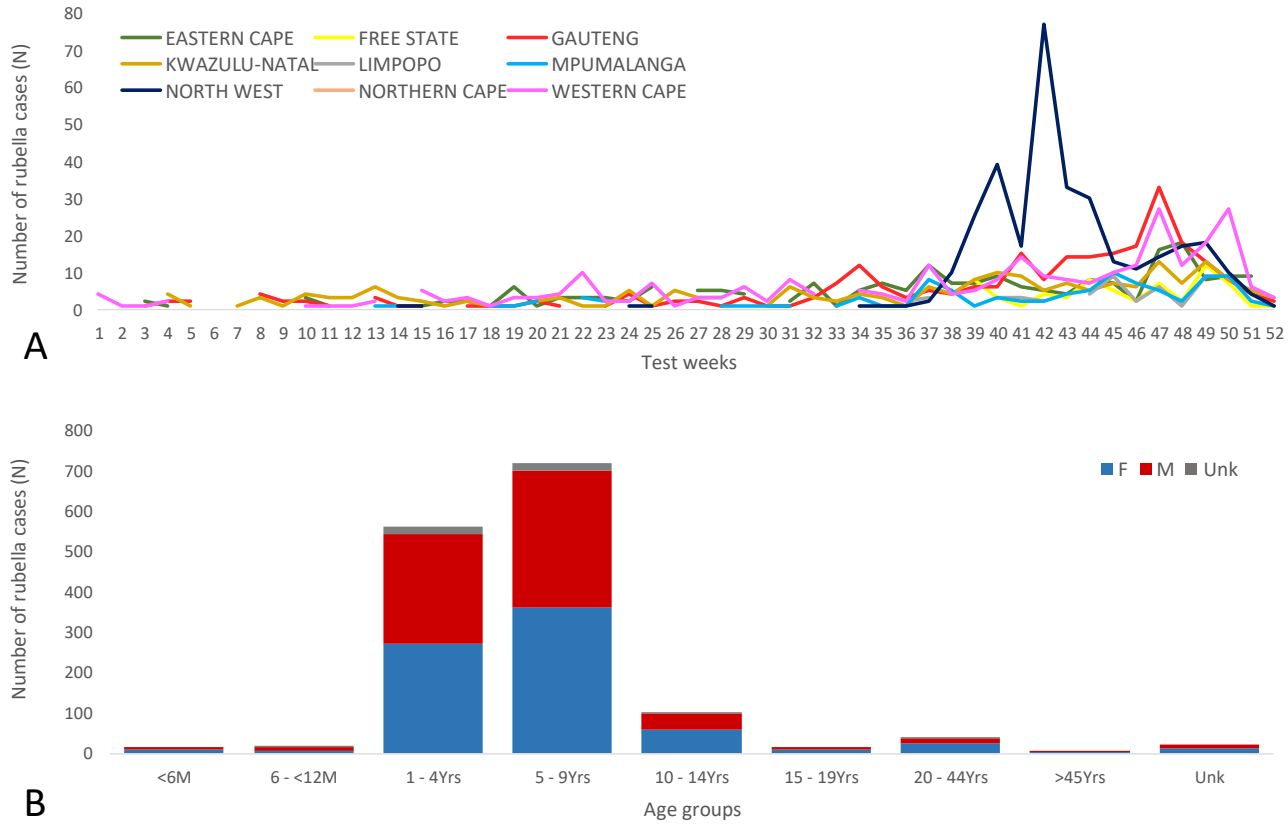

Figure 4. Provincial distribution (**A**), age and gender distribution (**B**) of laboratory-confirmed rubella cases in South Africa for the period 1 January to 31 December 2019 (N=1,496; males, N=695; females, N=757; unknown, N=44).

Notably in the North West Province, and specifically in the Bojanala Platinum district (Figure 5A), an outbreak of rubella was detected, beginning at the end September (weeks 39 to week 44). Rubella incidence was highest in the 5 - 9 year old age group, amounting to 56% of the total rubella infections (Figure 5B). There were more females than males with rubella (54% vs. 46%, respectively), and of the females with rubella, 1.2% (2 of 165) were aged between 15 - 44 years old. Moreover, due to investigation of a possible measles outbreak at the time, there was enhanced case-finding that may have contributed to the higher rubella numbers.

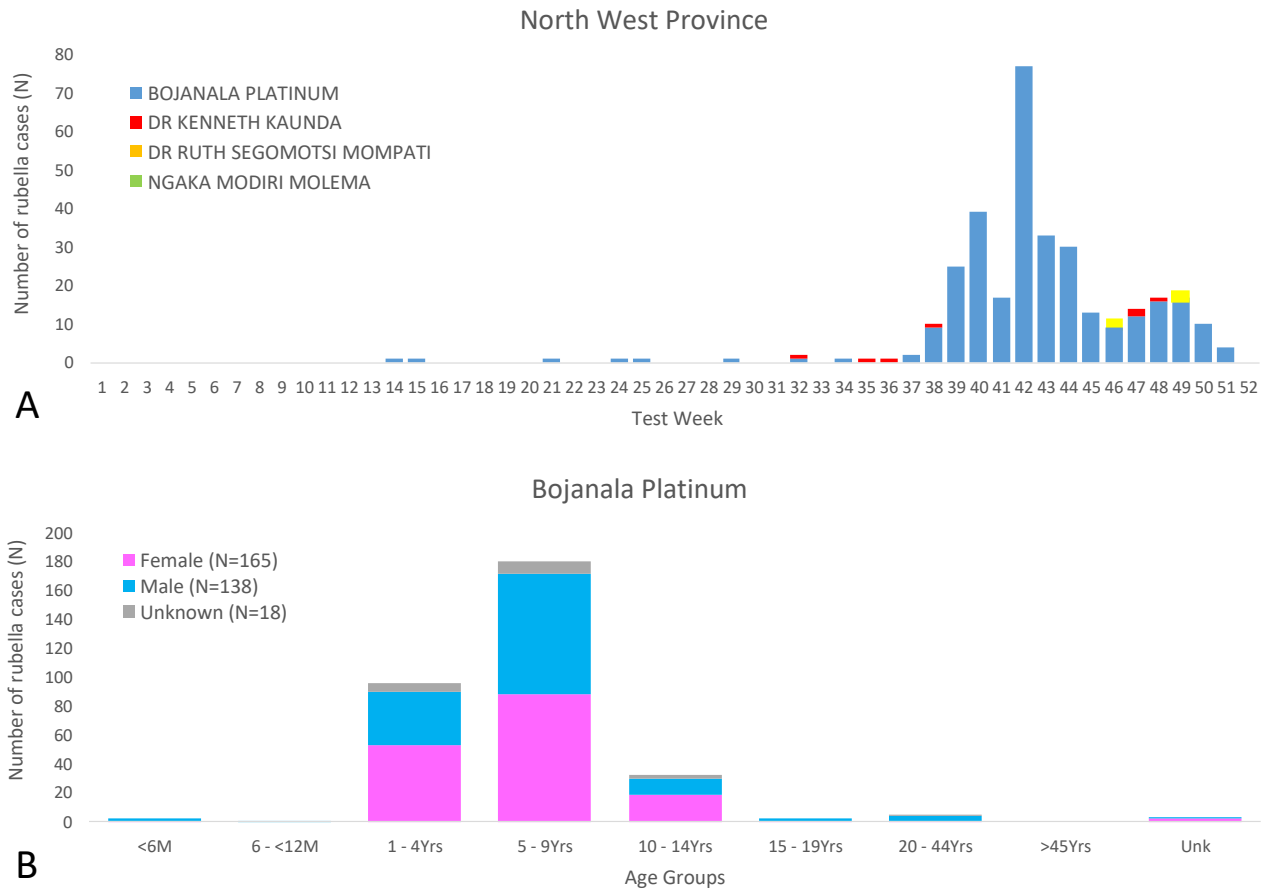

Figure 5A: Epidemic curve showing rubella distribution in the North West Province, South Africa, by district for the period 1 January to 31 December 2019 (N=332). **Figure 5B**. Age and gender distribution of rubella cases in the Bojanala Platinum district (N=321; males, N=139; females, N=165; unknown, N=18).

More than half of all measles and rubella cases had a case investigation form as well as a unique epidemiological (EPID) number (Table 3). In approximately half of measles cases, vaccination status was not recorded. Using the narrow case definition (measles positive serology only), 8.7% (2 of 23) were too young to have received their first measles vaccine (i.e. <6 months of age). Using the narrow case definition, 18 of 23 (78.3%) had not been vaccinated or had unknown vaccine status compared to 21 of 42 (50.0%) using the wide case definition (dual positive serology), suggesting that many of the dual positive cases likely did not have measles.

Measles genotyping and cluster detection

A total of 165 specimens (eight throat swab, one urine, one CSF and 155 sera) were tested for measles RNA using RT-PCR. Fourteen (8.54%) were positive for the presence of measles virus, three of which had the D8 genotype. The remainder had insufficient material for genotyping. Of these three cases, two had a European travel history (one travelled to Georgia and the other to Germany, Italy and France), and the third refused to meet with the outbreak response team, thus travel history could not be obtained.

Congenital rubella syndrome (CRS) surveillance

In 2019, responses to monthly e-mails sent to clinicians at study sentinel sites varied from 11% to 30%. Overall, there were four laboratory-confirmed CRS cases reported, two via the NMC system and two from sentinel site surveillance. This was less than the number reported in 2018 (N=5). Clinical information regarding infant's birthplace, gender, signs and symptoms as well as maternal information remains unknown.

Field and laboratory surveillance indicators for suspected rash cases

In 2019, the national detection rate for non-measles and non-rubella febrile rash illness was 4.41 per 100,000 population (Table 4). Eight of nine provinces exceeded the WHO target of detecting at least two non-measles, non-rubella febrile rash cases per 100,000 population. The detection rate in Limpopo province was 1.6 per 100,000. Overall, the surveillance system was sensitive to detect, notify and investigate suspected measles cases. Regarding the incidence rate for confirmed measles cases, using the wide case definition, the national target of less than one measles case per million population was not met. Specifically, four provinces (Eastern Cape, Free State, North West and Western Cape) had a measles incidence rate above 1 case per million population. However, a review of the measles cases using the narrow case definition (excluding those with concomitant rubella infection), shows that the measles incidence rate was less than 0.4 per million population.

Table 3. Surveillance indicators for laboratory-confirmed measles, rubella and discarded cases in South Africa for the period 1 January to 31 December 2019.

Category	Laboratory-confirmed				
	Measles single positive (narrow case definition) N=23	Measles dual positive (wide case definition) N=42	Rubella positive N=1,496	Discarded cases (non-measles, non-rubella N=2,591	Total laboratory cases N=4,608
Case investigation form (CIF)	12 (52.2%)	26 (61.9%)	862 (57.6%)	1293 (49.9%)	2397 (52.0%)
Epidemiological (EPID) number	19 (82.6%)	28 (66.7%)	1185 (79.2%)	2155 (83.2%)	3721 (80.8%)
Cases with a CIF & EPID number	9 (39.1%)	21 (50.0%)	790 (52.8%)	1200 (46.3%)	2207 (47.9%)
Measles vaccination status					
Too young (<6months)	2 (8.7%)	3 (7.1%)	15 (1.0%)	87 (3.4%)	112 (2.4%)
Blank	13 (56.5%)	18 (42.9%)	831 (55.5%)	1729 (66.7%)	2882 (62.5%)
No	3 (13.0%)	0 -	9 (0.6%)	31 (1.2%)	50 (1.1%)
Yes	5 (21.7%)	21 (50.0%)	641 (42.8%)	744 (28.7%)	1564 (33.9%)
Measles vaccine doses					
1	1 (20.0%)	2 (9.5%)	33 (5.1%)	111 (14.9%)	162 (10.4%)
2 or more	4 (80.0%)	18 (85.7%)	519 (92.2%)	611 (82.1%)	1361 (87.0%)
Dosage unknown	0 -	1 (4.8%)	17 (2.7%)	22 (3.0%)	41 (2.6%)

Table 4. Field surveillance adequacy by provinces, South Africa, January - December 2019.

Province	Measles single positive cases	Measles dual positive cases	Total measles cases	Non-measles non-rubella cases	Total population	Measles single positive cases	Measles dual positive cases	Total measles cases	Non-measles non-rubella cases
						Illness rate per 1 000 000 population			Illness rate per 100 000 population
ECP	0	9	9	227	6,712,277	0,00	1,34	1,34	3.38
FSP	1	3	4	104	2,887,466	0,35	1,04	1,39	3.60
GP	6	7	13	569	15,176,115	0,40	0,46	0,86	3.75
KZP	2	9	11	300	11,289,083	0,18	0,80	0,97	2.66
LPP	2	1	3	96	5,982,583	0,33	0,17	0,50	1.60
MP	1		1	213	4,592,185	0,22	0,00	0,22	4.64
NCP	0	1	1	94	1,263,874	0,00	0,79	0,79	7.44
NWP	2	7	9	664	4,027,160	0,50	1,74	2,23	16.49
WCP	9	5	14	324	6,844,272	1,31	0,73	2,05	4.73
South Africa	**23**	**42**	**65**	**2591**	**58,775,015**	**0,39**	**0,71**	**1,11**	**4.41**

Population estimates obtained from Statistics South Africa mid-year population estimates, 2019.[17] For confirmed measles cases, green shading indicates good performance meeting the pre-elimination goal of less than 1 case per 1 000 000 population, and red indicates poor performance. For non-measles, non-rubella illness rate per 100 000, green shading indicates good performance meeting the WHO surveillance target of non-measles febrile rash illness rate of more than 2 per 100 000 population, and red indicates poor performance i.e. not meeting the surveillance target. ECP = Eastern Cape Province, FSP = Free State Province, GP = Gauteng Province, KZP = KwaZulu-Natal Province, LPP = Limpopo Province, MP = Mpumalanga Province, NCP = Northern Cape Province, NWP = North West Province, WCP = Western Cape Province.

Discussion

There were 65 confirmed measles cases in South Africa in 2019. However, 23 were single positive and 42 were dual positive cases, indicating the complexities of measles serological testing in areas of high concurrent rubella. Although two measles cases required hospital admission no complications or deaths were reported. Overall, despite the 2020 measles elimination goal for South Africa, sporadic cases of measles as well as clusters still occurred. Using the wide case definition (all measles positive by serology), the pre-elimination target of less than one case per million was not achieved. However, when reviewing the measles incidence rate using the narrow case definition (exclusion of cases with dual rubella positive serology) (Table 2), the incidence rate was less than 0.4 per million population, suggesting that the South African measles elimination goal may be achievable within the next few years. Moreover, given that confirmed and suspected measles clusters were promptly identified, the National Surveillance System performed well and provincial health workers were able to respond rapidly with investigation and vaccination.

Measles cases occurred largely in the 1 – 4 year old age group (34.0%), similar to cases reported in 2018 (44.9%). However, the second highest proportion in 2019 was amongst the 20 - 44 year old age group (16.0%), indicating pockets of young adults who remain susceptible to measles infection. When comparing the 2019 provincial distribution of measles single positive cases, Western Cape Province had the highest burden of 1.31 per million population. This is due to the confirmed measles cluster with a recent travel history.

Incorporation of the NMC measles cases into the annual measles review is a recent strength. The fact that 86 cases were reported to the NMC system without a laboratory specimen having been received for testing highlights logistic difficulties, emphasizing the need to improve sample transportation.

The rubella incidence rate increased from 21.3 per million in 2017 to 25.5 per million in 2019. Rubella was predominant in children aged less than 10 years old. Of female cases, 4.2% were of reproductive age, highlighting a significant rubella immunity gap in females of reproductive age, indicative of the growing need to implement a RCV into the SA-EPI. In addition, there were four laboratory CRS cases. Thus, RCV introduction needs to be carefully planned, coordinated and maintained with high coverage in order to avoid increasing rubella incidence in females of childbearing age.

Many areas of surveillance still require improvement. These include CIF completion, EPID number allocation and follow-up investigation reports. For example, on average, less than half of the suspected cases had a CIF and EPID number. From a review of the discarded cases, many did not have information on vaccination history. More than 80% of those with vaccination history reported receiving two vaccine doses, giving an indication of vaccine coverage in South Africa. Confirmation of coverage figures awaits results from the ongoing national vaccine coverage survey.[18]

Conclusion

In South Africa in 2019, there was one imported cluster of four measles cases and no outbreaks. Two clusters of febrile rash illness, in which more than three individuals had dual positive measles and rubella serology, highlighted the complexities of serological surveillance in an area

with endemic rubella but low measles incidence. Using the narrow case definition (exclusion of dual positive rubella cases), the measles incidence was below the pre-elimination target of less than one case per million. While the African measles elimination goal of 2020 has lapsed, there is hope that measles elimination can be achieved in South Africa. Future inclusion of throat swabs for expansion of molecular testing for febrile rash surveillance is recommended. Four laboratory confirmed CRS cases emphasizes the need for introduction of rubella vaccination in the expanded programme on immunization, subject to sufficiently high vaccination coverage.

Acknowledgements

We acknowledge and thank the NHLS CDW team for extracting and sharing the measles reported for 2019.

References

1. Moss WJ. Measles. *Lancet* (London, England). 2017;390(10111):2490-502.
2. WHO Joint News Release. More than 140,000 die from measles as cases surge worldwide. 2019. Available at: https://www.who.int/news-room/detail/05-12-2019-more-than-140-000-die-from-measles-as-cases-surge-worldwide
3. Progress in global control and regional elimination of measles, 2000-2011. *Wkly Epidemiol Rec.* 2013;88(3):29-36.
4. Masresha B, Luce R, Shibeshi M, Katsande R, Fall A, Okeibunor J, et al. Status of measles elimination in eleven countries with high routine immunisation coverage in the WHO African Region. *J Immunol Sci.* 2018;Suppl:140-4.
5. Madhi SA, Rees H. Special focus on challenges and opportunities for the development and use of vaccines in Africa. *Human Vaccines & Immunotherapeutics.* 2018;14(10):2335-9.
6. WHO Africa. Experts caution against stagnation of immunization coverage in Africa. 2019. Availble at: https://www.afro.who.int/news/experts-caution-against-stagnation-immunization-coverage-africa
7. Massyn N, Pillay Y, Padarath A, editors. District Health Barometer 2017/18. Durban: Health Systems Trust; 2019. Available at: https://www.hst.org.za/publications/District%20Health%20Barometers/DHB+2017-18+Web+8+Apr+2019.pdf
8. Hong HA, Makhathini L, Mashele M, Malfeld S, Motsamai T, Sikhosana L, et al. Annual measles and rubella surveillance review, South Africa, 2017. Available at: http://wwwnicdacza/wp-content/uploads/2018/09/Annual-measles-and-rubella-surveillance-review-South-Africa-2017pdf 2018.

9. Ntshoe GM, McAnerney JM, Archer BN, Smit SB, Harris BN, Tempia S, et al. Measles outbreak in South Africa: epidemiology of laboratory-confirmed measles cases and assessment of intervention, 2009-2011. *PLoS One*. 2013;8(2):e55682.
10. Lambert N, Strebel P, Orenstein W, Icenogle J, Poland GA. Rubella. *Lancet* (London, England). 2015;385(9984):2297-307.
11. Grant GB, Desai S, Dumolard L, Kretsinger K, Reef SE. Progress toward rubella and congenital rubella syndrome control and elimination - Worldwide, 2000-2018. *MMWR Morb Mortal Wkly Rep*. 2019;68(39):855-9.
12. Lee JY, Bowden DS. Rubella virus replication and links to teratogenicity. *Clin Microbiol Rev*. 2000;13(4):571-87.
13. Panagiotopoulos T, Antoniadou I, Valassi-Adam E. Increase in congenital rubella occurrence after immunisation in Greece: retrospective survey and systematic review. *BMJ*. 1999;319(7223):1462-7.
14. Metcalf CJ, Cohen C, Lessler J, McAnerney JM, Ntshoe GM, Puren A, et al. Implications of spatially heterogeneous vaccination coverage for the risk of congenital rubella syndrome in South Africa. *J R Soc Interface*. 2013;10(78):20120756.
15. Cameron NA. When, and how, should we introduce a combination measles-mumps-rubella (MMR) vaccine into the national childhood expanded immunization programme in South Africa? *Vaccine*. 2012;30 Suppl 3:C58-60.
16. Schoub BD, Harris BN, McAnerney J, Blumberg L. Rubella in South Africa: An impending greek tragedy? *South African Med J*. 2009;99(7):515-9.
17. Motaze NV, Manamela J, Smit S, Rabie H, Harper K, duPlessis N, et al. Congenital rubella syndrome surveillance in South Africa using a sentinel site approach: a cross-sectional study. *Clin Infect Dis*. 2018.
18. Mid-year population estimates, 2019. Department of Statitics South Africa Stastistcal Release, P0302.
19. R J Burnett, Dlamini NR, Meyer JC, Mutevedzi P, Kibuuka DK, Mphahlele MJ, et al. South Africa's first national vaccination coverage survey since 1994. *South African Medical Journal*. 2019;109(5):289.

OVERVIEW OF ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF ESKAPE ORGANISMS ISOLATED FROM PATIENTS WITH BACTERAEMIA IN SOUTH AFRICA, 2016 – 2018

Husna Ismail[1], Olga Perovic[1,2]

[1]Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses, NICD
[2]School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

Summary

Antimicrobial resistance (AMR) in Gram-positive and Gram-negative bacteria has increased in recent years. According to the World Health Organization (WHO), the ESKAPE group (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter* spp.) are listed amongst 12 bacterial species against which new antimicrobial agents are urgently needed. The aim of this project was to describe these ESKAPE organisms and *Escherichia coli* isolated from patients with bacteraemia as reported from two health sectors in South Africa, and to compare their antimicrobial susceptibility profiles over a three-year period. Antimicrobial susceptibility testing data were extracted from a web-based electronic platform created by the National Institute for Communicable Diseases. Specific 'drug-bug' combinations following the WHO's Global Antimicrobial Surveillance System guidelines were included in the analysis. A total of 106 300 ESAKPE plus *E. coli* isolates from both private and public health sectors was analysed. There was an increase in the number of pathogens identified from 31 369 in 2016 to 34 928 in 2017 to 40 003 in 2018, with a two-fold increase in non-susceptibility to carbapenems among *K. pneumoniae* in both health sectors. The relative proportion of *A. baumannii* drug susceptible isolates from the public sector remained stable during 2017 and 2018 (20% were susceptible). *Pseudomonas aeruginosa* isolates reported from the private sector showed an increase in susceptibility to piperacillin-tazobactam, from 64% in 2017 to 74% in 2018. In this surveillance period the key findings include an increase in the numbers of ESKAPE pathogens and resistance to carbapenems among Enterobacteriaceae. This analysis provides AMR surveillance data for healthcare guidance at national level.

Introduction

Bacteria in the ESKAPE group of pathogens includes six healthcare-associated multidrug-resistant organisms (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter* spp.).[1] In addition, *Escherichia coli* causes the majority of life-threatening bacterial infections in community and healthcare facilities worldwide. According to the World Health Organization (WHO), these organisms are listed amongst 12 bacterial species against which new antimicrobial agents are urgently needed.[1] Surveillance for antimicrobial resistance (AMR) is key to understanding the current extent of resistance. This is necessary to inform health programmes that generate guidelines for treatment, and assists in the prevention of AMR transmission.[2] In South Africa (SA), one of the strategic objectives of the Antimicrobial Resistance National Strategy Framework document, formulated by the National Department of Health, is to optimize surveillance and early detection of AMR.[2,3] This strategy includes AMR reporting from the list of organisms of the Global Antimicrobial Resistance Surveillance System of the WHO. In addition to the ESKAPE group of organisms, *E. coli* was added because it is one of the most common community and hospital pathogens of the Enterobacteriaceae family.

The aim of this project was to describe the ESKAPE organisms and *E. coli* isolated from patients with bacteraemia as reported from public and private health sectors in SA, and to compare their antimicrobial susceptibility profiles over a three-year period.

Methods

Study design, population and setting

A secondary data analysis of antimicrobial susceptibility testing (AST) in South Africa from January 2016 to December 2018 was conducted. AST data were extracted from a secure web-based electronic platform created by the Surveillance Information Management Unit (SIMU) at the National Institute for Communicable Diseases (NICD). These data were available on the AMR dashboard hosted by the NICD website (http://www.nicd.ac.za). The study population included all patients who had a blood culture submitted either to the public National Health Laboratory Service (NHLS) or to one of the four accredited private pathology laboratories (Ampath, Lancet Laboratories, PathCare and Vermaak and Partners). Positive blood cultures for any one of the ESKAPE organisms or *E. coli* were included in the analysis. The working group of the South African Society for Clinical Microbiology made a decision in 2015 to exclude

surveillance of *Enterobacter* spp. owing to concerns about the lack of standardisation in the testing and reporting of susceptibility profiles between different laboratories.

Definitions

In line with the GERMS-SA laboratory-based surveillance programmes, duplicate isolates of the same organism obtained from the same patient within 21 days were excluded, in order to avoid bias induced by multiple investigations of severely ill patients. AST and interpretation of results were performed by individual laboratories according to current Clinical and Laboratory Standards Institute (CLSI) guidelines, or the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (at one private laboratory). There were only a few minor changes in the breakpoint interpretation in EUCAST during the three-year study period (for instance, cefepime zone sizes were changed from 19 mm to 25 mm), and no changes in CLSI breakpoint interpretive criteria were used in the analysis of drug-bug combinations. AST results were grouped, based on categorical data as provided by the submitting laboratories. Results were reported as susceptible or non-susceptible, which includes the intermediate and resistant categories. The reporting format of susceptibility profiles for drug-bug combinations was based on the WHO Global Antimicrobial Surveillance System (GLASS) early implementation manual.[4]

Results

Over the three-year study period 106 300 ESKAPE organisms and *E. coli* were reported, of which 67% (n=71 661) were from the public sector and 33% (n=34 639) from the private sector. Gram-negative bacteria accounted for 61% (43 571/71 661) in the public sector and 72% (24 971/34 639) in the private sector. *Escherichia coli* accounted for 17% and 31%, *K. pneumoniae* 25% and 28%, *A. baumannii* 13% and 3%, *P. aeruginosa* 6% and 10%, *E. faecalis* 8% and 8%, *E. faecium* 7% and 3%, and *S. aureus* 24% and 17% in the public and private sectors respectively. In the private sector, there was a decrease in the relative proportion of *E. coli* isolates from 35% in 2017 to 28% in 2018, an increase in the relative proportion of *K. pneumoniae* isolates from 27% in 2017 to 29% in 2018, and an increase in the relative proportion of *S. aureus* isolates from 15% in 2017 to 20% in 2018 (Table 1).

Table 1. Bacterial profile for ESKAPE organisms and *Escherichia coli* identified from blood cultures obtained from the public and private health sectors in South Africa, 2016 to 2018.

Sector	Group	Organism	2016 (N=22340) n (%)	2017 (N=22892) n (%)	2018 (N=26429) n (%)
Public	Enterobacteriaceae	*Escherichia coli*	3981 (18)	4085 (18)	4441 (17)
		Klebsiella pneumoniae	5533 (25)	5440 (24)	6688 (25)
	Non-fermentative Gram-negative bacteria	*Acinetobacter baumannii*	2736 (12)	3139 (14)	3509 (13)
		Pseudomonas aeruginosa	1197 (5)	1471 (6)	1351 (5)
	Gram-positive bacteria	*Enterococcus faecalis*	1710 (8)	1768 (8)	2101 (8)
		Enterococcus faecium	1669 (7)	1565 (7)	1944 (7)
		Staphylococcus aureus	5514 (25)	5424 (24)	6395 (24)
			2016 (N=9029) n (%)	**2017 (N=12036) n (%)**	**2018 (N=13574) n (%)**
Private	Enterobacteriaceae	*Escherichia coli*	2781 (31)	4187 (35)	3863 (28)
		Klebsiella pneumoniae	2466 (27)	3204 (27)	3921 (29)
	Non-fermentative Gram-negative bacteria	*Acinetobacter baumannii*	304 (3)	458 (4)	403 (3)
		Pseudomonas aeruginosa	914 (10)	1256 (10)	1214 (9)
	Gram-positive bacteria	*Enterococcus faecalis*	739 (8)	867 (7)	1014 (7)
		Enterococcus faecium	311 (3)	315 (3)	389 (3)
		Staphylococcus aureus	1514 (17)	1749 (15)	2770 (20)

Enterobacteriaceae

Escherichia coli: Differences in susceptibilities were observed for the fluoroquinolone ciprofloxacin and third- and fourth-generation cephalosporins in both health sectors. In the public sector, there was an increase in non-susceptibility to ciprofloxacin from 26% in 2017 to 29% in 2018, and in the private sector from 31% in 2016 to 37% in 2018. In the public sector, non-susceptibility to cefotaxime/ceftriaxone increased from 25% in 2017 to 31% in 2018, ceftazidime from 25% in 2017 to 30% in 2018 and cefepime from 25% in 2017 to 30% in 2018. Isolates from the private sector showed greater susceptibility to the cephalosporins compared to those from the public sector. A high proportion of isolates reported from both health sectors were susceptible to the carbapenems (ertapenem, imipenem and meropenem). Although there was no difference in susceptibility to the beta-lactam and beta-lactamase inhibitor piperacillin-tazobactam in the public sector, there was an increase in non-susceptibility for isolates reported from the private sector from 20% in 2016 to 24% in 2018 (Table 2).

Table 2. Antimicrobial susceptibility patterns of *Escherichia coli* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Amikacin	3842	3478 (91)	3885	3522 (91)	4275	4067 (95)
	Amoxicillin-clavulanic acid	3845	2462 (64)	3870	2456 (63)	4237	2509 (59)
	Ampicillin/amoxicillin	3834	614 (16)	3823	595 (16)	4191	607 (14)
	Cefepime	3668	2785 (76)	3750	2825 (75)	4232	2972 (70)
	Cefotaxime/ceftriaxone	3752	2798 (75)	3835	2874 (75)	4257	2941 (69)
	Ceftazidime	3780	2869 (76)	3791	2848 (75)	4253	2979 (70)
	Ciprofloxacin	3815	2818 (74)	3720	2756 (74)	4287	3056 (71)
	Cotrimoxazole	NR	NR	NR	NR	NR	NR
	Doripenem	NR	NR	NR	NR	NR	NR
	Ertapenem	3552	3518 (99)	3659	3645 (100)	4218	4198 (100)
	Gentamicin	3864	3168 (82)	3872	3175 (82)	4263	3470 (81)
	Imipenem	3727	3705 (99)	3774	3757 (100)	4267	4243 (99)
	Levofloxacin	9	7 (78)	19	16 (84)	17	13 (76)
	Meropenem	3716	3691 (99)	3810	3791 (100)	4247	4224 (99)
	Piperacillin-tazobactam	3485	3020 (87)	3736	3237 (87)	4259	3733 (88)
Private	Amikacin	2781	2598 (93)	4040	3725 (92)	3855	3724 (97)
	Amoxicillin-clavulanic acid	2780	1945 (70)	4171	2791 (67)	3859	2443 (63)
	Ampicillin/amoxicillin	1998	425 (21)	2310	466 (20)	3800	857 (23)
	Cefepime	2778	2283 (82)	4040	3254 (81)	3858	3018 (78)
	Cefotaxime/ceftriaxone	2777	2253 (81)	4171	3329 (80)	3623	2768 (76)
	Ceftazidime	2148	1755 (82)	2804	2231 (80)	3199	2489 (78)
	Ciprofloxacin	1997	1378 (69)	3534	2301 (65)	2713	1719 (63)
	Cotrimoxazole	1746	657 (38)	2298	839 (37)	2243	817 (36)
	Doripenem	2753	2748 (100)	4013	4007 (100)	3745	3731 (100)
	Ertapenem	2779	2769 (100)	4041	4026 (100)	3860	3836 (99)
	Gentamicin	2779	2368 (85)	4045	3448 (85)	3857	3280 (85)
	Imipenem	2777	2772 (100)	4043	4033 (100)	3862	3847 (100)
	Levofloxacin	792	593 (75)	1229	868 (71)	1152	859 75)
	Meropenem	2780	2777 (100)	4042	4034 (100)	3862	3849 (100)
	Piperacillin-tazobactam	2774	2212 (80)	3677	2868 (78)	3854	2923 (76)

NR = not reported

Klebsiella pneumoniae: Non-susceptibility to ciprofloxacin in both health sectors increased from 2016 to 2018: in the public sector from 34% to 37% and in the private sector from 40% to 51%. We also observed an increase in non-susceptibility to carbapenems over the three-year study period. In the public sector, non-susceptibility to ertapenem increased from 4% to 10%, imipenem from 5% to 12% and meropenem from 6% to 12%. In the private sector, non-susceptibility to ertapenem increased from 15% to 30%, imipenem from 10% to 18% and meropenem from 9% to 18%. No changes in susceptibility to piperacillin-tazobactam were noted for isolates reported from the public sector. Isolates reported from the private sector however showed an increase in non-susceptibility from 57% in 2016 to 64% in 2018 (Table 3).

Table 3. Antimicrobial susceptibility patterns of *Klebsiella pneumoniae* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Amikacin	5288	4278 (81)	5130	4164 (81)	6344	5109 (81)
	Amoxicillin-clavulanic acid	5284	1763 (33)	5085	1542 (30)	6283	1861 (30)
	Cefepime	5164	1687 (33)	5012	1548 (31)	6279	1595 (25)
	Cefotaxime/ceftriaxone	5192	1631 (31)	5008	1483 (30)	6314	1506 (24)
	Ceftazidime	5201	1661 (32)	5042	1523 (30)	6275	1534 (24)
	Ciprofloxacin	5280	3479 (66)	4893	3128 (64)	6315	3990 (63)
	Cotrimoxazole	NR	NR	NR	NR	NR	NR
	Doripenem	NR	NR	NR	NR	NR	NR
	Ertapenem	4769	4562 (96)	4696	4333 (92)	5924	5310 (90)
	Gentamicin	5308	2083 (39)	5125	1992 (39)	6306	2124 (34)
	Imipenem	5071	4800 (95)	4929	4492 (91)	6200	5442 (88)
	Levofloxacin	48	35 (73)	38	22 (58)	63	33 (52)
	Meropenem	5068	4772 (94)	4967	4537 (91)	6200	5466 (88)
	Piperacillin-tazobactam	4967	2799 (56)	4951	2718 (55)	6267	3408 (54)
Private	Amikacin	2444	1964 (80)	3162	2392 (76)	3895	3346 (86)
	Amoxicillin-clavulanic acid	2450	975 (40)	3175	1133 (36)	3902	1283 (33)
	Cefepime	2435	1070 (44)	3167	1231 (39)	3899	1471 (38)
	Cefotaxime/ceftriaxone	2442	1052 (43)	3169	1203 (38)	3625	1334 (37)
	Ceftazidime	1760	789 (45)	2307	895 (39)	3131	1182 (38)
	Ciprofloxacin	2068	1231 (60)	2824	1528 (54)	3341	1638 (49)
	Cotrimoxazole	1853	789 (43)	2625	1027 (39)	2819	1061 (38)
	Doripenem	2376	2185 (92)	3047	2683 (88)	3630	3071 (85)
	Ertapenem	2419	2056 (85)	3124	2403 (77)	3829	2672 (70)
	Gentamicin	2442	1405 (58)	3169	1727 (54)	3896	2061 (53)
	Imipenem	2410	2175 (90)	3121	2647 (85)	3802	3113 (82)
	Levofloxacin	509	382 (75)	551	378 (69)	899	634 (71)
	Meropenem	2431	2206 (91)	3123	2679 (86)	3816	3140 (82)
	Piperacillin-tazobactam	2443	1050 (43)	3169	1184 (37)	3896	1402 (36)

NR = not reported

Non-fermentative Gram-negative bacteria

Acinetobacter baumannii: There were differences in susceptibilities to the aminoglycosides (amikacin and gentamicin) in data both health sectors. In the public sector, non-susceptibility to amikacin increased from 56% to 67% and gentamicin from 68% to 77% between 2016 and 2017 (no change was noted in susceptibility to gentamicin between 2017 and 2018). In the private sector, non-susceptibility to amikacin increased from 37% to 49% and gentamicin from 47% to 59%. Although there were differences in susceptibilities for the carbapenems reported from the public sector between 2016 and 2017, the proportion of susceptible isolates remained stable in 2018 (~20% were susceptible). In the private sector, an increase in non-susceptibility was noted over the three-year period i.e. resistance to imipenem increased from 54% to 64% and to meropenem from 56% to 65%. In addition, non-susceptibility to tigecycline increased from 10% of isolates in 2016 to 29% in 2018 (Table 4).

Table 4. Antimicrobial susceptibility patterns of *Acinetobacter baumannii* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Amikacin	2064	913 (44)	2052	765 (37)	2050	671 (33)
	Doripenem	NR	NR	NR	NR	NR	NR
	Gentamicin	2629	837 (32)	2955	668 (23)	3315	749 (23)
	Imipenem	2581	684 (27)	2865	558 (19)	3322	663 (20)
	Meropenem	2602	654 (25)	2928	549 (19)	3322	661 (20)
	Minocycline	30	6 (20)	33	9 (27)	38	5 (13)
	Tetracycline	16	7 (44)	8	3 (38)	12	4 (33)
	Tigecycline	1279	1176 (92)	1745	1585 (91)	2356	2171 (92)
Private	Amikacin	288	182 (63)	439	249 (57)	390	197 (51)
	Doripenem	275	120 (44)	435	172 (40)	367	135 (37)
	Gentamicin	303	161 (53)	458	212 (46)	402	166 (41)
	Imipenem	304	139 (46)	458	174 (38)	380	137 (36)
	Meropenem	303	133 (44)	458	173 (38)	402	139 (35)
	Minocycline	NR	NR	NR	NR	NR	NR
	Tetracycline	NR	NR	NR	NR	NR	NR
	Tigecycline	212	190 (90)	326	285 (87)	271	192 (71)

NR = not reported

Pseudomonas aeruginosa: An increase in susceptibility to ceftazidime from 79% to 83% was noted for isolates reported from the public sector. In 2018, there was an increase in susceptibility for isolates reported from the private sector from 71% in 2017 to 75%. Isolates reported from the public sector showed no changes in susceptibilities to imipenem and meropenem. There was an increase in susceptibility for isolates reported from the private sector between 2017 and 2018. Susceptibility to imipenem increased from 58% to 66% and meropenem from 60% to 67%. Isolates reported from the private sector showed an increase in susceptibility to piperacillin-tazobactam from 64% in 2017 to 74% in 2018 (Table 5).

Table 5. Antimicrobial susceptibility patterns of *Pseudomonas aeruginosa* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Cefepime	1076	884 (82)	1324	1119 (85)	1247	994 (80)
	Ceftazidime	1150	906 (79)	1404	1173 (84)	1279	1060 (83)
	Doripenem	NR	NR	NR	NR	NR	NR
	Imipenem	1102	845 (77)	1362	1040 (76)	1263	956 (76)
	Meropenem	1123	873 (78)	1372	1063 (77)	1258	950 (76)
	Piperacillin/tazobactam	1118	812 (73)	1369	1112 (81)	1263	1011 (80)
Private	Cefepime	908	652 (72)	1240	862 (70)	1205	888 (74)
	Ceftazidime	892	657 (74)	1228	876 (71)	1203	903 (75)
	Doripenem	883	601 (68)	1208	762 (63)	1144	809 (71)
	Imipenem	911	567 (62)	1243	719 (58)	1208	793 (66)
	Meropenem	912	588 (64)	1244	745 (60)	1206	805 (67)
	Piperacillin/tazobactam	902	582 (65)	1226	780 (64)	1196	889 (74)

NR = not reported

Gram-positive bacteria

Enterococcus faecalis: No differences in susceptibilities to the various antimicrobial agents were observed (Table 6).

Enterococcus faecium: Less than 5% of isolates reported from both health sectors were non-susceptible to both vancomycin and teicoplanin. Isolates from both sectors showed an increase in susceptibility to teicoplanin from 2017 to 2018. No changes in susceptibility patterns were noted for linezolid during the three-year surveillance period (Table 7).

Staphylococcus aureus: Although there was an increase in susceptibility to the penicillinase-stable penicillin cloxacillin from 2016 to 2017, an increase in non-susceptibility from 2017 to 2018 was evident in both sectors i.e. public from 23% to 25% and private from 15% to 18%. A greater percentage of non-susceptible isolates were reported from the public sector compared to the private sector during the three-year surveillance period (Table 8).

Table 6. Antimicrobial susceptibility patterns of *Enterococcus faecalis* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Daptomycin	4	4 (100)	18	18 (100)	4	4 (100)
	Linezolid	1302	1292 (99)	1317	1306 (99)	1663	1644 (99)
	Penicillin/ampicillin	757	679 (90)	892	816 (91)	1292	1178 (91)
	Teicoplanin	947	933 (99)	978	966 (99)	1367	1334 (98)
	Vancomycin	1655	1632 (99)	1670	1643 (98)	1982	1955 (99)
Private	Daptomycin	168	168 (100)	263	263 (100)	244	244 (100)
	Linezolid	511	508 (99)	595	591 (99)	690	688 (100)
	Penicillin/ampicillin	88	66 (75)	82	67 (82)	58	46 (79)
	Teicoplanin	695	692 (100)	816	814 (100)	940	940 (100)
	Vancomycin	726	724 (100)	861	859 (100)	1011	1011 (100)

Table 7. Antimicrobial susceptibility patterns of *Enterococcus faecium* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Daptomycin	8	8 (100)	1	0 (0)	3	3 (100)
	Linezolid	1380	1369 (99)	1236	1224 (99)	1638	1632 (100)
	Penicillin/ampicillin	837	30 (4)	813	46 (6)	1165	64 (5)
	Teicoplanin	1033	1001 (97)	908	853 (94)	1277	1234 (97)
	Vancomycin	1636	1560 (95)	1509	1436 (95)	1878	1819 (97)
Private	Daptomycin	65	63 (97)	104	102 (98)	117	116 (99)
	Linezolid	215	210 (98)	191	190 (99)	241	239 (99)
	Penicillin/ampicillin	38	3 (8)	27	0 (0)	22	0 (0)
	Teicoplanin	295	283 (96)	299	282 (94)	361	350 (97)
	Vancomycin	309	295 (95)	312	294 (94)	389	379 (97)

Table 8. Antimicrobial susceptibility patterns of *Staphylococcus aureus* isolates identified from blood cultures in South Africa, 2016 to 2018.

		2016		2017		2018	
Health sector	**Drug**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**	**Total isolates tested (N)**	**Susceptible (%)**
Public	Cloxacillin	5118	3705 (72)	5108	3951 (77)	6167	4640 (75)
Private	Cloxacillin	1283	950 (74)	1508	1283 (85)	2094	1713 (82)

Discussion & conclusions

Two-thirds of blood culture isolates were reported from the public sector. Gram-negative bacteria were more commonly reported and the relative proportion was higher in the private sector. *Klebsiella pneumoniae* and *S. aureus* were the most common organisms reported from the ESKAPE group. The relative proportions for organisms within each sector were similar over the study period. However, differences were observed between the two sectors. These findings show that higher proportions of *A. baumannii*, *E. faecium* and *S. aureus* were reported from the public sector, while higher proportions of *E. coli* and *P. aeruginosa* were reported in the private sector. Proportions for *K. pneumoniae* and *E. faecalis* were similar between both sectors.

There were notable differences for the Enterobacteriaceae. Compared to 2017, *E. coli* isolates from both sectors displayed lower susceptibilities to ciprofloxacin, amoxicillin-clavulanic acid and the cephalosporins in 2018. In addition, almost 25% of *E. coli* isolates were non-susceptible to piperacillin-tazobactam in the private sector. *Klebsiella pneumoniae* showed a worrisome continuous decrease in susceptibility to the carbapenems in both health sectors. There were substantial differences in the susceptibility profile for *A. baumannii* between 2017 to 2018. Isolates showed a decrease in susceptibility to the aminoglycosides and carbapenems in both health sectors. Of note, there was a 20% drop in susceptibility against tigecycline. *Pseudomonas aeruginosa* isolates reported from the public sector showed no noteworthy differences in susceptibility profiles. However, isolates from the private sector showed increases in susceptibility to ceftazidime and piperacillin/tazobactam. Susceptibility to the traditional antimicrobial agents may suggest that these can be used for longer durations.

Several limitations are highlighted in this report. The retrospective design of the study was based on obtainable data but some information was missing. Confirmatory AST methods were not recorded due to capturing AST only from primary screening testing on the laboratory information system. Data may have been incomplete owing to missing information not captured on the laboratory information system; for instance, susceptibility to ertapenem for *K. pneumoniae* was higher compared to meropenem in the public sector. The converse was observed in the private sector, which is expected. Colistin testing was not standardised across the both public and private sectors and therefore it was omitted from this report. No

demographic, epidemiological, clinical or molecular data were available to distinguish between healthcare-associated and community-associated infections.

Surveillance during this period confirms that resistance rates are increasing for carbapenems among Enterobacteriaceae in both health sectors, and in *A. baumannii,* particularly in the public sector. The carbapenem resistance is of concern as this stimulates the use of colistin in SA as a treatment option for these multidrug-resistant organisms. *Staphylococcus aureus* showed a slight increase in cloxacillin susceptibility (i.e. decrease in MRSA) over this period. Evidence of increasing antimicrobial resistance shows that monitoring these trends is of critical importance for public health interventions in community and hospital settings.

Acknowledgements

The authors wish to thank S. Candy and her team from SIMU at the NICD for making the data available, the South African Society for Clinical Microbiology editorial committee (N. Govender, W. Lowman, C. Govind, M. Maloba, K. Swe Swe-Han, C. Bamford, C. Sriruttan, K. Moodley, I. Zietsman, B. Magazi, R Kularatne, and Y. Mahabeer) for comments and suggestions and T. Zwane for assistance with data analysis.

References

1. Mulani MS, Kamble EE, Kumkar SN, Tawre MS, Pardesi KR. Emerging strategies to combat ESKAPE pathogens in the era of antimicrobial resistance: A review. *Front Microbiol.* 2019;10.
2. Perovic O, Schultsz C. Stepwise approach for implementation of antimicrobial resistance surveillance in Africa. *Afr J Lab Med*. 2016;5(3):1–7.
3. Schellack N, Benjamin D, Brink A, Duse A, Faure K, Goff D, et al. A situational analysis of current antimicrobial governance, regulation, and utilization in South Africa. *Int J Infect Dis* [Internet]. 2017;64:100–6. Available from: https://doi.org/10.1016/j.ijid.2017.09.002
4. World Health Organization. Global antimicrobial resistance surveillance system. *WHO* [Internet]. 2015;36. Available from: http://apps.who.int/iris/bitstream/10665/188783/1/9789241549400_eng.pdf?ua=1

BLOOD CULTURE SPECIMEN COLLECTION PRACTICES AMONG PATIENTS WITH SUSPECTED BLOODSTREAM INFECTIONS AT AN EMERGENCY DEPARTMENT OF A TERTIARY HOSPITAL IN JOHANNESBURG, 14-20 JUNE 2018

Itumeleng Moema,[1,2,3] Liliwe Shuping,[2] Lazarus Kuonza,[1,2] Olga Perovic[3,4]

[1]School of Health Systems and Public Health, University of Pretoria, Tshwane
[2]South African Field Epidemiology Training Programme, NICD
[3]Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses, NICD
[4]Department of Clinical Microbiology and Infectious Diseases, University of the Witwatersrand, Johannesburg

Summary

Rapid diagnosis of bloodstream infections (BSIs) is critical to initiate appropriate treatment to reduce mortality and morbidity among patients. Blood culture remains the gold standard for diagnosis of BSIs and guidelines have been developed in order to optimise the benefits of this tool. Since the publication of the South African blood culture guidelines in 2010, few studies have evaluated healthcare workers' adherence to the recommended practices. The objectives of this study were to determine blood culture utilisation among healthcare workers in an emergency department, to quantify the contamination rates of blood cultures, and to assess the knowledge and practices of healthcare workers in a public-sector hospital in South Africa. A cross-sectional study was conducted at a Johannesburg tertiary hospital from 14-20 June 2018. The first fifty adult (≥17 years) patients admitted through the emergency department per day were screened for signs and symptoms of BSI/sepsis that qualify them for a blood culture, and the proportion that eventually received a blood culture was determined. Medical record reviews were conducted to collect demographic and clinical data, and laboratory information was obtained from the National Health Laboratory Service (NHLS) Central Data Warehouse. Knowledge, attitudes and practices of healthcare workers around recommended blood culture practices were assessed using a self-administered questionnaire. A total of 402 adult patients was admitted through the emergency department during the study period, and 165 (41%) of these were assessed for BSI/sepsis symptoms, including temperature of 38°C and above, or

tachycardia (abnormal heart rate), or tachypnoea (abnormally fast respiratory rate), or bradycardia (abnormally slow heart rate) or elevated white cell count. Of the 165 patients, 110 (67%) met the definition for suspected BSI/sepsis and were enrolled into our study, while 55 (33%) either had missing data or did not meet the inclusion definition. Among patients with suspected BSI/sepsis with available laboratory information (89), 25 (28%) had a blood culture done. Compared to patients who did not receive a blood culture, patients who had one done were more likely to be diagnosed with pulmonary conditions (36% versus 16%, p=0.031), infection-related conditions such as urinary tract infection, suspected sepsis, malaria, etc. (16% versus 5%, p=0.031), metabolic conditions (12% versus 8%, p=0.031), have abnormal white cell counts (57% versus 40%, p=0.179), be HIV-seropositive positive (73% versus 53%, p=0.296) and present with two or more BSI/sepsis signs and symptoms (70% versus 53%, p=0.144). Among 25 patients with blood cultures done, two (8%) had laboratory-confirmed BSI caused by *Escherichia coli* and *Proteus vulgaris*. Coagulase-negative *Staphylococcus* sp. (CNS) was isolated from two patients, yielding a contamination rate of 8%. We interviewed 56 healthcare workers, including 16 (29%) doctors, 32 (58%) professional nurses and 8 (14%) phlebotomists. Many (41%) healthcare workers had no knowledge of available blood culture guidelines and few (11%, 6/56) reported ever being trained on the 2010 guidelines above. There was varied knowledge on recommended practices such as appropriate hand antisepsis, volume of sample required and the effects of antibiotic administration prior to specimen collection. A majority of the doctors 87% (n=14) reported being satisfied with blood culture results and most reported that the reason was that results provided pathogen and susceptibility profiles that allow for targeted treatment. This study demonstrated that blood culture collection guidelines were not consistently adhered to leading to poor blood culture uptake at this facility. We also found poor and inconsistent knowledge of blood culture guidelines among healthcare workers. Periodic training to improve awareness of blood culture guidelines and blood culture practices is recommended.

Introduction

Bloodstream infections (BSIs) affect a substantial number of individuals worldwide, and without timely diagnosis, represent a medical emergency with high mortality rates.[1] Delayed diagnosis or treatment of BSIs may result in severe complications such as sepsis and septic shock, where invasion of microorganisms such as bacteria and fungi of the blood cause dysregulated inflammatory immune response, at times leading to multiple organ failure and death. A number of studies demonstrate the public health burden and impact of BSIs, with a major impact in low-income countries.[2–5] In 2011, BSIs accounted for about 19% of all healthcare-associated infections (HAIs) in low- and middle-income countries. African studies have reported case fatalities between 24% and 53% of children with bacteraemia.[4,5] South African studies have reported that HAIs form the majority of BSIs, accounting for 10% in a study of children and 73% in one adult study.[6,7] Furthermore, the overall cost impact of HAIs include additional hospitalisation days, antimicrobial use and additional laboratory investigations.[6]

Blood cultures are a gold standard laboratory-based diagnostic tool used by clinicians to diagnose and treat BSIs.[1,8] They allow for targeted treatment by providing clinicians with the pathogen identity as well as antimicrobial susceptibility patterns, and have been associated with a reduction in inappropriate antibiotic therapy and an improved reduction in 30-day mortality.[9,10] Despite the benefits of blood cultures, there is a lack of knowledge among healthcare workers on appropriate blood culture collection practices, which influence the diagnostic value of the methodology.[1,8,11–14] Good practice guidelines aimed at assisting clinicians to use blood cultures appropriately, such as identifying eligible patients and using the correct aseptic procedures to reduce contamination, have been published. In South Africa, guidelines aimed at optimizing blood culture yield and reducing contamination rates were published by clinicians and microbiologists in 2010.[15] In addition, the National Health Laboratory Service (NHLS), which provides laboratory diagnostic services for all public-sector hospitals in South Africa, has made available a handbook detailing standard operating procedures for blood culture sample collection.[16] However, available data in South Africa suggest that blood cultures are not used optimally and therefore their benefits are unlikely to be realised.

Several studies done among adults and children have shown a lack of universal implementation, and inconsistencies in blood culture practices as specified in guidelines.[6–8,11,17] For example, a study at a district hospital in Cape Town reported that indicators for performing blood cultures were diverse and inconsistent among clinicians, with fever and sepsis being the most common. In another study, some clinicians reported that they did not regard the above-mentioned 2010 guidelines nor the NHLS handbook as explicit guidelines for blood culture collection. Many studies also show lack of implementation of guidelines as demonstrated by high blood culture contamination rates, often exceeding the 3% recommended by the American Society of Microbiology.[8,11,17–19] In addition to delaying appropriate therapy, contaminants in blood cultures result in inappropriate therapy, which may lead to complications and ultimately death. Contaminants also increase the cost of healthcare, and are associated with 20% increased cost in subsequent laboratory charges, and 39% increased cost related to intravenous antibiotics.[20]

Although various studies have shown inappropriate or lack of use of blood culture guidelines, there is limited data on blood culture utility, and healthcare workers' blood culture practices and knowledge in hospitals in Gauteng. The first objective of this study was to determine whether clinicians at a tertiary hospital in Johannesburg collected blood culture specimens among all eligible patients as stipulated in available guidelines. The second objective was to quantify the contamination rates of blood culture specimens for patients who had a blood culture done. The third objective was to assess the knowledge and practices of blood cultures among healthcare workers.

Methods

Study design and setting: A cross-sectional study was conducted over a seven-day period (14-20 June 2018) at a tertiary hospital in Johannesburg, South Africa. This facility was selected firstly because it is a referral hospital that provides a variety of medical services to patients with multiple and complex medical conditions that makes them susceptible to BSIs. Secondly, it is an academic hospital with an onsite microbiology laboratory where blood cultures are routinely performed. This facility also provides 24-hour emergency services. After assessment or stabilisation, patients presenting at the emergency department are discharged or transferred to one of 21 in-patient wards. The hospital provides medical services to an urban population of

approximately one million people. For the first objective of the study, we identified and enrolled all patients that were eligible for a blood culture according to the 2010 guidelines and the NHLS handbook. On a daily basis, the first fifty patients admitted through the casualty service were screened for clinical criteria that qualified them for a blood culture, and the proportion that eventually received a blood culture was determined. In order to determine blood culture contamination rates among patients with blood cultures done, blood culture data from the NHLS Central Data Warehouse (CDW) were obtained. We then recruited healthcare workers who were on duty on any day during the study period to participate in a knowledge, attitudes and blood culture practices survey.

Study definitions: All eligible adults aged 17 years and above were included in the study. Suspected BSI was defined according to the Guideline for the optimal use of blood cultures, published in 2010.[15] Briefly, suspected BSI was defined as a temperature >38°C, or tachycardia (abnormal heart rate) of more than 90 beats per minute (bpm), or tachypnoea (abnormally fast respiratory rate) of more than 20 bpm, or $PaCO_2$<4.3 kPa (32 mmHg), or bradycardia (abnormally slow heart rate) of slower than 50 bpm, or white cell count (WCC) of more than 12 000 cells/mm^3 or >4-11x10^9 cells/L. Sepsis was defined as any patient with a documented infection who had a sequential organ failure assessment score (SOFA) of two or more points according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).[21] Laboratory-confirmed BSI was defined as a positive blood culture result with a known pathogen that was not a common skin contaminant.[22] Known or recognized pathogens were defined according to the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) organisms list.[22] According to the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) organisms list, contamination was defined as isolation of microorganisms commonly found on the skin and which contaminated specimens during specimen collection.[22] Patients who did not meet the suspected BSI/sepsis definition, those who could not be traced in the wards, and those with missing demographic, clinical and laboratory data necessary for case ascertainment, were excluded from the analysis.

Data collection: The emergency department admission books were used to identify patients and medical records were reviewed to identify suspected cases of BSI/sepsis. Minimal demographic and clinical data, including type of ward, gender, diagnosis, and signs and symptoms related to BSI/sepsis such as fever, white cell count, and tachycardia were collected using a standard data collection form. Medical records and the NHLS laboratory data were used to ascertain blood culture specimen collection. Microbiological laboratory results for all blood cultures done during the study period were accessed from the NHLS CDW. The onsite NHLS laboratory used an automated blood culture system, BACT/ALERT 3D (bioMerieux. Inc. Durham, USA), for culture of organisms, and identification and susceptibility testing was done using the Vitek2 automated system (bioMerieux). Data on knowledge, attitudes and practices (KAPs) of recommended blood specimen collection practices among healthcare workers was collected using a self-administered questionnaire. Sixteen questions were used to assess level of knowledge and practices. Included questions assessed knowledge of the 2010 guidelines or NHLS handbook, prior training, signs and symptoms necessitating a blood culture, number of specimen collection bottles required in a standard blood culture, volume of blood required, temperature at which blood cultures are incubated, the effect of prior antibiotics use on blood cultures, etc. Trained field workers distributed a questionnaire to healthcare workers, including doctors, registered nurses and phlebotomists who were on duty across the hospital during the study period.

Data management and analysis: Patient information was captured electronically onto Epi-Info 7 statistical software. Data quality checks were conducted to ensure all data were complete and accurate. Where possible, missing or incorrect data were sought or rectified using patient records or laboratory reports. Data were analysed using the statistical package STATA version 15.1 (StataCorp LP, College Station, Texas, USA). Summary measures including proportions and medians and corresponding interquartile ranges (IQRs) were reported. The chi squared or Fisher's exact tests were used to compare categorical variables of patients who received a blood culture to patients who did not.

Ethics: Ethical clearance to conduct the study was obtained from the Faculty of Health Sciences Research Ethics Committee of the University of Pretoria (58/2018). Permissions were also obtained from the Gauteng Department of Health and the hospital's research committee and heads of departments. Permission to use the NHLS data was obtained from the NHLS Academic Affairs and Research Department. All healthcare workers were informed about the purpose of the study and gave informed consent before participating. Confidentiality for patients was ensured by assigning a study-specific identity number to protect each patient's identity. Identifying information was not collected for healthcare workers. A unique identifier was assigned to each participant. All data were stored electronically on encrypted devices and were only accessible to study investigators.

Results

A total of 402 patients was admitted through the general casualty service (includes the medical, trauma, orthopaedic, and surgery departments) during the study period, and of the 350 consecutive patients selected, medical files for eligibility screening were available for 165 (47%) (Figure 1). Due to a two-day lag in identifying and enrolling patients, some of the selected patients could not be traced within the hospital wards and some files could not be recovered. Of the 165 patients screened, 110 (67%) met the definition of suspected BSI/sepsis and were enrolled into the study. Fifty-five patients (33%) were excluded because they did not meet the case definition or had missing data. Among the 110 patients with suspected BSI/sepsis, blood culture information could only be retrieved for 89 (81%), and 64 (72%) of these did not receive a blood culture.

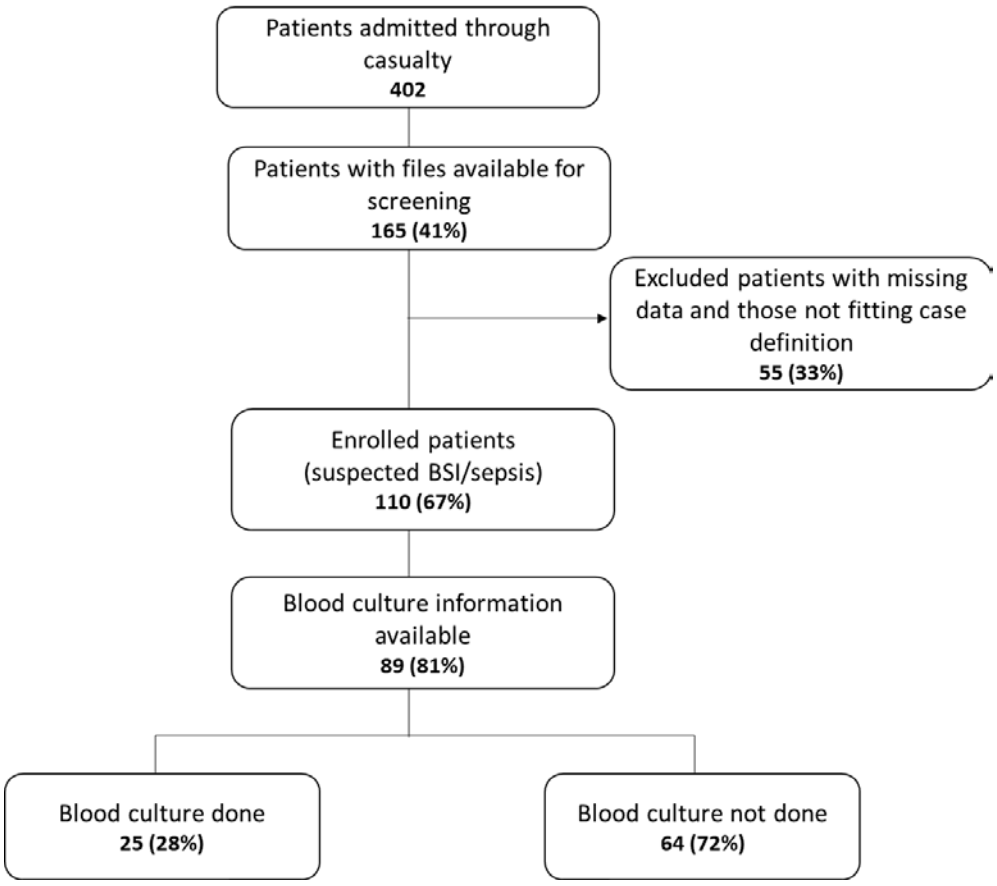

Figure 1. Study flow diagram. BSI = bloodstream infection

Enrolled patients were predominantly male (65/108 [60%]) and the median age was 44 years (IQR 34–61) (Table 1). The most common admission diagnoses (23% [25/106]) were pulmonary conditions such as pneumonia and respiratory failure. Trauma conditions such as vertebral fractures, gunshot wounds and motor-vehicle accidents accounted for 13% (14/106) of the diagnoses. Cardiac conditions such as hypertension and congestive cardiac failure, and infection-related conditions such as urinary tract infection and sepsis, each accounted for 10% (11/106) of the diagnoses. Skin and soft tissue infections accounted for 6% (6/106) of the conditions. Among patients with recorded HIV status, 26% (28/44) were HIV-seropositive. Most patients presented (58% [52/90]) with two or more symptoms related to BSI/sepsis. The median temperature was 36.5°C (IQR, 36°C–36.8°C) and three of the 71 patients with known information had fever (≥38°C). The median WCC was 8.88 x10^9 cells/L (IQR 6.81 – 13.49) and 42% (38/90) of patients had counts that were not within normal ranges. Most patients were transferred to medical units (64% [70/103]), followed by the surgical units (17% [14/103]), orthopaedic units (8% [9/103]) and intensive care units (2% [2/103]).

The proportion of male patients was not significantly higher among patients who had blood cultures done compared to those who did not (68% versus 51%, p=0.14). Compared to patients who did not receive a blood culture, those who had one done were more likely to be diagnosed with pulmonary conditions (36% versus 16.13%, p=0.03), infection related conditions (16% versus 5%, p=0.03), metabolic conditions (12% versus 8%, p=0.03), have abnormal white cell counts (57% versus 40%, p=0.18), and/or be HIV-seropositive (73% versus 53%, p=0.3). The proportion of patients presenting with two or more BSI/sepsis signs and symptoms was higher among those who received a blood culture compared to those who did not (70% versus 53%, p=0.14). Patients who did not receive a blood culture were more likely to have trauma conditions (23% versus 0%, p=0.03). The proportion of patients with fever (temperature ≥38°C) was higher among those who did not receive blood cultures (87% versus 100%, p=0.03). All patients in both groups with known information had tachycardia present. A higher proportion of patients who received blood cultures were given systemic antibiotics (100% versus 60%) and systemic antifungals (5% versus 2%) on admission. Sixty-five percent of patients with a blood culture received the broad-spectrum antibiotic amoxicillin-clavulanic acid (data not shown).

Table 1. Characteristics of patients with suspected blood stream infections (BSI)/sepsis (N=110) at a tertiary hospital in Johannesburg during the period 14-20 June 2018.

Characteristics	All patients n=110 n (%)[b] or median (IQR)	Blood culture done n=25	Blood culture not done n=64	p value
Age in years				
17-24	6 (5.50)	0 (0.0)	3 (4.7)	0.18
25-34	22 (20.2)	8 (32.0)	11 (17.2)	
35-44	28 (25.7)	9 (36.0)	13 (20.3)	
45-54	18 (16.5)	3 (12.0)	11 (17.2)	
55-64	15 (13.8)	1 (4.0)	12 (18.8)	
65+	20 (18.4)	4 (16.0)	14 (21.9)	
Sex				
Female	43 (39.8)	8 (32.0)	31 (49.2)	0.14
Male	65 (60.2)	17 (68.0)	32 (50.8)	
Ward type				
Medical unit	70 (68.0)	17 (70.8)	37 (59.7)	0.07
Surgical unit	19 (18.5)	3 (12.5)	16 (25.8)	
Orthopaedic unit	9 (8.7)	1 (4.2)	8 (12.9)	
Intensive care unit	3 (2.9)	2 (8.3)	0 (0.0)	
High care unit	2 (1.9)	1 (4.2)	1 (1.6)	

Admission diagnosis				
Pulmonary conditions	25 (23.4)	9 (36.0)	10 (16.1)	0.03
Trauma conditions	14 (13.1)	0 (0.0)	14 (22.6)	
Cardiac conditions	11 (10.3)	1 (4.0)	6 (9.7)	
Infectious diseases	11 (10.3)	4 (16.0)	3 (4.8)	
Metabolic conditions	9 (8.4)	3 (12.0)	5 (8.1)	
Skin and soft infections	6 (5.6)	2 (8.0)	4 (6.5)	
Neurological conditions	4 (3.7)	1 (4.0)	3 (4.8)	
Other conditions[a]	26 (24.3)	5 (20.0)	17 (27.4)	
HIV positive				
No	16 (36.4)	4 (26.7)	9 (47.4)	0.3
Yes	28 (63.6)	11 (73.3)	10 (52.6)	
Temperature (°C)	36.5 (36.0–36.8)	36.5 (36.0–37.0)	36.5 (36.1–36.7)	
Temperature ≥38°C	68 (95.8)	20 (87.0)	48 (100)	0.03
Temperature <38°C	3 (4.2)	3 (13.0)	0 (0.0)	
White cell count (10^9 cells/L)	8.9 (6.8–13.5)	8.4 (5.7–14.2)	9.1 (7.2–13.5)	
Within normal range	52 (57.8)	9 (42.9)	33 (60.0)	0.18
Above normal range	38 (42.2)	12 (57.1)	22 (40.0)	
Systolic blood pressure	126 (106–156)	126 (106–157)	125 (99–156)	
Tachycardia present	87 (100)	22 (100)	48 (100)	0.22
No tachycardia	0 (0.00)	0 (0.00)	0 (0.00)	
Respiratory rate	24 (22–28)	23 (21–29)	24 (22–26)	
Tachypnoea present	1 (3.0)	0 (0.0)	1 (5.0)	1.00
No Tachypnoea	32 (97.0)	6 (100)	19 (95.0)	
Number of BSI/sepsis				
One symptom	40 (43.5)	7 (30.4)	24 (47.1)	0.14
≥2 symptoms	52 (56.5)	16 (69.6)	27 (52.9)	
Antibiotics on admission				
No	25 (26.0)	0 (0.0)	22 (40.0)	0.001
Yes	71 (74.0)	22 (100.0)	33 (60.0)	
Antifungals on admission				
No	77 (96.3)	19 (95.0)	45 (97.8)	0.52
Yes	3 (3.7)	1 (5.0)	1 (2.1)	
Surgical treatment				
No	83 (80.6)	23 (95.8)	42 (70.0)	0.01
Yes	20 (19.4)	1 (4.2)	18 (30.0)	

IQR = interquartile range; [a]Other conditions include attempted suicide, systemic lupus erythematosus, etc. [b]Percentages may not sum to 100 due to rounding.

Among 25 patients for whom blood cultures were done, two (8% [2/25]) had laboratory-confirmed BSI due to *Escherichia coli* and *Proteus vulgaris*. Coagulase-negative *Staphylococcus* sp. (CNS) were isolated from two patients, yielding a contamination rate of 8%. No organism was isolated for 84% (21/25) of the patients who had blood cultures done. Both patients with a laboratory-confirmed BSI were above 60 years of age, had co-morbidities and had tachycardia as one of their enrolment criteria, and both received antimicrobial treatment on the day of

admission (data not shown). Overall, patients whose blood culture did not yield an organism had similar clinical characteristics (data not shown).

One hundred and seventy-four healthcare workers were approached and 56 consented to participate in the study, making the survey response rate 32%. The majority (77% [43/56]) of participants were females. Of the 56 healthcare workers, 29% (16) were doctors with a median age of 28 years (IQR, 25–31), 58% (32) were professional nurses with a median age of 36 years (IQR, 23–56), and 14% (8) were phlebotomists with a median age of 38 years (IQR,30–46]. The majority of the doctors (75%, n=12) worked in medical units and four (25%) worked in surgical units. Most nurses worked in the emergency department (31%), followed by surgical units (19%, n=6), high care units (19%, n=6), medical units (16%, n=5) and the orthopaedic unit (16%, n=5). When asked about knowledge of any currently available blood culture standard operating procedures (SOPs), 8 (100%) phlebotomists, 7 (44%) doctors and 3 (32%) nurses reported knowing about an SOP (p=0.04) (Table 3). Most doctors (19%, n=16), nurses (6%, n=2) and phlebotomists (13%, n=1) had not received training on blood culture practices according to the 2010 South African guidelines. All doctors reported that they sometimes make diagnoses that require a blood culture and 81% (n=13) reported taking a blood culture specimen each time it was required. Regarding procedures for specimen collection, 56% (n=9) of the doctors, 85% (n=23) of the nurses and 75% (n=6) of the phlebotomists reported using an appropriate antiseptic to prepare a venepuncture site (p=0.3). Most phlebotomists (75%, n=6) knew the minimum amount of blood required for a blood culture among adults compared to doctors (69%, n=11) and nurses (52%, n=14) (p=0.08). All phlebotomists, 88% (n=14) of the doctors and 50% (n=16) of the nurses knew that antibiotic use prior to specimen collection affects blood culture organism detection (p=0.04). A majority of the doctors (88%, n=14) reported taking a blood culture specimen if the patient was on antibiotics and specimen collection is still indicated. When asked if satisfied with the blood culture results, 87% (n=14) of the doctors and 53% (n=17) of the nurses reported being satisfied. Doctors' reasons (n=11) for satisfaction were that blood culture results provide pathogen and susceptibility profiles that allow for targeted treatment. One doctor (6%) reported not being satisfied with the results due to the high frequency of skin commensals isolation.

Discussion

This study shows that more than two-thirds of patients eligible for a blood culture did not have one done. Compared to the recommended standard, a higher blood culture contamination rate was found. This study however had a very small sample size. This study also found that familiarity with blood culture guidelines and blood culture procedure standards was low among healthcare workers, with phlebotomists generally having a greater awareness than doctors and nurses.

Diagnoses of BSI/sepsis is an important step in the treatment of patients and, consequently, reduction of community- and healthcare-associated infections through surveillance and antimicrobial stewardship. There are, however, limited studies that explore the extent to which healthcare workers use this diagnostic tool. This study found that an overwhelming majority of patients who qualified for blood culture according to available guidelines did not receive one. Among similar studies done in Canada and Denmark, variation in the use of blood cultures has been reported, with some studies showing high usage and some showing usage as low as 11%.[23,24] There is paucity of data regarding blood culture utilisation in our setting. Nonetheless, our study shows that in this Gauteng Province hospital, blood culture specimen collection practices were not in line with available guidelines. Whether this is a reflection of other hospitals in Gauteng Province or the whole of South Africa remains unclear. It is therefore recommended that hospitals assess blood culture utilisation in their own settings as this may improve diagnosis and treatment of BSI/sepsis.[25]

Blood culture guidelines and protocols have been developed so that healthcare workers have a guide on the most likely patients to have BSI/sepsis. The majority of patients with a blood culture investigation in our study had a pulmonary disease as an admission diagnosis, indicating that there may be a high index of suspicion of community-acquired pneumonia among casualty department clinicians. Inclusion of blood culture specimen collection recommendations in the current pneumonia management guidelines might have increased specimen collection among this group of patients.[26] No single symptom was strongly associated with blood culture specimen collection in our study. Instead, patients presenting with two or more BSI/sepsis symptoms were most likely to receive a blood culture. Although we did not ascertain this, clinicians in this study were likely to collect blood culture specimens when patients presented

with a combination of symptoms instead of one, likely due to prior experience with low yield of blood cultures among patients with only one symptom.[27,28]

Despite low blood culture specimen collection in this hospital, the yield of blood cultures was marginally below the generally reported rate of 10%, and similar to the 7.8% reported by a South African study conducted in the same setting.[25,28] There are several factors that affect blood culture yield, including blood volume and antibiotic use prior to specimen collection.[29,30] All patients in our study who received a blood culture were also treated with antibiotics, which may explain the low blood culture yield in this study. However, time stamps of blood culture collection and antibiotic administration were not available. We could therefore not ascertain whether specimens were collected prior to or post-antibiotic administration. Of note, two-thirds of patients who did not get a blood culture were given antibiotics on the day of admission. This is concerning as antimicrobial stewardship programs recommend that empirical treatment be given after taking specimens for microbial cultures and selecting the most appropriate narrow-spectrum antimicrobials based on invading pathogen and susceptibility testing. Antibiotic stewardship through dedicated programmes and infection control practice should be strengthened in this hospital in order to improve practices.[31]

According to The American Society of Microbiology, the proportion of contaminants in blood cultures should not exceed 3%.[19] Similar to what we found in this study, high rates of contamination have been reported in other South African studies.[6–8,11,17] One study conducted at peripheral hospitals reported decreased blood culture contamination rates, from 7-9% in 2006-2007 to 4.6% in 2010; however, the current rate was still higher than that recommended.[18] Taken together, these results suggests that blood culture procedures in South African hospitals are not optimally performed, necessitating widespread awareness and training on currently available guidelines. Such interventions have been shown to be effective at bringing about changes in blood culture practice and decreasing contamination rates.[32,33] Feedback on blood culture practice errors, contamination rates, adverse effects on patient outcomes and costs incurred because of guidelines and standard practice deviation, should be communicated to healthcare workers.

Best blood culture practices require a thorough understanding and knowledge of recommended guidelines such as appropriate indications for ordering and drawing of specimens, recommended drawing site, appropriate application of skin antiseptics and the blood collection process.[12,13,34,35] In this study, knowledge and practice of blood cultures among healthcare workers was unsatisfactory and suboptimal, although phlebotomists generally demonstrated better knowledge compared to other healthcare workers. Overall, these findings were similar to studies that reported a gap in knowledge, attitudes and practices among nursing staff, phlebotomists, patient care assistants and laboratory technicians.[12,34] One of the reasons for these findings is likely that a low proportion of healthcare workers surveyed were familiar with or had ever received training on available guidelines. Interestingly, nearly 90% of all doctors reported collecting blood culture specimens each time when indicated. This was contrary to a Nigerian study that reported that only 39.8% of doctors request a blood culture when indicated.[12] In addition, the high number of doctors in this study reporting specimen-taking did not match the low rates of blood cultures done among the study patients, indicating that blood culture practices among healthcare workers might be inappropriate. Furthermore, we found that a quarter of all healthcare workers did not know the minimum blood volume required for a blood culture among adults, and nearly 40% of doctors did not identify the correct hand antiseptic solution for use when collecting blood culture specimens. These findings indicate that some healthcare workers may not follow the recommended antiseptic techniques required, nor the volume of specimen needed, resulting in low yields of blood cultures and high rates of contamination.[33,34]

This study had several limitations, which limits interpretation and generalisation to other South African public-sector hospitals. Low utilisation of blood cultures was ascertained using information on the first day of admission, which means we might have missed additional blood cultures that were taken on subsequent hospital days as the conditions of the patients progressed. Only 47% of selected patients were screened for enrollment in the study and some of the medical records of enrolled patients had missing information, further limiting identification of patients with suspected BSI/sepsis who had a blood culture done, and resulting in data sparsity for statistical analysis. Furthermore, the short duration of our study likely did not account for periodic changes such as the type of diseases most prevalent during specific seasons, which may affect clinicians' decisions to do a blood culture. Additionally, variation in

blood culture practices may differ between sessional staff rotating in the emergency department. Although efforts were made to include as many healthcare workers in this survey as possible, the response rate was low, and therefore the findings of this survey may not be representative of the entire hospital. Lastly, blood cultures were collected by doctors working in the emergency department, none of whom participated in our survey, making it difficult to directly correlate survey findings to blood culture practices. Although this study was conducted at only one hospital, findings were in line with other studies done in South Africa. We therefore believe that these findings give an indication of knowledge and awareness among healthcare workers on blood culture guidelines, and the extent at which blood cultures are utilised at emergency departments of tertiary public-sector hospitals.

Conclusion

Low knowledge and adherence to blood culture guidelines among healthcare workers was evident from this study, with the exception of phlebotomists. Periodic training on blood culture guidelines is therefore recommended. Development of a blood culture task team and feedback system on blood culture practices and contamination rate could improve guideline adherence among all healthcare workers.[36,37]

Acknowledgements

We thank the South African Field Epidemiology Training Programme (SAFETP) and the Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM), National Institute for Communicable Diseases (NICD) for their financial and human resources support. The National Health Laboratory Service is thanked for providing laboratory data. Lastly, we thank the Helen Joseph Hospital management and the healthcare staff for their assistance and participation in this study.

References

1. Lamy B, Dargère S, Arendrup MC, Parienti JJ, Tattevin P. How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the art. Vol. 7, *Frontiers in Microbiology*. 2016.
2. Etyang AO, Scott JAG. Medical causes of admissions to hospital among adults in Africa: A systematic review and 2003. *Glob Health Action*. 2013;6(1).

3. World Health Organization (WHO). Report on the burden of endemic health care-associated infection Worldwide. WHO Library Cataloguing-in-Publication Data, WHO Document Production Services. 2011.
4. Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among children admitted to a rural hospital in Kenya. *N Engl J Med* [Internet]. 2005;352(1):39–47. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa040275
5. Aiken AM, Mturi N, Njuguna P, Mohammed S, Berkley JA, Mwangi I, et al. Risk and causes of paediatric hospital-acquired bacteraemia in Kilifi District Hospital, Kenya: A prospective cohort study. Vol. 378, *The Lancet*. 2011. p. 2021–7.
6. Dramowski A, Whitelaw A, Cotton MF. Burden, spectrum, and impact of healthcare-associated infection at a South African children's hospital. *J Hosp Infect*. 2016;94(4):364–72.
7. McKay R, Bamford C. Community-versus healthcare-acquired bloodstream infections at groote schuur hospital, Cape Town, South Africa. *South African Med J*. 2015;105(5):363–9.
8. Abrahams MS, Whitelaw AC, Orth H. Time for a culture change? Suboptimal compliance with blood culture standards at a district hospital in Cape Town. South *African Med J*. 2015;105(12):1039–43.
9. Meehan TP. Quality of care, process, and outcomes in elderly patients with pneumonia. *J Am Med Assoc* [Internet]. 1997;278(23):2080. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.1997.03550230056037
10. Metersky ML, Ma A, Bratzler DW, Houck PM. Predicting bacteremia in patients with community-acquired pneumonia. *Am J Respir Crit Care Med* [Internet]. 2004 Feb 1 [cited 2019 Jan 10];169(3):342–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14630621
11. Lochan H, Bamford C, Eley B. Blood cultures in sick children. *South African Med J*. 2013;103(12):918–20.
12. Ojide CK, Onwuezobe AI, Asuquo EE, Obiagwu CS. Knowledge, attitude and practice of blood culture: A cross sectional study among medical doctors in a Nigerian Tertiary Hospital. *African J Clin Exp Microbiol* [Internet]. 2013;14:174–9. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=awn&AN=ajcem-91755&site=ehost-live http://www.ajol.info/index.php/ajcem/article/view/91755
13. Park WB, Myung SJ, Oh MD, Lee J, Kim NJ, Kim EC, et al. Educational intervention as an effective step for reducing blood culture contamination: A prospective cohort study. *J Hosp Infect.* 2015;91(2):111–6.
14. Nair A, Elliott SP, Al Mohajer M. Knowledge, attitude, and practice of blood culture contamination: A multicenter study. *Am J Infect Control* [Internet]. 2017 May 1 [cited 2019 Oct 12];45(5):547–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28214162

15. Ntusi N, Aubin L, Oliver S, Whitelaw A, Mendelson M. Guideline for the optimal use of blood cultures. *South African Med J*. 2010;100(12):839–43.
16. National Health Laboratory Service Handbook Technical Working Group. NHLS Handbook: Document number: GPQ0064: Version number: 1[Internet]. [cited 2019 Jan 10]. Available from: http://www.pathology.uct.ac.za/sites/default/files/image_tool/images/231/documents/NHLS_Handbook_2015.pdf
17. Kenyon CR, Fatti G, Schrueder N, Bonorchis K, Meintjes G. The value of blood culture audits at peripheral hospitals. Vol. 102, *South African Medical Journal*. 2012. p. 224–5.
18. Weddle G, Jackson MA, Selvarangan R. Reducing blood culture contamination in a pediatric emergency department. *Pediatr Emerg Care*. 2011;27(3):179–81.
19. Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RB, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the infectious diseases society of America (IDSA) and the American Society for Microbiology (ASM). *Clin Infect Dis.* 2013;57(4).
20. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: The true consequences of false-positive results. *J Am Med Assoc*. 1991;265(3):365–9.
21. Singer M, Deutschman CS, Seymour C, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). Vol. 315, *Journal of the American Medical Association*. 2016. p. 801–10.
22. Centers for Disease Control and Prevention. National Healthcare Safety Network (NHSN) Patient Safety Component Manual. [Internet]. [cited 2020 June 4]. Available from: https://www.cdc.gov/nhsn/PDFs/pscManual/pcsManual_current.pdf
23. Laupland KB, Church DL, Gregson DB. Blood cultures in ambulatory outpatients. BMC Infect Dis [Internet]. 2005 May 17 [cited 2019 Feb 12];5:35. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15904503
24. Gubbels S, Nielsen J, Voldstedlund M, Kristensen B, Schønheyder HC, Vandenbroucke-Grauls CMJE, et al. Utilization of blood cultures in Danish hospitals: A population-based descriptive analysis. *Clin Microbiol Infect*. 2015 Apr 1;21(4):344.e13-344.e21.
25. Boyles TH, Davis K, Crede T, Malan J, Mendelson M, Lesosky M. Blood cultures taken from patients attending emergency departments in South Africa are an important antibiotic stewardship tool, which directly influences patient management. *BMC Infect Dis* [Internet]. 2015 Oct 6 [cited 2020 Mar 16];15(1):410. Available from: http://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-1127-1
26. Boyles TH, Brink A, Calligaro GL, Cohen C, Dheha K, Maartens G, et al. South African guideline for the management of community-acquired pneumonia in adults [Internet]. [cited 2019 Dec 9]. Available from: https://www.fidssa.co.za/Content/Documents/Boyles-et-al-SA-CAP-Guideline-J-Thoracic-Diseases-2017.pdf

27. Linsenmeyer K, Gupta K, Strymish JM, Dhanani M, Brecher SM, Breu AC, et al. Culture if spikes? Indications and yield of blood cultures in hospitalized medical patients. *J Hosp Med* [Internet]. 2016 May 1 [cited 2019 Apr 15];11(5):336–40. Available from: http://www.journalofhospitalmedicine.com/jhospmed/article/127949/yield-blood-cultures
28. Kelly AM. Clinical impact of blood cultures taken in the emergency department. *J Accid Emerg Med* [Internet]. 1998 Jul [cited 2019 Jan 14];15(4):254–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9681310
29. Neuhauser M. National Center for Emerging and Zoonotic Infectious Diseases Antibiotic Stewardship: optimizing antibiotic use in inpatient settings annual NHSN Training-March 2, 2018 [Internet]. 2018 [cited 2019 Jan 14]. Available from: https://www.cdc.gov/antibiotic-use/stewardship-report/index.html
30. Riedel S, Bourbeau P, Swartz B, Brecher S, Carroll KC, Stamper PD, et al. Timing of specimen collection for blood cultures from febrile patients with bacteremia. *J Clin Microbiol* [Internet]. 2008 Apr 1 [cited 2019 Apr 28];46(4):1381–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18305133
31. Morrill HJ, Caffrey AR, Jump RLP, Dosa D, LaPlante KL. Antimicrobial stewardship in long-term care facilities: A call to action. Vol. 17, *Journal of the American Medical Directors Association*. 2016. p. 183.e1-183.e16.
32. Hall KK, Lyman JA. Updated review of blood culture contamination. Vol. 19, *Clinical Microbiology Reviews*. 2006. p. 788–802.
33. Denno J, Gannon M. Practical steps to lower blood culture contamination rates in the emergency department. *J Emerg Nurs*. 2013;39(5):459–64.
34. Nair A, Elliott SP, Al Mohajer M. Knowledge, attitude, and practice of blood culture contamination: A multicenter study. *Am J Infect Control*. 2017;45(5):547–8.
35. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008. *Intensive Care Med* [Internet]. 2008 Jan 4 [cited 2019 Jan 10];34(1):17–60. Available from: http://link.springer.com/10.1007/s00134-007-0934-2
36. Al-Hamad A, Al-Ibrahim M, Alhajhouj E, Al-Alshaikh Jaffer W, Altowaileb J, Alfaraj H. Nurses' competency in drawing blood cultures and educational intervention to reduce the contamination rate. *J Infect Public Health* [Internet]. 2016 [cited 2019 Jan 11];9:66–74. Available from: http://dx.doi.org/10.1016/j.jiph.2015.06.0071876-0341/
37. Bowen CM, Coleman T, Cunningham D. Reducing blood culture contaminations in the emergency department: It takes a team. *J Emerg Nurs* [Internet]. 2016 Jul [cited 2019 Jan 14];42(4):306–11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27063211

CASE REPORT: ODYSSEAN MALARIA AT A RESIDENTIAL ESTATE, CITY OF TSHWANE, 14 JANUARY 2020

Jessica Yun

Centre for Respiratory Diseases and Meningitis, NICD

Summary

In November 2019, the National Institute for Communicable Diseases (NICD) was notified of a malaria case at a residential estate, City of Tshwane, Gauteng Province. The case was investigated on 14 January 2020. An interview was conducted with the case-patient to gather information on demographics, clinical and exposure history, and an environmental assessment of the residence and immediate surroundings was conducted. The patient was a 48-year-old male. He and family members had no travel history to a malaria-endemic area. Following an initial misdiagnosis, the patient was hospitalized for 9 days and recovered following antimalarial treatment. The patient's residence is in close proximity (approximately 50-60 meters) to the N4 national highway on which vehicles from malaria-endemic areas may travel through. There was no evidence of local free-standing water that could enable mosquito breeding. The outbreak was most likely caused by the accidental introduction of an infected mosquito by a vehicle returning from a malaria transmission area, an event known as Odyssean malaria.

Background

Malaria is endemic to only three of South Africa's nine provinces including the northeastern areas of KwaZulu-Natal (KZN), Mpumalanga and Limpopo provinces.[1] Malaria in South Africa is seasonal, and peaks during the warmer, wetter summer months from September to May.[2] The malaria season overlaps with the festive period during which there is increased traffic flow between Gauteng Province and malaria endemic areas within South Africa and neighboring countries, especially Mozambique and Zimbabwe. This increases the incidence of a category known as Odyssean malaria. Odyssean malaria is acquired locally through a bite of an infective

Anopheles mosquito that has been inadvertently imported from a malaria endemic area via ground or air transport.[3]

Malaria is transmitted by certain *Anopheles* mosquito species that are endemic to South Africa's low altitude northeastern regions. This is the southernmost extent of their distribution in sub-Saharan Africa in which these species are common. Malaria generally presents as a 'flu-like febrile illness that can be fatal if not diagnosed and treated soon after the onset of symptoms.[2]

In South Africa, malaria is a class I notifiable medical condition (NMC). This means that notification should be made immediately upon the identification of a case that meets either the suspected, probable or confirmed case definition as given in the NMC guidelines.[4] Following notification of a case for which there is no travel history (i.e. a case of locally acquired malaria), an entomological assessment of the index house and the surrounding geographical location should be conducted by environmental health officials.[4] This is to identify potential *Anopheles* mosquito breeding sites that may indicate a need for insecticide-based control measures in the immediate area.

On 11 November 2015, the Outbreak Response Unit, Division of Public Health Surveillance and Response of the National Institute of Communicable Diseases (NICD), received a notification of a confirmed malaria case by the Gauteng Province Department of Health. The case-patient was a 49-year-old male who was admitted to a private hospital on 11 December 2019. The patient reported symptoms including fever, headache, nausea, vomiting and flu-like illness. As the patient had no travel history (within the past 3 months) to a malaria-endemic area, an investigation was subsequently conducted by the provincial/district Department of Health environmental health officers, district communicable disease coordinator and NICD to identify contacts and determine the possible cause of transmission. The objectives of the follow-up investigation were: 1) to describe the characteristics of the laboratory-confirmed malaria case; 2) to visit the index house and establish if there were breeding sites for mosquitoes, collect mosquito larvae and, if possible, to collect and identify mosquito vectors of malaria and 3) to conduct a site investigation in the immediate vicinity of the index house to identify possible routes of mosquito importation.

Methods

A descriptive study was conducted using the following case definitions as per NMC guidelines[4]:

- A suspected case in a non-endemic malaria area was defined as an individual presenting with fever, headache and/or 'flu-like illness (acute febrile 'flu-like illness) with no other cause for illness and non-specific laboratory findings.
- A probable case was defined as a clinically suspected case in an endemic area.
- A confirmed case demographics as an individual with a positive laboratory malaria test (malaria rapid antigen test, blood smear, or PCR) for *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* or *P. knowlesi*.

To establish the magnitude and possible source/s of the outbreak, the following activities were conducted during the site visit:

Epidemiological investigation: An in-depth key informant interview was conducted with the case-patient to gather information on demographics, clinical and malaria exposure history. Informed consent was granted.

Laboratory investigation: Blood smear microscopy and PCR analysis for the detection of malaria parasites was conducted by the hospital laboratory service at the time case-patient was admitted. No additional laboratory investigations were undertaken during the investigation for the confirmed case.

Environmental investigation: An environmental assessment of the case-patient's residence (index house) and immediate surroundings was conducted to identify possible mosquito breeding sites.

Public health intervention measures: Information pamphlets were distributed to the patient and health/promotion activities about malaria were conducted among community members and clinicians at nearby hospitals in the City of Tshwane by the provincial/district Department of Health.

Results

Epidemiological and clinical information: On 10 December 2019, a 48-year-old male developed symptoms of fever and fatigue and visited a nearby clinic. However, he was incorrectly diagnosed as having a stomach lining issue and was given treatment to alleviate the symptoms. As the day progressed his symptoms worsened and he reported a headache, nausea, vomiting, flu-like symptoms, sweating and was not able to sleep. On 11 December 2019, he went to a private hospital and was put on an IV drip. Blood tests were conducted and viral hepatitis was initially suspected. The patient was later admitted to ICU and was diagnosed with malaria following microscopy and PCR analysis of a blood sample. He was hospitalised for 9 days and recovered following antimalarial treatment. He was discharged on 20 December 2019.

The patient resides on a secure residential estate on the east side of Pretoria. He is a white-collar office worker and commutes to Johannesburg (Sandton) daily. He had no history of travel to a malaria-endemic area, and no recent needlesticks or blood transfusions were reported. He does not have a domestic worker and had no knowledge of other contacts (friends, family, neighbours and colleagues) who had travelled to an endemic area during the epidemiologically relevant period.

Environmental investigation: The patient's residence is immediately adjacent to the N4 national highway. As it is possible for mosquitoes to be transported long distances by road transport, there is an increased risk of imported malaria from vehicles that use highways as arterial routes between provinces.[3] An environmental investigation revealed no mosquitoes in the home and there was no evidence of free-standing water that could enable mosquito breeding. Therefore, no specific vector control measures were conducted at the residence.

Discussion & conclusion

This investigation shows a sporadic case of Odyssean malaria in a non-endemic area, with no evidence of an epidemiological link to any other case. The patient had no history of travel to any malaria-endemic areas, resulting in a delayed diagnosis. The high case fatality rates associated with Odyssean malaria are generally attributable to late presentation at health facilities and delayed or missed diagnoses.

Odyssean malaria can have a case fatality rate as high as 50% (current average is 17%) as compared to the national malaria case fatality rate of 0.7% in 2018.[5,6] The initial misdiagnosis in the case reported here highlights the importance of keeping malaria as a differential diagnosis for patients presenting with febrile illness, even in the absence of a travel history to a malaria endemic area.

Based on date of symptom onset and the typical incubation period for malaria, the patient in this case most likely acquired malaria from the bite of an infective *Anopheles* mosquito during the last week of November 2019. The mosquito in question could have alighted from a car, taxi, bus or truck that had stopped on the N4 highway in close proximity to the patient's residence.

Community outreach and recommendations

Upon completion of the investigation, malaria information pamphlets were provided to the patient. Additionally, health/promotion activities about malaria were conducted among community members and clinicians at nearby hospitals in the City of Tshwane by the provincial Department of Health. More specifically, healthcare workers were advised to consider malaria when a patient presents with 'flu-like illness, fever (>38°C) and headache, and progressively worsens over a short period of time, regardless whether there is a travel history to an endemic area or not. It was further advised that potential mosquito breeding sites should be drained or treated with an appropriate larvicide.

Acknowledgements

We thank staff and management of the provincial Departments of Health (surveillance officers, communicable disease control coordinators, local health authorities/healthcare workers) and the National Institute for Communicable Diseases (Parasitology and Vector Control Reference Laboratories, Outbreak Response Unit and the South African Field Epidemiology Training Programme), who made the investigation possible.

References

1. Maharaj R, Raman J, Morris N, Moonasar D, Durrheim DN, Seocharan I, et al. Epidemiology of malaria in South Africa: From control to elimination. *South African Med J.* 2013;103(10):779–83.
2. National Department of Health (NDoH) South Africa. National guidelines for the prevention of malaria, South Africa, 2018. 2018.
3. Frean J, Brooke B, Thomas J, Blumberg L. Odyssean malaria outbreaks in Gauteng Province, South Africa, 2007 - 2013. *South African Med J.* 2014;104(5):335–8.
4. National Institute for Communicable Diseases. NMC guideline. 2018.
5. National Institute for Communicable Diseases. Clusters of odyssean malaria in Gauteng Province—December 2018. *Communicable Diseases Communique*. 2019;18(1):6–7. Available from: www.nicd.ac.za
6. World Health Organization. World malaria report 2019. 2019. Available from: www.who.int/malaria

MALARIA VECTOR SURVEILLANCE REPORT, SOUTH AFRICA, JANUARY – DECEMBER 2019

Yael Dahan-Moss[1,2], Eunice Jamesboy[1,2], Leanne Lobb[1,2], Blazenka Letinic[1,2], Jacek Zawada[1,2], Zandile Langa[1,2], Miriam Mwamba[1,2], Erica Vogel[2], Maria Kaiser[1,2], Thabo Mashatola[1], Shune Oliver[1,2], Givemore Munhenga[1,2], Power Tshikae[1,2], Michael Samuel[1,2], Oliver Wood[1,2], Eric Raswiswi[3], Dumisani Dlamini[3], Nondumiso Mabaso[3], Zuziwe Manyawo[3], Silindile Sibambo[4], Busisiwe Nkosi[4], John Govere[2], Bryan Silawu[4], Lazarus Mkhabela[4], Fanuel Ndlovu[4], Thembekile Mgwenya[4], Maureen Coetzee[1,2], Lizette Koekemoer[1,2], Basil Brooke[1,2]

[1]Centre for Emerging Zoonotic & Parasitic Diseases, NICD
[2]Wits Research Institute for Malaria, MRC Collaborating Centre for Multidisciplinary Research on Malaria, Faculty of Health Sciences, University of the Witwatersrand
[3]Environmental Health, Malaria and Communicable Disease Control, KwaZulu-Natal Department of Health
[4]Malaria Elimination Programme, Mpumalanga Department of Health

Summary

Malaria in South Africa is seasonal and primarily occurs in the Limpopo, Mpumalanga and KwaZulu-Natal provinces. The control of malaria vector mosquito species is based on indoor spraying of residual insecticides (IRS) and limited larval source management. There were 13780 malaria cases resulting in 79 confirmed deaths in South Africa in 2019. Vector surveillance in collaboration with the National Institute for Communicable Diseases (NICD) during 2019 revealed the presence of four malaria vector species - *Anopheles arabiensis* (n=3,054, 60%), *An. merus* (n=427, 8%), *An. parensis* (n=424, 8%) and *An. vaneedeni* (n=141, 6%). These have previously been shown to contribute to ongoing residual malaria transmission in South Africa. Several closely related non-vector *Anopheles* species were also collected. The specimens analysed were collected from KwaZulu-Natal (85%, n=4,352) and Mpumalanga (15%, n=773) provinces. The surveillance information by province and municipality shows that IRS based vector control needs to be maintained at a high rate of coverage and that spraying should ideally be completed before the onset of each malaria season. Given that all sporozoite positive (and therefore malaria infective) adult *Anopheles* females recently collected were found resting outdoors, and given that there are no large-scale vector control tools targeting outdoor-resting mosquitoes, larviciding, including the treatment of winter breeding sites, should continue to be used as a complimentary method to enhance the effect of IRS in high incidence areas. In the

context of the current COVID-19 pandemic, it is further recommended that all vector malaria control activities be conducted especially timeously and efficiently. This will reduce the risk of co-infection in affected communities and reduce malaria-related hospitalizations.

Introduction

South Africa's malaria affected areas include the low altitude border regions of Limpopo, Mpumalanga and KwaZulu-Natal Provinces. These regions typically experience active malaria transmission, especially during the peak malaria season that spans the summer months of November to April. Malaria incidence in 2019 (13,780 cases) was substantially lower than that recorded in 2018 (18,638 cases), but still higher than that of 2016 (9,478 cases).[1]

Each of South Africa's malaria endemic provinces have developed well-coordinated malaria control operations including routine vector control, which is primarily based on the application of indoor residual insecticide spraying (IRS) and, to a lesser extent, larval source management.[2] Although IRS has proven efficacy spanning many decades, residual malaria transmission continues and is likely caused by outdoor feeding and resting *Anopheles* vector mosquitoes that are unaffected by indoor applications of insecticide.[3,4] In addition, populations of the major malaria vector species, *Anopheles funestus* and *An. arabiensis*, have developed resistance to insecticides, especially in northern KwaZulu-Natal.[2,5] The pyrethroid resistance phenotype in *An. arabiensis* in this region is however of low intensity currently and is not considered to be operationally significant at this stage, unlike the pyrethroid-carbamate resistance profile in *An. funestus* which is of high intensity, is highly significant epidemiologically and was at least partly causative of the malaria epidemic experienced in South Africa during the period 1996 to 2000.[6]

Residual malaria transmission, comparatively high incidence and burgeoning insecticide resistance in malaria vector populations within South Africa's borders necessitate ongoing and enhanced vector surveillance to inform best practices for control. This is especially pertinent in terms of South Africa's malaria elimination agenda[7] and the current COVID-19 pandemic, during which it is especially important to reduce disease burden as far as possible. Currently, surveillance is routinely conducted by the entomology teams of Mpumalanga, KwaZulu-Natal and Limpopo provinces with support from partner institutions including the National Institute for Communicable Diseases (NICD), the Wits Research Institute for Malaria (WRIM) of the

University of the Witwatersrand, the Institute for Sustainable Malaria Control of the University of Pretoria, and the South African Medical Research Council.

This report summarises malaria vector surveillance in South Africa in 2019 based on specimens referred to the Vector Control Reference Laboratory (VCRL) of the Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD), NICD.

Methods

During 2019, *Anopheles* mosquitoes were collected from sentinel sites in KwaZulu-Natal and Mpumalanga provinces (Figure 1). These specimens were either collected by VCRL personnel or were referred to the VCRL by partner institutions and provincial malaria control programme entomology teams during the period January to December 2019.

Adult *Anopheles* mosquitoes were collected by human-baited net traps, human landing catches, CO_2 net traps, and outdoor placed clay pots, modified buckets and tyres. Other specimens were collected as larvae and were reared to adults for subsequent analysis. One or more of these collection techniques were deployed at each sentinel site (Figure 1). Adult specimens were preserved on silica gel in 1.5ml tubes and were identified as far as possible using external morphological characters by VCRL, partner institution and/or provincial malaria control programme personnel. Specimens identified as members of the *An. gambiae* complex or *An. funestus* group were subsequently identified to species using standard polymerase chain reaction (PCR) assays. Quality assurance based on the ISO 17025:2017 standard was used to ensure the quality of results.

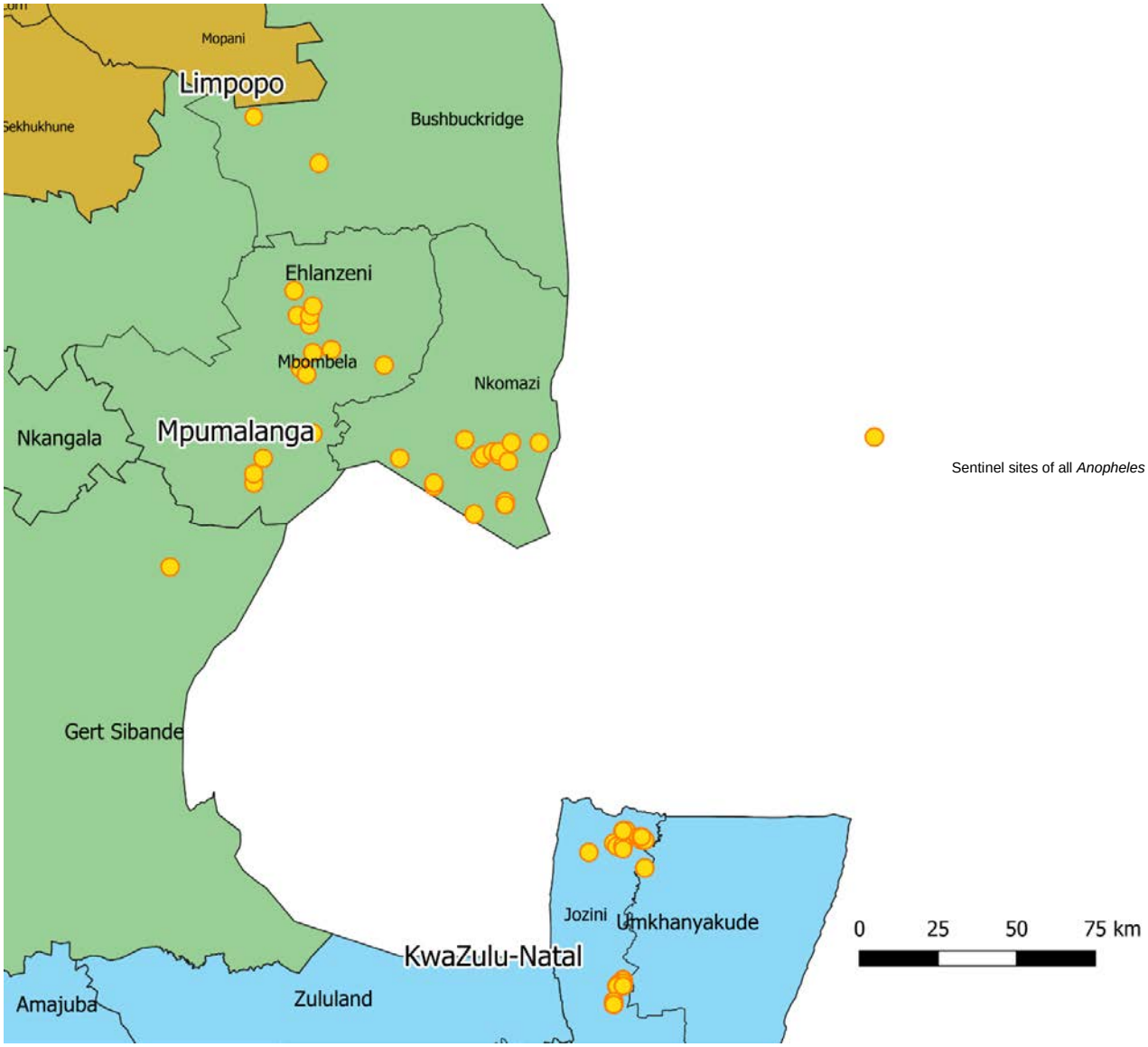

Figure 1. Sentinel sites in KwaZulu-Natal and Mpumalanga provinces from which *Anopheles* species were collected, South Africa, 2019.

Results

A total of 5,125 *Anopheles* mosquitoes was collected from sentinel sites in the Umkhanyakude district of KwaZulu-Natal Province and the Ehlanzeni and Gert Sibande districts of Mpumalanga Province. Most of the specimens were collected from KwaZulu-Natal (85%, n=4,352) followed by Mpumalanga (15%, n=773) (Table 1). These were subsequently identified as members of the *An. gambiae* complex (70%, n=3,574), *An. funestus* group (15%, n=760) or other *Anopheles* species (15%, n=791). *Anopheles arabiensis* predominated the collections (60%, n=3,054) although substantial numbers of *An. marshallii group, An. merus*, *An. parensis*, *An. rivulorum* and *An. vaneedeni* were also obtained (Table 1).

Table 1. Numbers of *Anopheles* specimens collected by species and province, South Africa, 2019.

***Anopheles* species complex, group or other**	***Anopheles* species**	**KwaZulu-Natal**	**Mpumalanga**	**Total**
***An. gambiae* complex**	*An. arabiensis*	2,765	289	3,054
	An. merus	104	323	427
	An. quadriannulatus	23	70	93
***An. funestus* group**	*An. leesoni*	45	8	53
	An. parensis	424		424
	An. rivulorum	112	30	142
	An. vaneedeni	125	16	141
Other *Anopheles* species	*An. coustani*	76		76
	An. caliginosus	1		1
	An. demeilloni	6		6
	An. listeri		23	23
	An. maculipalpis	4	4	8
	An. marshallii group	566		566
	An. pharoensis	17		17
	An. pretoriensis	33	9	42
	An. rufipes	40	1	41
	An. schwetzi	1		1
	An. squamosus	6		6
	An. tenebrous	2		2
	An. ziemanni	2		2
Total		4,352	773	5,125

The malaria vectors *An. arabiensis* and *An. merus* (members of the *An. gambiae* species complex) were collected from sentinel sites in both endemic provinces (Figure 2). In KwaZulu-Natal Province, populations of these species were found in the Jozini, Umhlabuyalingana and Mtubatuba municipalities of the Umkhanyakude District. In Mpumalanga, populations of these species were found in Nkomazi, Bushbuckridge and Mbombela of the Ehlanzeni District and in the Gert Sibande District.

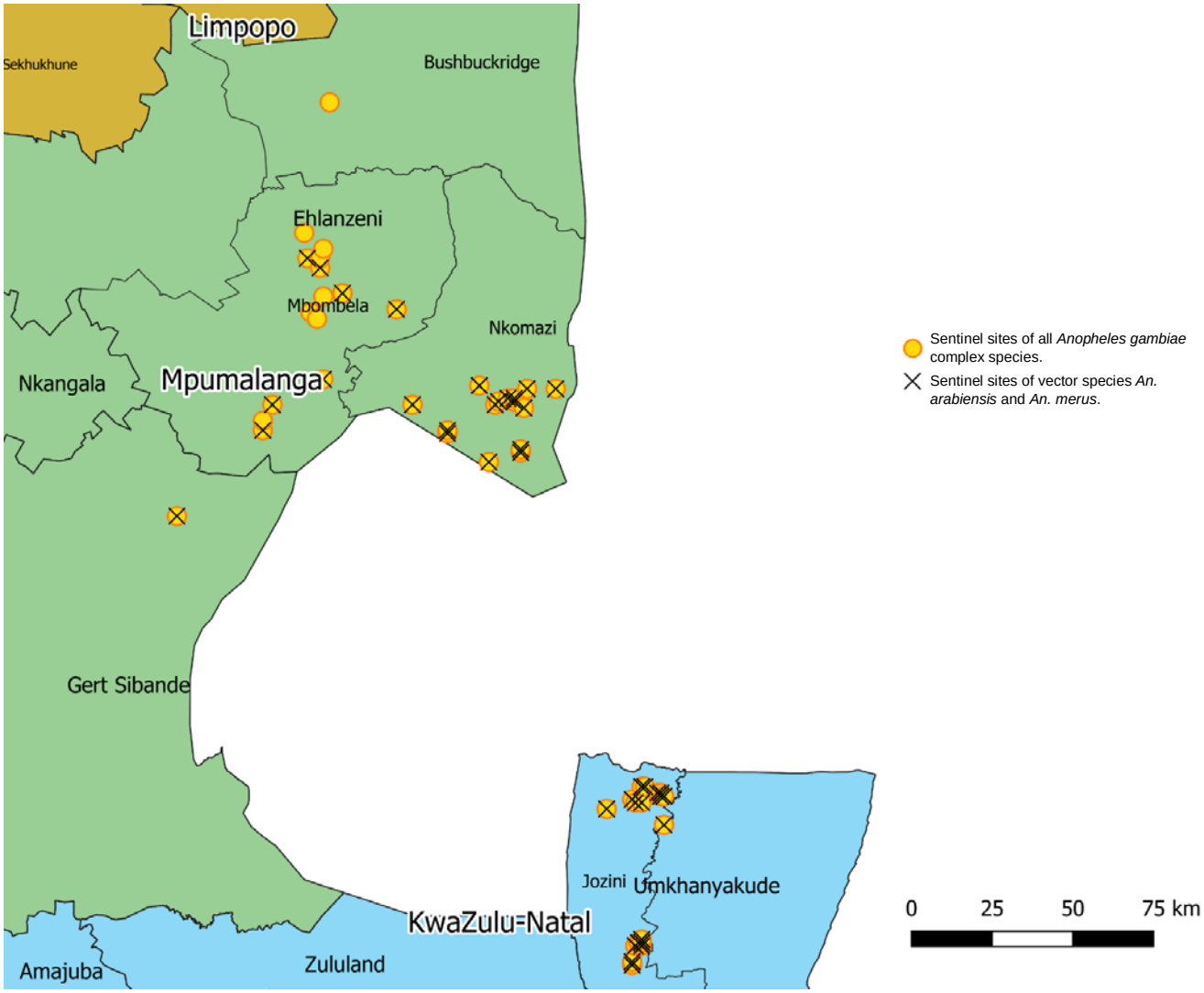

Figure 2. Sentinel sites in KwaZulu-Natal and Mpumalanga provinces from which samples of *Anopheles gambiae* complex species (yellow circle) were collected. Those sites from which the malaria vectors *An. arabiensis* and *An. merus* (black "x") were collected are indicated by an X, South Africa, 2019.

The secondary malaria vector species *An. vaneedeni* [3] was collected from sentinel sites in both provinces while *An. parensis*, also a secondary vector [8], was collected only in KwaZulu-Natal (Table 1). Other potential malaria vector species within the *An. funestus* group that were collected from sentinel sites in both provinces include *An. leesoni* and *An. rivulorum* (Table 1). The distribution of all known and suspected vector species within the *An. funestus* group is shown in Figure 3. Specimens of these species were collected in Jozini in the Umkhanyakude District of KwaZulu-Natal Province and in Nkomazi and Bushbuckridge of the Ehlanzeni District of Mpumalanga Province.

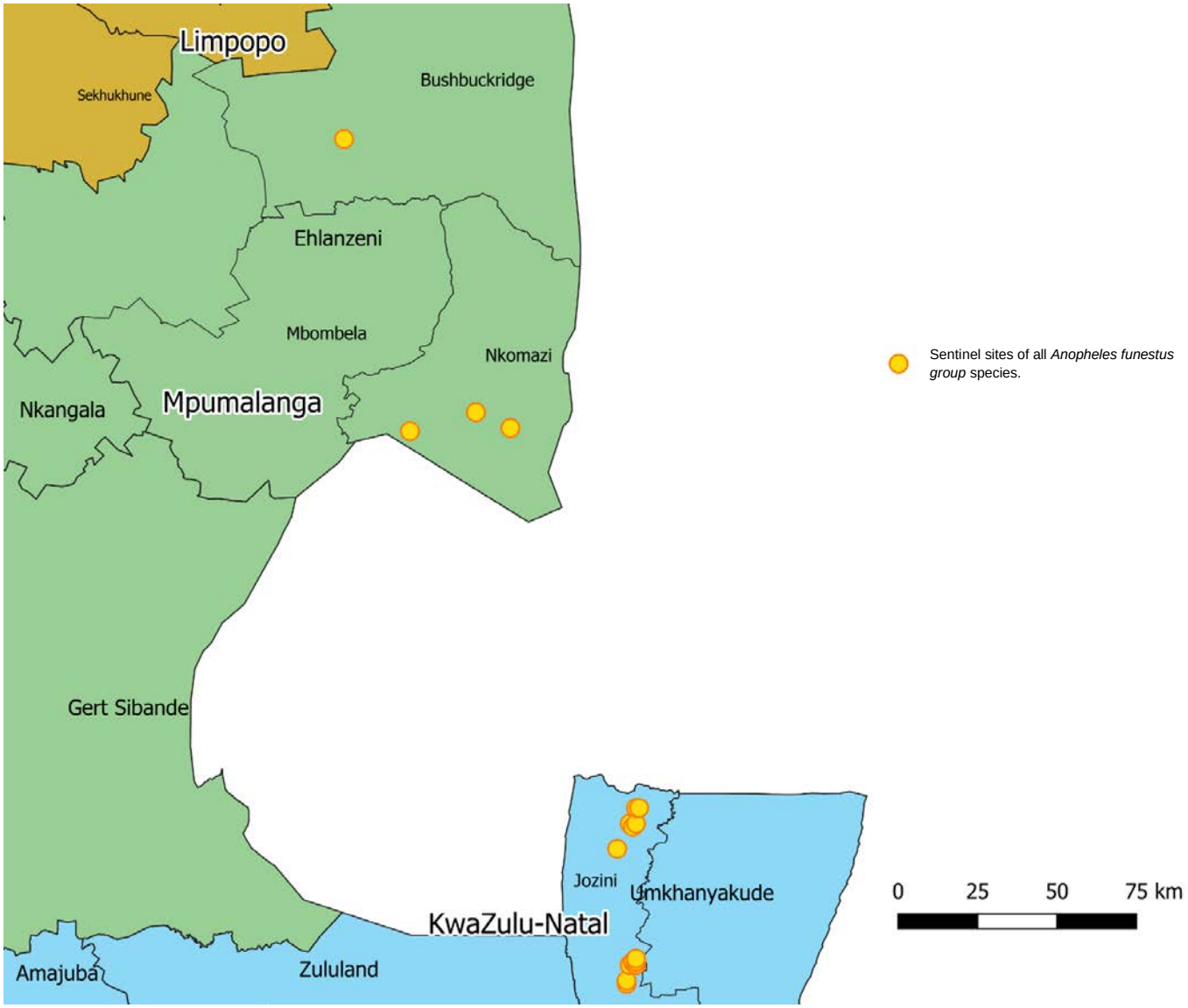

Figure 3. Sentinel sites in KwaZulu-Natal and Mpumalanga provinces from which samples of the known and potential secondary malaria vectors *Anopheles vaneedeni*, *An. parensis*, *An. rivulorum* and *An. leesoni* were collected, South Africa, 2019.

Anopheles coustani, *An. demeilloni*, *An. marshallii* group, *An. pharoensis*, *An. rufipes*, *An. squamosus* and *An. ziemanni* have been incriminated as malaria vectors in other regions of Africa[9,10,11,12] but not in South Africa. The distribution of these potential vector species is shown in Figure 4. Specimens of these species were collected in Jozini in the Umkhanyakude District of KwaZulu-Natal Province and in Nkomazi and Bushbuckridge of the Ehlanzeni District of Mpumalanga Province.

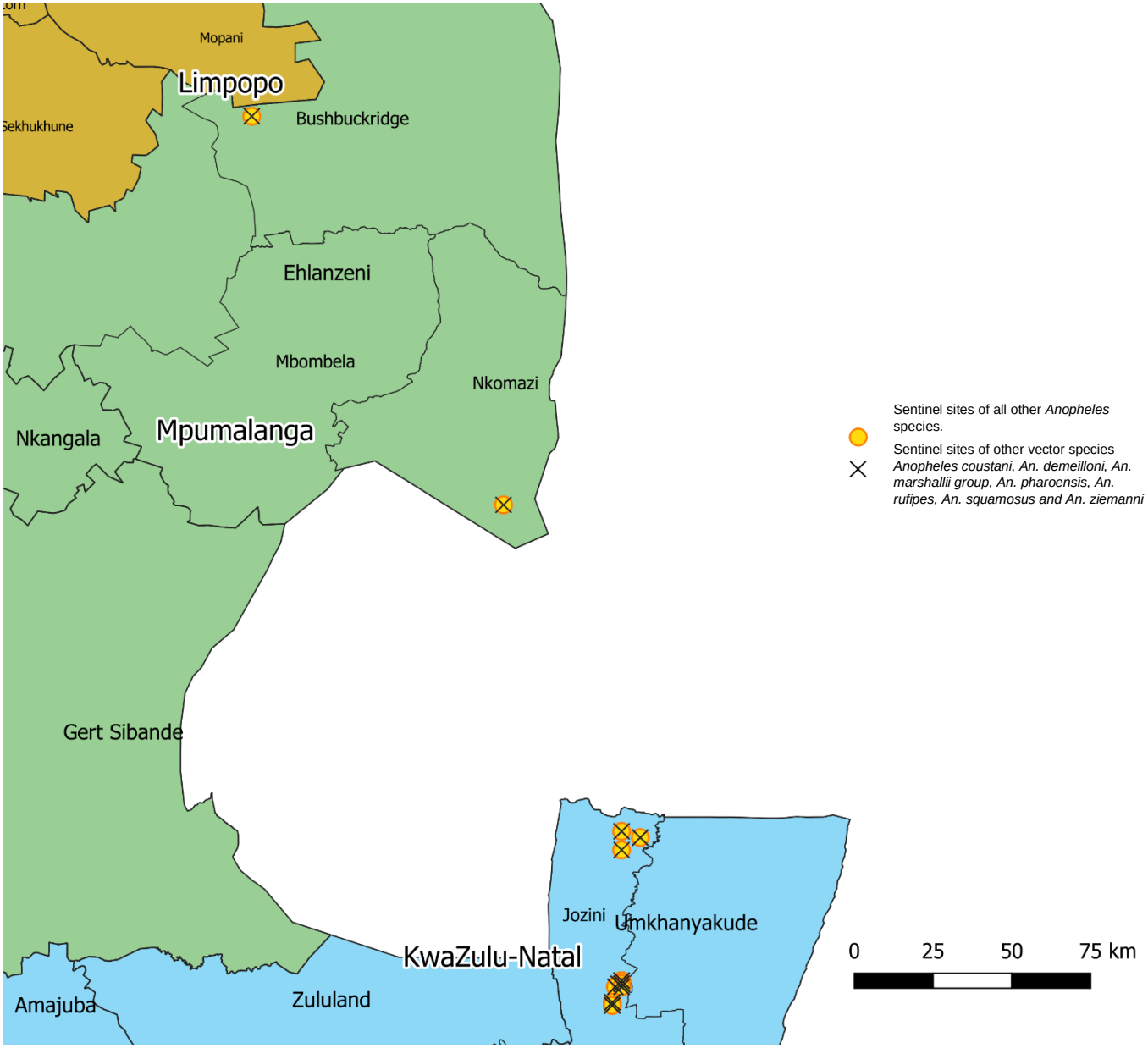

Figure 4. Sentinel sites in KwaZulu-Natal and Mpumalanga provinces from which samples of all other *Anopheles* species (yellow circle) were collected. Sites from which the potential secondary malaria vectors *Anopheles coustani*, *An. demeilloni*, *An. marshallii* group, *An. pharoensis*, *An. rufipes*, *An. squamosus* and *An. ziemanni* were collected are indicated by an X, South Africa, 2019.

The number of anophelines collected by species and locality was highly variable across seasons. For example, *An. arabiensis* was most prevalent during spring and summer in KwaZulu-Natal Province while *An. merus* was particularly prevalent during winter and spring in Mpumalanga Province (Figure 5). *Anopheles parensis* and *An. rivulorum* were most common during summer in KwaZulu-Natal and *An. rivulorum* predominated in autumn in Mpumalanga (Figure 6). There

was a comparatively high prevalence of *An. marshallii* group through most of the year in KwaZulu-Natal (Figure 7).

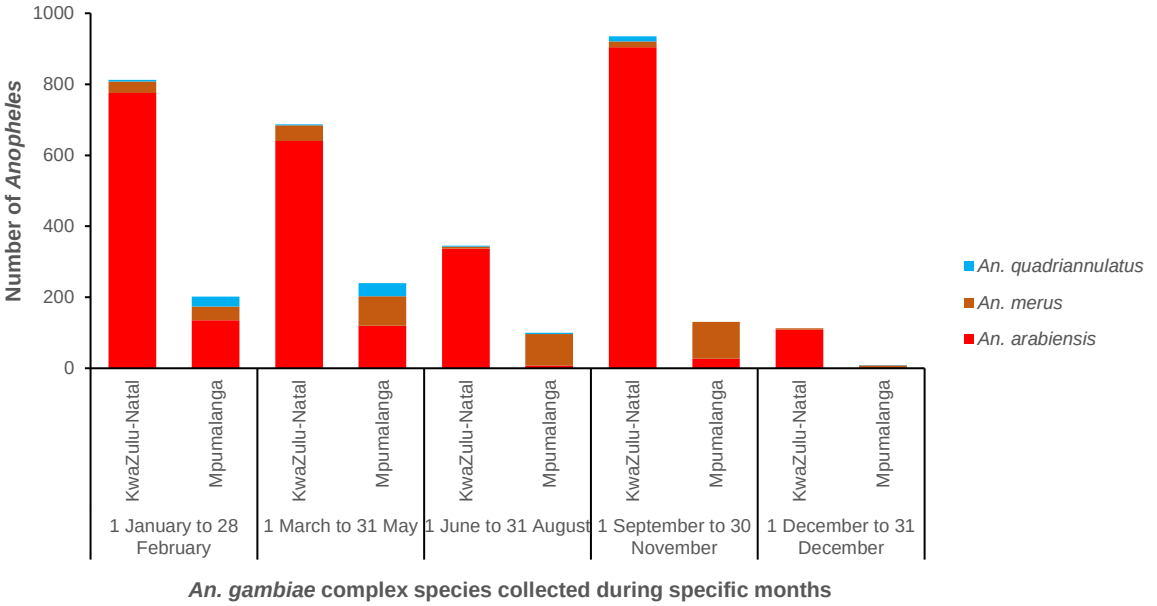

Figure 5. Distribution (in absolute numbers) of *Anopheles gambiae* complex specimens collected by species, province and season, South Africa, 2019.

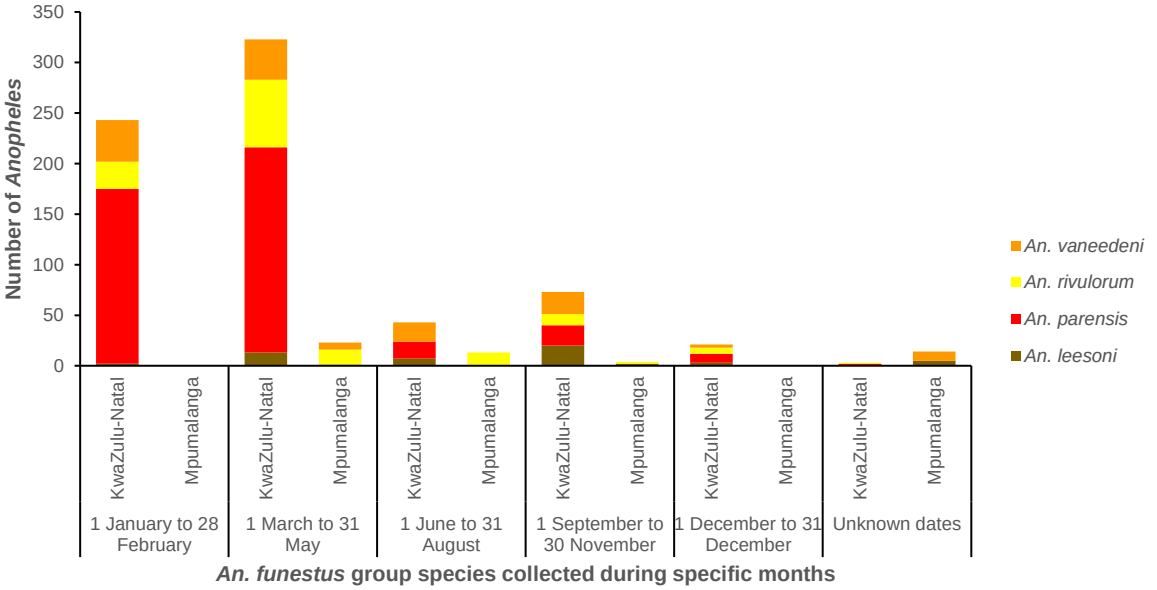

Figure 6. Distribution (in absolute numbers) of *Anopheles funestus* group specimens collected by species, province and season, South Africa, 2019.

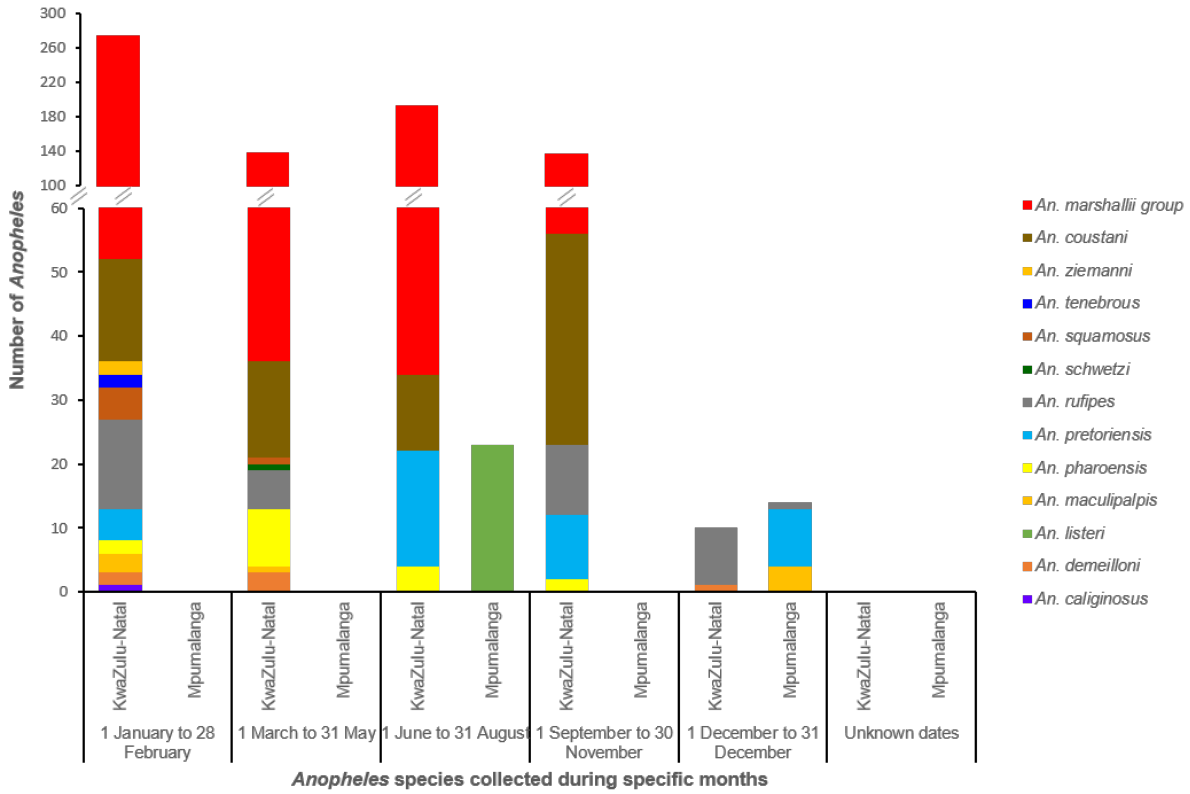

Figure 7. Distribution (in absolute numbers) of miscellaneous *Anopheles* specimens collected by species, province and season, South Africa, 2019.

Discussion

Malaria vector surveillance during 2019 in the KwaZulu-Natal and Mpumalanga provinces of South Africa revealed 19 *Anopheles* species. These included species incriminated as vectors within South Africa as well as suspected vector species that have been incriminated in other African countries.

Anopheles arabiensis is a major malaria vector in South Africa with variable feeding and resting behaviours. Outdoor feeding and resting components of *An. arabiensis* populations are at least partially responsible for ongoing residual malaria transmission.[4]

Anopheles merus is likely an important secondary malaria vector in South Africa[2] and has also been implicated in transmission in southern Mozambique. Interestingly, this species is traditionally described as a salt-water coastal breeder but the larval collections from which most of these specimens accrued were found in what were likely fresh-water breeding sites (salinity was not tested in these sites at time of collection). Data from Mpumalanga Province

suggest that this species is increasing its inland range and abundance by adapting to breeding in fresh-water habitats.[13]

Anopheles vaneedeni tends to rest outdoors and will readily feed on humans. It has been implicated as a secondary malaria vector in Mpumalanga and KwaZulu-Natal provinces[3] and likely plays an important role in residual transmission in South Africa.

Anopheles parensis has recently been incriminated as a malaria vector in South Africa.[8] Its contribution to residual malaria transmission is however likely to be minimal at best owing to its strong tendency to feed on livestock animals. This species will nevertheless feed on humans as well and will rest indoors and outdoors.

Although no *An. funestus* were collected in KwaZulu-Natal and Mpumalanga provinces during 2019, there is a recent record of this species in Limpopo Province.[14] In the absence of vector control, this species is the predominant malaria vector in the southern African region where it is especially prevalent in neighbouring Mozambique and Zimbabwe.[2] Although the eastern Lowveld regions of South Africa form part of the natural range of this species, its absence is likely attributable to intensive IRS programmes in KwaZulu-Natal, Mpumalanga and Limpopo provinces.[2] However, in light of the recent detection of *An. funestus* in Limpopo, the possibility of transmission by this species in the border regions of the Vhembe and Mopani districts cannot be ruled out. Other members of the *An. funestus* group detected during 2019 include *An. leesoni* and *An. rivulorum*. Of these, both have been implicated as a minor malaria vector in East Africa [9].

Other species that occur in South Africa and that have been incriminated as malaria vectors in various African localities include *An. marshallii*, *An. coustani*, *An. demeilloni*, *An. pharoensis*, *An. rufipes*, *An. squamosus* and *An. ziemanni*.[9,10,11,12] It is possible that one or more of these species plays a role in residual malaria transmission in South Africa.

Relative *Anopheles* population densities tend to fluctuate between seasons and are generally highest during the summer months congruent with increased rainfall.[4] These increased densities coincide with South Africa's summer malaria season because greater numbers of

vector mosquitoes invariably translate into higher rates of transmission assuming there are adequate parasite populations.

Conclusion & recommendations

Several anophelines, including malaria vector species, occur in the north-eastern Lowveld regions of South Africa, with their relative abundances varying considerably by season. Despite coordinated provincial IRS programmes that usually achieve high spray coverage rates (80% or more of targeted structures in endemic areas), populations of these species persist and at least four of them - *An. arabiensis*, *An. merus*, *An. vaneedeni* and *An. parensis* – have previously been implicated in ongoing residual transmission in South Africa (tentative in the cases of *An. merus* and *An. parensis*). The reasons for this are multiple and certainly include outdoor-biting and outdoor-resting components of these species.

Based on this information it is recommended that:

- IRS based vector control be maintained at a high rate of coverage in endemic districts
- IRS activities should ideally be completed before the onset of each malaria season
- Larval source management[15], including the treatment of winter breeding sites, be maintained so as to enhance the effect of IRS in high incidence areas
- Insecticide resistance management practices be maintained and periodically revised based on surveillance information
- In the context of the current COVID-19 pandemic, malaria control activities should be conducted especially timeously and efficiently. This will reduce the risk of co-infection in affected communities and reduce malaria-related hospitalizations

Acknowledgements

Entomology team members of the provincial Malaria Control Programmes of KwaZulu-Natal and Mpumalanga are thanked for the referral of surveillance specimens to the VCRL. Dr Patrick Moonasar, Dr Eunice Misiani, Prof Rajendra Maharaj, Mr Aaron Mabuza, Mr Eric Raswiswi, Mr Philip Kruger and all members of the South African Malaria Elimination Committee (SAMEC) are

especially thanked for their support for vector surveillance. These activities were sponsored by the Mpumalanga and KwaZulu-Natal Malaria Control Programmes, the National Institute for Communicable Diseases, the International Atomic Energy Agency, the Industrial Development Corporation and the South African Nuclear Energy Corporation (NECSA) through its Nuclear Technologies in Medicine Biosciences Initiative (NTeMBI) – a national platform funded by the Department of Science and Technology. MC and LK are supported by a NRF/DST Research Chair Initiative grant.

References

1. South Africa National Department of Health malaria statistics. Unpublished data.
2. Brooke BD, Koekemoer LL, Kruger P, Urbach J, Misiani E, Coetzee M. Malaria Vector Control in South Africa. *S Afr Med J* 2013; 103(10 Suppl 2): 784-788.
3. Burke A, Dandalo L, Munhenga G, Dahan-Moss Y, Mbokazi F, Ngxongo S, Coetzee M, Koekemoer L, Brooke B. A new malaria vector mosquito in South Africa. *Sci Rep* 2017; 7: 43779.
4. Dandalo LC, Brooke BD, Munhenga G, Lobb LN, Zikhali J, Ngxongo SP, Zikhali PM, Msimang S, Wood OR, Mofokeng M, Misiani E, Chirwa T, Koekemoer LL. 2017. Population dynamics and *Plasmodium falciparum* (Haemosporida: Plasmodiidae) infectivity rates for the malaria vector *Anopheles arabiensis* (Diptera: Culicidae) at Mamfene, KwaZulu-Natal, South Africa. *J Med Entomol* 2017; 54(6): 1758-1766.
5. Brooke BD, Robertson L, Kaiser ML, Raswiswi E, Munhenga G, Venter N, Wood OR, Koekemoer LL. Insecticide resistance in the malaria vector *Anopheles arabiensis* in Mamfene, KwaZulu-Natal. *S Afr J Sci* 2015; 111(11/12): 0261.
6. Venter N, Oliver SV, Muleba M, Davies C, Hunt RH, Koekemoer LL, Coetzee M, Brooke BD. Benchmarking insecticide resistance intensity bioassays for *Anopheles* malaria vector species against resistance phenotypes of known epidemiological significance. *Parasit Vectors* 2017; 10: 198.
7. South Africa National Department of Health, Malaria elimination strategy for South Africa 2019-2013, Pretoria, NDoH, 2019.
8. Burke A, Dahan-Moss Y, Duncan F, Qwabe B, Coetzee M, Koekemoer L, Brooke B. Anopheles parensis contributes to residual malaria transmission in South Africa. *Malar J* 2019; 18: 257.
9. Kyalo D, Amratia P, Mundia CW, Mbogo CM, Coetzee M, Snow RW. A geo-coded inventory of anophelines in the Afrotropical Region south of the Sahara: 1898-2016. *Wellcome Open Res*. 2017; 2: 57.
10. Ogola EO, Fillinger U, Ondiba IM, Villinger J, Masiga DK, Torto B, Tchouassi DP. Insights into malaria transmission among *Anopheles funestus* mosquitoes, Kenya. *Parasit Vectors* 2018; 11: 577.

11. Daygena TY, Massebo F, Lindtjørn B. Variation in species composition and infection rates of *Anopheles* mosquitoes at different altitudinal transects, and the risk of malaria in the highland of Dirashe Woreda, south Ethiopia. *Parasit Vectors* 2017; 10: 343.
12. Gillies MT, De Meillon B. The Anophelinae of Africa south of the Sahara, vol. 54. Johannesburg: Publications of the South African Institute for Medical Research; 1968.
13. Mbokazi F, Coetzee M, Brooke B, Govere J, Reid A, Owiti P, Kosgei R, Zhou S, Magagula R, Kok G, Namboze J, Tweya H, Mabuza A. Changing distribution and abundance of the malaria vector *Anopheles merus* in Mpumalanga Province, South Africa. *Public Health Action*. 2018; 8(Suppl 1): S39-S43.
14. Braack LEO, Bornman R, Kruger T, Dahan-Moss Y, Gilbert A, Kaiser M, Oliver S, Cornel AJ, Lee Y, Norris DE, Coetzee M, Brooke BD, de Jager C. Review of malaria vectors and vector surveillance in Limpopo Province, South Africa. *Int J Environ Res Pub Hlth* 2020 (Submitted)
15. Larval source management - a supplementary measure for malaria vector control. An operational manual, WHO 2013. http://www.who.int/malaria/publications/atoz/larval_source_management_2-pager_eng.pdf

PUBLIC HEALTH SURVEILLANCE BULLETIN

The Public Health Surveillance Bulletin is published by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service (NHLS)

Private Bag X4, Sandringham 2131,
Johannesburg, South Africa

Suggested Citation: [Authors' names or National Institute for Communicable Diseases (if no author)]. [Article title].

Request for e-mail subscription are invited - please send requests to:
Mrs Sinenhlanhla Jimoh
SinenhlanhlaJ@nicd.zc.za

This bulletin is available on the NICD website:
http:\\www.nicd.ac.za