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Surveillance of viral haemorrhagic fevers, Rift Valley fever and yellow fever in humans, South Africa, 2019-2023

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Summary

Viral haemorrhagic fevers are infections associated with blood clotting abnormalities, which may lead to bleeding manifestations and life-threatening disease. Various zoonotic and/or vector-borne RNA viruses may cause haemorrhagic fevers, while human-to-human transmission may also occur following the initial spillover from reservoir or vector. Viral haemorrhagic fevers are typically associated with intensive public health preparedness and response to prevent and contain outbreaks effectively. In South Africa, viral haemorrhagic fevers are listed as category 1 notifiable medical conditions that require immediate reporting upon clinical suspicion, in accordance with Regulation 1434, Surveillance and the Control of Notifiable Medical Conditions of the National Health Act of 2003 (Act no 61 of 2003). In addition, Rift Valley fever (in humans) and yellow fever are category 1 notifiable medical conditions, often present clinically as a haemorrhagic syndrome, and are therefore included in this surveillance programme. We conducted a retrospective review of suspected and confirmed viral haemorrhagic fevers cases, Rift Valley fever and yellow fever. This report summarises the detection of these infections in humans through passive surveillance in South Africa for the period 2019-2023. We conclude that although the risk of importation of non-endemic VHF, RVF and YF in South Africa is low, and cases of locally acquired CCHF and RVF are infrequent, improved and integrated surveillance and response capabilities are necessary to ensure that any importations are subject to rapid detection and public health responses, especially to contain possible outbreaks.

Introduction

RNA viruses belonging to several viral families may cause haemorrhagic fever. From a public health perspective, important ones in Africa are Ebola virus (EBOV) and Marburg virus (MARV) (family *Filoviridae*), Crimean-Congo haemorrhagic fever virus (CCHFV) (family *Nairoviridae*), and Lassa and Lujo viruses (family *Arenaviridae)*.[1] In addition, Rift Valley fever virus (RVFV) (family *Phenuiviridae*) and yellow fever virus (YFV) (family *Flaviviridae*) infection in some cases present with a haemorrhagic clinical syndrome.[1-3] Of these, CCHFV, RVFV and MARV are considered endemic (or naturally occurring) in South Africa.[1-4]

The VHFs are zoonotic infections involving various animal species such as (but not limited to) bats, rodents and primates in intricate ecological cycles. Spillover may occur directly from the reservoir animal or transmission may be arthropod-borne as with CCHF, RVF and YF.[1-3] Human-to-human transmission may occur, typically requiring close contact with contaminated bodily fluids and fomites, with a higher risk of transmission in the nosocomial setting.[1-3,5] The clinical presentations of VHF, RVF and YF vary in degree of severity, but clinical features in mild to severe cases may include abrupt onset of headaches, fever, malaise, anorexia, arthralgia, nausea with vomiting, and diarrhoea.[1-3] In severe cases rapid deterioration with progression to haemorrhage, multi-organ failure and shock are common.[1-3] The case fatality rates vary by disease, with Marburg virus disease (MVD) outbreaks

associated with up to 90% fatal outcomes. Owing to the non-specific initial signs and symptoms, detection and appropriate management of cases is often challenging and delayed. Suspected cases of VHF, RVF and YF are diagnosed clinically, usually prompted by an epidemiological link (i.e. tick or mosquito bites, contact with an infected person or with animals in geographic locations where these diseases occur), which may explain exposure. Confirmation of the diagnosis is achieved through detection of viral RNA in the blood of infected persons by reverse transcription polymerase chain reaction (RT-PCR) assays, or the detection of anti-virus IgG and/or IgM using various serological assays.[1-3,6]

The National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service (NHLS), is the national reference laboratory for investigations of VHF, RVF and YF in humans in South Africa. Based on clinical suspicion, notification is required immediately (i.e. category 1 notifiable medical condition or NMC). The suspected cases are notified by healthcare professionals through the NMC surveillance platform, after which laboratory investigation is performed at the NICD/NHLS to confirm or discount the clinical diagnoses. The following VHFs are included as category 1 NMCs in South Africa: Ebola virus disease (EVD), MVD, Lassa fever (LF), Lujo fever, VHF associated with New World arenaviruses, CCHF and other newly identified viruses causing haemorrhagic fever.

This report summarizes surveillance for VHF, RVF and YF in humans in South Africa for the period 2019-2023.

Methods

Study design and cases

This is a retrospective record review using documents submitted to the Special Viral Pathogens Laboratory and the Arbovirus Reference Laboratory, Centre for Emerging Zoonotic and Parasitic Disease, NICD/NHLS, for suspected cases of VHF, RVF and YF. All requests for laboratory investigation for VHF, RVF and YF in humans in South Africa were referred to this laboratory during the reporting period. The documents included in the review were case submission forms, case investigation forms (as publically available from the NICD website, www.nicd.ac.za), unstructured case notes collected from referring physicians and/or medical officers attending to the NICD hotline, laboratory staff during laboratory investigation, and/or district and provincial Department of Health investigation teams. The data obtained from the laboratory records were verified against the data reported on the NMC platform. Included in the study were cases submitted for VHF (including EVD, MVD, LF, Lujo fever, VHF associated with New World arenavirus infections, CCHF or newly identified viruses causing haemorrhagic fever), RVF and YF investigations from 1 January 2019 to 31 December 2023. Only cases suspected or confirmed in South Africa were included. Suspected and confirmed cases were defined as per NMC case definitions (available from https://www.nicd.ac.za/nmc-overview/). Briefly, laboratory confirmed cases were defined as cases that tested positive by RT-PCR, were positive for anti-virus IgM, or when seroconversion was demonstrated through a four-fold rise in anti-virus IgG titer in serially collected blood samples.

Data extraction and analysis

Data extracted from the laboratories' records were collected in a database prepared in Microsoft® Excel. Descriptive epidemiological analysis was performed for laboratory-confirmed cases considering age, reported sex, geographical distribution, source of exposure and outcome of disease. Geographic distribution of laboratory-confirmed CCHF cases was mapped using ArcGIS Pro 3.2 (ESRI, CA, USA).

Results

The numbers of suspected and confirmed cases of VHF, RVF and YF in South Africa from 2019-2023 are summarised in Table 1. A total of 232 cases (not the number of tests conducted) was investigated during the reporting period. The endemic diseases, CCHF and RVF, were most frequently investigated, i.e. 77 and 90 cases, respectively. A single case of Lassa fever (LF) was reported in 2022, and ten cases of CCHF were confirmed in South Africa during the reporting period. No cases of other VHF, RVF, YF or haemorrhagic fever associated with newly identified viruses were detected during the reporting period.

Table 1. Numbers of suspected (in parentheses) and laboratory-confirmed human cases of viral haemorrhagic fevers per year in South Africa, 2019-2023. No newly identified viruses causing haemorrhagic fever were reported during this period.

Disease	Year					Total confirmed per disease
	2023	**2022**	**2021**	**2020**	**2019**	
EVD	0 (1)	0 (2)	0 (1)	0 (1)	0 (6)	0 (11)
MVD	0 (0)	0 (2)	0 (1)	0 (0)	0 (5)	0 (8)
LF	0 (2)	1(3)	0 (1)	0 (0)	0 (2)	1 (8)
Lujo fever	0 (0)	0 (2)	0 (1)	0 (0)	0 (2)	0 (5)
New World arenaviruses	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CCHF	1(7)	3(15)	1(10)	2 (11)	3 (34)	10 (77)
RVF	0 (3)	0 (19)	0 (21)	0 (12)	0 (35)	0 (90)
YF	0 (8)	0 (9)	0 (2)	0 (2)	0 (12)	0 (33)
Total confirmed per year	**1**(21)	**4** (52)	**1**(37)	**2** (26)	**3** (96)	**11 (232)**

EVD=Ebola virus disease; MVD=Marburg virus disease, LF=Lassa fever, CCHF=Crimean-Congo haemorrhagic fever, RVF=Rift Valley fever, YF=yellow fever.

Figure 1 shows the age and sex of laboratory-confirmed cases of LF and CCHF. The age range of these cases was 30–71 years. Males accounted for nine of the eleven reported cases.

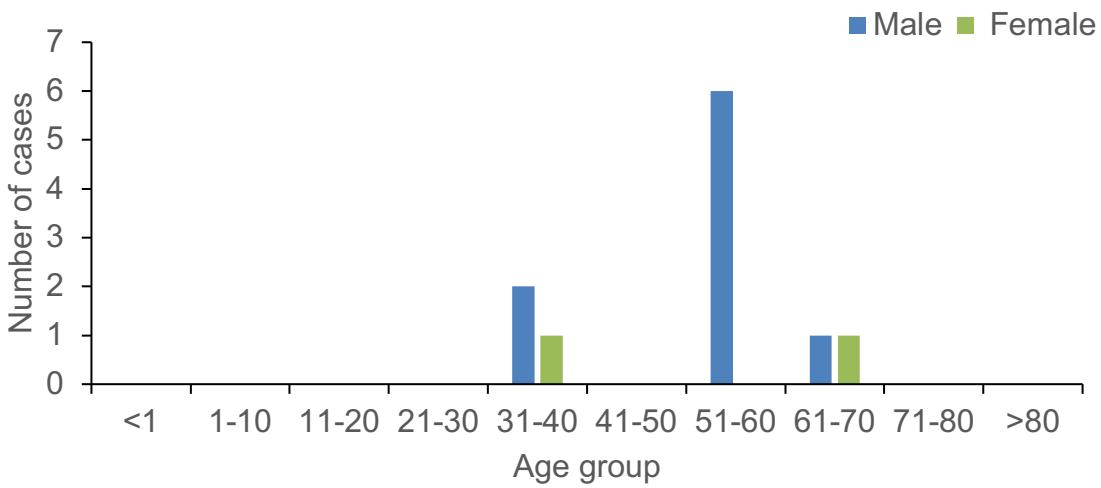

Figure 1. Age and sex distribution of confirmed viral haemorrhagic fever (VHF) cases, South Africa, 2019-2023.

The LF case and one CCHF case had fatal outcomes. Table 2 shows the exposure histories for the confirmed cases. The LF case involved a person with a history of extensive travel in Nigeria prior to returning to South Africa. Given the incubation period of LF, it is most likely that the patient was exposed to the virus during those travels. The exposures reported for confirmed CCHF cases were mostly tick bites or likely tick exposure (n=7). These cases were predisposed to tick bites due to their occupations, which included livestock farming (n=4), veterinary work (n=1) and game management (i.e. culling industry) (n=1). One case involved a hiker who reported a tick bite. One case was associated with an abattoir worker who may have been exposed to ticks or had contact with blood and tissues of viraemic animals. The remaining cases had unclear exposure histories, but tick or blood-borne exposures are plausible given their occupations (n=3). The latter included livestock farming, abattoir work and veterinary work.

Table 2. Exposure histories of laboratory-confirmed cases of Lassa fever (LF) and Crimean-Congo haemorrhagic fever (CCHF), South Africa, 2019-2023.

Disease	Source of exposure	Details of exposure	Geographic location of exposure
LF	Not reported	Travel to rural mining areas where exposure to rodents is possible	Various locations in Nigeria
CCHF	Tick	Occupational exposure: veterinarian	Free State Province, South Africa
	Tick	Occupational exposure: livestock farmer	Northern Cape Province, South Africa
	Tick	Occupational exposure: livestock farmer	North West Province, South Africa
	Tick	Occupational exposure: livestock farmer	North West Province, South Africa
	Tick	Occupational exposure: livestock farmer	Free State Province, South Africa
	Tick	Retired, exposed during hiking	Western Cape Province, South Africa
	Not reported	Occupational exposure: Sheep farmer	Western Cape Province, South Africa
	Probably ticks	Occupational exposure: Game culling on farms and nature reserves	Eastern Cape Province, South Africa
	Slaughter	Occupational exposure: Abattoir worker (sheep)	Western Cape Province, South Africa
	Not reported	Occupational exposure: Veterinarian	North West Province, South Africa

The laboratory-confirmed CCHF cases were associated with local exposure events. During the reporting period, cases occurred in the North West (n=3), Western Cape (n=3), Free State (n=2), Eastern Cape (n=1) and Northern Cape (n=1) provinces (Figure 2).

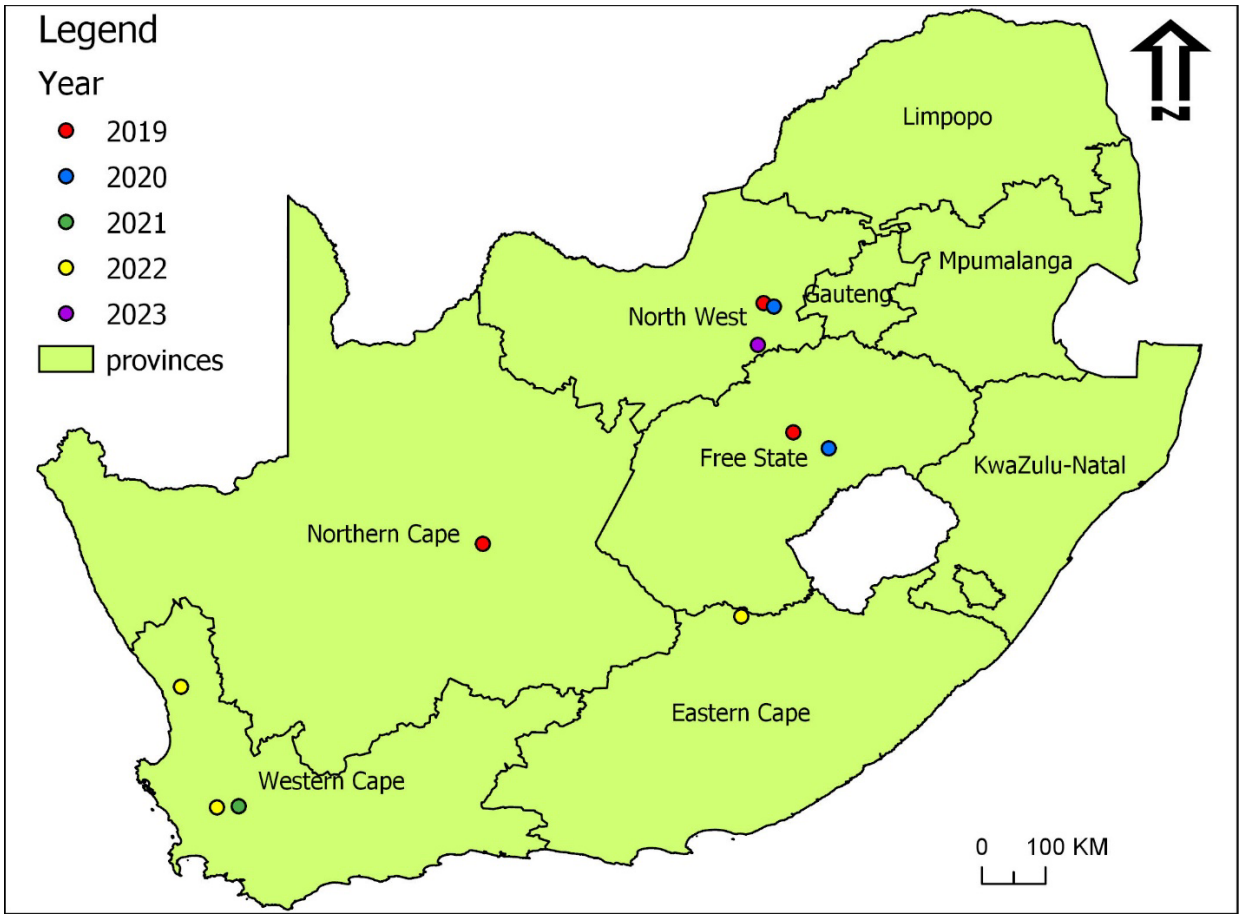

Figure 2. Distribution of human cases of Crimean-Congo haemorrhagic fever (CCHF) by year across South Africa, 2019-2023.

Discussion

The capacity to detect and respond to cases of VHF is important, especially in terms of support for the implementation of the International Health Regulations (https://www.who.int/health-topics/international-health-regulations#tab=tab_1) and adherence to the Global Health Security Agenda (https://globalhealthsecurityagenda.org/) in South Africa. This is particularly relevant for VHF, RVF and YF, as these diseases may spread across borders and affect international travel and trade. To date in South Africa, reports of EVD, MVD, LF and Lujo fever have been rare, and are associated with travelers or patients evacuated to South Africa. During the past 10 years, large-scale outbreaks of EVD (i.e. West African outbreak) and YF, and the emergence of MVD in locations in Africa where it has not occurred previously, present a risk for importation of these diseases into South Africa. Although CCHF and RVF reports in South Africa are infrequent, the epidemiology of these vector-borne diseases may be affected as vector ecology is impacted by factors such as climate change and changes in land use. Preventative vaccines and therapeutics currently remain unavailable for most of these diseases.

In South Africa, surveillance for VHF, RVF and YF in humans is passive. This entails the clinical diagnosis of cases followed by laboratory investigation to confirm or disprove the presumptive clinical diagnosis. These cases, both suspected and laboratory-confirmed, are notified and reported through the NMC platform in adherence to national regulations for the notification of these diseases. By promptly notifying cases, health authorities can rapidly implement measures to prevent or curtail the spread of diseases.

Reports of endemic and non-endemic VHF and RVF are sporadic in South Africa. During the reporting period, 232 suspected cases of VHF, RVF or YF were subject to laboratory investigation. The number of cases investigated fluctuated by year and may relate to the occurrence of outbreaks in other African countries, which may lead to an increased index of suspicion and a need for laboratory investigation. There were no case reports of EVD, MVD, Lujo fever, infections associated with New World arenaviruses, RVF or YF during this period. In 1996, a case of EVD was reported in a healthcare worker returning from Gabon, being the only confirmed case of imported EVD in South Africa.[7] This case was associated with a secondary transmission of EVD within South Africa.[7] In 1975, a case of MVD was reported in a tourist in South Africa and was also associated with subsequent secondary transmission in-country.[8] The tourist had extensive travel history in Zimbabwe and South Africa, and the source of the exposure remains speculative.[8] Genetic analysis of MARV from Egyptian fruit bats in Limpopo province and the virus isolated from the tourist showed high similarity.[4] Lujo fever was reported in a highly fatal outbreak of hemorrhagic fever in 2008 involving healthcare workers in Johannesburg, South Africa, and associated with a newly-described virus.[9] No cases of haemorrhagic fever associated with New World arenaviruses have been reported from South Africa to date. Rift Valley fever is periodically reported in South Africa, with the most recent outbreak in 2018.[10] This outbreak was isolated with only four cases of RVF in farm workers from one farm in the Free State Province.[10] No cases of yellow fever have been confirmed from South Africa to date.

There was a single case of imported LF in 2022. Lassa fever is endemic to countries in West Africa, and therefore only expected in South Africa in travelers returning from endemic areas. This is the second case of imported LF in South Africa. In 2007, LF was recorded in a physician who contracted the disease following extensive travel for a polio vaccination campaign in rural Nigeria. The patient was evacuated to South Africa for medical treatment, after which the diagnosis was suspected and confirmed. Likewise, the case reported in 2022 was a patient who had travelled to Nigeria. In this case, the patient presented to a hospital in South Africa for medical management after returning from Nigeria. Both cases of LF had fatal outcomes. Globally, LF is the most frequently reported VHF in travellers.[11]

CCHF is endemic in South Africa and has been recognised in the country since 1981. There are sporadic case reports from all nine provinces with larger numbers from the Northern Cape, Free State and North West provinces. More than two-thirds of cases reported since 1981 involved tick exposures.[12] The remaining cases reported exposure to animal tissues and/or blood, or were residing or working in rural areas where tick exposures would be expected. CCHF cases were most common among those predisposed to tick exposures and/or exposures to animal tissues and blood such as livestock farmers, veterinarians, abattoir workers and hunters. During the reporting period, there were ten cases of CCHF from the Western Cape, Free State, North West, Eastern Cape and Northern Cape provinces. The features of the confirmed CCHF cases were in keeping with those of cases reported in the country since 1981.[12]

Conclusion

Although the risk of importation of non-endemic VHF, RVF and YF in South Africa is low, and cases of locally acquired CCHF and RVF are infrequent, improved and integrated surveillance and response capabilities are necessary to ensure that any importations are subject to rapid detection and public health responses, especially to contain possible outbreaks.

Recommendations

- Healthcare workers should remain vigilant for cases of VHF, RVF and YF presenting to healthcare facilities in South Africa. Prompt notification of suspected cases through the NMC platform is key to trigger public health responses to contain possible outbreaks.
- Astute and comprehensive laboratory investigation for suspected cases is crucial to justify and ensure the implementation of appropriate public health responses. The national reference laboratory at the NICD conducts testing for VHF, RVF and YF.
- Preparedness for VHF, RVF and YF in South Africa requires updating of strategic and actionable plans, guidelines and standard operating procedures on a regular basis. Additionally, simulation exercises involving all relevant sectors should be conducted using an inter-sectoral and One Health approach as applicable.

Ethical considerations

The Human Research Ethics Committee of the University of the Witwatersrand approved the analysis and reporting of these data - reference number: M210752 and protocol title: Essential communicable disease surveillance and outbreak investigation activities of the National Institute for Communicable Diseases.

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Conflict of interest

The authors declare no conflicts of interest.

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