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Review Article

Epidemiology of Crimean-Congo Hemorrhagic Fever (CCHF) in Africa—Underestimated for Decades

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Abstract. Crimean-Congo hemorrhagic fever (CCHF) is endemic in Africa, but the epidemiology remains to be defined. Using a broad database search, we reviewed the literature to better define CCHF evidence in Africa. We used a One Health approach to define the impact of CCHF by reviewing case reports, human and animal serology, and records of CCHF virus (CCHFV) isolations (1956–mid-2020). In addition, published and unpublished collection data were used to estimate the geographic distribution of *Hyalomma* ticks and infection vectors. We implemented a previously proposed classification scheme for organizing countries into five categories by the level of evidence. From January 1, 1956 to July 25, 2020, 494 CCHF cases (115 lethal) were reported in Africa. Since 2000, nine countries (Kenya, Mali, Mozambique, Nigeria, Senegal, Sierra Leone, South Sudan, Sudan, and Tunisia) have reported their first CCHF cases. Nineteen countries reported CCHF cases and were assigned level 1 or level 2 based on maturity of their surveillance system. Thirty countries with evidence of CCHFV circulation in the absence of CCHF cases were assigned level 3 or level 4. Twelve countries for which no data were available were assigned level 5. The goal of this review is to inform international organizations, local governments, and healthcare professionals about shortcomings in CCHF surveillance in Africa to assist in a movement toward strengthening policy to improve CCHF surveillance.

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a severe tick-borne zoonosis caused by Crimean-Congo hemorrhagic fever virus (CCHFV; *Bunyavirales*: *Nairoviridae*: *Orthonairovirus*).[1] CCHF was first described during an outbreak among Soviet military personnel stationed in Crimea in 1944–1945.[2–4] CCHF is broadly endemic in both Africa and Eurasia, with more than 30 countries having reported cases since the first cases emerged in Crimea.[1,5–7] CCHF epidemiology in Africa is not well described. However, there has been a global increase in the number of reported CCHF cases since 2000, with nine countries in Africa (Table 1) and 11 countries in Asia[7] reporting their first confirmed human CCHF cases.

CCHFV virus is transmitted to humans via tick bites or through direct contact with infected animals or infected people. In the CCHFV life cycle, ticks (mainly of the species *Hyalomma marginatum* and *Hyalomma rufipes*) are both reservoirs and vectors.[5,8] Many mammals (including cattle, dromedaries, goats, and sheep), reptiles, and some birds (in particular ostriches) can be infected with the virus and remain asymptomatic while the virus amplifies. As a result, livestock, animal herders, slaughterhouse workers, and healthcare workers in endemic areas are at high risk of acquiring infection.[8–11]

Most CCHF cases are mild or asymptomatic. Mild cases may present with nonspecific symptoms or clinical signs, such as headache, myalgia, joint pain, fever, nausea, and vomiting. A small proportion of cases are severe with sudden onset, quickly developing bruising, and severe hemorrhage. Death may occur within days of disease onset.[3,12–18] CCHF lethality (5–80%) has been associated with different factors, such as access to medical care, age, virus strain, preexisting medical conditions, and route of transmission.[19–22]

Most reports on first autochthonous CCHF cases in individual countries were preceded by epidemiologic surveys or CCHFV isolation from ticks that provided evidence of local CCHFV circulation. For example, in Kenya (then British Kenya), evidence of CCHFV infection may have been described in as early as 1961,[23] and serological evidence of human CCHFV infection was first obtained in the early 1980s.[24] CCHFV was first isolated from ticks in Kenya in 1975.[5] Yet, it was not until 2000 that the first Kenyan human case was encountered.[25] In Sudan, serologic evidence of CCHFV in animals was obtained in 1986[26] and in humans in 1989.[27] CCHFV was identified in ticks collected during an outbreak in 1995.[28] Yet, it was not until 2008 that the first human case was described.[29] In Nigeria, serologic evidence of CCHFV was first obtained in animals in the early 1960s[30] and in humans in 1973.[31] CCHFV was identified in Nigerian ticks in 1964.[32,33] Yet, the first human case was identified in 2010.[34]

Thus, little is known about CCHF epidemiology in Africa, and published epidemiologic/epizootiologic data are mostly from outbreak investigations and rarely systematic. In a multistage analysis, a cohesive framework was developed to assess substantial pandemic potential for endemic high-consequence infectious disease in Africa, and CCHFV was identified with substantial index case, outbreak, epidemic, and pandemic potential compared with Ebola and Marburg virus disease and Lassa fever.[35] A predictive model of CCHF distribution in Africa also pinpointed large areas in Southern, Eastern, Central, and Western Africa as being suitable for CCHFV transmission.[36] The absence of additional epidemiological data is the consequence of only a

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TABLE 1
Total confirmed CCHF cases in Africa by country from 1956 to July 2020

Country (current designation)	Total confirmed cases	Total deaths	Year(s)	References
Burkina Faso	1	0	1983	80
Central African Republic	1	0	1976	5
Democratic Republic of the Congo	3	1	1956, 2008	43,46
Egypt	4	1	1981, 2012	68,75
Kenya	6	1	2000, 2010, 2020	25,88,89
Mali	40	7	2009–2013, 2017, 2020	90–92
Mauritania	50	12	1983, 1988, 2003, 2007, 2012, 2017, 2018, 2019	57,81–86,93
Mozambique	8	0	2015	94
Namibia	20	10	1986–2001, 1987, 2002, 2010, 2014, 2017–2019	57,95–104
Nigeria	50	0	2010–2014	34
Senegal	8	1	2003, 2004, 2015, 2017, 2020	57,105–109
Sierra Leone	1	0	2016	110
South Africa	215	52	1981–2018, 2018, 2019	58–62
South Sudan	1	0	2013	111
Sudan	34	16	2008, 2009, 2010, 2013, 2014, 2015–2016, 2018	29,57,69–73
Tanzania	1	0	1986	112
Tunisia	5	0	2014	74
Uganda	45	13	1958–1965, 1963–1964, 1967, 1972, 1978, 2013, 2015, 2017, 2018, 2019, 2020	5,43,67,113–128
Zimbabwe	1	1	1997	129

CCHF = Crimean-Congo hemorrhagic fever. Total deaths are those among confirmed cases only. Therefore, lethality was not calculated. We were limited to available data, but this approach likely underestimates the true CCHF burden.

few African countries entertaining active CCHF (V) surveillance systems.[37]

This article focuses on Africa to recognize highly CCHF-affected countries with an emphasis on regions that may not have been (known to be) CCHFV endemic in the past. We used a One Health approach to integrate vector, animal, human, and virus data to define disease status in each country. This article is in follow-up of our previous publication on Southern and Western Asia[7] and is part of a series of publications mapping CCHF in the world.

METHODS

We searched PubMed, GenBank, GIDEON, Google Scholar, Scopus, ProMED, and Web of Science, among other more minor databases, for records indexed from the original descriptions of CCHF in 1944 through July 25, 2020 to identify and review the scientific literature on reported CCHF cases from all countries in Africa as defined by the UN Geoscheme (Eastern Africa: British Indian Ocean Territory; Burundi; Comoros; Djibouti; Eritrea; Ethiopia; French Southern Territories; Kenya; Madagascar; Malawi; Mauritius; Mayotte; Mozambique; Réunion; Rwanda; Seychelles; Somalia; South Sudan; Uganda; United Republic of Tanzania; Zambia; and Zimbabwe; Middle Africa: Angola; Cameroon; Central African Republic; Chad; Democratic Republic of the Congo [COD]; Equatorial Guinea; Gabon; Republic of the Congo; and São Tomé and Príncipe; Northern Africa: Algeria; Egypt; Libya; Morocco; Sudan; Tunisia; and Western Sahara; Southern Africa: Botswana; Eswatini; Lesotho; Namibia; South Africa; Western Africa: Benin; Burkina Faso; Cabo Verde; Côte d'Ivoire; Gambia; Ghana; Guinea; Guinea-Bissau; Liberia; Mali; Mauritania; Niger; Nigeria; Saint Helena, Ascension, and Tristan da Cunha; Senegal; Sierra Leone; and Togo).[38]

Our review included articles published in any language. We also collected information from conference presentations (if indexed in the listed electronic databases) and unpublished data/reports through personal communications. We accessed available online government reports (the National Institute for Communicable Diseases [NICD] in South Africa) and communicated with government officials (Ministries of Health in South Africa, Uganda, Zimbabwe, Kenya, and Mozambique) for confirmation of unpublished data. In addition, we accessed and reviewed published animal and human serology data, CCHFV detection or isolation data from ticks or vertebrates, and information regarding CCHFV surveillance systems. We also reviewed the U.S. National Tick Collection database[39] for data that indicated the presence of CCHFV vectors in any geographic area of interest. We limited our search and consideration to *H. marginatum* and *H. rufipes* ticks because of their undisputed capacity to transmit CCHFV transstadially, transovarially, and to animals.[40,41] We used Boolean combinations of search terms, including "Hyalomma," "CCHFV," "CCHF," "CHF," "Crimean," "Crimean-Congo," "Congo-Crimean," "Congo virus"; "Crimean hemorrhagic fever"; "nairovirus," and "orthonairovirus" and the names of each of the countries (or their predecessor names).

One Health country-level classification scheme. We used a classification scheme developed by our team and previously published in an article that focused on epidemiology of CCHF in Southern and Western Asia.[7] This classification system integrated vector, animal, and human data to identify CCHFV circulation in an area of interest. Countries were classified as follows: level 1 CCHF cases reported annually through established surveillance; level 2 CCHF cases reported intermittently in absence of robust surveillance; level 3 no CCHF cases reported and no robust surveillance established, but available data point toward the possibility of undetected/unreported CCHF cases (animal/human serology, CCHFV detected in *Hyalomma* ticks); level 4 no CCHF cases reported and no robust surveillance or

epidemiologic/epizootiologic studies, but *Hyalomma* ticks are present; and level 5 no available data.[7]

RESULTS

From January 1, 1956 to July 25, 2020, 19 African countries reported a total of at least 494 human CCHF cases (115 lethal), with the first case being described in COD. The regional distribution of the countries was as follows: six were in Eastern Africa, two in Middle Africa, three in Northern Africa, two in Southern Africa, and six in Western Africa (Tables 2–5). Most cases were reported from Mali, Mauritania, Namibia, Nigeria, South Africa, Sudan, and Uganda. Most countries reported cases randomly or through outbreak investigations, but South Africa and Uganda used established surveillance systems. All countries were organized into five categories by the level of evidence (Figure 1). Since 2000, nine countries (Kenya, Mali, Mozambique, Nigeria, Senegal, Sierra Leone, South Sudan, Sudan, and Tunisia) have reported their first cases (Table 5), most of which were identified via random detection in people with acute febrile disease or through outbreak investigations.

DISCUSSION

CCHFV is considered a significant threat to human health in endemic areas, including Africa. The World Health Organization (WHO) included CCHF in its blueprint of priority diseases, which lists emerging diseases that are understudied.[42] CCHF was first described in 1956 in Africa,[43–45] although evidence of this disease in Africa has not been clearly described. Recently, the number of CCHF cases has increased on the continent, with some countries reporting their first cases. We collected available evidence of CCHF epidemiology and classified each country based on the level of evidence. One caveat is that we were not able to establish a category for studies reporting negative data on CCHFV animal or human serology and virus isolation in ticks because of the extremely low number of such publications/reports and their limited scopes.

There are significant variability or gaps in surveillance activities and capabilities between countries. The knowledge gap resulting from the likely lack of active zoonosis surveillance, including CCHF, in resource-limited African countries can impair their awareness of, preparedness for, decision-making during, and countering emerging zoonotic infections that may cause large disease outbreaks on the continent.[37]

Most countries in Middle Africa do not have the diagnostic capability to detect CCHF cases, although there is a significant level of evidence that CCHFV is actively circulating. Lack of diagnostic capability is likely the major factor contributing to underestimation of CCHF endemicity in Africa compared with other endemic regions, such as the Mediterranean Basin. For example, COD is the second largest country in Africa and reported Africa's first CCHF case in 1956,[43–45] but no subsequent cases were identified until 2008.[46] Animal serology

TABLE 2
Current evidence for CCHFV circulation in Eastern Africa

Country (current designation)	CCHF cases reported	Human serology	Animal serology	*Hyalomma* ticks	CCHFV detected in ticks	Level of evidence
British Indian Ocean Territory	No	No	No	No	No	5
Burundi	No	No	No	No	No	5
Comoros	No	No	No	No	No	5
Djibouti	No	No	1992[130]	Yes[131]	2010[132]	3
Eritrea	No	No	No	Yes[39]	No	4
Ethiopia	No	No	No	Yes[133]	1975[134]	3
French Southern Territories	No	No	No	No	No	5
Kenya	2000, 2010, 2020[25,88,89]	1980, 1983, 1987, 2010, 2009–2012, 2020[24,88,89,135–137]	1961, 1972, 1974, 1986[5,26,44,138]	Yes[39]	1975,2008[5,139]	2
Madagascar	No	1989, 2008[140,141]	No	No[142]	1985[143]	3
Malawi	No	No	No	Yes[131,144]	No	4
Mauritius	No	No	No	No	No	5
Mayotte	No	No	No	No	No	5
Mozambique	2015[94]	No	No	Yes[39,145]	No	2
Réunion	No	No	No	No	No	5
Rwanda	No	No	No	Yes[131]	No	4
Seychelles	No	No	No	No	No	5
Somalia	No	No	1993, 1994, 1996[146–148]	Yes[39]	1994, 1996, 2009[147–149]	3
South Sudan	2013[111]	No	No	Yes[150]	No	2
Uganda	1958–1965,1963–1964, 1967,1972,1978,2013, 2015,2017,2018, 2019,2020[5,43,67,113–128]	1984, 2006[151,152]	1970, 1972[138,153]	Yes[154]	1970, 1978, 1981, 2015[5,67,155,156]	1
United Republic of Tanzania	1986[112]	No	1974[5]	Yes[39,157]	No	2
Zambia	No	No	No	Yes[39]	No	4
Zimbabwe	1997[129]	1980[158]	1964–1985, 1973–1978[112,159]	Yes[39]	No	2

CCHF = Crimean-Congo hemorrhagic fever; CCHFV = Crimean-Congo hemorrhagic fever virus. Years are listed if there is evidence of anti-CCHFV antibodies in humans or animals, CCHFV vector endemicity, or CCHFV antigen or genome detection.

TABLE 3
Current evidence for CCHFV circulation in Middle, Northern, and Southern Africa

Country (current designation)	CCHF cases reported	Human serology	Animal serology	*Hyalomma* ticks	CCHFV detected in ticks	Level of evidence
Middle Africa						
Angola	No	No	No	Yes[160]	No	4
Cameroon	No	1985, 2005–2012[161,162]	2013[163]	Yes[39]	2015[163]	3
Central African Republic	1976[5]	1966–1979, 1979, 1979–1982, 1984 1980–1985, 1993[49–52,164,165]	1979–1982, 1983, 1988, 1992[50,51,53,54]	Yes[39]	1972–1979, 1973, 1975[5,55,56]	2
Chad	No	No	No	Yes[39,166]	No	4
Democratic Republic of the Congo	1956, 2008[43,46]	No	2013[163,167]	Yes[168,169]	No	2
Equatorial Guinea	No	1985[161]	No	No	No	3
Gabon	No	No	2005, 2008, 2009[170]	No	No	3
Republic of the Congo	No	1985[161]	No	No	No	3
São Tomé and Príncipe	No	No	No	No	No	5
Northern Africa						
Algeria	No	No	No	Yes[39,171]	2009[172]	3
Egypt	1981, 2012[68,75]	1976[173]	1976, 1986, 2004, 2009[26,76–78,173]	Yes[39]	2009[149]	2
Libya	No	No	No	Yes[39]	No	4
Morocco	No	No	No	Yes[39]	2011[174]	3
Sudan	2008, 2009, 2010, 2013, 2014, 2015–2016, 2018[29,57,69–73]	1989, 1998, 2012, 2015–2016[27,69,175,176]	1986–1987, 1994, 2013, 2014, 2015[26,177–180]	Yes[39]	1995, 2009, 2017[28,149,181]	2
Tunisia	2014[74]	2014[74]	No	Yes[39]	No	2
Western Sahara	No	No	No	No	No	5
Southern Africa						
Botswana	No	No	No	Yes[39,64]	No	4
Eswatini	No	No	No	Yes[65]	No	4
Lesotho	No	No	No	Yes[66]	No	4
Namibia	1986–2001, 1987 2002, 2010, 2014, 2017–2019[57,95–104]	1984[182]	No	Yes[183]	No	2
South Africa	1981–2018, 2018, 2019[58–62]	1981, 1983, 1984–1988, 2016[184–188]	1964–1985, 1981, 1983, 1984, 1984–1988, 1993, 2002[10,112,159,184,186,187,189–194]	Yes[39]	1981[104,184]	1

CCHF = Crimean-Congo hemorrhagic fever; CCHFV = Crimean-Congo hemorrhagic fever virus. Years are listed if there is evidence of anti-CCHFV antibodies in humans or animals, CCHFV vector endemicity, or CCHFV antigen or genome detection.

yielded positive results in 2013.[47] CCHFV likely has been circulating in COD for years. COD has been mired in conflict for decades and has the largest number of internally displaced people in Africa. As another example, the Central African Republic reported only one human CCHF case in 1976,[48] whereas positive human and animal serology[49–54] and virus isolation from ticks[5,55,56] strongly support virus circulation in the area. Civil wars in the region, especially in COD and Central African Republic, have weakened the local healthcare infrastructures. Both countries would benefit from assistance by international organizations, cross-governmental support, and multi-institutional collaborations to build diagnostic capabilities by establishing, developing, or strengthening human and ecologic CCHF surveillance networks and systems.

Among countries in Southern Africa, South Africa reported 215 CCHF cases (1981–2019), the highest number of cases on the continent.[57–62] The annual number of cases is available through the National Institute for Communicable Diseases (NICD) in Sandringham, Johannesburg. South Africa has a well-established surveillance system, implementing national guidelines for recognition and management of viral hemorrhagic fevers such as CCHF, and NICD's Special Pathogen Unit is capable of diagnosing these diseases.[63] However, some countries that have a border with South Africa (i.e., Botswana, Eswatini, Lesotho, and Mozambique) have not reported any cases despite the prevalence of *Hyalomma* ticks,[39,64–66] supporting the notion that CCHFV may be circulating but has not been detected due to limited diagnostic capabilities. These countries would benefit from testing of *Hyalomma* ticks for CCHFV and seroprevalence studies in humans and animals.

In Eastern Africa, Uganda reported 44 cases (Table 2). There is an appreciable gap in CCHF case detection from 1978 to 2013, which could have been due to lower CCHFV activity during this period. The increased detection of cases since 2013 could have been due to any biological vector or human risk factors but is more likely due to maturity of Uganda's surveillance system and improved diagnostic capabilities. Since 2010, to rapidly identify infectious disease outbreaks, including Ebola and Marburg virus diseases, the Uganda Virus Research Institute (UVRI) has cultivated relationships with multiple international partners and established a surveillance system in collaboration with the Ugandan Ministry of Health.[67] Most newly diagnosed CCHF cases in Uganda have been confirmed through this surveillance system. Kenya, South Sudan, Tanzania, and Zimbabwe have each reported at least

TABLE 4
Current evidence for CCHFV circulation in Western Africa

Country (current designation)	CCHF cases reported	Human serology	Animal serology	*Hyalomma* ticks	Virus detected in ticks	Level of evidence
Benin	No	1981–1983[195]	No	Yes[39,196]	No	3
Burkina Faso	1983[80]	1983[80,197]	No	Yes[198,199]	No	2
Cabo Verde	No	No	No	Yes[200]	No	4
Côte d'Ivoire	No	No	No	Yes[201,202]	No	4
Gambia	No	No	No	Yes[203]	No	4
Ghana	No	2011[19]	2009[170]	Yes[39,204]	2011[19]	3
Guinea	No	No	No	Yes[205,206]	1978–1991[207]	3
Guinea-Bissau	No	No	No	No	No	5
Liberia	No	1981[208]	No	No	No	3
Mali	2009–2013, 2017, 2020[90–92]	1991, 2009–2013[90,209]	2005–2014, 2013[163,210]	Yes[211,212]	2011[213]	2
Mauritania	1983, 1988, 2003, 2007, 2012, 2017, 2018, 2019[57,81–86,93]	1983, 1984, 1985, 1988, 2003[85,86,197,214–218]	1983, 1984, 1988, 2003, 2013[85,86,163,197,214,215]	Yes[215]	1983, 1984,2003[85,197,214,215]	2
Niger	No	No	1984–1988[219,220]	Yes[221,222]	No	3
Nigeria	2010–2014[34]	1973, 1988, 2011, 2010–2014[31,34,223,224]	1964–1968, 1976, 1983, 1984–1988, 2015[32,219,225–227]	Yes[32,228]	1964, 1964–1968, 1966, 1976[5,32,227,229]	2
Saint Helena, Ascension and Tristan da Cunha	No	No	No	No	No	5
Senegal	2003, 2004, 2015, 2017, 2020[57,105–109]	1986, 1989, 1987–1995[230–233]	1969, 1972, 1983, 1986, 1987–1995, 1989–1992, 1991, 2014[5,197,230,232,234–238]	Yes[239,240]	1963–1974, 1969–1991, 1969, 1970–1974, 1983, 1985, 1987, 1990, 1989–1992, 1991–1992, 1992[5,41,197,230,232,235–237,241–244]	2
Sierra Leone	2016[110]	2007–2014[245]	No	Yes[239]	No	2
Togo	No	No	No	Yes[246]	No	4

CCHF = Crimean-Congo hemorrhagic fever; CCHFV = Crimean-Congo hemorrhagic fever virus. Years are listed if there is peer-reviewed evidence of anti-CCHFV antibodies in humans or animals, CCHFV vector endemicity, or CCHFV antigen or genome detection.

one case of CCHF; if they had the same diagnostic capabilities as Uganda, it is likely that more cases would have been detected.

Among Northern African countries, Egypt, Sudan, and Tunisia have reported CCHF cases. Egypt was the first country in the region to experience CCHF in 1981.[68] Sudan detected its first case in 2008[29] and has been reporting cases annually since.[29,59,69–73] Tunisia's first case dates to 2014.[74] Although Egypt only recognized CCHF in 1981 and 2012,[68,75] positive animal serology and CCHFV detection in ticks have been reported intermittently, supporting the notion that CCHFV is circulating in the region.[26,76–78] Although Sudan has reported 34 CCHF cases since 2008, most of these cases have been diagnosed in the setting of outbreak investigations. Libya, which borders Egypt, Sudan, and Tunisia, has not reported any CCHF cases. Among Northern African countries, Egypt has a unique infrastructure and a long-standing history of partnership with the U.S. Naval Medical Research Unit Three (NAMRU-3) as long as it was situated in Cairo Egypt. NAMRU-3 worked closely with Egypt's Ministry of Health and Population, the U.S. National Institutes of Health (NIH), the WHO, the U.S. Agency for International Development, and the U.S. Centers for Disease Control and Prevention (CDC).[79] NAMRU-3 was recently relocated to Italy, but a similar entity with a similar infrastructure associated with international collaboration in partnership with local governments could be developed to (re)establish a CCHF diagnostic surveillance system in the region.

In Western Africa, Burkina Faso and Mauritania reported their first CCHF cases in 1983.[80] Burkina Faso has not reported any cases since then, whereas Mauritania has been reporting cases intermittently through outbreak investigations.[59,81–86] Mali, Nigeria, Senegal, and Sierra Leone have each reported at least one case since 2003. Although not bordering other countries that have reported CCHF cases, Nigeria has reported the highest number of cases (50) in Western Africa since 2014.[34] Niger, located between Nigeria and Mali, may therefore be affected by numerous undiagnosed CCHF cases.

Diagnosis of new CCHF cases in eight African countries (Table 1; mainly in Eastern Northern and Western Africa) since 2000 is most likely primarily due to improvement in diagnostic capabilities rather than ecological changes related to vector and human behavior. These countries still lack established surveillance systems and would benefit significantly from collaboration with within and outside their regions to diagnose additional cases and better estimate the epidemiology of CCHF on the continent.

TABLE 5
Since 2000, nine countries have reported their first autochthonous CCHF cases in Africa

Year	Country
2000[25]	Kenya
2003[107]	Senegal
2008[29]	Sudan
2009[90]	Mali
2010[34]	Nigeria
2013[111]	South Sudan
2014[74]	Tunisia
2015[94]	Mozambique
2016[110]	Sierra Leone

CCHF Burden Level	Countries
Level 1 (2 countries)	South Africa, Uganda
Level 2 (16 countries)	Burkina Faso, Central African Republic (CAR), Democratic Republic of the Congo (DRC), Egypt, Kenya, Mali, Mozambique, Namibia, Nigeria, Sierra Leone, South Sudan, Sudan, Senegal, United Republic of Tanzania, Tunisia, Zimbabwe
Level 3 (14 countries)	Algeria, Cameroon, Djibouti, Equatorial Guinea, Ethiopia, Gabon, Ghana, Guinea, Liberia, Madagascar, Morocco, Niger, Republic of the Congo, Somalia
Level 4 (15 countries)	Angola, Benin, Botswana, Cabo Verde, Chad, Côte d'Ivoire, Eritrea, Eswatini, Gambia, Lesotho, Libya, Malawi, Rwanda, Togo, Zambia
Level 5 (13 countries)	British Indian Ocean Territory, Burundi, Comoros, French Southern Territories, Guinea Bissau, Mauritius, Mayotte, Réunion, São Tomé and Príncipe, Saint Helena, Ascension and Tristan da Cunha, Seychelles, Western Sahara

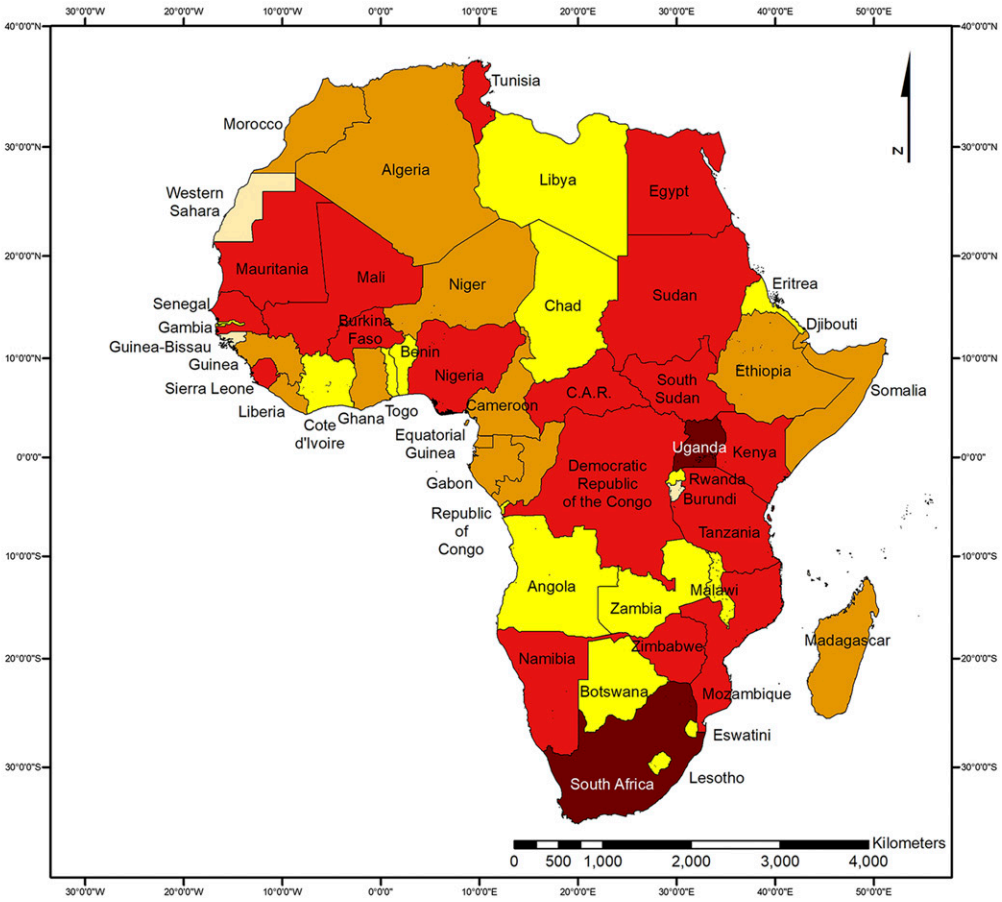

FIGURE 1. Evidence of CCHF in Africa using a One Health approach. The following level classification is applied: level 1, CCHF cases reported annually through established surveillance; level 2, CCHF cases reported intermittently in absence of robust surveillance; level 3, no CCHF cases reported and no robust surveillance established, but available data point toward the possibility of undetected/unreported CCHF cases (animal/human serology, CCHFV detected in *Hyalomma* ticks); level 4, no CCHF cases reported and no robust surveillance or epidemiologic/epizootiologic studies, but *Hyalomma* ticks present; and level 5, no available data. Classification at the country level was performed for policy implications. Country boundaries do not necessarily reflect the geographic area at risk and are not necessarily endorsed by the authors. The map was created using ArcGIS Release 10.61. Source: Database of Global Administrative Areas. This figure appears in color at www.ajtmh.org.

The current (2017) WHO map outlining CCHF endemicity in Africa[87] is based on reports of cases, human serology, and presence of CCHFV tick vectors. However, most countries in Africa do not have CCHF diagnostic capability, likely leading to underestimation of cases. Our One Health approach to country classification more comprehensively integrates additional factors, such as animal serology and inclusion of more granular data on vector presence. This approach revealed evidence of CCHFV circulation in Northern and Middle African regions that were not considered high risk in a previous CCHFV distribution modeling effort.[36] Based on our examination of CCHFV epidemiology in Africa, we recommend the following:

1. Egypt, South Africa, and Uganda, that is, countries with diagnostic capabilities, should provide rapid diagnostic support during CCHF outbreaks. Furthermore, we propose that these countries collaborate to establish a network and act as regional diagnostic centers to define a realistic epidemiology of CCHF for the entire continent. To be most effective, this collaboration effort should include active CCHF surveillance, testing of *Hyalomma* ticks for CCHFV, animal and human serology testing, improved healthcare infrastructure, community education about CCHFV transmission, and providing personal protective equipment (PPE).
2. Burkina Faso, Central African Republic, COD, Kenya, Sierra Leone, South Sudan, Tanzania, and Zimbabwe, which have rarely reported cases despite serological and tick surveillance data being in support of virus circulation (level 2), would benefit most from establishing active CCHF surveillance systems.
3. *Hyalomma* ticks are present in most African countries, but information about CCHFV circulation is limited. Countries assigned level 4 (Angola, Benin, Botswana, Cabo Verde, Chad, Côte d'Ivoire, Eritrea, Gambia, Lesotho, Libya, Malawi, Rwanda, Swaziland, Togo, and Zambia) will benefit from testing of *Hyalomma* ticks for CCHFV and from animal/human seroprevalence studies in collaboration.
4. Countries with limited evidence of *Hyalomma* tick presence, assigned level 5 (Burundi, Comoros, Guinea Bissau, Mauritius, Mayotte, Réunion, São Tomé and Príncipe, Saint Helena, Ascension, and Tristan da Cunha, Seychelles, and Western Sahara), would benefit from tick surveillance studies.
5. Most African countries also lack healthcare infrastructures to support outbreak investigations, early case detection, patient isolation, and patient medical care. Multi-institutional

collaboration should focus on raising awareness about routes of CCHFV transmission and providing PPE to prevent community and nosocomial outbreaks.

Our study has important limitations. First, we were dependent on publications and reports indexed in public databases or referenced in works indexed in databases. Consequently, we may have missed important datasets that were never officially published or circulate only within governments or institutions as internal reports. Second, we had to assume that all studies within a category (virus isolation, human serology, and animal serology) were of the same quality and hence could be treated equally. However, studies considerably differ in approach and rigor, and hence a positive result reported in one work could have been considered a negative result using a different method or vice versa. Third, artificially created geographic borders of course do not affect virus ecology and transmission, but biotopes and ecological niches may differ considerably in adjacent areas. Thus, two countries may have been counted as CCHFV endemic despite one of them having a homogenous CCHFV distribution throughout, whereas the second country may only have a single CCHFV hotspot. We erred on the side of caution by assuming that countries adjacent to CCHF-endemic countries may also have circulating CCHFV, but, of course, this does not have to be the case. Ecologic niche modeling might be a solution for addressing both issues, but is outside the scope of this manuscript. Finally, our study does not address climate change over time, nor the increasing human activity and human-induced changes of biotopes, both of which could be associated with CCHFV vector and host migrations and therefore changes in CCHF prevalence over time. We call on international public health organizations (the WHO and the World Organization for Animal Health) to create or expand partnerships with local governments to provide support for human, tick, and animal CCHFV surveillance in Africa and to ultimately increase knowledge about CCHFV ecology and CCHF epidemiology.

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