International Journal of Infectious Diseases 109 (2021) 174–181

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Seroprevalence and associated risk factors of selected zoonotic viral hemorrhagic fevers in Tanzania

Sima Rugarabamu[a,b,c], Gaspary O. Mwanyika[a,b,d], Susan F. Rumisha[e,f], Calvin Sindato[a,g], Hee-Young Lim[h], Gerald Misinzo[a,b], Leonard E.G. Mboera[a,*]

[a] SACIDS Foundation for One Health, Sokoine University of Agriculture, Morogoro, Tanzania
[b] Department of Veterinary Microbiology, Parasitology and Biotechnology, Sokoine University of Agriculture, Morogoro, Tanzania
[c] Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
[d] Mbeya University of Science and Technology, Mbeya, Tanzania
[e] National Institute for Medical Research, Headquarters, Dar es Salaam, Tanzania
[f] Malaria Atlas Project, Geospatial Health and Development, Telethon Kids Institute, Perth, Western Australia
[g] National Institute for Medical Research, Tabora Research Centre, Tabora, Tanzania
[h] Korea Disease Control and Prevention Agency, National Institute of Health, Osong, Chungchungbukdo, Republic of Korea

ARTICLE INFO

Article history:
Received 5 March 2021
Revised 1 July 2021
Accepted 3 July 2021

Keywords:
viral hemorrhagic fever
antibodies
seroprevalence
risk factors
Tanzania

ABSTRACT

Objective: To determine the seroprevalence of selected zoonotic viral hemorrhagic fevers (VHFs) and their associated risk factors in Tanzania.
Methods: Blood samples were collected from consenting outpatients and community members in eight districts selected from five ecological zones of Tanzania. Serum was harvested and tested for the presence of immunoglobulin G (IgG) and M (IgM) antibodies against Crimean-Congo hemorrhagic fever (CCHF), Ebola virus disease (EVD), Marburg virus disease (MVD), Rift Valley fever (RVF), and yellow fever (YF).
Results: The presence of IgM and IgG antibodies against CCHF, EVD, MVD, RVF, and YF was detected in 64 of 500 samples (12.8%). The prevalences of IgM and IgG antibodies to CCHF, EVD, MVD, RFV, and YF were 2.0%, 3.4%, 1.2%, 4.8%, and 1.4%, respectively. Contact with wild animals (OR = 1.2, CI = 1.3–1.6) and keeping goats (OR = 1.3, CI = 1.5–1.9) were significantly associated with RVF, while contact with bats (OR = 1.2, CI = 1.1–1.5) was associated with MVD.
Conclusion: The findings of this study provide evidence of exposure to CCHF, EVD, MVD, RVF, and YF in Tanzania. Since most of these VHFs occurred without apparent clinical forms of the disease, these findings call for the need to strengthen the surveillance system and management of febrile illnesses in Tanzania.

Introduction

Viral hemorrhagic fevers (VHFs) are a group of zoonotic diseases caused by several distinct groups of viruses from the families *Flaviviridae, Phenuiviridae, Arenaviridae*, and *Filoviridae*. The VHFs reported in Sub-Saharan Africa include Crimean-Congo hemorrhagic fever (CCHF), Ebola virus disease (EVD), Lassa fever (LF), Lujo hemorrhagic fever (LUHF), Marburg virus disease (MVD), Rift Valley fever (RVF), and yellow fever (YF) (Bray, 2005; Changula et al., 2014; Iannetta et al., 2019; Mboussou et al., 2019). The World Health Organization considers CCHF, EVD, MVD, and RVF as being among the top 10 pathogens that pose the most significant risk to public health (WHO, 2018). VHFs have become more prevalent in Africa in recent years, causing either sporadic or large-scale epidemics (Isaäcson, 2001; Nicastri et al., 2019; Iannetta et al., 2019; Rugarabamu et al., 2020).

Ebola virus disease is the deadliest of the VHFs. It was first reported in the Democratic Republic of the Congo (DRC) and South Sudan in 1976, but later reported in several other countries in Africa (Rugarabamu et al., 2020). During the past decade, outbreaks

* Corresponding author: Dr. Leonard E.G. Mboera, SACIDS Foundation for One Health, Sokoine University of Agriculture, P.O. Box 3297, Morogoro, Tanzania.
Tel.: +255754314701.
E-mail addresses: sima.rugarabamu@sacids.org (S. Rugarabamu), gaspary.mwanyika@sacids.org (G.O. Mwanyika), siaeli@gmail.com (S.F. Rumisha), csindato@gmail.com (C. Sindato), limhy0919@korea.kr (H.-Y. Lim), gerald.misinzo@sacids.org (G. Misinzo), lmboera@gmail.com (L.E.G. Mboera).

https://doi.org/10.1016/j.ijid.2021.07.006

of MVD in Africa have been reported in DRC, Kenya, and Uganda (Smith et al., 1982; Nyakarahuka et al., 2019). While LUHF has been reported in South Africa (Briese et al., 2009), LF outbreaks have been reported in Nigeria, Sierra Leone, Guinea, and Liberia (Keïta et al., 2019). Of the viral hemorrhagic fevers, RVF has been reported most widely in Africa, including Egypt, Gambia, Kenya, Madagascar, Mauritania, Mayotte, Niger, Somalia, South Africa, Sudan, Tanzania, and Uganda (Adam et al., 2010; LaBeaud et al., 2010; Hassan et al., 2011; Aradaib et al., 2013; Archer et al., 2013; Drake et al., 2013; Himeidan et al., 2014; Sindato et al., 2014; Kenawy et al., 2018; Cook et al., 2017; Jansen van Vuren et al., 2018; WHO, 2019). Yellow fever has been recently reported in Angola, DRC, Ethiopia, Kenya, Nigeria, Republic of Congo, and Uganda (Kwagonza et al., 2018; Tsegaye et al., 2018; Iannetta et al., 2019).

Despite the widespread occurrence of VHFs, the true burden in Sub-Saharan African countries is still not sufficiently known. The low incidence of VHFs and their non-specific initial clinical presentations make diagnosis difficult. This partly affects the management of febrile illnesses because, in addition to VHFs, there are several diseases that are characterised by fever as one of the manifestations (Bannister, 2010). Some studies have reported serological responses to VHFs in asymptomatic individuals from countries where no outbreaks were reported, suggesting that VHF viruses have a broader range of hosts and geographical locations (Fhogartaigh and Aarons, 2015; Malvy et al., 2019). Studies in DRC and Nigeria have reported a seroprevalence of 2% for EVD and MVD in apparently healthy individuals (Tomori et al., 1988; Bausch et al., 2003; Moyen et al., 2015). On the other hand, studies in Cameroon, Central African Republic, Chad, Republic of Congo, Equatorial Guinea, and Gabon have reported low prevalences of CCHF, RVF, LF, EVD, and MVD among the general population (Gonzalez et al., 1989, 2000).

VHFs are becoming a major public health problem partly because of increasing interconnectedness and ease of travel in African locations characterized by low diagnostic capacity and functional epidemiological surveillance, inadequate infection control practices at healthcare facilities, and weak vector control programmes. Understanding their local epidemiology is critical to guiding differential diagnoses and evidence-based clinical management and control (Beeching et al., 2014). Our study aimed to determine the seroprevalence of CCHF, EVD, MVD, RVF, and YF and their associated risk factors in selected districts, representing different ecological zones of Tanzania.

Methods

Study areas and design

Eight districts were selected for the study using a multistage cluster sampling design. Initially, the ecological zones of the country were identified and categorized based on rainfall patterns, vegetation, land-use patterns, and altitude. The country was subsequently divided into five distinct ecological zones. Zone 1 included the western areas, with tropical forest, a unimodal rainfall pattern, and altitude $<$ 2300 m above sea level. Zone 2 was the southern-highland area, with high precipitation, tropical forest, a bimodal rainfall pattern, low temperatures, and elevation $>$ 2300 m. Zone 3 was the northeastern area, with a bimodal rainfall pattern and seasons of high temperatures. Zone 4 comprised the central part of the country, which is a semi-arid area characterized by moderate precipitation and a unimodal rainfall pattern. Zone 5 included the Lake Victoria area, characterized by a bimodal rainfall pattern and intermediate temperatures.

RVF and CCHF have already been reported in Tanzania (Swanepoel et al., 1987; Sindato et al., 2014). Thus, characterizing the risk of occurrence of mosquito- and tick-borne viral diseases in Tanzania has been associated with areas with suitable habitat for primary vectors, including the coastal, western, southern-highland, and Lake Victoria zones (Mweya et al., 2016). Other high-risk areas include those located at low altitudes, experiencing high precipitation and bimodal rainfall, with proximity to forests, and where contact with wild animals is prevalent; these are characteristic features of the northeastern, southern-highland and Lake Victoria zones of the country (Sindato et al., 2014, 2016). Although there are limited data on the distribution of ticks in Tanzania, the available information suggests that they are widely distributed in different ecological zones of the country (Swai et al., 2005; Kwak et al., 2014; Kerario et al., 2017).

Individuals encroaching into forest areas for different activities, including hunting and timber extraction, who are likely to be exposed to the preparation and consumption of bush meat or handling of dead primates, and/or who reside in areas that border high disease-risk areas are considered to be at increased risk for EVD (Bannister, 2010; Feldmann and Geisbert, 2011). These are the characteristic features of the Lake Victoria and western zones of Tanzania. In addition, exposure to fruit bat excreta in caves/mines has been reported as one of the risk factors for MVD (Bannister, 2010; Mehedi et al., 2011).

The selected districts were Buhigwe, Kalambo (Zone 1), Kyela (Zone 2), Kilindi, Kinondoni (Zone 3), Kondoa, Mvomero (Zone 4), and Ukerewe (Zone 5) (Figure 1). In each district, three wards and nine villages were selected to account for local ecological biodiversity variations. Ten households from each village were selected and all eligible members ($\geq$ 9 months old) of the household who consented to participate were included. One hospital, two health centres, and four dispensaries were selected in each district. Recruitment was carried out at health facilities until the target sample was obtained. The geographical coordinates of the study villages and health facilities were recorded. Blood samples were collected from selected consenting outpatients (facility settings) and community members (at household level) following a protocol approved by the Medical Research Coordinating Committee of the National Institute of Medical Research in Tanzania.

Sample size calculation

Based on the variations in ecology, the number of individuals to be included in the study was calculated independently for each zone. Next, population-weighted samples were allocated among the districts. There is lack of accurate information on the prevalence of these viruses in the study areas. Since fever is the main clinical manifestation, a conservative approach was taken, utilizing the regional and zonal prevalences of febrile populations, as reported in Tanzania (TMIS, 2017), to facilitate calculation. The respective fever prevalences for Zone 1, Zone 2, Zone 3, Zone 4, and Zone 5 were 23.9%, 19.9%, 20.1%, 18.1%, and 18.9%. A desired absolute precision of 5% was used, with a confidence level of 95%. The minimum estimated sample size was 492 individuals, broken down as follows: Zone 1, $n = 127$ (Buhigwe = 71; Kalambo = 55); Zone 2 (Kyela), $n = 68$; Zone 3, $n = 121$ (Kilindi = 61; Kinondoni = 59); Zone 4: $n = 112$ (Kondoa = 57; Mvomero = 54); and Zone 5 (Ukerewe), $n = 64$. The sample size assumed a contingency of 10% to account for non-responses, refusals, or absence. Since this study planned to collect data in both households and health facilities, a 50:50 split was allocated between these two sampling settings.

Data and sample collection

This study was carried out between June and November 2018. The research team received guidance on the study objectives, procedures, research ethics, and data collection tools, and was in-

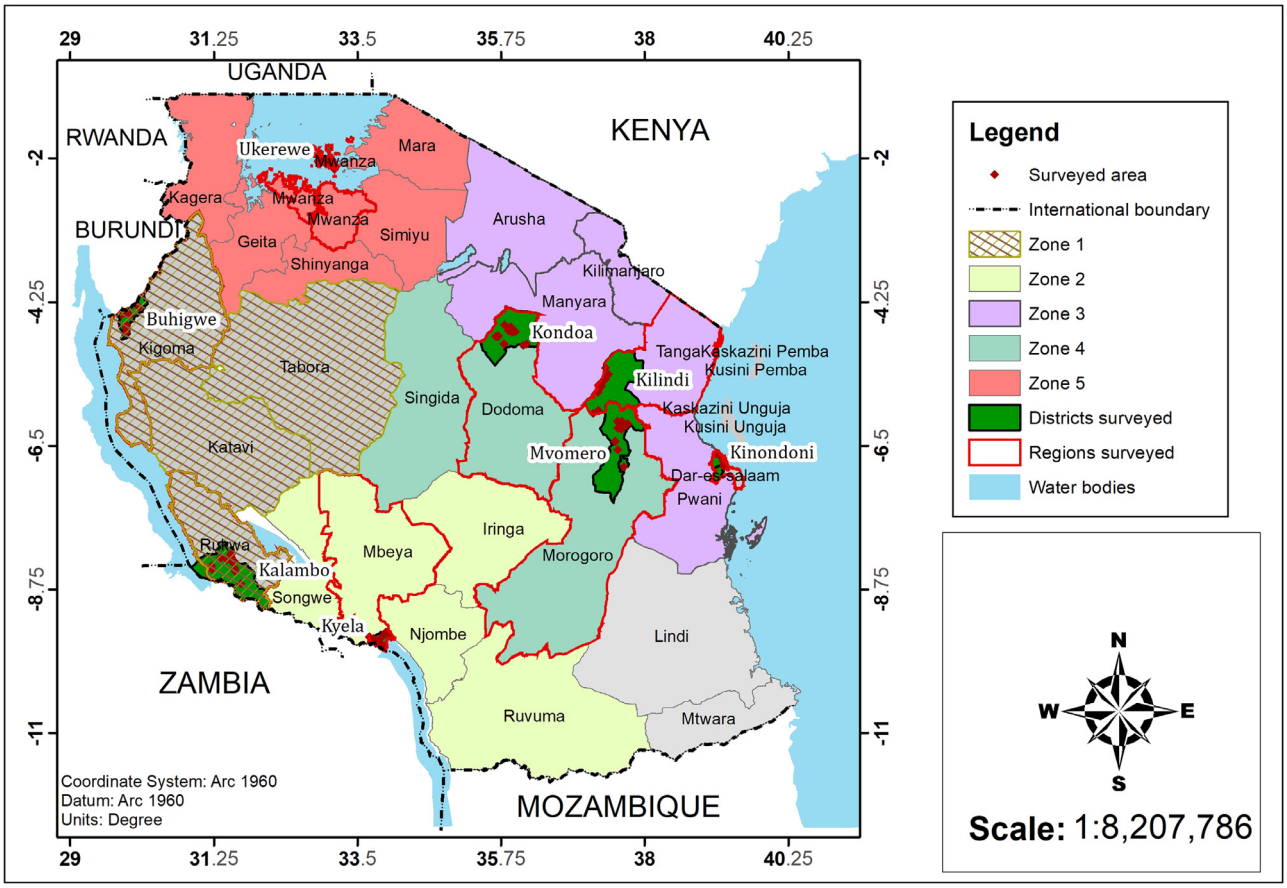

Figure 1. Map of Tanzania, showing the study districts.

volved in data collection and sampling of participants at the study sites. The study objectives were presented to officials in the respective study regions, districts, wards, and villages. Similarly, details on the study, its importance, and the sampling approach were explained to study participants prior to the signing of informed consent forms. All age groups were targeted, except those under 9 months of age (potentially considered to have maternally derived immunity against VHF).

Using a semi-structured questionnaire programmed into the *AfyaData* app installed on smartphones (Karimuribo et al., 2017), face-to-face interviews were conducted in Kiswahili (the national language) to collect socio-demographic characteristics and epidemiological data on risk exposure practices. The socio-demographic characteristics collected included age, sex, occupation, village, workplace, and area of residence. The potential exposure risk practices included contact with wild animals, consumption of game meat, having stagnant water around homes, and experience of mosquito bites.

Each participant was assigned a unique identification code to avoid direct identification. All study participants were examined for clinical manifestations suggestive of the targeted VHFs. Body temperature was recorded using a digital clinical thermometer. Around 5 ml of blood was collected from adults and children > 10 years, and 2 ml from children ≥ 9 months and ≤ 10 years of age, by venepuncture with standard sterile technique. Malaria infection testing was performed on site using malaria rapid diagnostic test kits (CareStart™ Malaria HRP-2/pLDH; American Access Bio Company, USA). The collected data were submitted to the server located at Sokoine University of Agriculture (SUA), while quality assessment was conducted throughout the sampling period by examining the data submitted to the server on a daily basis.

Laboratory examination

Serum was harvested from collected blood samples by centrifugation in the laboratory in the respective district hospitals. The samples were labelled using a unique identification number, archived, and stored in liquid nitrogen (−196°C) before being transferred to the laboratory at SUA, where they were stored at −80°C until examination. Aliquots of the sera were tested for the presence of human IgG and IgM antibodies against CCHF, EVD, MVD, RVF, and YF using commercial ELISA kits, according to the manufacturer's instructions (My BioSource, Inc., San Diego, CA, USA).

Data analysis

Data were cleaned and analysed using IBM SPSS Statistics for Windows, version 23. Frequencies, medians, and associated interquartile ranges (IQRs) were calculated. The chi-square test (or Fisher's test where relevant) was used to compare the proportions of VHF seropositivity by sex, age group, education level, and fever on the day of sample collection. Analysis of variance was used to compare means. To obtain the independent risk factors, all the variables were entered in the multiple logistic regression model to estimate adjusted matched odds ratios and associated 95% confidence intervals (CI). The differences were considered statistically significant when the *p*-value was below 0.05. Statistical cut-off values for ELISA antibody analysis were determined according to the manufacturer's instructions, using the average optical density value of the negative control wells + 0.15. The assay performance was considered effective when both the intra-assay and inter-assay coefficients of variability (CV) were less than 15%.

Table 1
Socio-demographic characteristics of study participants by district

Characteristics	Buhigwe	Kalambo	Kyela	Kinondoni	Kilindi	Kondoa	Mvomero	Ukerewe	Total
Sex	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Female	37 (51.4)	35 (59.3)	42 (62.7)	32 (61.5)	41 (53.2)	24 (49.0)	37 (62.7)	43 (66.2)	291 (58.2)
Male	35 (48.6)	24 (40.7)	25 (37.3)	20 (38.5)	36 (46.8)	25 (51.0)	22 (37.3)	22 (33.8)	209 (41.8)
Age (years)									
0–15	16 (22.2)	4 (6.8)	12 (17.9)	3 (5.8)	8 (10.4)	5 (10.2)	12 (20.3)	12 (18.5)	72 (14.4)
16–30	17 (23.6)	24 (40.7)	24 (35.8)	16 (30.8)	22 (28.6)	16 (32.6)	16 (27.1)	16 (24.6)	151 (30.2)
31–45	22 (30.6)	15 (25.4)	18 (26.8)	15 (28.8)	22 (28.6)	16 (32.6)	11 (18.6)	17 (26.2)	136 (27.2)
46–60	15 (20.8)	16 (27.1)	10 (14.9)	10 (19.2)	25 (32.4))	9 (18.4)	16 (27.2)	16 (24.6)	117 (23.4)
≥ 61	2 (2.8)	0	3 (4.5)	8 (15.3)	0	3 (6.2)	4 (6.8)	4 (6.1)	24 (4.8)
Education level									
None	25 (34.7)	17 (28.8)	15 (22.4)	6 (11.5)	27 (35.1)	10 (20.4)	14 (23.7)	14 (21.5)	128 (25.6)
Primary	44 (61.1)	37 (62.7)	38 (56.7)	32 (61.5)	43 (55.8)	32 (65.3)	38 (64.4)	45 (69.2)	308 (61.6)
Secondary	2 (2.8)	5 (8.5)	10 (14.9)	12 (23.1)	4 (5.2)	7 (14.3)	5 (8.5)	4 (6.2)	51 (10.2)
College	1 (1.4)	0	3 (4.5)	2 (3.8)	3 (3.9)	0	2 (3.4)	2 (3.1)	13 (2.6)
Main occupation									
Livestock keeping	1 (1.4)	3 (5.1)	5 (7.7)	3 (5.8)	12 (15.6)	12 (24.5)	2 (3.4)	2 (3.1)	40 (8.0)
Business	1 (1.4)	2 (3.4)	1 (1.5)	11 (21.2)	10 (13.0)	3 (6.1)	3 (5.1)	2 (3.1)	33 (6.7)
Crop farming	48 (66.7)	41 (69.5)	39 (60.0)	8 (15.3)	38 (49.4)	18 (36.7)	32 (54.2)	40 (61.5)	264 (52.8)
Employed	2 (2.8)	2 (3.4)	6 (9.2)	16 (30.8)	5 (6.5)	2 (4.0)	3 (5.1)	8 (12.3)	44 (8.9)
Student	5 (6.9)	1 (1.7)	5 (7.7)	5 (9.6)	4 (5.2)	6 (12.2)	5 (8.5}	7 (10.8)	38 (7.7)
Others	15 (20.8)	10 (16.9)	17 (27.2)	9 (17.3)	8 (10.3)	8 (16.3)	14 (23.7)	6 (9.2)	79 (15.9)

Results

Socio-demographic characteristics

A total of 500 participants from health facilities (n = 259) and households (n = 241) participated in the study (Table 1). Over half (58.2%) of the study participants were females, and the overall mean age was 35 (SD ± 18.9) years. In all districts, over half (57.4%) of participants were in the 16–45 years of age category, followed by the older age group of those ≥ 46 years (28.2%). Less than two-thirds (60%) of participants had received primary school education. Half (51.9%) of the participants were crop farmers, while a small proportion (7%) were livestock keepers (Table 1).

Clinical findings

Overall, 26.4% (n = 132) were found to have fever during the clinical examination. A total of 56 individuals (11.2%) tested positive for malaria. Of those with fever, 56 (42.4%) tested positive for malaria. The prevalence of malaria was highest in Kyela (23.8%), followed by Ukerewe (18.4%) and Kalambo (15.3%). It was lowest among individuals in Kondoa (2.0%).

Seroprevalence of VHFs

Overall, the VHF antibodies were detected in 64 study participants (12.8%). The seroprevalence was highest in Zone 1 (6.0%), followed by Zone 3 (3.6%), Zones 4 and 5 (1.4%), and Zone 2 (Kyela; 0.4%). The association between seroprevalence of VHFs and zone was found to be significant. District-wise, the highest seroprevalence (all VHFs combined) was recorded in Buhigwe (4.4%; n = 22), followed by Kinondoni (2.8%; n = 14) (Table 2).

The prevalence of the specific IgM and IgG antibodies against RVF, EVD, MVD, CCHF, and YF were 4.8%, 3.4%, 1.2%, 2.0%, and 1.4%, respectively. Comparing the prevalences of IgG and IgM antibodies for specific diseases, there was a significant association between ecological zone, geographical location, and seropositivity (Table 3). Ecological zones 2, 4, and 5 showed no evidence of EVD, MVD, or YF but low (<2%) IgG and IgM positivity against RVF and CCHF. Ecological zones 1 and 3 showed evidence of all tested viruses (Table 3).

Significant differences were found between groups based on age, sex, residence, sampling site, or those with and without fever.

Table 2
Number and percentage (%) of respondents with fever and malaria by district

District	No. of respondents	No. (%) with fever	No. (%) with malaria
Buhigwe	72	22 (30.5)	7 (9.7)
Kalambo	59	10 (16.9)	9 (15.3)
Kyela	67	13 (19.4)	16 (23.8)
Kinondoni	52	14 (26.9)	2 (3.8)
Kilindi	77	21 (27.3)	3 (3.9)
Kondoa	49	17 (34.6)	1 (2.0)
Mvomero	59	18 (30.5)	6 (10.2)
Ukerewe	65	17 (26.2)	12 (18.4)
Total	500	132 (26. 4)	56 (11.2)

The seroprevalence of IgM antibodies among participants with fever was higher (37%; n = 50) than in those without fever (11%; n = 14) (p = 0.01). The majority of those with IgG seropositivity (53%) were found in the health facility setting. Overall VHF seroprevalence was significantly lower among people infected with malaria than in those without malaria (p = 0.004) (Table 4).

Potential risk factors for VHF seropositivity

In the multivariate analysis, three variables were identified as independent risk factors for VHF. Contact with wild animals (OR = 1.2, CI = 1.3–1.6) and keeping goats (OR = 1.3, CI = 1.5–1.9) were significantly associated with RVF, while contact with bats (OR = 1.2, CI = 1.1–1.5) was associated with MVD (Table 5).

Discussion

This was the first serological survey of VHFs to include five viruses in eight districts from different ecological zones in Tanzania. Each district showed serological evidence of at least one virus, with seroprevalences of 0.4–4.4%. Our results indicate that VHF infections are prevalent among human populations in Tanzania. The highest VHF antibody seroprevalence was recorded in western Tanzania, characterised by a unimodal rainfall pattern and an altitude below 2300 m. The lowest seroprevalence was observed in the semi-arid central Tanzania, characterized by moderate precipitation and a unimodal rainfall pattern. VHF virus activity in the country's diverse environments was significantly associated with

Table 3
Seroprevalence (%) of IgG and IgM antibodies against RVF, CCHF, EVD, MVD VD , and YF by zone and district

District/zone	No. Table 2 tested	RVF		CCHF		EVD		DVVD		YF		Overall	*p*-value*
		IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	(IgG+IgM)%	
District													
Buhigwe	72	1	1	2	0	6	6	2	3	1	0	4.4	
Kinondoni	52	3	4	1	2	0	0	0	0	2	2	2.8	
Mvomero	59	1	1	0	0	0	0	0	0	0	0	0.4	
Kyela	67	0	1	1	0	0	0	0	0	0	0	0.4	0.001
Kalambo	59	2	0	1	0	1	2	0	0	1	1	1.6	
Kondoa	49	2	1	1	1	0	0	0	0	0	0	1.0	
Kilindi	77	0	1	0	0	2	0	1	0	0	0	0.8	
Ukerewe	65	6	0	0	1	0	0	0	0	0	0	1.4	
Total	500	3.0	1.8	1.2	0.8	1.8	1.6	0.6	0.6	0.8	0.6	12.8	
Zone													
Zone 1	131	3	1	3	0	7	8	2	3	2	1	6.0	0.0017
Zone 2	67	0	1	1	0	0	0	0	0	0	0	0.4	
Zone 3	129	3	5	1	2	2	0	1	0	2	2	3.6	
Zone 4	108	3	2	1	1	0	0	0	0	0	0	1.4	
Zone 5	65	6	0	0	1	0	0	0	0	0	0	1.4	
Total	500	3.0	1.8	1.2	0.8	1.8	1.6	0.6	0.6	0.8	0.6	12.8	

Key: RVF = Rift Valley fever; EVD= Ebola virus disease; MVD = Marburg virus disease; YF = yellow fever; CCHF = Crimean-Congo hemorrhagic fever; *Probabilities estimated using chi-square test.

Table 4
Seroprevalence of IgG and IgM antibodies against RVF, CCHF, EVD, MVD, and YF by socio-demographic and clinical characteristics

Variable		No. tested	RVF		CCHF		EVD		DVD		YF		Overall	*p*-value*
			IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	(IgG+IgM)%	
Age (years)	0–15	72	2	1	2	0	1	2	1	2	–	–	2.2	
	16–30	151	6	3	2	2	3	2	1	1	3	2	5.0	0.91
	31–45	136	3	1	1	2	3	4	1	–	–	1	3.2	
	46–60	117	2	3	1	–	1	–	–	–	1	–	1.6	
	61–75	15	1	1	–	–	1	–	–	–	–	–	0.6	
	≥76	9	1	–	–	–	–	–	–	–	–	–	0.2	
Sex	Female	291	8	7	3	3	6	4	1	1	3	2	7.4	0.662
	Male	209	7	2	3	1	3	4	2	2	1	1	5.4	
Education level	None	22	5	3	2	3	3	4	1	1	1	–	4.6	
	Primary	29	7	2	2	1	5	2	2	2	3	3	5.8	
	Secondary	10	2	4	1	–	1	2	–	–	–	–	2.0	0.828
	College	2	1	–	1	–	–	–	–	–	–	–	0.4	
Residence	Urban	279	10	4	3	3	4	4	2	2	2	2	7.2	
	Rural	221	5	5	3	1	5	4	1	1	2	1	5.6	0.960
Sampling location	Household	241	4	3	2	2	2	4	2	2	2	0	4.6	
	Facility	259	11	6	4	2	7	4	1	1	2	3	8.2	0.083
Current fever	Yes	132	11	5	5	4	7	5	2	3	3	3	9.4	
	No	368	4	4	1	0	2	3	1	0	1	0	3.2	0.073
Malaria	Positive	56	2	0	1	0	2	1	2	2	2	0	2.4	
	Negative	444	13	9	5	4	7	7	1	1	2	3	10.4	0.004
Total		500	3.0	1.8	1.2	0.8	1.8	1.6	0.6	0.6	0.8	0.6	12.8	

Key: RVF = Rift Valley fever; EVD = Ebola virus disease; MVD = Marburg virus disease; YF = yellow fever; CCHF = Crimean-Congo hemorrhagic fever; *Probabilities estimated using chi-square test.

contact with wild animals generally, or specifically bats, and with keeping goats. However, in this study the seropositivity rate appeared not to be associated with overt clinical symptoms, suggesting that VHF viruses may be less pathogenic in their natural settings than commonly thought. Most human VHF diseases have been described in epidemic settings, involving atypical exposure modes (Johnson, 1978; WHO, 1978).

Serological evidence of RVF and CCHF has been reported consistently for high-risk groups in Tanzania's diverse ecological zones (Mohamed et al., 2010; Heinrich et al., 2012; Ahmed et al., 2018). A significantly high proportion of YF, EVD, and MVD seropositivity identified in our study expressed selected VHF group specificity, reacting with YF, EVD, and MVDVD strains. The observed seropositivities for EVD and MVD in our study support those reported elsewhere in Africa in the absence of severe clinical manifestations, associated with asymptomatic or mild infections, suggesting subclinical forms of the diseases (Boisen et al., 2015; Brainard et al., 2016; Budodo et al., 2020). Similar low prevalences of VHFs (including YF, MVD, and EVD) have been reported in Ethiopia and Uganda (Tsegaye et al., 2018; Nyakarahuka et al., 2020). In a similar study in Central African Republic (CAR), slightly higher prevalences of EVD (5.3%) and MVD (2.4%) were reported (Gonzalez et al., 2000). In a previous study in CAR, a relatively higher seroprevalence of EVD (21.3%) but lower rates for MVD (3.1%) and CCHF (1.1%) were reported by Johnson et al. (1993). Recently, Steffen et al. (2019) reported serological prevalences of 2.0–3.5% in the Republic of Congo and DRC, and 1.3% in Cameroon.

Given the high mortality and very low incidence of mild or subclinical infections observed in previously reported outbreaks, the virus-specific reactions observed in our study might reflect distinct VHFs strain activity. An alternative interpretation of our data could be that EVD and MVD VD induce the formation of group-reactive antibodies of varying specificities depending upon the virus strain, nature of exposure, and host reactivity. Our study identified reactivity to IgG and IgM antibodies in some tested sera reflecting past and recent exposure. This finding is supported by the obser-

Table 5
Univariate and multivariate/logistic regression analysis of the association between exposure risk factors and seropositivity by infection

Infection	Exposure risk factor	IgG +ve	IgG −ve	IgM +ve	IgM −ve	Univariate analysis		Multivariate analysis	
						OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
RVF	Contact with wild animals	–	–	5 (5.7)	82 (94.1)	1.1 (1.2–1.4)	< 0.001	1.2 (1.3–1.6)	< 0.0001
	Water bodies around home	–	–	46 (15.3)	254 (84.7)	0.926 (0.91–0.93)	< 0.001	–	
	Livestock farming	3 (1.4)	199 (98.6)	–	–	1.2 (1.1–1.4)	0.014	–	
	Business	5 (2.5)	195 (97.6)	–	–	1.7 (1.6–1.9)	0.019	–	
	Keeping goat	6 (0.6)	94 (99.4)	–	–	1.6 (1.5–1.7)	0.007	1.3 (1.5–1.9)	0.014
CCHF	Contact with wild animals	4 (3.1)	125 (96.9)	–	–	1.1 (1.0–1.3)	< 0.001	–	
	Consumption of raw milk	4 (3.6)	107 (99.1)	–	–	1.2 (1.1 – 1.3)	0.006	–	
	Consumption of raw blood	1 (16.6)	5 (83.4)	–	–	1 .1 (1L08–1.2)	0.003	–	
EVD	Handling dead primates	–	–	9 (23.6)	29 (98.2)	1.9 (1.8–2.2)	< 0.001	–	
MVD	Handling dead primates	8 (21.6)	29 (78.4)	–	–	1 (0.98–1.002)	0.087	–	
	Contact with bats	2 (5.2)	36 (94.6)	–	–	1 (0.98–1.001)	0.23	1.2 (1.1–1.5)	0.04
YF	Use mosquito net	3 (0.9)	312 (99.1)	3 (o.95)	312 (99.05)	1 (0.1–1.0021)	0.073	–	

Key: RVF = Rift Valley fever; EVD = Ebola virus disease; MVD = Marburg virus disease; YF = yellow fever; CCHF= Crimean-Congo hemorrhagic fever

vation that asymptomatic VHF infections have been found more frequently in areas where the clinical cases have been reported (Chamberlin and Philippon, 2002). The specific characteristics of individual immunity leading to the production of specific antibodies, and early and healthy inflammatory responses (Rucker and Tiemann, 2012), may explain the presence or absence of symptomatic presentations. Additionally, a population may have been exposed to an unidentified virus with low pathogenicity or produced asymptomatic antibodies against various linear epitopes located in different structural and non-structural proteins of the virus (Johnson et al.,1993; Moyen et al., 2015).

The findings of our study indicate a significantly lower seroprevalence of VHF among those infected with malaria. Concurrent malaria parasite and YF and RVF infections have been reported among patients seeking care in Senegal (Sow et al., 2016). A recent study in Gabon reported a strong positive association between EVD-specific IgG seropositivity and the presence of malaria parasite infection, suggesting within-host interaction between the two pathogens (Abbate et al., 2020). There is currently limited information on the epidemiological link between exposure to various VHF viruses and malaria. However, these findings confirm observations by other studies (Sow et al., 2016; Abbate et al., 2020) that concurrent malaria and VHF virus infections are common, and that they are most often likely to be missed during routine screening for malaria because they are not included in the differential diagnosis. Our study also found out that people with VHF were more likely to be identified in a health facility than in a household setting because health-seeking behaviours are more likely to occur when individuals experience clinical symptoms (Latunji and Akinyemi, 2018; Zhang et al., 2020).

Our findings indicated that contact with wild animals and keeping goats were significantly associated with RVF seropositivity. Domestic and wild animals may play a role as maintenance hosts of RVF virus, and serve as sources of the virus during inter-epidemic periods, contributing to sporadic outbreaks (Matiko et al., 2018; Wright et al., 2019; Lubisi et al., 2020). In a study in Kenya, risk factors for RVF infection were found to include consumption or handling of products from sick animals, and being a herdsperson or handling aborted animal fetal material (Anyangu et al., 2010). In our study, exposures relating to animal contact were associated with acute RVF infection, whereas exposures to mosquitoes were not independent risk factors. In a previous study in Mbeya, Tanzania, residence altitude, high vegetation density, and higher minimum and lower maximum temperatures were associated with RVF virus positivity (Heinrich et al., 2012). Our study also identified contact with bats as a potential risk for MVD seropositivity, as reported previously by other studies (Monath, 1999; Towner et al., 2007). Several studies in Africa have reported close interactions with non-human primates and bats during outbreaks of MVD (Adjemian et al., 2011; Wood et al., 2012; Green, 2012).

Our results showed that a considerable number of participants had antibodies against VHF. This may not necessarily be generalizable to the entire population. However, this is not surprising, given the high incidence of febrile illnesses of unknown origin reported in Tanzania (Crump et al., 2013; Dalrymple et al., 2019). Continued surveillance and intense epidemiological investigations are needed to evaluate VHF pathogenicity and the likelihood that unidentified, serologically cross-reacting, and non-pathogenic members of the VHF families are present in Tanzania. Additionally, a significant association between seropositivity and region may have implications for future prevention strategies.

The most likely limitations of our study, which may affect interpretation of these findings, include the recall accuracy of answers to questions by the study's participants during face-to-face interviews. The study was conducted during the dry season. Although mosquito activity would have been lower during this period than in the wet season, the cross-sectional nature of the study did not offer the opportunity to estimate the likely period/time of exposure to infection. Therefore, the presented serological results based on antibody detection were likely a reflection of cumulative exposure and should therefore be interpreted with caution. The estimation of virus-specific risk factors was based on models with a small sample size, which may have influenced their accuracy.

Conclusion

Viral hemorrhagic fevers due to CCHF, EVD, MVD, RVF, and YF viruses were found to be prevalent in Tanzania, and to vary from one ecological zone to another. While RVF antibodies were found in all eight districts, CCHF was detected in six districts, and

EVD, MVD, and YF in four districts. Contact with wild animals and keeping goats were significantly associated with RVF seropositivity, while contact with bats was a potential risk for MVDVD seropositivity. Our study provides evidence of exposure to CCHF, EVD, MVD, RVF, and YF in Tanzania. These findings call for the need to strengthen the surveillance system and management of febrile illnesses in Tanzania.

Declaration of Competing interest

All authors declare no conflicts of interest.

Funding

This research was supported by a research program funded by the Korea National Institute of Health/Korea Disease Control and Prevention Agency (fund code: 4845-300-340-01).

Ethical approval

This study was approved by the Medical Research Coordinating Committee of the National Institute of Medical Research in Tanzania (NIMR/HQ/R.8a/Vol.IX/2724). Written informed consent was obtained from each participant aged ≥ 18 years. For all individuals aged < 18 years, written informed consent was sought from the respective parent or guardian. Each study subject was assigned a unique identification number to ensure confidentiality.

Acknowledgements

The authors are grateful to Alexander Raphael, Martin Anditi, Lucas Lazaro, and Feliciana Rawille for their support in data and sample collection. They would also like to thank Mariam Makange, Anna Rogath, and Mhoja Ndalahwa for their technical assistance in the laboratory examination of samples. Finally, the authors acknowledge the World Bank through the Government of United Republic of Tanzania for providing PhD scholarships to Sima Rugarabamu and Gaspary Mwanyika, who were part of the research team.

References

Abbate JL, Becquart P, Leroy E, Ezenwa VO, Roche B. Exposure to Ebola virus and risk for infection with malaria parasites, rural Gabon. Emerg Infect Dis 2020;26(2):229–37. doi:10.3201/eid2602.181120.

Adam AA, Karsany MS, Adam I. Manifestations of severe Rift Valley fever in Sudan. Int J Infect Dis 2010;14:e179–80 http://dx.doi.org/. doi:10.1016/j.ijid.2009.03.029.

Adjemian J, Farnon EC, Tschioko F, Wamala JF, Byaruhanga E, et al. Outbreak of Marburg hemorrhagic fever among miners in Kamwenge and Ibanda districts, Uganda, 2007. J Infect Dis 2011;204(3):S796–9 Suppl. doi:10.1093/indices/jir312.

Ahmed A, Makame J, Robert F, Julius K, Mecky M. Sero-prevalence and spatial distribution of Rift Valley fever infection among agro-pastoral and pastoral communities during interepidemic period in the Serengeti ecosystem, northern Tanzania. BMC Infect Dis 2018;18:276. doi:10.1186/s12879-018-3183-9.

Anyangu AS, Gould LH, Sharif SK, Nguku PM, Omolo JO, Mutonga D, et al. Risk factors for severe Rift Valley fever infection in Kenya, 2007. Am J Trop Med Hyg 2010;83(2):14–21 Suppl. doi:10.4269/ajtmh.2010.09-0293.

Aradaib IE, Erickson BR, Elageb RM, Khristova ML, Carroll SA, Elkhidir IM, et al. Rift Valley fever, Sudan, 2007 and 2010. Emerg Infect Dis 2013;19:246–53 http://dx.doi.org/. doi:10.3201/eid1902.120834.

Archer BN, Thomas J, Weyer J, Cengimbo A, Landoh DE, Jacobs C, et al. Epidemiologic investigations into outbreaks of Rift Valley fever in humans, South Africa, 2008–2011. Emerg Infect Dis 2013;19:1918–25 http://dx.doi.org/. doi:10.3201/eid1912.121527.

Bannister B. Viral haemorrhagic fevers imported into non-endemic countries: risk assessment and management. Br Med Bull 2010;95(1):193–225. doi:10.1093/bmb/ldq022.

Bausch DG, Borchert M, Grein T, Roth C, Swanepoel R, et al. Risk factors for Marburg haemorrhagic fever, the Democratic Republic of the Congo. Emerg Infect Dis 2003;9:1531–7. doi:10.3201/eid0912.030355.

Beeching NJ, Fenech M, Houlihan CF. Ebola virus disease. BMJ 2014;349:g7348 doi:. doi:10.1136/bmj.g7348.

Boisen ML, Schieffelin JS, Goba A, Oottamasathien D, Jones AB, Shaffer JG, et al. Multiple circulating infections can mimic the early stages of viral haemorrhagic fevers and possible human exposure to filoviruses in Sierra Leone before the 2014 outbreak. Viral Immunol 2015;28(1):19–31. doi:10.1089/vim.2014.0108.

Brainard J, Hooper L, Pond K, Edmunds K, Hunter PR. Risk factors for transmission of Ebola or Marburg virus disease: a systematic review and meta-analysis. Int J Epidemiol 2016;45(1):102–16 https://doi.org/10.1093.

Bray M. Pathogenesis of viral haemorrhagic fever. Curr Opin Immunol 2005;17(4):399–403. doi:10.1016/j.coi.2005.05.001.

Briese T, Paweska JT, McMullan LK, Hutchison S, et al. Genetic detection and characterization of Lujo virus: a new haemorrhagic fever-associated arenavirus from Southern Africa. PLoS Pathog 2009;5(5). doi:10.1371/journal.ppat.1000455.

Budodo RM, Horumpende PG, Mkumbaye SI, Mmbaga BT, Mwakapuja RS, Chilongola JO. Serological evidence of exposure to Rift Valley, Dengue and Chikungunya viruses among agro-pastoral communities in Manyara and Morogoro regions in Tanzania: a community survey. PLoS Negl Trop Dis 2020;14(7). doi:10.1371/journal.pntd.0008061.

Chamberlin P, Philippon N. The East African March–May rainy season: associated atmospheric dynamics and predictability over the 1968–97 period. J Clim 2002;15(9):1002–19 https://doi.org/10.1175/1520-0442(2002)015<1002:teammr>2.0.CO;2.

Changula K, Kajihara M, Mweene AS, Takada A. Ebola and Marburg virus diseases in Africa: increased risk of outbreaks in previously unaffected areas? Microbiol Immunol 2014;58(9):483–91. doi:10.1111/1348-0421.12181.

Cook EAJ, Grossi-Soyster EN, de Glanville WA, Thomas LF, Kariuki S, Bronsvoort BM, et al. The seroepidemiology of Rift Valley fever in people in the Lake Victoria Basin of western Kenya. PLoS Negl Trop Dis 2017;11(7). doi:10.1371/journal.pntd.0005731.

Crump JA, Morrissey AB, Nicholson WL, Massung RF, Stoddard RA, et al. Etiology of severe non-malaria febrile illness in northern Tanzania: a prospective cohort study. PLoS Negl Trop Dis 2013;7(7):e2324. doi:10.1371/journal.pntd.0002324.

Dalrymple U, Cameron E, Arambepola R, Battle KE, Chestnutt EG, Keddie SH, et al. The contribution of non-malarial febrile illness co-infections to *Plasmodium falciparum* case counts in health facilities in sub-Saharan Africa. Malar J 2019;18:195. doi:10.1186/s12936-019-2830-y.

Drake JM, Hassan AN, Beier JC. A statistical model of Rift Valley fever activity in Egypt. J Vector Ecol 2013;38:251–9 http://dx.doi.org/. doi:10.1111/j.1948-7134.2013.12038.x.

Feldmann H, Geisbert TW. Ebola haemorrhagic fever. Lancet 2011;377:849–62 2011. doi:10.1016/S0140-6736(10)60667-8.

Fhogartaigh CN, Aarons E. Viral haemorrhagic fever. Clin Med 2015;15(1):61–6 2015. doi:10.7861/clinmedicine.15-1-61.

Gonzalez JP, Josse R, Johnson ED, Merlin M, Georges AJ, et al. Antibody prevalence against haemorrhagic fever viruses in randomized representative Central African populations. Res Virol 1989;140:319–31. doi:10.1016/S0923-2516(89)80112-8.

Gonzalez JP, Nakouné E, Slenczka W, Morvan JM. Ebola and Marburg virus antibody prevalence in selected populations of the Central African Republic. Microb Infect 2000;2(1):39–44. doi:10.1016/S1286-4579(00)00287-2.

Green A. Uganda battles Marburg fever outbreak. Lancet 2012;380(9855):1726. doi:10.1016/s0140-6736(12)61973-4.

Hassan OA, Ahlm C, Sang R, 2007 Evander MThe. Rift Valley fever outbreak in Sudan. PLoS Negl Trop Dis 2011;5(9):e1229. doi:10.1371/journal.pntd.0001229.

Heinrich N, Saathoff E, Weller N, Clowes P, Kroidl I, et al. High seroprevalence of Rift Valley fever and evidence for endemic circulation in Mbeya region, Tanzania, in a cross-sectional study. PLoS Negl Trop Dis 2012;6:e1557. doi:10.1371/journal.pntd.0001557.

Himeidan YE, Kweka EJ, Mahgoub MM, El Rayah EA, Ouma JO. Recent outbreaks of Rift Valley fever in East Africa and the Middle East. Front Public Health 2014;2:169 http://dx.doi.org/. doi:10.3389/fpubh.2014.00169.

Iannetta M, Di Caro A, Nicastri E, Vairo F, Masanja H, Kobinger G, et al. Viral hemorrhagic fevers other than Ebola and Lassa. Infect Dis Clin North Am 2019;33:977–1002. doi:10.1016/j.idc.2019.08.003.

Isaäcson M. Viral haemorrhagic fever hazards for travelers in Africa. Clin Infect Dis 2001;33(10):1707–12 doi: 10.1086/322620.

Jansen van Vuren P, Kgaladi J, Patharoo V, Ohaebosim P, Msimang V, Nyokong B, Paweska JT. Human cases of Rift Valley fever in South Africa, 2018. Vector-Borne Zoonotic Dis 2018;18(12). doi:10.1089/vbz.2018.2357.

Johnson ED, Gonzalez JP, Georges A. Haemorrhagic fever virus activity in equatorial Africa: distribution and prevalence of filovirus reactive antibody the Central African Republic. Trans Royal Soc Trop Med Hyg 1993;87(5):530–5. doi:10.1016/0035-9203(93)90075-2.

Johnson KM. Ebola haemorrhagic fever in Zaire, 1976. Bulletin of the World Health Organization 1978;56:271–93.

Kerario II, Muleya W, Chenyambuga S, Koski M, Hwang S-G, Simuunza M. Abundance and distribution of Ixodid tick species infesting cattle reared under traditional farming systems in Tanzania. Afr J Agric Res 2017;12(4):286–99. doi:10.5897/ajar2016.12028.

Karimuribo ED, Mutagahywa E, Sindato C, Mboera L, Mwabukusi M, Kariuki Njenga M, et al. A smartphone app (*AfyaData*) for innovative one health disease surveillance from community to national levels in Africa: intervention in disease surveillance. JMIR Public Health Surveill 2017;3(4):e94. doi:10.2196/publichealth.7373.

Keïta M, Kizerbo GA, Subissi L, Traoré FA, Doré A, Camara MF, et al. Investigation of a cross-border case of Lassa fever in West Africa. BMC Infect Dis 2019;19(1):606. doi:10.1186/s12879-019-4240-8.

Kenawy MA, Abdel-Hamid YM, Beier JC. Rift Valley fever in Egypt and other African countries: historical review, recent outbreaks and possibility of disease occurrence in Egypt. Acta Trop 2018;181:40–9. doi:10.1016/j.actatropica.2018.01.015.
Kwagonza L, Masiira B, Kyobe-Bosa H, Kadobera D, Atuheire EB, Lubwama B, et al. Outbreak of yellow fever in central and southwestern Uganda, February–May 2016. BMC Infectious Diseases 2018;18:548. doi:10.1186/s12879-018-3440-y.
Kwak YS, Kim TY, Nam S-H, Lee IY. Ixodid tick infestation in cattle and wild animals in Maswa and Iringa, Tanzania. Korean J Parasitol 2014;52(5):565–8. doi:10.3347/kjp.2014.52.5.565.
LaBeaud AD, Kazura JW, King CH. Advances in Rift Valley fever research: insights for disease prevention. Curr Opin Infect Dis 2010;23:403–8 http://dx.doi.org/. doi:10.1097/QCO.0b013e32833c3da6.
Latunji OO, Akinyemi OO. Factors influencing health-seeking behaviour among civil servants in Ibadan, Nigeria. Ann Ib Postgrad Med 2018;16(1):52–60.
Lubisi BA, Ndouvhada PN, Neiffer D, Penrith ML, Sibanda D-R, Bastos A. Seroprevalence of Rift Valley fever in South African domestic and wild suids (1999–2016). Transbound Emerg Dis 2020;67(2):811–21. doi:10.1111/tbed.13402.
Malvy D, McElroy AK, de Clerck H, Günther S, van Griensven J. Ebola virus disease. Lancet 2019;393(10174):936–48. doi:10.1016/S0140-6736(18)33132-5.
Matiko MK, Salekwa LP, Kasanga CJ, Kimera SI, Evander M, Nyangi WP. Serological evidence of inter-epizootic/inter-epidemic circulation of Rift Valley fever virus in domestic cattle in Kyela and Morogoro, Tanzania. PLoS Negl Trop Dis 2018;12(11). doi:10.1371/journal.pntd.0006931.
Mboussou F, Ndumbi P, Ngom R, Kamassali Z, Ogundiran O, Van Beek J, et al. Infectious disease outbreaks in the African region: an overview of events reported to the World Health Organization in 2018. Epidemiol Infect 2019;147:e299. doi:10.1017/S0950268819001912.
Mehedi M, Groseth A, Feldmann H, Ebihara H. Clinical aspects of Marburg hemorrhagic fever. Future Virol 2011;6:1091–106. doi:10.2217/fvl.11.79.
Mohamed M, Mosha F, Mghamba J, Zaki SR, Shieh WJ, Paweska J, et al. Epidemiologic and clinical aspects of a Rift Valley fever outbreak in humans in Tanzania, 2007. Am J Trop Med Hyg 2010;83(2):22–7 Suppl. doi:10.4269/ajtmh.2010.09-0318.
Monath TP. Ecology of Marburg and Ebola viruses: speculations and directions for future research. J Infect Dis 1999;179(1):S127–38 Suppl. doi:10.1086/514281.
Moyen N, Thirion L, Emmerich P, Dzia-Lepfoundzou A, Richet H, Boehmann Y, et al. Risk factors associated with Ebola and Marburg viruses seroprevalence in blood donors in the Republic of Congo. PLoS Negl Trop Dis 2015;9(6). doi:10.1371/journal.pntd.0003833.
Mweya CN, Kimera SI, Stanley G, Misinzo G, Mboera LEG. Climate change influences potential distribution of infected *Aedes aegypti* co-occurrence with dengue epidemics risk areas in Tanzania. PLoS ONE 2016;11(9). doi:10.1371/journal.pone.0162649.
Nicastri E, Kobinger G, Vairo F, Montaldo C, Mboera LEG, Ansunama R. Ebola virus diseases: epidemiology, clinical features, management, and prevention. Infect Dis Clin North Am 2019;33(4):953–76 2019. doi:10.1016/j.idc.2019.08.005.
Nyakarahuka L, Shoemaker TR, Balinandi S, Chemos G, Kwesiga B, Mulei S, et al. Marburg virus disease outbreak in Kween District Uganda, 2017: epidemiological and laboratory findings. PLoS Negl Trop Dis 2019;13. doi:10.1371/journal.pntd.0007257.
Nyakarahuka L, Schafer IJ, Balinandi S, Mulei S, Tumusiime A, Kyondo J, et al. A retrospective cohort investigation of seroprevalence of Marburg virus and Ebola viruses in two different ecological zones in Uganda. BMC Infect Dis 2020;20:461. doi:10.1186/s12879-020-05187-0.
Rucker G, Tiemann J. Eleven years of MODIS burned areas: a GIS analysis for the United Republic of Tanzania territory. Project report for Tanzania Forest Services. Dar es Salaam: Ministry of Natural Resources and Tourism; 2012.
Rugarabamu S, Mboera L, Rweyemamu M, Mwanyika G, Lutwama J, Paweska J, et al. Forty-two years of responding to Ebola virus outbreaks in Sub-Saharan Africa: a review. BMJ Glob Health 2020;5. doi:10.1136/bmjgh-2019-001955.
Sindato C, Karimuribo ED, Pfeiffer DU, Mboera LEG, Kivaria F, Dautu G, et al. Spatial and temporal pattern of Rift Valley fever outbreaks in Tanzania; 1930 to 2007. PLoS ONE 2014;9(2):e88897. doi:10.1371/journal.pone.0088897.
Sindato C, Kim B, Stevens KB, Karimuribo ED, Mboera LEG, Paweska JT, et al. Spatial heterogeneity of habitat suitability for Rift Valley fever occurrence in Tanzania: an ecological niche modelling approach. PLoS Negl Trop Dis 2016;10(9). doi:10.1371/journal.pntd.0005002.
Smith DH, Isaacson M, Johnson KM, Bagshawe A, Johnson BK, Swanapoel R, et al. Marburg-virus disease in Kenya. Lancet 1982;319(8276):816–20. doi:10.1016/s0140-6736(82)91871-2.
Sow A, Loucoubar C, Diallo D, Faye O, Ndiaye Y, Senghor CS, et al. Concurrent malaria and arbovirus infections in Kedougou, southeastern Senegal. Malar J 2016;15:47. doi:10.1186/s12936-016-1100-5.
Steffen I, Lu K, Yamamoto LK, Hoff NA, Mulembakani P, Wemakoy EO, et al. Serologic prevalence of Ebola virus in Equatorial Africa. Emerg Infect Dis 2019;25(5):911–18 https://dx.doi.org/. doi:10.3201/eid2505.180115.
Swai ES, Mbise AN, Kessy V, Kaaya E, Sanka P, Loomu PM. Farm constraints, cattle disease perception and tick management practices in pastoral Maasai community, Ngorongoro, Tanzania. Livest Res Rural Dev 2005;17(2) http://www.lrrd.org/17/2/cont1702.
Swanepoel R, Shepherd AJ, Leman PA, Shepherd SP, McGillivray GM, et al. Epidemiologic and clinical features of Crimean-Congo hemorrhagic fever in southern Africa. Am J Trop Med Hyg 1987;36(1):120–32. doi:10.4269/ajtmh.1987.36.120.
TMIS (2017) Tanzania Malaria Indicator Survey 2017. Ministry of Health, Community Development, Gender, Elderly and Children (Tanzania Mainland), Ministry of Health (Zanzibar), National Bureau of Statistics, Office of the Chief Government Statistician, and ICF 2017. Dar es Salaam, Tanzania, and Rockville, Maryland, USA.
Tomori O, Fabiyi A, Sorungbe A, Smith A, McCormick JB. Viral haemorrhagic fever antibodies in Nigerian populations. Am J Trop Med Hyg 1988;38:407–10. doi:10.4269/ajtmh.1988.38.407.
Towner JS, Pourrut X, Albariño CG, Nkogue CN, Bird BH, Grard G, et al. Marburg virus infection detected in a common African bat. PLoS ONE 2007;2(8):e764. doi:10.1371/journal.pone.0000764.
Tsegaye MM, Beyene B, Ayele W, Abebe A, Tareke I, Sall A, et al. Seroprevalence of yellow fever and related Flaviviruses in Ethiopia: a public health perspective. BMC Public Health 2018;18:1011. doi:10.1186/s12889-018-5726-9.
WHO. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO international study team. Bull World Health Org 1978;56:247–70.
WHO. Annual Review of Diseases Prioritized under the Research and Development BluePrint. Geneva, Switzerland: World Health Organization; 2018 February https://www.who.int/emergencies/diseases/2018prioritization-report.pdf?ua=1 .
WHO. Weekly Bulletin on Outbreak and Other Emergencies. Week 27. Geneva, Switzerland: World Health Organization; 2019 https://apps.who.int/iris/bitstream/handle/10665/325777/OEW27-0107072019.pdf.
Wood JLN, Leach M, Waldman L, MacGregor H, Fooks AR, Jones KE, et al. A framework for the study of zoonotic disease emergence and its drivers: spillover of bat pathogens as a case study. Philos Trans R Soc Lond B Biol Sci 2012;367(1604):2881–92. doi:10.1098/rstb.2012.0228.
Wright D, Kortekaas J, Bowden TA, Warimwe GM. Rift Valley fever: biology and epidemiology. J Gen Virol 2019;100(8):1187–99. doi:10.1099/jgv.0.001296.
Zhang Q, Feng S, Wong IOL, Ip DK, Cowling BJ, et al. A population-based study on healthcare-seeking behavior of persons with symptoms of respiratory and gastrointestinal-related infections in Hong Kong. BMC Public Health 2020;20:402. doi:10.1186/s12889-020-08555-2.