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GROSSI-SOYSTER AND OTHERS

RIFT VALLEY FEVER

Rift Valley Fever Seroprevalence in Coastal Kenya

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Abstract.

Rift Valley fever virus (RVFV) causes severe disease in both animals and humans, resulting in significant economic and public health damages. The objective of this study was to measure RVFV seroprevalence in six coastal Kenyan villages between 2009 and 2011, and characterize individual-, household-, and community-level risk factors for prior RVFV exposure. Sera were tested for anti-RVFV IgG via enzyme-linked immunosorbent assay. Overall, 51 (1.8%; confidence interval [CI₉₅] 1.3–2.3) of 2,871 samples were seropositive for RVFV. Seroprevalence differed significantly among villages, and was highest in Jego Village (18/300; 6.0%; CI₉₅ 3.6–9.3) and lowest in Magodzoni (0/248). Adults were more likely to be seropositive than children ($P < 0.001$). Seropositive subjects were less likely to own land or a motor vehicle ($P < 0.01$), suggesting exposure is associated with lower socioeconomic standing ($P = 0.03$). RVFV exposure appears to be low in coastal Kenya, although with some variability among villages.

BACKGROUND

Rift Valley fever virus (RVFV) is a zoonotic phlebovirus that can be transmitted to livestock and humans by a number of mosquito species, including *Aedes ochraceus*, *Aedes mcintoshi*, *Culex tritaeniorhynchus*, and *Aedes vexans*, or by direct contact with, or aerosols from, contaminated fluids and tissues.^{1–7} A majority of infected humans experience mild disease, with roughly 1% of cases suffering severe symptoms such as hemorrhagic fever and encephalitis.^{2,4,5,8} RVFV is highly pathogenic in domestic livestock, specifically goats, sheep, and cattle.^{6,9} Outbreaks have had detrimental impacts on livestock trade, and meat and dairy industries, as infection can cause a catastrophic decline in animal breeding and productivity.⁶

It is difficult to determine the true public health impact of RVFV and principle risk factors associated with exposure and disease, as human cases are not reliably reported. The weight of many factors, specifically as biological sex and gender dynamics, differ by study scope and regional focus.¹⁰ Similarly, community knowledge and perception of described risks, methods of transmission, and symptoms and severity of disease vary by study region, populations surveyed, and access to health interventions and public health efforts to minimize disease.^{11–13} The objective of this study was to measure RVFV prevalence in six coastal villages in Kenya. Variability in prevalence between these villages was used to identify risk factors associated with

RVFV exposure by linking seropositivity to demographic data such as socioeconomic standing (SES), occupation, and clinical history. Household mosquito abundance was also measured to test for correlation between mosquito exposure, in and near the home, and seropositivity for RVFV.

MATERIALS AND METHODS

This study was part of a larger project on polyparasitism in communities on the southern coast of Kenya.^{14,15} Study participants were recruited in 2009–2011 from the rural villages of Jego, Kinango, Magadzoni, Milalani, Nganja, and Vuga located in the southeastern corner of Kenya, in Kwale County (Figure 1)¹⁴ Jego, the southern-most village, is located on the border with Tanzania. Milalani, Nganja, Magadzoni, Vuga, and Jego are very close to the Indian Ocean, whereas Kinango is situated inland by 50 km. Kinango, located in a semiarid inland area, has a much drier climate compared with villages such as Milalani, Nganja, and Magadzoni located in the coastal plains region.^{15,16}

Biobanked sera collected from 2,871 study participants during the 2009–2011 recruitment phase were tested for anti-RVFV IgG by standardized indirect enzyme-linked immunosorbent assay (ELISA) protocols as previously described.^{2–5} Institutional Review Board (IRB) approval was obtained for this project from Children’s Hospital of Oakland Research Institute (IRB No. 2013-023), University Hospitals Case Medical Center of Cleveland (IRB No. 11-07-42), and Kenya Medical Research Institute (IRB SSC No. 087) before testing biobanked samples. All consenting long-term residents of designated study villages in Kwale District, Coast Province, Kenya, ≥ 5 years of age, were selected for inclusion. Those who refused consent or assent, and/or were not a long-term resident of the study area were excluded from participation.

Demographic, household inventory, and environmental exposure questionnaires were administered to all participants at the time of enrollment. Questions referred to SES, occupation, basic clinical history, livestock exposures, and exposure to mosquitoes. An SES index was established with the use of Principal Component Analysis of demographic and household data relating to land ownership, homestead construction (i.e., materials used for roof and floor), light sources available, mobility (i.e., ownership of a bicycle or motor vehicle), drinking water sources, and the type of primary latrine and its proximity to their homestead (Table 1).¹⁷

Resting mosquitoes were captured inside study households in the early morning using the Pyrethrum Spray Catch (PSC) method, and outside using clay pot traps and Prokopack aspirators.¹⁰ PSC collections were performed monthly in 10 randomly selected households from April 2009 to 2013.^{14,16} Approximately 95% of the collected mosquitoes were culicine (*Culex* spp.).¹⁴ Culicine density per household was tested for association with household RVFV seroprevalence.

The relationship of each potential predictor with odds of RVFV seropositivity was assessed in bivariate analysis with the use of χ^2 test.

RESULTS

Of the 2,871 serum samples tested, 51 (1.8%; confidence interval [CI]₉₅ 1.3–2.3) were RVFV seropositive (Table 1). Distribution of seropositives was significantly different among the six villages ($P < 0.001$). Jego had the highest seroprevalence (18/300; 6.0%; CI₉₅ 3.6–9.3), whereas Magadzoni had the lowest (0/248). The four other villages also had low seroprevalence, with

only 1.0% of residents in Vuga (8/835; CI₉₅ 0.4–1.9), 1.0% in Kinango (5/524; CI₉₅ 0.3–2.2), 1.7% in Nganja (7/404; CI₉₅ 0.1–3.5), and 2.3% in Milalani (13/560; CI₉₅ 1.2–3.9) having positive tests (Table 1 and Figure 2). Adults were more likely to be seropositive than children (1.7% and 0.1%, respectively; $P < 0.001$) (Table 1). Participants who tested seropositive for anti-RVFV antibodies ranged from 13 to > 90 old. No statistically significant difference in seropositivity was noted between genders.

Questionnaire data identified few statistically significant correlations between subject lifestyle, behaviors, and health history, and RVFV exposure. Seropositive subjects were less likely to own land or a motor vehicle ($P < 0.01$). Seropositivity was not associated with documented livestock exposure at the household (Figure 2).

DISCUSSION

Our data suggest that RVFV exposure is not common in the extreme southern part of rural coastal Kenya. Studies conducted in rural northeastern Kenya in 2006 reported seroprevalence rates of > 13% in two areas of the semi-arid Ijara District,² located north of our present study region (coastal Kwale County).^{2–4,18} A study by Mohamed and others described a 2007 outbreak of RVFV in Tanzania, located south of our study region, with 511 suspected cases, 36.4% of which were laboratory confirmed.¹⁹ Previous reports from Kwale County indicate that there have been at least 21 RVFV outbreaks in that location since the first recorded case in 1961.²⁰

Historical outbreak data compared with the average age of seropositive subjects may elucidate the frequency of outbreaks in Kwale County villages. Median age of seropositive subjects was significantly higher than those who tested seronegative in Nganja ($P = 0.003$), Milalani ($P < 0.001$), Jego ($P < 0.001$), and Kinango ($P = 0.002$), and in the total study cohort overall ($P < 0.001$). Across the villages surveyed in our study, adults were 1.7 times more likely to be seropositive than children. The higher likelihood for seropositivity in adults may be due to exposure earlier in their lives, such as through an outbreak that occurred before many of the children of our study population were born, or, alternatively, through age-specific occupational exposures.^{8,13} Our data suggest that cumulative exposure has been relatively low, despite the number of previous outbreaks in Kwale County, and nationally over time.

Low rates of RVFV exposure on the coast may be attributed to diversity in the types of jobs available in those regions. Human seroprevalence was not significantly correlated with household livestock in our study. In contrast, a study in the northeastern province by Munyua and others indicates that livestock infections typically multiply before human exposure.⁹ Most studies analyzing the zoonotic nature of RVFV have shown a significant link between exposure to animals and seropositivity for RVFV.⁸ Although number of animals kept was not significantly associated with RVFV exposure, occupational exposures that may contribute more significantly to RVFV exposure (e.g., herding, butchering) may be more influential than keeping animals at home. A 2010 study of a population of nomadic herders by Aagaard-Hansen and others confirms a higher risk of disease exposure in individuals with occupational handling of animals.²¹ Additionally, studies by Ng'ang'a and others (2016) and Owange and others (2014) suggest that these risks may also be due to specific perceptions of risk and overall disease impact in these populations.^{12,13}

Gender was not a significant factor for exposure in our study, which may be a limitation of our sample size. Many studies that indicate gender as a risk factor for RVFV exposure have shown that males are more likely to be seropositive for RVFV than females, with differences in

prevalence ranging between 5% and 14% between genders.^{5,18} This may suggest differential exposure to RVFV through labor distribution and gender roles, with the expectation of significant regional and cultural variation. In contrast, other studies do not report gender as a risk factor for RVFV exposure.^{5,10,22}

The World Health Organization (WHO) has declared that RVFV is a significant emerging infectious disease that impacts primarily poor and marginalized populations.²³ Although there are many individual- and household-level factors that are associated with lower SES and poverty that may create a higher likelihood of exposure to mosquito-borne diseases, many of the traditional risk factors identified in previous studies of RVFV exposure were not significant risk factors for our populations. SES data in this study indicated that subjects of lower standing were more likely to be seropositive, yet occupation could not be correlated with seropositivity.

Human seroprevalence was not significantly correlated to household *Culex* density in our study. *Culex* density near the homestead may not be representative of overall mosquito exposure during daytime. Overall, households in Kinango, the most inland village surveyed, had the highest density of *Culex* in the homestead, but some of the lowest rates of seropositivity. Further research is required to determine whether this may suggest exposure to RVFV can be attributed to other modes of transmission or by other mosquito species.

Our data indicate a significant variation in exposure at the village level, with the highest seroprevalence found in Jego. The higher seroprevalence in Jego may be related to periodic flooding of the area, which is predominantly low-lying estuary. Jego is also adjacent to a herding community that had exceptionally high livestock and cattle numbers. Historically, RVFV outbreaks have occurred during years with significant and extensive rainfall, which creates new mosquito habitats through flooding, thus increasing mosquito populations.^{6,24} The importance of heavy rainfall and flooding for mosquito-borne diseases has also been identified at the community level. Owange and others report that high rainfall and the creation of dambos from flooding are perceived by community members as one of the most important risk factors of the RVFV disease pathway.¹³

There were a number of limitations to our study. This cross-sectional study of selected villages does not represent extensive variations in climate other than rainfall. Data collected using questionnaires, addressing health history, environment, and lifestyle factors, were self-reported and subject to reporting bias. Mosquito analysis only included the most abundant *Culex* spp., and did not include testing to detect RVFV in these vectors. Analysis of livestock included only goats and cattle, as other species were too rare for meaningful analysis.

In conclusion, the results presented suggest that RVFV is transmitting at low levels on the coast of Kenya, with exposure varying by village. Despite the lack of a significant correlation between culicine density, household livestock, and RVFV prevalence, our data did illustrate the impacts of age and SES on exposure to RVFV. Additionally, there are public health implications highlighted by our findings in this region, specifically environmental and occupational risks that may be higher for adults or those of lower SES. These findings point to the need for more extensive local and regional studies to further elucidate the influence of mosquito exposure, occupational exposure, and livestock trade on RVFV transmission.

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FIGURE 1. Map of study area; inset: map of Kenya showing study sites within Kwale County.

FIGURE 2. Culicine and livestock densities per house and Rift Valley fever virus (RVFV) seropositivity per village.

TABLE 1

Risk factor analysis of demographic and lifestyle factors

Factor	Level	Nganja			Milalani			Vuga			Jego			Kinango			Magodizoni			Total			Total	Test		
		Negative	Positive	P value	Negative	Positive	P value	Negative	Positive	P value	Negative	Positive	P value	Negative	Positive	P value	Negative	Positive	P value	Negative	Positive	P value				
N		397 (13.8%)	8 (0.3%)		541 (18.8%)	12 (0.4%)		842 (29.3%)	8 (0.3%)		282 (9.8%)	16 (0.6%)		516 (18%)	5 (0.2%)		247 (8.6%)			2,825 (98.3%)	49 (1.7%)		2,874 (100%)			
Age, median (IQR)		20 (11, 36)	49.5 (37.5, 53)	0.003*	17 (11, 35)	44.5 (31.5, 75)	< 0.001*	17 (12, 36)	37.5 (21.5, 51)	0.021	20 (14, 34)	44 (29.5, 61.5)	< 0.001*	14 (10, 28)	63 (53, 66)	0.002*	14 (9, 30)			17 (11, 34)	48 (30, 61)	< 0.001*	16 (8, 33)	Wilcoxon rank-sum		
Sex	Female	213 (12.9%)	5 (0.3%)	0.73	317 (19.2%)	7 (0.4%)	1.00	473 (28.6%)	7 (0.4%)	0.15	149 (9%)	8 (0.5%)	1.00	330 (19.9%)	3 (0.2%)	1.00	143 (8.6%)			1,625 (98.2%)	30 (1.8%)	0.77	1,655 (100%)	Fisher's exact		
	Male	183 (15.3%)	3 (0.3%)		224 (18.8%)	5 (0.4%)		356 (29.8%)	1 (0.1%)		133 (11.1%)	8 (0.7%)		182 (15.3%)	2 (0.2%)		96 (8%)			1,174 (98.4%)	19 (1.6%)				1,193 (100%)	
Tribe	Digo	354 (17.2%)	8 (0.4%)	1.00	513 (25%)	12 (0.6%)	1.00	738 (35.9%)	6 (0.3%)	0.34	149 (7.3%)	4 (0.2%)	0.063	51 (2.5%)	0 (0.0%)	1.00	219 (10.7%)			2,024 (98.5%)	30 (1.5%)	0.28	2,054 (100%)	Fisher's exact		
	Ditiana	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		1 (100%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)		0 (0.0%)			1 (100%)
	Dumma	20 (3.3%)	0 (0.0%)		14 (2.3%)	0 (0.0%)		66 (10.9%)	2 (0.3%)		96 (15.9%)	8 (1.3%)		380 (62.8%)	5 (0.8%)		14 (2.3%)			590 (97.5%)	15 (2.5%)				605 (100%)	
	Kamba	7 (1.2%)	0 (0.0%)		3 (5.2%)	0 (0.0%)		7 (12.1%)	0 (0.0%)		12 (20.7%)	2 (3.4%)		25 (43.1%)	0 (0.0%)		2 (3.4%)			56 (96.5%)	2 (3.5%)				58 (100%)	
	Swahili	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		7 (58.3%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		5 (41.7%)	0 (0.0%)		0 (0.0%)			12 (100%)	0 (0.0%)				12 (100%)	
	Other	15 (12.6%)	0 (0.0%)		11 (9.2%)	0 (0.0%)		13 (10.9%)	0 (0.0%)		25 (21%)	2 (1.7%)		51 (42.9%)	0 (0.0%)		2 (1.7%)			117 (98.3%)	2 (1.7%)				119 (100%)	
	0-25%	81 (11.6%)	3 (0.4%)		235 (33.7%)	8 (1.1%)		138 (19.8%)	1 (0.1%)		94 (13.5%)	6 (0.9%)		59 (8.5%)	2 (0.3%)		71 (10.2%)			678 (97.1%)	20 (2.9%)				698 (100%)	
25-50%	109 (13.4%)	2 (0.2%)	143 (17.6%)	2 (0.2%)	234 (28.7%)	2 (0.2%)	101 (12.4%)	7 (0.9%)	142 (17.4%)	2 (0.2%)	70 (8.6%)			799 (98.2%)	15 (1.8%)		814 (100%)									
50-75%	53 (9.7%)	0 (0.0%)	63 (11.5%)	1 (0.2%)	218 (39.8%)	2 (0.4%)	54 (9.9%)	3 (0.5%)	97 (17.7%)	0 (0.0%)	57 (10.4%)			542 (98.9%)	6 (1.1%)		548 (100%)									
75-100%	154 (18.9%)	3 (0.4%)	100 (12.3%)	1 (0.1%)	252 (31%)	3 (0.4%)	33 (4.1%)	0 (0.0%)	218 (26.8%)	1 (0.1%)	49 (6%)			806 (99.0%)	8 (0.98%)		814 (100%)									
Highest level of education completed	None	34 (16.1%)	2 (0.9%)	1.00	37 (17.5%)	4 (1.9%)	0.31	54 (25.6%)	2 (0.9%)	0.86	24 (11.4%)	4 (1.9%)	0.55	39 (18.5%)	1 (0.5%)	1.00	10 (4.7%)			198 (93.8%)	13 (6.2%)	0.28	211 (100%)	Fisher's exact		
	Primary	51 (16.5%)	3 (1%)		64 (20.6%)	2 (0.6%)		95 (30.6%)	2 (0.6%)		28 (9%)	2 (0.6%)		42 (13.5%)	2 (0.6%)		19 (6.1%)			299 (96.4%)	11 (3.5%)				310 (100%)	
	Secondary	12 (15.4%)	1 (1.3%)		18 (23.1%)	1 (1.3%)		20 (25.6%)	0 (0.0%)		4 (5.1%)	1 (1.3%)		19 (24.4%)	0 (0.0%)		2 (2.6%)			75 (96.1%)	3 (3.8%)				78 (100%)	
	University/adult education	9 (11.3%)	0 (0.0%)		24 (30%)	0 (0.0%)		24 (30%)	0 (0.0%)		9 (11.3%)	1 (1.3%)		7 (8.8%)	0 (0.0%)		6 (7.5%)			79 (98.8%)	1 (1.3%)				80 (100%)	
Mosquito avoidance behavior	None	27 (9.7%)	1 (0.4%)	0.71	48 (17.3%)	2 (0.7%)	0.40	107 (38.6%)	0 (0.0%)	0.91	28 (10.1%)	1 (0.4%)	0.58	43 (15.5%)	1 (0.4%)	0.35	19 (6.9%)			272 (98.2%)	5 (1.8%)	0.38	277 (100%)	Fisher's exact		
	0-33%	202 (14%)	4 (0.3%)		328 (22.7%)	9 (0.6%)		383 (26.5%)	4 (0.3%)		151 (10.4%)	11 (0.8%)		220 (15.2%)	1 (0.1%)		133 (9.2%)			1,417 (97.9%)	29 (2.0%)				1,446 (100%)	
	33-66%	128 (15.3%)	3 (0.4%)		117 (14%)	1 (0.1%)		242 (29%)	3 (0.4%)		72 (8.6%)	4 (0.5%)		188 (22.5%)	2 (0.2%)		74 (8.9%)			821 (98.4%)	13 (1.6%)				834 (100%)	
	66-100%	40 (16.6%)	0 (0.0%)		48 (15.1%)	0 (0.0%)		110 (34.7%)	1 (0.3%)		31 (9.8%)	0 (0.0%)		65 (20.5%)	1 (0.3%)		21 (6.6%)			315 (99.4%)	2 (0.6%)				317 (100%)	
Yellow fever vaccine	No	90 (16.5%)	1 (0.2%)	1.00	51 (9.3%)	0 (0.0%)	1.00	121 (22.2%)	0 (0.0%)	1.00	42 (7.7%)	0 (0.0%)	1.00	156 (24%)	1 (0.2%)	1.00	104 (19%)			544 (99.6%)	2 (0.4%)	1.00	546 (100%)	Fisher's exact		
	Yes	37 (39.4%)	0 (0.0%)		8 (8.5%)	0 (0.0%)		5 (5.3%)	0 (0.0%)		7 (7.4%)	0 (0.0%)		35 (37.2%)	0 (0.0%)		2 (2.1%)			94 (100%)	0 (0.0%)				94 (100%)	
	No data	270 (9.4%)	7 (0.25%)		482 (16.8%)	12 (0.42%)		716 (24.9%)	8 (0.28%)		233 (8.1%)	16 (0.56%)		345 (12%)	4 (0.14%)		247 (8.74%)			2,825 (98.3%)	47 (1.7%)				2,874 (100%)	

Figure 1



Figure 2

