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Seroepidemiological Reconstruction of Long-term Rift Valley Fever Virus Circulation in Nouakchott, Mauritania

Meïli Baragatti,[1,a] Bedia Abdoullah,[2,a] Nicolas Gomez,[3,4,5] Nazli Ayhan,[6,7] Rémi Charrel,[7] Leonardo K. Basco,[5,8] Ali Ould Mohamed Salem Boukhary,[2] and Sébastien Briolant[3,4,5]

[1]Unité mixte de recherche en Mathématiques, Informatique et Statistique pour l'Environnement et l'Agronomie, Université Montpellier, Institut national de recherche pour l'agriculture, l'alimentation et l'environnement, Institut Agro, Montpellier, France; [2]Unité de Recherche Génomes et Milieux, Université de Nouakchott, Nouakchott, Mauritania; [3]Unité Parasitologie et Entomologie, Département Microbiologie et Maladies Infectieuses, Institut de Recherche Biomédicale des Armées, Marseille, France; [4]Unité mixte de recherche Risques Infectieux Tropicaux et Microorganismes Emergents, Aix Marseille Université, Service de santé des armées, Assistance publique-Hôpitaux de Marseille, Marseille, France; [5]Institu Hospitalo-Universitaire Méditerranée Infection, Marseille, France; [6]Centre National de Référence des Arbovirus, Institut national de la santé et de la recherche médicale-Institut de Recherche Biomédicale des Armées, Marseille, France; [7]Unité des Virus Émergents, Aix-Marseille Université, Università di Corsica, IRD 190, Inserm 1207, Institut de Recherche Biomédicale des Armées, Marseille, France; and [8]Unité mixte de recherche Vecteurs – Infections Tropicales et Méditerranéennes, Institut de Recherche pour le Développement, Marseille, France

Background. Although Rift valley fever (RVF) is endemic in Mauritania, with 8 epidemics documented since 1987, infections among human populations, particularly in Nouakchott, the capital city of Mauritania, remain limited. The objectives of the present study were to assess the seroprevalence of RVF in humans and reconstruct the epidemiological history of RVF virus (RVFV) circulation within the city.

Methods. Using data from a cross-sectional and descriptive serological study among asymptomatic subjects conducted in Nouakchott in 2021, a mathematical model was developed to trace the seroepidemiological evolution of RVFV between 1927 and 2020 in the capital city.

Results. A total of 1319 participants were included, of whom 12.0% (158/1319) were positive for anti-RVFV immunoglobulin G (IgG). Sex, age group, district of residence, and use of mosquito nets or repellents at night were not statistically associated ($P > .05$) with anti-RVFV IgG positivity. Using the Hamiltonian Monte Carlo algorithm, posterior estimates of annual infection rates and probabilities of annual outbreak were calculated. The model suggested the absence of RVFV circulation before 1960, and the estimated outbreaks were concentrated between 1960 and 1972 and between 2017 and 2020.

Discussion. The present study provides the first overview of the evolution of RVF epidemiology in Nouakchott and the serological evidence that RVFV has been circulating in human populations in Nouakchott for a longer period of time than previously thought. Therefore, close surveillance in animals, humans, and mosquito vectors is necessary to detect the presence of RVFV and interrupt any future epidemics in the country.

Keywords. Rift Valley fever; Africa; Mauritania; Nouakchott; seroepidemiology.

Rift Valley fever (RVF) is a mosquito-borne zoonotic disease caused by Rift Valley fever virus (RVFV), a negative-sense, tri-segmented single-stranded RNA virus of the genus *Phlebovirus* in the family Phenuiviridae [1]. RVFV affects not only domestic ruminants, leading to economic losses due to mortality in their newborns and high abortion rates among pregnant animals, but it also poses a risk to human health, as it can cause flu-like symptoms, as well as hemorrhagic and nervous disorders [2, 3]. The World Organization for Animal Health has designated RVF as a notifiable disease [4].

RVFV is primarily transmitted to animals through the bite of infected *Aedes* or *Culex* mosquitoes [5]. *Aedes* spp may also transmit the virus vertically to their offsprings (ie, transovarial transmission), contributing to the persistence of the virus in nature during interepizootic and/or dry periods [6]. Humans, primarily those in direct contact with animals, such as butchers, animal breeders, slaughterhouse workers, and veterinary workers, usually get infected by handling body fluids of diseased animals. Although less common, human infection can also occur through infected mosquito bites [5]. To date, no human-to-human transmission has been documented.

RVF is endemic in different parts of Mauritania. Eight major outbreaks have been reported over the past 4 decades (1987, 1998, 2003, 2010, 2012, 2015, 2020, and 2022), with an average of an outbreak every 4.5 years and an overall case-fatality rate

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[a]M. B. and B. A. contributed equally.

Correspondence: Sébastien Briolant, MD, PhD, Unité Parasitologie et Entomologie, Département Microbiologie et Maladies Infectieuses, Institut de Recherche Biomédicale des Armées, Allée du Médecin Colonel Jamot, Marseille 13005, France (sbriolant@wanadoo.fr).

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of 21.1% in humans [7]. Human and animal cases have been reported from almost all regions of Mauritania [7–9]. Exceptional climatic conditions, such as heavy and prolonged rainfall, have been suspected to be the main drivers of RVF outbreaks in these regions [10, 11]. The possibility of regional spread of the outbreak cannot be ruled out given the presence of a competent mosquito vector in the majority of the regions, high density of livestock animals, and uncontrolled cross-border pastoral movements to and from neighboring countries related to the practice of transhumance and nomadic herding.

RVFV infections among human populations, particularly in large cities, remain limited. The historical epidemiology of RVF in Nouakchott, the capital and largest city in the country, is unknown. However, in the 2015, 2020, and 2022 RVF epidemics, human cases and fatalities due to RVFV were reported in Nouakchott, suggesting the circulation of the virus within the city [12–14]. Our study was conducted with the aim of assessing the recent seroprevalence of RVF in humans in Nouakchott and, based on these data, study the historical expansion of RVFV in the city. Mathematical modeling has been previously successfully applied in epidemiological studies to reconstruct the historical circulation of pathogenic agents in a number of emerging and reemerging arboviruses, such as Chikungunya [15–17], dengue [18], Zika [19], and RVFV [20]. Using data from a cross-sectional and descriptive serological study among asymptomatic individuals conducted in Nouakchott in 2021, mathematical modeling was used to trace the seroepidemiological evolution of RVFV between 1927 and 2020 in the city.

METHODS

Study Design, Population, and Covariates

A cross-sectional serological screening was conducted from January to June 2021 in the National hospital Center (NHC), situated in the city center. The inclusion criteria of the participants were age > 3 days old, the absence of fever (axillary temperature < 37.5°C), consultation at NHC for a routine checkup, and permanent residence in Nouakchott. After informed consent was obtained, 3 mL of blood was collected by venipuncture into a sterile blood collection tube without anticoagulant. The serum was separated by centrifugation and stored at −20°C until analysis.

A short questionnaire on sociodemographic characteristics was administered to each participant (or their legal guardians). Sociodemographic variables included age, sex, and district of residence in the city of Nouakchott. Information on the possession and use of bed nets, as well as the use of mosquito repellents, was also recorded. The collected data and the corresponding blood samples were anonymized to protect confidentiality.

Serological Testing

The presence of anti-RVFV IgG was tested using a commercial multispecies competitive enzyme-linked immunosorbent assay (ELISA) kit (ID Screen; IDVet), which has already been used in several previous studies to estimate anti-RVFV immunoglobulin G (IgG) levels in humans [21–23]. If a serum sample was positive for anti-RVFV IgG, serum neutralization assay was performed as previously described [24, 25] on 2-fold serial dilutions (1:20 to 1:160) to verify the absence of cross-reactivity against Toscana virus (TOSV) and sandfly fever Sicilian virus (SFSV). Viruses were titrated in Vero cells (American Type Culture Collection CCL81), and 100 50% tissue culture infectious dose ($TCID_{50}$) virus was added into each well, except for the blank control. Following incubation at 37°C for 1 hour, a suspension of 2×10^5 Vero cells/mL was added to each well, and the plates were further incubated at 37°C in a 5% CO_2 incubator. After 5 days for TOSV and 6 days for SFSV, the microplates were observed under an inverted microscope to detect signs of cytopathic effects.

Outcomes

The primary outcome was the prevalence of positive anti-RVFV IgG in study participants. After inclusion, a review of the database showed that 3 were not permanent residents of Nouakchott, and 3 additional patients were assigned the same anonymized code number by error. The results of these 6 participants were excluded from analysis. The final total of samples included in analysis was 1319.

Statistical Analysis

Data were recorded in Excel files (Microsoft) and checked for consistency before statistical analysis using the R statistical environment (version 2024.4.2.0) [26]. Qualitative variables were adjusted to obtain levels with similar numbers. The covariates were assessed as a function of the positivity of anti-RVFV IgG using a logistic regression model.

Modeling

For infections that induce life-long immunity and persistence of antigen-specific immunological markers, serological surveys in which the serological status and age of the enrolled individuals are available enable the reconstruction of the history of annual "force of infection" (FOI). To quote Ferguson et al [27], "the proportion of seropositive increases with age, in which case the rate of increase with age can be interpreted as a measure of the 'intensity' of infection experienced by the population in the past." Generally, the FOI (denoted λ) depends on time and age and is defined as the instantaneous per capita rate at which susceptible individuals of age (a) at time (t) acquire infection.

Three assumptions were made to develop our model. First, the FOI of RVFV is age-independent. Based on this working assumption, the FOI would depend only on time and can be estimated on an annual basis. Secondly, because only a few persons born before 1960 were sampled in our survey, it was assumed that the FOI is constant prior to 1960. Thirdly, it was

assumed that all individuals were susceptible in 1950 (due to the fact that data on age pyramids in Mauritania are available only from 1950 to 2021). This last assumption implies that the force of RVFV infection is null before 1950. It is in agreement with the available data in the literature and from what we observed and estimated when developing the analytic method. The second and third assumptions can be summarized as follows: the FOI is constant between 1950 and 1960, and null before 1950.

For modeling purposes, a simple differential equation was applied to trace the history of annual FOI [27, 28]. Using the fact that the number of individuals of age a at time t who are seropositive among the total number of persons of age a at time t follows a binomial distribution, the likelihood of the annual FOI can be obtained. To estimate these annual FOI values, we used a Bayesian approach. We assumed a bimodal prior distribution for the annual FOI which is a mixture of 2 Gaussian distributions: the first centered at 0 with a standard deviation (SD) of 0.001, and the second centered at 0.1 with a SD of 0.03, as performed earlier by Lim et al [17]. This approach allows there to be a priori no outbreak for a given year (first component), or an outbreak involving a low proportion of the population infected (second component). The model was fitted using a Hamiltonian Monte Carlo (HMC) algorithm (which is a particular case of a Markov chain Monte Carlo algorithm), with "cmdstanr" R library and CmdStanR (Command Stan R) [29]. Samples from the posterior distribution were kept for inference: 4 chains of length 3000, including 1000 iterations of burn-in which were generated.

The HMC algorithm enabled us to obtain samples from the posterior distribution of the annual FOI from 1950 to 2020. Using these samples, the annual FOI values were estimated by calculating posterior means. For each year, the probability of an outbreak was calculated as the proportion of postburn-in iterations in which the annual FOI was greater than 0.5%. Data on age pyramids of the Mauritanian populations from 1950 to 2020 were recovered (https://www.populationpyramid.net) to be able to reconstruct the proportion of susceptible population by year. Based on these data and the estimated annual FOI, the expected number of individuals who were seropositive in the entire population for each year between 1950 and 2020 was estimated at each iteration of the algorithm. The estimated annual proportion of the population susceptible to RVFV infection was then deduced. Details of the model used, assumptions, formulae, equations, calculations, estimates of various parameters using simulations obtained a posteriori, and full Stan and R codes are shown in detail in the Supplementary Material.

Ethics Approval

The objectives of the study were explained to all participants in their respective local dialect. Written informed consent was obtained from each adult participant or, in the case of children <18 years old, from their parents or legal guardians, prior to their enrollment. In addition, adolescents aged between 12 and <18 years old provided their assent. The study was approved by the Ethics Committee of the University of Nouakchott Al-Aasriya (approval No. 003/2020/CE/UNA) on 12 May 2020.

RESULTS

A total of 1319 participants were included in the present study. The mean and median ages of the participants were 38.9 years (95% confidence interval [CI], 37.9–39.8 years) and 37.0 years (interquartile range [IQR], 26–51 years), respectively, and the range was 5 days–94 years. Among the included patients, 53.1% (701/1319) were female and 46.9% (618/1319) were

Table 1. Association Between Patient Characteristics and Anti-Rift Valley Fever Virus IgG Positivity

Variable	No. Tested	Anti-RVFV IgG Positive, No. (%)	Crude OR (95% CI)[a]	*P* Value
Overall	1319	158 (12.0)		
Sex				
Female	701	79 (11.3)	Ref	
Male	618	79 (12.8)	1.15 (.83–1.61)	.39
Age, y				
0–19	141	15 (10.4)	Ref	
20–34	455	55 (12.1)	1.15 (.63–2.12)	.64
35–49	348	33 (9.48)	0.88 (.46–1.68)	.70
≥50	375	55 (14.7)	1.44 (.79–2.65)	.24
Residence				
N Nouakchott				
Teyarett	132	17 (12.9)	…	
Dar Naim	98	13 (13.3)	…	
Toujounin	98	15 (15.3)	…	
Total in N Nouakchott	328	45 (13.7)	Ref	
W Nouakchott				
Sebkha	144	12 (8.3)	…	
Tevragh Zeina	163	21 (12.9)	…	
Ksar	75	9 (12.0)	…	
Total in W Nouakchott	382	42 (11.0)	0.78 (.50–1.22)	.27
S Nouakchott				
Riadh	178	18 (10.1)	…	
Arafat	246	32 (13.0)	…	
El Mina	185	21 (11.4)	…	
Total in S Nouakchott	609	71 (11.7)	0.83 (.56–1.24)	.36
Use of impregnated bed net				
No	1066	129 (12.1)	Ref	
Yes	253	29 (11.5)	0.94 (.61–1.44)	.78
Sleeping under bed net				
Never	552	74 (13.4)	Ref	
Always	767	84 (11.0)	0.79 (.57–1.11)	.18
Repellent use				
Never	1088	135 (12.4)	Ref	
Always	231	23 (9.97)	0.78 (.49–1.25)	.30

Abbreviations: CI, confidence interval; IgG, immunoglobulin G; N, northern; OR, odds ratio; Ref, reference for OR calculation; RVFV, Rift Valley fever virus; S, southern; W, western.

[a]Odds ratios of each covariate were estimated using logistic regression model.

male, resulting in a sex ratio of 0.88 (Table 1). Overall, 12.0% (158/1319) of the participants were positive for anti-RVFV IgG. The seroprevalence was lower in females (11.3%) than males (12.8%), but the difference was not statistically significant ($P = .39$; Table 1). Participants aged 50 years and older had the highest seroprevalence (55/375, 14.7%), and participants aged between 35 and 49 years (38/355, 10.7%) had the lowest rate of anti-RVFV IgG seropositivity, but the observed differences in 4 age groups were not statistically significant ($P > .05$; Table 1). Data analysis by districts suggested that there appears to be an east-west gradient in RVFV seroprevalences within the city, with higher seroprevalences in the east and lower in the west (Figure 1). Toujounin district, located at the eastern fringe of the city, had the highest seroprevalence (15.3%)

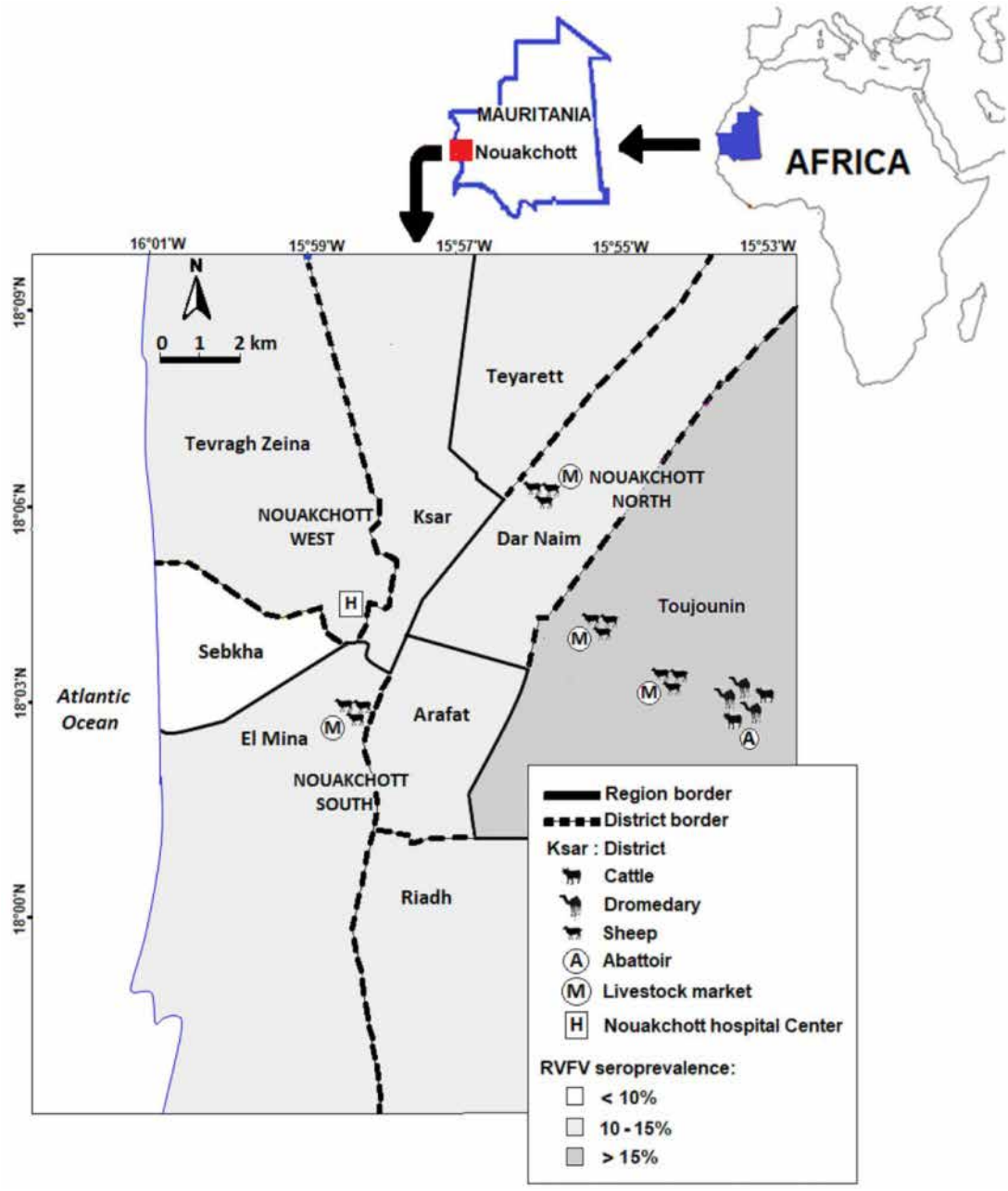

Figure 1. Map of Nouakchott, Mauritania, showing the location of the study site. The National Hospital Center is located in Tevragh Zeina district. Colored areas correspond to 1 of 3 levels of anti-Rift Valley fever virus immunoglobulin G (IgG) seropositivity: <10% (light green) in the district of Sebkha; 10%–15% (yellow) including the districts of Dar Naim, Teyarett, Arafat, Riadh, El Mina, Tevragh Zeina, and Ksar; and >15% (light purple), corresponding to the district of Toujounin. The Atlantic Ocean lies to the west of the city. Adapted from Choplin [30].

while Sebkha, situated at the western limit of the city bordering the Atlantic Ocean, showed the lowest seroprevalence (8.3%) (Table 1). Intermediate RVFV seroprevalences (ie, 10%–15%) were observed in the remaining districts. Preventive measures such as sleeping under bed nets at night and using insecticide-treated bed nets or repellents were not associated with anti-RVFV IgG positivity ($P > .05$; Table 1).

The serum samples that yielded a positive anti-RVFV IgG result (n = 158) were further tested to rule out TOSV and SFSV by seroneutralization tests. All 158 samples were negative for both of these phleboviruses.

Posterior estimations of the annual FOI were determined using HMC algorithm, and the probabilities of annual outbreak were calculated. Our model suggested that there had been almost no RVFV circulation in Nouakchott prior to 1960 (Figure 2) and that the estimated outbreaks appeared to be concentrated during 2 time periods: between 1960 and 1972 and between 2017 and 2020. We refer the reader to the Supplementary Material for exact values of the annual FOI estimate and the associated SD. For most of the birth years groups, the observed proportions of seropositive (cross-sectional study) and the proportions predicted by the model were close (Figure 3). The largest differences were observed in the periods before 1950, periods for which it is difficult to be precise given the small number of individuals still alive and present in our dataset (47 individuals).

DISCUSSION

This is the first study to evaluate the seroprevalence of RVFV in humans in Nouakchott, revealing a prevalence of 12%. The results of our study are in agreement with those of the systematic review on published seroprevalence studies, which concluded that 12.6% of human samples collected a year following a RVF outbreak were positive for RVFV antibodies [31]. In a previous study conducted in 2020 in Senegal, a country bordering the south of Mauritania, a much lower anti-RVFV IgG positivity rate (3.9%) was reported [32]. In East and Central African countries, high seroprevalences (36.4% and 28.1%) were observed during interepidemic periods among Kenyan [33] and Chadian populations, respectively [34]. These disparities in seroprevalences across different regions highlight the variability in RVFV exposure and the influence of factors such as geography, climate, and vector dynamics on the transmission of RVFV.

In the present study, the seroprevalence was comparable between males and females, and we do not know if close contact with livestock is a risk factor in Nouakchott. A similar observation was made in studies conducted in other African countries [32–35]. In Madagascar and Somalia, however, the RVF seroprevalence in men was twice as high as in women [22, 36], probably because men are more frequently in close contact with livestock than women. This is particularly true for regions other than Nouakchott in Mauritania and the Sahel where livestock farming is practiced exclusively by males [7].

The age group ≥50 years had a relatively higher IgG positivity rate than the younger age groups. Our observation is in agreement with that of several previous studies, notably those performed in Senegal and Uganda, where the prevalence of RVF was associated with age [32, 35]. Likewise, in East Africa (Somalia and Kenya), studies have also shown that RVFV seropositivity increases with age possibly due to multiple contact with livestock animals [22, 37]. However, in contrast to our findings that 11% of Mauritanians aged 0–20 years were

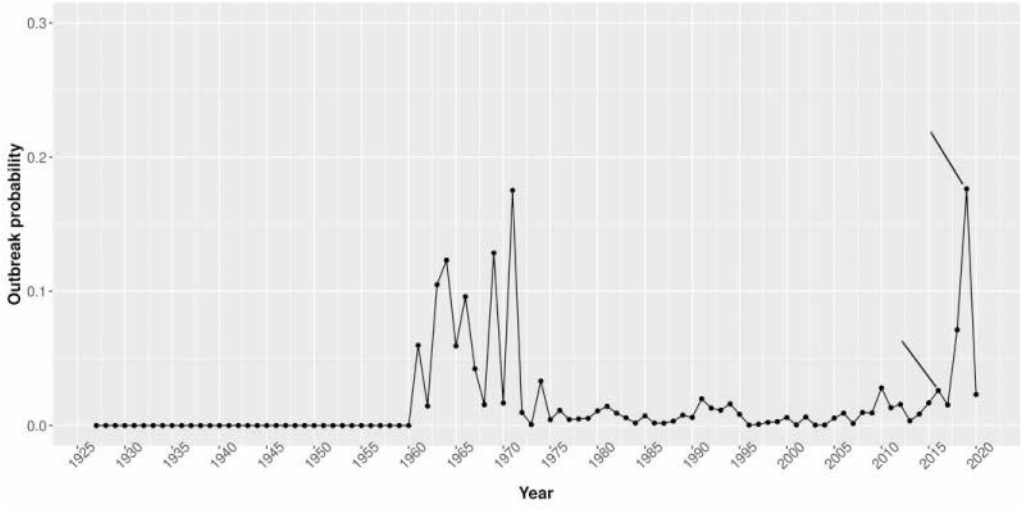

Figure 2. Probabilities of the estimated annual outbreak in Nouakchott, Mauritania. Probabilities were calculated as the proportion of model iterations that have an annual force of infection of at least 0.005 each year between 1927 and 2020. The arrows correspond to the epidemics detected by epidemiological surveillance in Nouakchott.

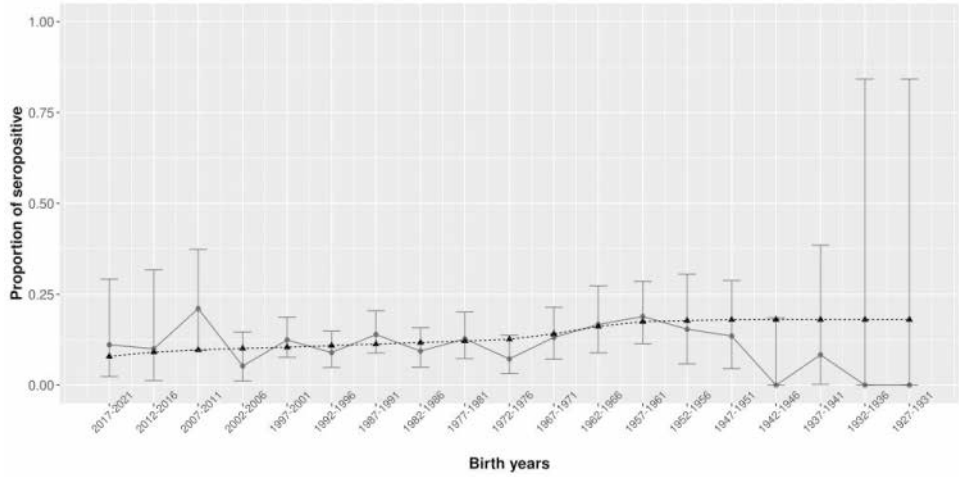

Figure 3. Proportions of seropositive individuals by 5-year age groups. The observed (red circles and bars corresponding to 95% confidence intervals) and fitted (green triangles) proportions of RVFV seropositivity by 5-year age groups from 1927 to 2021 in Nouakchott, Mauritania.

RVFV IgG-positive, in the Ugandan study [35], the authors did not observe any evidence of past RVFV infection in individuals under 20 years of age. Those authors hypothesized that the absence of young individuals with anti-RVFV IgG may be due to the absence of RVF cases in the study area since 1968 [35]. These findings on RVFV seropositivity in relation to age from different African countries highlight the importance of regional epidemiological history in shaping the current seroprevalence patterns.

An analysis of seroprevalence data by location of the patients' habitual residence suggested that patients with anti-RVFV IgG were present in all districts of Nouakchott. A relatively higher prevalence of positive IgG was observed among residents in Toujounin district, which may be due to its economic activity related to livestock production. Several livestock markets are located in this district, including the largest market and abattoir for the sale and slaughter of ruminants. Although the difference in RVFV seroprevalence among the districts in Nouakchott was not statistically significant, there was a higher risk of humans coming in contact with the virus in Toujounin, as well as in Dar Naim and El Mina. Other risk factors associated with the lifestyle of residents also need to be taken into consideration. These include hygienic practices in food processing, food consumption trends, and the diet of Nouakchott residents, which is characterized by a large consumption of red meat, in particular camel meat, which is cheaper than that of cattle and small ruminants. In addition to the occupational hazard in handling livestock, sociocultural practices, such as the ritual sacrifice of lamb during religious feasts and the widespread consumption of crude, unpasteurized camel milk, may also enhance exposure and vulnerability to RVFV [37–39]. Although the major mode of RVFV transmission to animals and humans is through mosquito bites [40, 41], we did not find that RVFV seropositivity is influenced by the use of bed nets or repellents. The most likely underlying reason is that, unlike *Anopheles* mosquitoes that mostly bite at night, in which case sleeping under a bed net may be beneficial to prevent malaria, *Aedes* and *Culex* spp are day-biting mosquitoes.

Cross-reactivity between RVFV and other phleboviruses such as Arumowot, Gordil, Saint-Floris, and Gabek Forest virus was recorded as negligible in artificially infected sheep [42]. In our study, all RVFV-positive samples tested negative for both TOSV and SFSV, indicating the absence of immunological cross-reactivity between RVFV and these 2 viruses belonging to the same genus.

Data from the present seroprevalence study were used to reconstruct the long-term historical circulation of RVFV in Nouakchott. Our model strongly suggests that RVF outbreaks occurred in Nouakchott during 2 periods: 1 (or more epidemics) between 1960 and 1972 and the other(s) between 2017 and 2020. Therefore, it can be assumed that several unreported RVF outbreaks occurred in Nouakchott during the period 1960–1972. Historical meteorological data indicate that Nouakchott, situated in the Saharan zone, and the adjacent Saharo-Sahelian zone have undergone a succession of 3 phases: (1) the so-called wet years (1950–1969), (2) the great drought (1970–1987), and (3) regular cycles of short rainy season and long dry season (2015–2020) [43]. During the first period, rainfall was much more abundant than the amount of precipitation seen in recent years, with an annual average of 150 mm (compared to an average of 112 mm during the period 1988–2010). These prolonged extreme environmental conditions during the wet years created permanent pools of water that probably led to significant mosquito proliferation. Mauritania's accession to independence in 1960, rapid development of the newly founded capital city of Nouakchott, and mass influx of human populations to the city

brought together animal and human hosts, vectors, and physical environment, and created the conditions that are necessary and favorable for the emergence of RVF outbreaks. During the second phase (1970–1987), the annual rainfall rarely reached 70 mm (mean, 58 mm; range, 3–191 mm) [43], a condition that is unfavorable for the development of mosquito habitats. Despite the continuous influx of humans and livestock into Nouakchott to escape drought (ie, rural exodus), our model does not suggest an occurrence of RVF outbreaks during this period, probably due to a relatively limited number of mosquito vectors. Since the end of the drought, the annual rainfall has increased to an average of 112 mm. The current third phase is marked by an increase in annual rainfall, together with the continuous rural exodus and development of livestock production sector within the city. These conditions were associated with the occurrence of major RVF epidemics in Nouakchott over the period 2015–2020.

Several limitations of the model should be noted. First, the inclusion of children under 2 years of age, in whom passive transfer of RVFV IgG from the mother may have occurred during breastfeeding, may have led to an overestimation of RVFV seropositivity in this age group. However, only 17.6% (4/17) of children under 2 years of age were positive for anti-RVFV IgG, which is not statistically different ($P > .05$) from the overall seropositivity of 12%. Secondly, the overall low number of seropositive individuals was reflected by the wide 95% CI of the proportions of seropositive individuals, especially in older persons born between 1927 and 1931 (n = 2, both seronegative) and younger children born after 2012. Thirdly, the age pyramid of the individuals enrolled in the study was different from that of the general population, which implies that our patient population is not totally representative of the Mauritanian population in Nouakchott. In our study, which was conducted in a hospital, people under 25 years were underrepresented, possibly due to the better health of older children and young adults, as compared to older adults. Patient selection bias may have led to an underestimation of RVF epidemic risk since the early 2000s, while 5 major outbreaks have been reported between 2000 and 2020 in Mauritania (2003, 2010, 2012, 2015, and 2020) [7].

In conclusion, the history of RVF in Nouakchott seems to extend further back than previously documented. The present study provides the first overview of the epidemiology of RVF in Nouakchott, and indirect and direct evidence of RVFV circulation in humans in Nouakchott in the past and in recent years, respectively, through modeling of recent seroprevalence data. As RVFV endemicity is established in Mauritania, animal and mosquito surveillance is necessary to prevent and control the spread of epidemics in the country.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Author contributions. S. B., A. O. M. S. B., L. K. B., and R. C. conceived and planned experiments. B. A. and A. O. M. S. B. managed participant enrollment. S. B., N. G., B. A., and N. A. supervised and performed experiments. M. B. and S. B. led the statistical analyses. B. A., L. K. B., and A. O. M. S. B. verified the data. S. B., A. O. M. S. B., M. B., B. A., and N. A. wrote the manuscript with input from L. K. B and R. C. All authors reviewed the manuscript, provided scientific input to the manuscript, and agreed with the decision to submit the manuscript. All authors had full access to all the data in the study.

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Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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