Kenema

Government

Hospital

Epidemiology and pathobiology of Lassa fever in Sierra Leone

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ABSTRACT

BACKGROUND

Lassa fever is a viral hemorrhagic fever (VHF) that is endemic in Sierra Leone, Guinea, Liberia and Nigeria, with cases reported in several other West African countries. Lassa virus (LASV; family *Arenaviridae* is transmitted to humans by contact with the excretions of its major reservoir *Mastomys natalensis*. Little work has been done to determine the seroprevalence of Lassa fever in Africa and characterize its clinical risk factors.

METHODS

We carried out two studies for laying the groundwork for determining prior Lassa exposure rates and its risk factors. One of the studies measured seroprevalence for LASV in the Districts of Kenema, Tonkilili, and Port Loco. Based on historical hospitalizations, we hypothesized that these districts would classify as high, medium, and low endemic areas, respectively. We also collected data on volunteer demographics, the local environment, and trapped rodents in and around households with Lassa fever cases In a separate study, we captured and analyzed clinical and laboratory data from clinical presentations to the Kenema Government Hospital to link patient signs and symptoms with survival outcomes and characterize Lassa fever epidemiology and its risk factors.

RESULTS

In Kenema District, LASV IgG seroprevalence varied from 10 to 62%. While Kenema district remains among the highest district in terms of Lassa fever prevalence in Sierra Leone, other districts are now increasingly reporting cases. Some villages in Tonkolili have seroprevalence rates similar to those of high prevalence villages in Kenema district. While we observed high variability within each of the districts, their overall mean prevalence rates were between 12% and 18%). Some villages were showed seroprevalence increases with increasing age (suggesting a long-term exposure to LASV) while others showed similar seroprevalence across age groups (suggesting a more recent introduction of LASV). Lassa fever case-fatality rates were 69%, but this estimate is likely inflated due to self-presentation bias. Self-presentation among acute Lassa cases was associated with bleeding, conjunctivitis, head and neck edema, and sore throat.

CONCLUSIONS

LASV infection in Sierra Leone is more widespread than previously known. Longitudinal studies investigating Lassa fever seroprevalence and incidence are critical for proper design of public health interventions, including LASV vaccine studies in humans. A better understanding of Lassa fever pathobiology is needed to improve case management.

Pathobiology of Lassa fever

Because Kenema Government Hospital is the only hospital for the diagnosis and treatment of Lassa fever in the country, cases recruited in consecutive order will represent all detectable cases of Lassa fever in Sierra Leone. To elucidate risk factors for LASV infection in pregnant women and children in a case-control study, pregnant women and children testing positive for Lassa fever will be compared to controls matched for age, sex, and ethnicity. Few risk factors for Lassa fever have been identified. Because of the limited access to diagnostics for Lassa fever, there have been few studies to identify risk factors leading to Lassa virus infection. Using with well-defined cases and controls is critical to assessing risk. Cases have been defined at individuals with clear signs and symptoms of Lassa fever with a positive ELISA test (antigen), admission to the Lassa Ward and commencement of ribavirin.

Hypothesis: LASV infection among pregnant women and children is directly related to rodent exposure and can be explained by a set of risk factors.

Table 1. Characteristics of study subjects.

Characteristic	Ag+/IgM+- (n = 222)	Ag-/IgM+ (n = 459)	Ag-/IgM- (n = 1221)	P[a]
Survival outcome				
Discharged	52 (33)	132 (73)	164 (66)	< .001
Died	104 (67)	49 (27)	85 (34)	
Admission status				
Admitted	111 (50)	131 (29)	124 (10)	< .001
Not admitted	111 (50)	328 (71)	1097 (90)	
District of residence				
Kenema	150 (73)	320 (72)	851 (73)	.536
Bo	19 (9)	45 (10)	88 (8)	
Other	36 (18)	80 (18)	222 (19)	
Age, yrs.				.007
<5	34 (15)	50 (11)	158 (13)	
5-14 yrs.	46 (21)	67 (15)	182 (15)	
15 – 40 yrs.	124 (56)	276 (60)	671 (56)	
> 40 yrs.	17 (8)	64 (14)	197 (71)	
Gender				
Female	123 (55)	261 (57)	682 (56)	.862
Male	99 (45)	197 (43)	533 (44)	
Pregnancy status[b]				
Pregnant	26 (32)	33 (20)	45 (11)	< .001
Nonpregnant	55 (68)	130 (80)	369 (89)	
Duration of illness[c]				
< 7 days	52 (26)	164 (38)	581 (52)	< .001
≥ 7 days	149 (74)	271 (62)	535 (48)	

Note. All results based expressed as frequency (%) unless indicated otherwise. Subgroup data unavailable for some subjects.
a. Corresponds to Pearson's chi-square test for assessing characteristic differences among the serostatus groups.
b. Sample population restricted to females between 15 and 40 years of age.
c. Defined as the number of days between dates of illness onset and initial clinical evaluation.

EPIDEMIOLOGY OF LASSA FEVER IN SIERRA LEONE

Kenema District has long been considered the area of highest Lassa fever incidence in the world and surveillance and research has been concentrated in this area. Many districts to the north and west of Kenema are believed to have limited Lassa virus circulation, however, it is unknown if lower Lassa fever incidence is due to limited efforts to detect virus, inability of clinical staff to recognize the disease, or if, indeed, there is no virus circulating in the area. We undertook a cross-sectional seroprevalence study is the first step to estimate risk of exposure to LASV in these two areas of varying Lassa fever incidence.

Hypothesis: Age and gender distributions of LASV exposure differ between endemic and non-endemic areas.

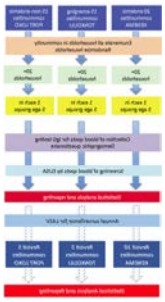

Figure 1. PEER sampling plan.

Figure 2. Seroprevalence in by village in Kenema District.

For our seroprevalence study the target populations included the entire populations the Districts of Kenema, Tonkolili, and Port Loko. 50 villages have participated with over 11,000 samples collected (Fig. 1). Currently lab assays, data entry and cleaning is nearly complete. Lassa virus seroprevalence is highly variable in different communities. For example in Kenema District LASV IgG seroprevalence varies from 10 to 62% (Fig. 2). While Kenema district remains the highest district in terms of prevalence for Lassa fever in Sierra Leone, other districts are now increasingly reporting cases (Fig. 3). One village Hamdalai in Port Loko district on the border with Guinea showed an extremely high seroprevalence for Lassa virus. Some villages in Tonkolili have seroprevalence rates similar to those of high prevalence villages in Kenema district. While we observed high variability within each of the districts, their overall mean prevalence rates were between 12% and 18%). Some villages were showed seroprevalence increases with increasing age (suggesting a long-term exposure to LASV) while others showed similar seroprevalence across age groups (suggesting a more recent introduction of LASV (Fig. 4).

Table 2. Clinical signs and symptoms of patients presenting to the KGH VHF Ward 2010-2016.

Symptom	Ag+/IgM+ -(n = 222)	Ag-/IgM+ (n = 459)	Ag-/IgM- (n = 1221)	P[a]
Fever	195 (88)	359 (78)	1027 (84)	.002
No fever	27 (12)	100 (22)	194 (16)	
Weakness	172 (77)	335 (73)	825 (68)	.004
No weakness	50 (23)	124 (27)	396 (32)	
Sore throat	122 (55)	153 (33)	367 (30)	<.001
No sore throat	100 (45)	306 (67)	854 (70)	
Vomiting	144 (65)	235 (51)	566 (46)	<.001
No vomiting	78 (35)	224 (49)	655 (54)	
Cough	159 (72)	258 (56)	616 (50)	<.001
No cough	63 (28)	201 (44)	605 (50)	
Abdominal pain	107 (48)	208 (45)	457 (37)	<.001
No abdominal pain	115 (52)	251 (55)	764 (63)	

Note. All results based expressed as frequency (%) unless indicated otherwise. Subgroup data unavailable for some subjects.
a. Corresponds to Pearson's chi-square test for assessing characteristic differences among the serostatus groups.

Although patients presenting to KGH with signs and symptoms of Lassa fever were all ill, subjects that presented with active LASV infection were at significantly increased risk of death (Table 1, 2). The majority of suspected cases continue to be from Kenema district. Patients with active LASV infection we generally younger . More females than males presented with signs and symptoms of Lassa fever, but the sex ratio did not vary significantly with serostatus. Most patients with active LASV infection presented after 7 days of illness.

Pregnant women with active LASV infection were over represented among patients presenting to KGH with signs and symptoms of Lassa fever (Table 1, 3). Case fatality rates were not significantly different between pregnant and non-pregnant women regardless of serostatus.

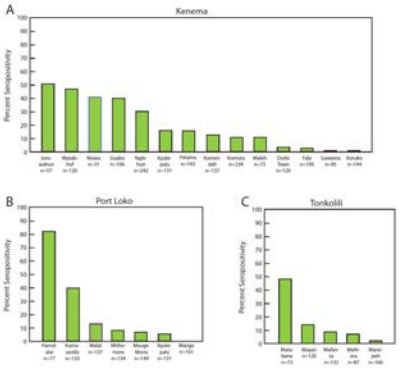

Figure 3. Seroprevalence in by village in Kenema, Port Loko and Tonkolili Districts.

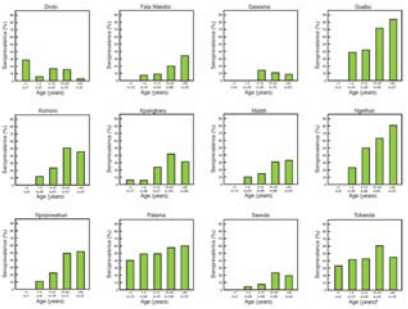

Figure 4. Seroprevalence in Kenema District by village and age group.

Table 3. Increased risk of LASV infection among pregnant women

	Odds Ratio	95% CI
Ag+/IgM+-	3.14	1.74-5.68
Ag-/IgM+	1.57	0.902-2.72
Ag-/IgM-	Ref	

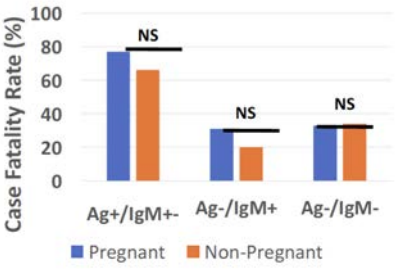

Figure 5. Case fatality rates in pregnant women and non-pregnart women presenting to Kenema Government Hospital by LASV serostatus.

Clinical signs and symptoms of patients presenting to KGH Varied depending on serostatus (Table 2). Fever was the most common symptom amongst all patents, followed by weakness, sore throat, vomiting, cough and abdominal pain. Significant differences were observed in each of these clinical parameters. Further analysis is underway to determine whether the case definition for Lassa fever can be refined.

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