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Serological Evidence of Hantavirus Infection in Suspected Cases of Viral Haemorrhagic Fever in Conakry, Guinea

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Abstract: Background: Hantaviruses are enzootic haemorrhagic fever viruses whose transmission to humans can cause serious illness with mortality rates ranging from 12% to 40%. Objective: This study aimed to estimate the seroprevalence of IgG antibodies against hantaviruses in the Conakry region. Methods: This was a cross-sectional study of suspected haemorrhagic fever cases. Blood samples were analysed at the Guinea Virology Research Center, Conakry, Republic of Guinea. The indirect enzyme-linked immunosorbent assay (Euro-Immun, vector-best, Russia) was used to detect the presence of specific IgG antibodies to hantaviruses according to the manufacturer's instructions. Results: A total of 368 suspected cases of haemorrhagic fever were reported between 2021 and 2022 in public health facilities in Conakry. The seroprevalence of IgG in patients was 8.7% (95% CI: 6.1-12.0). Patients under 30 years of age were the group most affected (14.9%). The seroprevalence of hantaviruses was significantly higher in trades worker (16.0%) than in other socio-professional categories ($p<0.001$). Patients with fever associated with anorexia and cough had a hantavirus IgG seroprevalence of 45.5% and 28.9% respectively. Conclusion: This study provided serological evidence of hantavirus circulation in the Conakry region. Active surveillance of hantaviruses, including molecular biology and serotyping, would be necessary to improve our understanding of the ecology of circulating hantavirus strains.

Keywords: Guinea, Hantavirus, Hemorrhagic Fevers, Serological

1. Introduction

Hantaviruses are zoonotic viruses that are spread by the aerosolised feces of rodents and other small mammals [1]. Although hantavirus infection causes chronic and inapparent infections in animal reservoirs, transmission of these viruses to humans can lead to serious illness, which can present as haemorrhagic fever with renal syndrome (HFRS) and pulmonary syndrome (SPH), with mortality rates ranging from 1% to 12% for HFRS and 40% for SPH [2, 3]. The known clinical symptoms in patients infected with the hantavirus include high fever, hemorrhage, thrombocytopenia, abdominal pain, flu-like symptoms and finally organ failure; these symptoms are also known to be caused by many other hemorrhagic fever viruses [4, 5].

Worldwide, there are an estimated 150,000 to 200,000 cases of HFRS, most of which occur in Asia (particularly China and

Korea) [6], although this number could increase in many countries as new strains are identified. However, climatic and environmental changes could affect the geographical distribution, abundance and dynamics of carrier rodents, and therefore the epidemiology of these infections [6]. The circulation of hantaviruses in countries with sufficient resources to meet the health needs of their populations could lead to speculation about the risk of these viruses emerging in other hosts and geographical areas [7]. Particularly in Africa, where many diseases remain neglected or under-reported due to poor health conditions, ineffective surveillance systems and insufficient laboratory capacity [7].

The first indigenous African hantavirus, named Sangassou virus, was discovered in Guinea in 2006 [8], and the first serological studies carried out on patients with fever indicated human hantavirus infections, implying an underestimation of the impact of hantavirus on public health on the African continent [8-10]. In addition, Guinea regularly experiences epidemics of Lassa haemorrhagic fever, which has become endemic in the border area with Liberia and Sierra Leone [11]. Then, there are the recent epidemics of zoonotic diseases, such as the Ebola virus [12, 13], which demonstrate the great need for intensive studies on highly pathogenic zoonotic viruses in Guinea in order to prepare for their emergence and major epidemics.

Infectious diseases are the main cause of fever in Guinea. Since hantavirus infections share the same clinical symptoms with other common infectious diseases in the country, they are often difficult to diagnose. In addition, health facilities lack accurate diagnostic tools, so misdiagnosis can easily occur, leading to inappropriate clinical management. In this case, a seroprevalence study could be used to assess rodent-human transmission. The aim of this study was to identify the presence of antibodies to hantaviruses in suspected cases of viral hemorrhagic fever in Guinea.

2. Methods

2.1. Study Area

This study took place in the Conakry region, the capital of the Republic of Guinea. Located on the south-west coast of the country, it covers an area of 450 km2, with an estimated population of 1,660,973 [14]. Administratively, Conakry is divided into five (5) urban communes: Kaloum, Dixinn, Matam, Matoto and Ratoma (Figure 1). The Conakry region has three national hospitals, six municipal medical centers and 18 primary health centers. The analyses were carried out at the Guinea Virology Research Center. This is a reference center for viral diseases, in particular viral hemorrhagic fevers and other viral infections with epidemic potential. Its mission is to implement national/international research projects and programmes on infectious diseases, including viral hemorrhagic fevers.

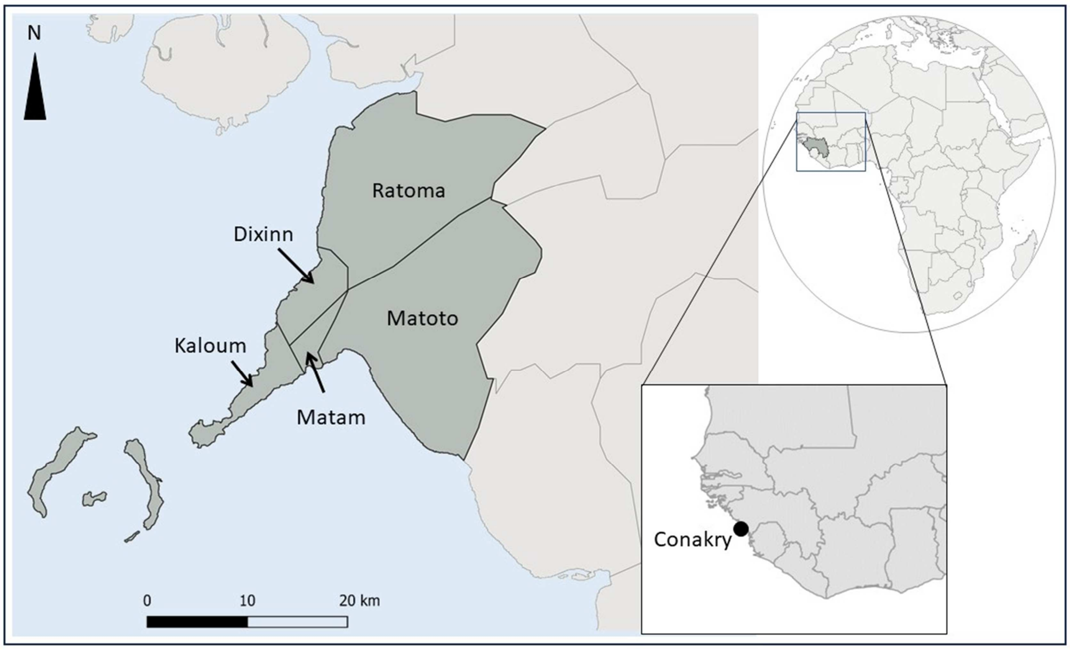

Figure 1. *Map of Conakry and its five communes (Map created with QGIS software: source of administrative boudaries map layer: https://www.gadm.org/; Link to the GADM license: https://www.gadm.org/license.html).*

2.2. Study Design and Population

This was a cross-sectional study based on haemorrhagic fever surveillance activities in public health facilities in the Conakry region, conducted between 1st January 2021 and 31st December 2022. Healthcare workers, including laboratory staff, were trained in clinical identification and asked to submit serum samples and information from suspected haemorrhagic fever cases. A suspected case was defined as a patient presenting with an acute febrile illness (i.e. fever ≥ 38°C for ≤ 7 days) unresponsive to any treatment for the usual causes of fever in the region (such as malaria) and at least one of the following signs: headache, rash, cough, myalgia, arthralgia, bloody diarrhoea, gingival haemorrhage, skin haemorrhage, etc.

2.3. Serological Analysis

Blood samples from suspected cases of viral haemorrhagic fever stored in the biobank of the Guinea Virology Research Center and with available socio-demographic and clinical information were analysed for the presence of specific IgG antibodies against hantaviruses using the indirect enzyme-linked immunosorbent assay (ELISA, Euro-Immun, vector-best, Russia), following the manufacturer's instructions.

2.4. Statistical Analysis

A descriptive analysis of the data was carried out. Patient characteristics were summarised with numbers and percentages for categorical variables. The mean and standard deviation were calculated for quantitative variables. The Chi-square test was used to determine the existence of a statistical association between seropositivity and the study variables. A value of $p<0.05$ was considered statistically significant. All statistical analyses were performed using RStudio software version 4.3.1 (R Foundation for Statistical Computing, Austria, Vienna).

3. Results

A total of 368 suspected cases of hemorrhagic fever were reported in public health facilities in Conakry between 2021 and 2022, 243 of whom were men (66.0%). The mean age of the patients was 43.9 years (±15.2) and most were civil servants (57.9%). The characteristics of the study participants are presented in Table 1.

Table 1. *Patient characteristics, Conakry 2021-2022.*

Characteristics	N = 368	Percentage
Sex		
Female	125	34.0
Male	243	66.0
Age (years)		
Mean (Standard deviation)	43.9 (15.2)	
< 30	67	18.2
30-45	145	39.4
>45	156	42.4
Occupation		
Retailer	30	8.1
Civil servant	213	57.9
Trades worker	81	22.0
Unemployed*	44	12.0

* Unemployed: students (n= 9), housewives (n= 31) and retired (n= 4)

The prevalence of IgG in patients in this study was 8.7% (95% CI: 6.1-12.0). Hantavirus IgG seroprevalence was 9.1% in men and 8.0% in women, but the difference observed was not significant (p= 0.70). Patients under 30 years of age were the group most affected (14.9%). The 31-45 and over-45 age groups had a prevalence of IgG antibodies to hantaviruses of 9.0% and 5.8% respectively. Hantavirus seroprevalence was significantly higher in trades worker (16.0%) than in other socio-professional categories ($p<0.001$) (Table 2).

Table 2. *Seroprevalence of IgG antibodies to hantavirus according to patient characteristics, Conakry 2021-2022.*

Characteristics	Number of subjects tested	IgG seroprevalence n (%)	*p-value*
Seroprevalence (% [95% CI])	368	32 (8.7 [6.1 - 12.0])	
Sex			0.70
Female	125	10 (8.0)	
Male	243	22 (9.1)	
Age (years)			0.083
< 30	67	10 (14.9)	
31-45	145	13 (9.0)	
>45	156	9 (5.8)	
Occupation			<0.001
Retailer	30	1 (3.3)	
Civil servant	213	6 (2.8)	
Trades worker	81	16.0	
Unemployed	44	27.3	

Clinical symptoms associated with fever were mainly headache (n=342), physical asthenia (n=138) and nausea (n=103). Patients with fever associated with anorexia and cough had a hantavirus IgG seroprevalence of 45.5% and 28.9% respectively. The results of the hantavirus seroprevalence analyses according to clinical symptoms are presented in Table 3.

Table 3. *Seroprevalence of IgG antibodies to hantavirus according to patients' clinical symptoms, Conakry 2021-2022.*

Characteristics	Number of subjects tested	IgG seroprevalence n (%)	*p-value*
Headache	342	24 (7.0)	<0.001
Asthenia	138	21 (15.2)	<0.001
Nausea	103	2 (1.9)	0.004
Cough	38	11 (28.9)	<0.001
Skin rash	39	7 (17.9)	0.063
Anorexia	33	15 (45.5)	<0.001

4. Discussion

Hantavirus infection is a rarely diagnosed disease in Guinea, although it is one of the haemorrhagic fevers under surveillance in the country. The resurgence of viral haemorrhagic fevers in Guinea, including hantaviruses, must now be anticipated, given the global health threat they represent, through proactive surveillance strategies that enable epidemic situations to be detected early.

This study showed a seroprevalence of IgG antibodies to hantaviruses of 8.7% in suspected cases of viral haemorrhagic fevers. In a previous study carried out in two rural villages in the Faranah region, the seroprevalence of IgG antibodies against hantaviruses was estimated at 12.2% in patients with a history of high fever in the previous 3 months using the ELISA technique [10]. This difference could probably be influenced by the populations studied. Serological studies carried out in Africa in the human population and in febrile patients have reported lower seroprevalences of IgG hantavirus antibodies, with respective prevalences of 3.9% in Côte d'Ivoire [15], 2.4% in the Democratic Republic of Congo [15], 2.0% in Mozambique [16], 1.7% in Madagascar [17] and 1.0% in South Africa [7].

Our study shows that trades worker and the unemployed including housewives, were more affected by hantavirus infection. Given that the IgG seropositivity observed reflects evidence of exposure in the past, we cannot assert specific sources of infection. However, the highest risk of hantavirus infections associated with the domestic environment could be due to routine activities (i.e. weeding, cleaning spaces, etc.) carried out in areas where rodents approach the peri-domestic environment in search of food [18]. This result corroborates the conclusion of a previous study which stated that the populations at risk are those who are active and take part in outdoor activities [19].

Most patients who tested positive for hantavirus IgG had fever followed by anorexia, cough, rash and physical asthenia as associated clinical symptoms. This clinical presentation is similar to that described in the literature. The initial symptoms of infection include the sudden onset of high fever, myalgias, back and abdominal pain and other flu-like symptoms [20]. However, the clinical implications remain unclear, as some hantaviruses can cause benign or even non-existent disease. In addition, hantavirus infections share similar clinical symptoms of acute febrile syndromes with other endemic diseases in Guinea, such as malaria, which is the main cause of consultation, hospitalisation and death in healthcare facilities. It is therefore important to raise awareness of hantavirus infections among healthcare workers, so that they understand the different types of exposure, the measures to take and the reporting of any suspected cases.

This study assessed the presence of previous hantavirus infection in suspected cases of haemorrhagic fever presenting to public health facilities in Conakry, so our results do not reflect the true seroprevalence of hantavirus infection in the general population. Due to a shortage of hantavirus IgM-specific diagnostic kits, we were unable to analyse the presence of recent hantavirus infection in patients. In addition, other diagnostic techniques, such as reverse transcriptase polymerase chain reaction (RT-PCR) and plaque reduction neutralisation tests, have not been used to characterise hantaviruses. Sangassou and Tanganya Viruses are currently the hantaviruses isolated in Guinea [10], it is therefore not known whether the anti-hantavirus IgG antibodies result from infection by these viruses or by another hantavirus. Other hantaviruses may remain unknown, as most hantavirus infections are rarely diagnosed. Future studies should include molecular biology and characterisation by sequencing to gain a better understanding of the ecology of circulating strains of hantavirus, as well as analysing the factors linked to the potential risk of environmental exposure to the excrement of infected rodents.

5. Conclusion

This study provides an overview of the circulation of hantaviruses in Conakry, which are of major importance due to their impact on public health. Our results confirm the hypothesis that hantaviruses contribute to morbidity in Guinea and should draw the attention of the country's public health authorities to the need to put in place measures to prevent hantavirus-related epidemics.

Author Contributions

Conceptualization, A. C. and S. B.; Data acquisition and biological analysis, S. T. and N. I.; Validation, A. C. and S. B.; Methodology, S. T. B., S. S. and A. T.; Writing - Original Draft Preparation, S. T. and S. T. B.; Writing - Review & Editing, A. C., Y. Y., N. I., M. D., K. J. J. O. K., S. C. C., T. V. B., F. T. B., S. S., A. T., S. B.

Ethical Considerations

The study was approved by the Institutional Review Board of the Guinea Virology Research Center. All patients were well informed about the study procedures. Informed consent was obtained from patients. Confidentiality of patient information was strictly preserved.

Ethics of Human Subject Participation

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Good Clinical Practice guidelines.

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Conflicts of Interest

The authors declare no conflicts of interest.

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