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Integrated viral haemorrhagic fever surveillance and response in public healthcare facilities in Guinée Forestière after the 2014-2016 Ebola epidemic

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1. List of abbreviations

EVD	Ebola virus disease
GDP	Gross domestic product
HCW	Healthcare worker
IDSR	Integrated disease surveillance and response
IPC	Infection prevention and control
KAP	Knowledge, attitudes and practices
RT-PCR	Reverse transcriptase polymerase chain reaction
USD	United States Dollar
VHF	Viral haemorrhagic fever(s)

2. List of publications

2.1. Thesis publications

Raab, M., Pfadenhauer, L.M., Nguyen, VK. *et al.* Period prevalence and identification challenges of viral haemorrhagic fever suspect cases in a tertiary referral hospital in Guinea: a cross-sectional, retrospective study of triage and emergency room patient profiles. *BMC Infect Dis* 20**,** 838 (2020). https://doi.org/10.1186/s12879-020-05573-8

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2.2. Further publications

Raab, M, Pfadenhauer, L.M, Doumbouya, D. Froeschl, G. Clinical presentations, diagnostics, treatments and treatment costs of children and adults with febrile illness in a tertiary referral hospital in south-eastern Guinea: a retrospective longitudinal cohort study. *PLoS ONE* 17(1): e0262084 (2022). https://doi.org/10.1371/journal.pone.0262084

Raab M, Roth E, Nguyen V-K, Froeschl G. The 2021 Ebola virus outbreak in Guinea: Mistrust and the shortcomings of outbreak surveillance. *PLoS Negl Trop Dis* 15(6): e0009487 (2021). https://doi.org/10.1371/journal.pntd.0009487

Roth E., Raab M. What do people know about Ebola? Reflections on knowledge surveys during outbreaks. *Virologie*. 2020;24(2): 61–7. doi:10.1684/vir.2020.0840

3. Contribution to publications

Prior to executing the research these publications are based on, I conceptualized and wrote the project. I gained the necessary approval from the LMU medical ethics committee. The project was financially supported by the LMU MeCuM International scholarship with 4000.- Euros. All of the work steps were supervised by Günter Fröschl (GF), Lisa Pfadenhauer (LP) and Michael Hölscher (MH). All made essential contributions through thorough readings and important comments.

The project translation into French - which was necessary for the Guinean health authorities - was drawn up by myself (MR) and corrected by a French native speaker.

3.1. Contribution to publication I

MR, LP, Dansira Doumbouya (DD), MH and GF were responsible for conceiving the study. MR and DD executed the data collection. MR, GF and Vinh-Kim Nguyen (VN) analysed the data. MR wrote the article. All authors read and reviewed the final submitted version of this manuscript.

3.2. Contribution to publication II

MR, LP, Tamba Jacques Milimonou (TJM), MH and GF were responsible for conceiving the study. MR and TJM executed the data collection. MR and GF analysed the data. MR wrote the article. All authors read and reviewed the final submitted version of this manuscript.

4. Introduction

4.1. The role of integrated disease surveillance and response after the 2014–2016 West African Ebola epidemic

From 2014 until 2016, the world's largest known viral haemorrhagic fever (VHF) epidemic struck in Liberia, Sierra Leone and Guinea. Caused by *Zaire ebolavirus*, 15,000 laboratory confirmed cases and 10,000 deaths were recorded. The outbreak started in *Guinée Forestière*, (Forest Guinea), a remote region in South-eastern Guinea bordering Liberia, Sierra Leone and Ivory Coast. The virus initially spread undetected to Sierra Leone and Liberia until an international health emergency was declared in August 2014 (1). National and international health authorities responded months after the outbreak had started. This was partly because of the absence of a well-functioning integrated disease surveillance and response (IDSR) system for VHF in the affected countries (2).

IDSR in African countries aims at preventing epidemics through rapid outbreak detection, timely reporting of signal cases and the implementation of adequate containment strategies (3). It consists of triage algorithms for suspect case screening, recommendations for laboratory testing and proposed measures for infection prevention and control (IPC) in case of outbreaks (4).

After the 2014-2016 Ebola virus disease (EVD) epidemic, IDSR for VHF was revitalized in affected West African countries, becoming one of several public health priorities. As part of this strategy, national agencies for health security were formed; laboratories were equipped with diagnostic capacities for VHF; their staff was trained to comply with biosafety procedures; specialized treatment centres for diseases with epidemic potential were built; standardized guidelines for screening and reporting of VHF were distributed in healthcare facilities and healthcare workers (HCW) were trained in the clinical application of those guidelines (5–8).

Forest Guinea has been identified as a region with a particularly high risk for future outbreaks of VHF: parts of the region are often inaccessible during the

rainy season; populations frequently cross permeable borders; interethnic and political tensions are unpredictable, making violent rejection of outbreak response teams more likely; several VHF are known to circulate in animal reservoirs within the region and the healthcare system has been structurally neglected due to its spatial and political distance to the country's capital (9–11).

4.2. Guinea's public healthcare system

Guinea is one of the poorest African countries with 55% of its population living below the poverty line before the EVD epidemic (12). It reported the highest fatality rate of EVD cases in all three West African countries with 67% (13). As of 2014, the Guinean government spent 5.6 % of its national GDP on the public healthcare system amounting to approximately $ 300 million USD per year (14). However, the public budget eventually available for healthcare may fare even lower due to administrative weaknesses in the public healthcare system (15). Guinea's healthcare system is set up as a pyramid: at the top are national university hospitals, prefectural and regional hospitals. Prefectural and regional hospitals have less service capacities than the country's only university hospital, located in Conakry. The middle of the pyramid is formed by multiple Health Centres distributed in the sub-prefectures' and districts' capitals. These provide for maternal and child care, vaccinations and family planning. The broad base of the public healthcare system is formed by Community Health Agents working in Health Posts, who constitute the healthcare infrastructure in villages (6).

The building of healthcare facilities, their equipment and staff salaries are officially financed by the national government. The Guinean constitution grants its population free universal health services, but the government's fiscal constraints do not allow for such. Rather, pay-as-you-go user fees in any public healthcare facility are common. Moreover, the national government depends on loans and partnerships with foreign (non-) governmental organizations to support its current healthcare system. Social, community-based and private health insurance schemes exist but with a very marginal total coverage of less than 5% (16).

Like Sierra Leone and Liberia, Guinea's national healthcare system was already fragile for many years prior to the EVD epidemic (17). The mentioned pay-as-you-go user fees are expansive relative to the average income. Moreover, the quality of care is often poor due to an informal economy within healthcare facilities and there is a shortage of properly trained staff and diagnostic capacities. Finally, many populations have to travel long distances to receive specialized care (18). All of the above apply even more in rural and remote regions such as Forest Guinea (19).

4.3. Clinical aspects of viral haemorrhagic fevers

VHF refer to several illnesses caused by infection with different RNA viruses. The most prominent VHF are Ebola virus disease, Marburg virus disease, yellow fever, dengue, Lassa fever, Crimean-Congo haemorrhagic fever and Rift Valley fever (20). They are transmitted through animal-to-human or human-to-human contact. Infection can be mild or severe, and the latter case may lead to multiple organ failure and death. While the various VHF may feature different clinical signs at different stages of infection, they are grouped together because infected patients often show a similar set of symptoms. These usually include fever, vomiting, diarrhoea, malaise, muscle pain and other non-specific symptoms, while late stage infection is often characterized by vascular damage leading to dehydration and sometimes bleeding (21).

Distinguishing VHF from other tropical diseases like malaria, typhoid fever or meningitis based on the clinical presentation of patients can be difficult. In field settings, molecular diagnosis of VHF is usually done through reverse transcriptase polymerase chain reaction (RT-PCR), even though RT-PCR is not commonly available in remote African regions (22). Rapid diagnosis and treatment of VHF is crucial for reducing case fatality rates, for recognizing outbreaks early and for improving occupational safety of HCW and others who are in contact with infected patients. Management of infected patients usually consists of strict isolation, symptomatic treatment and supportive intensive care (23).

4.4. Project rationale

The thesis asks how integrated VHF surveillance and response are practiced in the daily clinical reality of public healthcare facilities in Forest Guinea in the aftermath of the 2014–2016 EVD epidemic. The mentioned structural measures to rebuild IDSR within fragile healthcare settings have been considered key to detecting and responding to new VHF outbreaks and other infectious diseases (24). However, it is currently unknown whether and how the clinical integration of these newly established epidemiological surveillance mechanisms works within healthcare facilities in Guinea, especially in more remote regions. While some reports and studies from other West African countries on this topic have recently been published (5,7,25–27), Guinea has remained largely absent from this discussion.

The first publication is entitled “Period prevalence and identification challenges of viral haemorrhagic fever suspect cases in a tertiary referral hospital in Guinea: A cross-sectional, retrospective study of triage and emergency room patient profiles.” It examines VHF surveillance performance in a daily clinical setting in the largest tertiary hospital in Forest Guinea. This is done by determining VHF suspect case prevalence based on different screening criteria and comparing the detected case load to surveillance and response measures available to hospital staff and eventually taken by them. The publication further describes clinical trajectories of selected patients in order to discuss challenges in VHF suspect case identification.

The necessity to establish such basic epidemiological data emerged from after months of observation and participation at the N’zérékoré regional hospital. The hospital had several triage protocols in place for identifying VHF suspect cases. It also possessed an isolation ward and laboratory capacities to carry out RT-PCR tests to identify VHF in patients if necessary. However, we observed challenges in the application of triage protocols and suspect case management.

To explore this contradiction, we recorded patient symptoms for a period of three months and ascertained how many patients at the moment of hospital entry should be considered VHF suspect cases based on specific screening criteria. We analysed whether these patients were tested for EVD or other VHF to compare our initial observations with clinical data. We recorded all additional

diagnostic measures taken, as well as the diagnosis patients received. This data gave us more fine-grained insight into the processes of VHF suspect case recognition and its potential challenges.

Based on the analyses of the collected data as well as further observations and informal conversations with healthcare staff, we concluded that the hospital failed to test for VHF in patients when their symptoms would have formally required surveillance and response measures such as reporting and isolating a suspect case until RT-PCR results were obtained. This failure to integrate basic surveillance steps into clinical routine practice means that the hospital faced – and is still facing – several difficulties regarding IDSR of VHF. Based on the data analyses and observations we assume that the EVD epidemic generated a deep unease in regard to VHF and other highly infectious diseases in the clinical context. Directly identifying and reporting a VHF suspect case appeared to have various negative consequences, so staff circumvented taking responsibility for "bringing back" the fearful routines related to the EVD epidemic. By disregarding the application of VHF suspect case criteria, hospital staff avoided defiant and at times violent reactions by patients when were told they were suspected of having a VHF. Each VHF suspect case had the potential to disrupt the normal functioning of the healthcare facility by triggering a fearful response in HCW, patients and visitors. In post-Ebola times, it thus seems important to understand the traces that the EVD epidemic has left on healthcare professionals VHF surveillance practices if we wish to improve IDSR of VHF in Guinea and possibly beyond.

The second publication - entitled "Knowledge, attitudes and practices towards viral haemorrhagic fevers amongst healthcare workers in urban and rural public healthcare facilities in the N'zérékoré prefecture, Guinea: a cross-sectional study" - develops some of the conclusions of the first publication. It assesses the current understanding and potential gaps in knowledge, attitudes and practices (KAP) towards VHF amongst HCW in Forest Guinea's most populated prefecture.

The first publication suggested that certain misconceptions and attitudes could underlie the observed neglect regarding VHF suspect case recognition and

reporting. However, our KAP study found that HCW had an overall excellent knowledge of VHF such as their symptoms, infectivity, transmission, etc. Furthermore, reported attitudes and practices were favourable to early suspect case recognition and outbreak containment within the clinical setting. Our study noted no notable differences in KAP between urban and rural facilities even though HCW income and training level are usually higher in urban facilities. Interestingly, our study did not find differences in KAP between those HCW with prior training in IPC and those without. Participants did, however, report minor gaps in VHF suspect case identification practices as well as the notable shortage of protective gear within healthcare facilities.

We concluded that the 2014–2016 EVD outbreak left HCW with a very high awareness of EVD and other VHF regardless of whether or not they received IPC training during or after the epidemic. Regarding the project's rationale, the KAP study suggests that more training in IPC would not necessarily improve integrated VHF surveillance and response in public healthcare facilities. The underlying reasons for the deficiencies in the performance of viral surveillance can – as suggested above – only be assumed based on our data analyses, several observations and informal conversations. A further exploration of this topic would possibly require a qualitative research design (28).

However, both publications combined give a strong incentive to policymakers and clinical practitioners to monitor how newly established surveillance systems for VHF after the EVD epidemic work in West Africa. While it appears common sense that difficulties arise within the first years of integrating disease surveillance in the clinical setting – especially in already fragile and chronically underfunded healthcare systems – it is important not to overlook deficiencies and address them adequately. After all, VHF outbreaks with epidemic potential may recur in Guinea and other West African countries since corresponding pathogens are endemic in these regions. IDSR can only function if HCWs accept, understand and apply screening, testing and reporting protocols, considering they have the necessary protective and diagnostic equipment available. While infrastructural changes within West African healthcare systems are essential to IDSR, studies like ours additionally emphasize the importance

of understanding how viral surveillance protocols are translated into the daily clinical routines of West African healthcare facilities.

5. Summary

5.1. Abstract

Integrated disease surveillance and response (IDSR) in African countries aims at preventing epidemics through rapid outbreak detection, timely reporting of signal cases and the implementation of containment strategies. After the 2014–2016 West African Ebola virus disease epidemic, the IDSR for viral haemorrhagic fevers was revitalized to minimize the risk of future epidemics in the region. *Guinée Forestière* (Forest Guinea) – where the 2014-2016 Ebola outbreak started – is considered to be at a particularly high risk for future viral haemorrhagic fever outbreaks. The aim of this dissertation is to explore how the IDSR of viral haemorrhagic fevers is practiced in the clinical reality of public healthcare facilities in *Guinée Forestière* in the aftermath of the 2014-2016 Ebola virus epidemic.

Our first publication examines viral haemorrhagic fever surveillance performance in a daily clinical setting in the largest tertiary hospital in *Guinée Forestière*. It ascertains suspect case prevalence based on different screening criteria for a time period of three months. It further describes clinical trajectories of patients who fit screening criteria in order to discuss challenges associated with viral haemorrhagic fever suspect case identification. The study shows that regardless of which suspect case criteria are applied, suspect cases are usually not recognized at hospital entry. Further identification of suspect cases during their hospitalization seems equally challenging. This is due non-application of viral haemorrhagic fever suspect case definitions in daily clinical practice and low use of laboratory diagnostics to support important differential diagnosis.

To ascertain whether certain misconceptions of healthcare workers explain the findings of the first publication, the second publication assesses the knowledge, attitudes and practices towards viral haemorrhagic fevers amongst healthcare workers in public healthcare facilities in the most populated prefecture of *Guinée Forestière*. While the great majority of respondents demonstrated good knowledge and favourable attitudes towards viral haemorrhagic fevers, some reported gaps in preventive practices such as suspect case detection. Respondents also reported a shortage of protective medical equipment used in

everyday clinical work. Whether or not healthcare workers had been trained in infection prevention and control prior to our study did not seem to influence their level of knowledge, attitudes and practices towards viral haemorrhagic fevers.

Both studies provide a strong incentive to monitor the application of IDSR of viral haemorrhagic fevers in public healthcare facilities in Guinea and beyond. Minor gaps in knowledge, attitudes and practices amongst healthcare workers towards viral haemorrhagic fevers do not seem to account for the observed deficiencies in viral surveillance. Further research may illuminate why structural changes to improve viral surveillance in the aftermath of the Ebola outbreak are not translated into clinical practice.

5.2. Deutsche Zusammenfassung

Integrated Disease Surveillance and Response (IDSR) in afrikanischen Ländern zielt darauf ab, Epidemien zu verhindern. Ausbrüche sollen schneller erkannt und Signalfälle gemeldet werden, damit angemessene Eindämmungsstrategien umgesetzt werden können. Nach der westafrikanischen Ebola-Epidemie 2014-2016 wurde IDSR für virale hämorrhagische Fieber in betroffenen Ländern gestärkt, um das Risiko für zukünftige Epidemien zu minimieren. *Guinée Forestière* (Waldguinea) – die Region in der die Ebola-Epidemie 2014-2016 begann - ist einem besonders hohen Risiko für künftige Ausbrüche von viralen hämorrhagischen Fiebern ausgesetzt. Ziel dieser Dissertation ist es zu untersuchen, wie IDSR für virale hämorrhagische Fieber in der klinischen Realität öffentlicher Gesundheitseinrichtungen in *Guinée Forestière* nach der Ebola-Epidemie 2014-2016 umgesetzt wird.

Die erste Studie beobachtet die praktische Anwendung von Screening-Maßnahmen auf virale hämorrhagische Fieber im klinischen Alltag des größten Tertiärkrankenhauses in *Guinée Forestière*. Die Studie ermittelt die Prävalenz von Verdachtsfällen anhand verschiedener Screening-Kriterien für einen Zeitraum von drei Monaten. Ferner werden klinische Verläufe von Patienten beschrieben, die Screening-Kriterien erfüllen. Daran werden die Herausforderungen für die Erkennung von Verdachtsfällen verdeutlicht. Die Studie zeigt, dass Verdachtsfälle – unabhängig der Screening-Kriterien – im

klinischen Alltag im Untersuchungszeitraum nicht erkannt wurden. Die weitere Erkennung von Verdachtsfällen während deren Krankenhausaufenthaltes scheint ebenso schwierig zu sein. Dies ist sowohl auf den geringen Einsatz von Labordiagnostik zur Unterstützung bestimmter Diagnosen im klinischen Alltag, als auch auf die Missachtung von Falldefinitionen für virale hämorrhagische Fieber zurückzuführen.

Um festzustellen, ob bestimmte Bildungsdefizite bzw. Missverständnisse von Personal im öffentlichen Gesundheitswesen in *Guinée Forestière* die Ergebnisse der ersten Studie erklären, erhebt die zweite Studie deren Wissen, Einstellungen und Praktiken bezüglich viraler hämorrhagischer Fieber. Während die große Mehrheit der Befragten gute Kenntnisse und eine positive Einstellung zu viralen hämorrhagischen Fieber zeigte, berichteten einige über Lücken in der Präventionspraxis sowie der Erkennung von Verdachtsfällen. Die Befragten berichteten auch über einen Mangel an medizinischer Schutzausrüstung für deren tägliche klinische Arbeit. Ob Gesundheitspersonal vor unserer Studie in Infektionsschutz geschult worden war oder nicht schien deren Kenntnisstand, Einstellungen und Praktiken bezüglich viraler hämorrhagischer Fieber nicht zu beeinflussen.

Beide Studien unterstreichen die Wichtigkeit, die Anwendung von IDSR im klinischen Alltag von Gesundheitseinrichtungen in Guinea und den Nachbarländern regelmäßig zu evaluieren. Kleinere Wissenslücken und wenige fehlerhafte Praktiken des Gesundheitspersonals bezüglich viraler hämorrhagischer Fieber schienen nicht für die beobachteten Mängel im alltäglichen Screening verantwortlich zu sein. Weitere Studien könnten hilfreich sein, um genauer zu beleuchten warum strukturelle Veränderungen zur Verbesserung der Virusüberwachung nach der Ebola-Epidemie unzureichend in den klinischen Alltag übersetzt werden.

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