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Diagnostic Laboratories' Capacities and Preparedness for Emerging Viral Diseases in Guinea and Mali

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Abstract

The 2014-2016 Ebola epidemic in Guinea highlighted the need for more extensive evaluation of laboratories diagnostic capacities and preparedness in anticipation of future emerging viral disease outbreaks. We developed a questionnaire to assess the diagnostic capacities and preparedness of the four major medical laboratories in Guinea and Mali that are responsible for the provision of Ebola, Lassa, and Dengue diagnostics. The questionnaire inquired about the current state and need for equipment and reagents and adequacy of equipment and training received. In Guinea, all three diagnostic laboratories have the capacity and are well-prepared to perform Ebola diagnostics, however, only two have the capacity and trained staff to diagnose Lassa and none are currently prepared to diagnose Dengue infection. In Mali, the University Clinical Research Center (UCRC) laboratory, which was in charge of Ebola diagnostics during the last epidemic, currently has the capacity and is prepared to diagnose Ebola, Lassa, and Dengue infections. Combined, Guinea and Mali appear to have complementary capacity and preparedness to diagnose these Category A Priority Pathogens. While, the equipment, reagents and training efforts should be maintained, the gap in Dengue diagnostic capability in Guinea should be addressed with further equipping and training of additional district laboratories to strengthen the public health response for all viral diseases in these high-risk, yet, low-resource settings.

Keywords: Diagnostic; Emerging Viral Diseases; Guinea; Mali; Preparedness

Introduction

The 2014 Ebola epidemic in West Africa was the largest Ebola outbreak in history. More than 28,000 cases and over 11,000 deaths were reported in the West African countries of Guinea, Liberia, Sierra Leone, Mali and Senegal with nearly 40% of cases being fatal [1]. The Democratic Republic of Congo (DRC) has experienced several Ebola outbreaks and the most recent outbreak. which began in August 2019, is the second largest outbreak. These devastating Ebola epidemics have highlighted the need for more extensive evaluation of diagnostic capacities and preparedness, in anticipation of future viral disease epidemics in these regions [2,3]. Specifically, in Guinea during the 2014 epidemic, there was a paucity of essential trained health professionals, lack of diagnostic equipment and supplies, and general lack of laboratory preparedness

of trained staff, which likely contributed to the exponential spread of the disease. In addition to Ebola, other emerging viral diseases like Lassa and Dengue also pose serious threats to Guinea, Mali and neighboring countries [4,5]. Researchers and health professionals in Guinea, Mali and the United States are working together to identify areas for improvement and, eventually, to create an international network of trained professionals on emerging viral diseases, which could be activated across the region to intervene when needed [6]. Additionally, evaluating the maintenance of practices put in place during the last epidemic is essential to be prepared for early intervention and prevention of future outbreaks.

We created a questionnaire to assess the capacities and preparedness of the major health research and diagnostic facilities in Guinea and Mali for three Category A Priority Pathogens with a high epidemiological likelihood of emergence in these settings: Ebola, Lassa, and Dengue viral diseases. Although few cases of Dengue have been reported in Africa, the 2004 WHO Global Epidemiology of Infectious Diseases Study estimated that 20% of the population is at risk. While these diseases are under-reported mostly because of lack of diagnostic tools, available data still suggest that Dengue transmission is endemic in at least 34 African countries, including Guinea and Mali [7]. Moreover, Lassa fever has been reported to cause between 5,000 to 10,000 deaths each year in West Africa with Guinea designated as a high-risk country [8,9].

Methods

Questionnaire Development

We developed a questionnaire to evaluate diagnostic capacities of laboratories for the three Category A Priority Pathogens. The laboratory-targeted questions were developed based on the literature describing the most commonly used tests [10,11] "Dengue", 2009 and the necessary equipment and reagents for conducting the diagnostic tests for each viral disease [12-18]. The questionnaire had separate sections for Ebola, Lassa, and Dengue. Within each section, subsections included questions pertaining to the diagnostic tests recommended for each viral disease.

Perceived preparedness of training and funding were assessed by two self-reported questions, on a scale of 1 to 10. Each laboratory was also asked to report the number of positive cases diagnosed of each viral disease and the number of tests performed since the 2014 Ebola outbreak.

The questionnaire also queried about the quantity and types of equipment, adequacy of reagents for each diagnostic test, the number of personnel trained to perform each test, and the qualifications and experience of the personnel conducting the training.

Data Collection

The questionnaire was emailed to the heads of research and clinical laboratories specialized in viral infectious diseases in Guinea and Mali. We sent the questionnaire to three laboratories in Guinea (Gueckedou Hemorrhagic Fever Laboratory, Laboratory of Molecular Biology of N'Zérékoré, and Laboratory of Hemorrhagic Fevers of the Gamal Abdel University of Conakry) and one laboratory in Mali (University Clinical Research Center [UCRC] of Bamako). Two laboratories in Mali that are also involved in the diagnostics of viral diseases declined to participate to the survey.

Results

EBOLA

Overall Readiness

On a scale of 1-10 (10 being the best prepared/0 being completely unprepared), all four laboratories in Guinea and Mali rated their overall preparedness for Ebola as a 9 or 10 out of 10. In terms of funding, preparedness ranged from 5-8 out of 10 (Table 1). These positive findings are supported by the high number of suspected-cases tested in each of the centers since the last major outbreak.

	Guinea				Mali
	Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
How prepared do you feel [for Ebola]?	9	9	9	9	10
How prepared do you feel in terms of funding?	8	8	8	8	5
How many suspected cases have you seen since the last outbreak?	18,486	1,896	925	7,102	13

Table 1: Self-reported preparedness for an Ebola outbreak.

RT-PCR for Ebola

Every laboratory had received in-person training to perform RT-PCR testing for Ebola with both theoretical and practical training (Table 2). However, the Laboratory of Molecular Biology in N'Zérékoré reported a lack of reagents and equipment to perform RT-PCR.

ELISA for Ebola

Three of the four laboratories have some personnel who were trained in-person and had sufficient equipment and reagents to conduct ELISA to detect Ebola (Table 2). However, similarly to RT-PCR testing, the Laboratory of Molecular Biology in N'Zérékoré reported a lack of reagents and equipment to perform ELISA.

ReEBOV for Ebola Antigen Rapid Diagnostic Test

The ReEBOV Antigen Rapid Test Kit (Corgenix, USA) was approved by the World Health Organization (WHO) to be used during the 2014 West African outbreak. Three out of the four laboratories have personnel who were trained in-person by the Centers for Disease Control (CDC), however, none of these laboratories have any reagents/kits to perform ReEBOV, although none have received requests to perform the test. In Mali, 7 personnel are trained to perform ReEBOV and kits were reported as being available (2019). It should be noted that ReEBOV has been shown to be a potentially beneficial rapid point-of-care test and, therefore, useful for triage during large outbreaks [19].

		Guinea				Mali
		Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
RT-PCR	**How many personnel do you have who are trained to perform this?**	8	2	4	4.67	15
	Who trained you?	Institute of Tropical Medicine in Hamburg (Germany)	Hemorrhagic Fevers Laboratory of Conakry, the Pasteur Institute of Dakar	Institute of Tropical Medicine, Hamburg (Germany)	--	Dr. Heinz Feldmann, NIAID
	Do you have the necessary equipment and reagents?	Yes	No	Yes	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	11828	1896	0	4574.67	120

ELISA	**How many personnel do you have who are trained to perform this?**	5	0	4	3	4
	Who trained you?	Pasteur Institute of Dakar	-	Institute of Tropical Medicine, Hamburg (Germany)	--	NIAID
	Do you have the necessary equipment and reagents?	Yes	No	Yes	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	12	0	26	12.67	0
ReEBOV	**How many personnel do you have that are trained to perform this?**	8	0	4	4	7
	Who trained you?	CDC	--	CDC	--	A French Group
	Do you have the necessary equipment and reagents?	No	No	No	--	No
	How many testing requests have you received since the last Ebola outbreak?	0	0	0	0	0

Table 2: Personnel trained in and testing requests received for common methods of diagnosing EBOLA.

LASSA

Overall Preparedness for Lassa

Two of the three laboratories in Guinea rated their preparedness to conduct diagnostic tests for Lassa as 9 out of 10, however, one (Laboratory of Molecular Biology in N'Zerékoré) rated it as a 0 out of 10 (Table 3). The UCRC laboratory in Mali rated its preparedness as 10 out of 10.

	Guinea				Mali
	Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
How prepared do you feel [for Lassa]?	9	0	9	6	10
How prepared do you feel in terms of funding?	9	0	9	6	6
How many suspected cases have you seen since the last?	94	0	29	41	13

Table 3: Self-reported preparedness for Lassa outbreaks.

RT-PCR for Lassa

Two of the three laboratories in Guinea have personnel trained to use RT-PCR for Lassa and have sufficient equipment and reagents (Table 4). The Laboratory of Molecular Biology in N'Zérékoré described a lack of both equipment and reagents to perform RT-PCR for Lassa. The UCRC in Mali has six trained personnel and has all necessary equipment and reagents.

ELISA for Lassa

Two of the three laboratories in Guinea have four personnel who are trained to perform an ELISA for Lassa and have the necessary equipment and reagents (Table 4). The Laboratory of Molecular Biology in N'Zérékoré lacks equipment and reagents to perform an ELISA for Lassa. Additionally, although the diagnostic center in Mali has the necessary equipment, they do not have any personnel trained to perform an ELISA for Lassa.

		Guinea				Mali
		Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
RT-PCR	**How many personnel do you have who are trained to perform this?**	4	0	4	4.67	6
	Who trained you?	Institute of Tropical Medicine in Hamburg (Germany)	--	Institute of Tropical Medicine in Hamburg (Germany)	--	Dr. Heinz Feldmann, NIAID
	Do you have the necessary equipment and reagents?	Yes	No	Yes	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	69	0	29	32.67	0

ELISA	**How many personnel do you have who are trained to perform this?**	6	0	4	3	0
	Who trained you?	Institute of Tropical Medicine in Hamburg (Germany)	--	Institute of Tropical Medicine in Hamburg (Germany)	--	--
	Do you have the necessary equipment and reagents?	Yes	No	Yes	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	59	0	645	234.67	0

Table 4: Personnel trained in and testing requests received for common methods of diagnosing Lassa.

Dengue

Overall Preparedness for Dengue

Two of the three laboratories in Guinea rated their preparedness to conduct diagnostic tests for Dengue as 8 out of 10, and the Laboratory of Molecular Biology in N'Zérékoré rated it as a 0 out of 10. None of the laboratories have diagnosed any cases of Dengue since the 2014 Ebola outbreak (Table 5). The UCRC, however, only rated preparedness as 6 out of 10 in terms of funding.

	Guinea				**Mali**
	Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
How prepared do you feel?	8	0	8	5.33	10
How prepared do you feel in terms of funding?	9	0	8	5.33	6
How many suspected cases have you seen since the last?	0	0	0	0	20

Table 5: Self-reported preparedness for a Dengue outbreak in diagnostic laboratories in Guinea and Mali.

RT-PCR for Dengue

Two of the three laboratories in Guinea have four trained personnel to conduct RT-PCR for Dengue, but the Laboratory of Molecular Biology in N'Zérékoré has no one. Of the two laboratories with trained personnel, only the Laboratory of Hemorrhagic Fevers in Guinea has a sufficient amount of both equipment and reagents to conduct RT-PCR for Dengue. Overall, no testing requests have been made (Table 6). In Mali, there are 15 personnel trained to perform RT-PCR to diagnose Dengue. The UCRC has performed 20

Dengue RT-PCR tests since 2014. It should be noted that there is currently a Dengue outbreak in Mali (started in November 2019) and the number of diagnostic tests for Dengue continues to increase.

MAC-ELISA for Dengue

Both laboratories in Guinea that are self-described as "prepared" for Dengue and have two personnel each that are trained to perform a MAC-ELISA. Although they have the equipment, neither of these laboratories has all of the reagents necessary to perform a MAC-ELISA (Table 6). The UCRC in Mali has four personnel trained to diagnose Dengue using a MAC-ELISA and reported sufficient reagents and equipment for the test.

PRNT for Dengue

Dengue Plaque Reduction Neutralization Test (PRNT) is the current "gold standard" for quantify circulating anti-DENV neutralizing antibody. No one in any of the diagnostic laboratories in Guinea or Mali is trained to perform PRNT, no do any of the laboratories have the necessary reagents and equipment. While, the PRNT is considered the gold standard, it has been shown recently that PRNT has a significant amount of variability between serotypes [20].

		Guinea				Mali
		Gueckedou Hemorrhagic Fever Laboratory	**Laboratory of Molecular Biology in N'Zérékoré**	**Laboratory of Hemorrhagic Fevers in Guinea**	**Average**	**UCRC**
RT-PCR	**How many personnel do you have who are trained to perform this?**	4	0	4	2.67	15
	Who trained you?	Institute of Tropical Medicine in Hamburg (Germany)	--	Institute of Tropical Medicine in Hamburg (Germany)	--	Life Technologies, for using Applied Biosystems™ 7500 Real-Time PCR Systems
	Do you have the necessary equipment and reagents?	No	No	Yes	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	0	0	0	0	20

MAC-ELISA	**How many personnel do you have who are trained to perform this?**	2	0	2	1.33	4
	Who trained you?	Pasteur Institute of Dakar	--	Pasteur Institute of Dakar	--	CDC Platform
	Do you have the necessary equipment and reagents?	Yes for equipment but No for reagents	No	Yes for equipment but No for reagents	--	Yes
	How many testing requests have you received since the last Ebola outbreak?	0	0	0	0	0
PRNT	**How many personnel do you have who are trained to perform this?**	0	0	0	0	0
	Who trained you?	--	--	--	--	--
	Do you have the necessary equipment and reagents?	No	No	No	--	No
	How many testing requests have you received since the last Ebola outbreak?	0	0	0	0	0

Table 6: Personnel trained in and testing requests received for common methods of diagnosing Dengue.

Discussion

This study evaluated the current preparedness laboratories in Guinea, where the 2014 West African Ebola epidemic originated [2], and in Mali, a country bordering Guinea, for three Category A Priority Pathogens: Ebola, Lassa, and Dengue [21]. In 2014, Mali was better prepared to detect Ebola, which ultimately allowed for rapid detection and management of cases [22]. Subsequently, authorities in Mali and Guinea have worked together to synergize their efforts to prepare for future outbreaks of these emerging viral diseases. This study now seeks, four years after the end of the Ebola epidemic, to understand the lessons learned during the epidemic and to assess the capacity and preparedness of the laboratories to address future epidemics.

We found that all three diagnostic laboratories in Guinea are prepared to perform diagnostic tests for Ebola; however, while two of these laboratories have capacity and are prepared to diagnose Lassa, none has the capacity to diagnose Dengue. The UCRC in Mali, however, currently has the capacity and is generally well-prepared to diagnose all three emerging viral diseases. This preparedness of the Mali UCRC team is in part explained by its three-decade collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) intramural program which

has significantly developed the Mali laboratory and research infrastructure.

Of note, none of the three laboratories in Guinea have reagents to perform ReEBOV, which is a quick diagnostic test for Ebola. Although ReEBOV is not a gold standard test, having ReEBOV could be an important alternative to PCR or could be used as a triage test [19]. Adequate equipment, reagents, and training should be maintained for a rapid response of outbreaks.

The UCRC in Mali, while self-rated preparedness of funding as low, nevertheless, currently has excellent capacity to perform diagnostic tests for all three viral diseases. High levels of funding may not be needed when there is no ongoing outbreak. However, a key factor in the preparedness of the UCRC is current NIAID funding for a research study about the diagnostics on potential emerging infectious diseases, including Lassa fever, yellow fever, Ebola virus disease, Zika virus disease, Chikungunya, Dengue, Leptospirosis and flu viruses. This model of research funding appears to also be an effective strategy for maintaining capacity and preparedness for epidemics and should be considered for other high-risk, low-resource settings. Indeed, the same study is being considered for extension to Guinea under the same NIAID funding mechanism.

This cross-sectional descriptive study has some limitations. First, data are self-reported, which may have led to some bias. But, responses about capacity and preparedness for diagnostic tests for each viral disease and the overall preparedness score are largely concordant. Second, some responses are purely speculative since the real test of capacity and preparedness will only be known during an outbreak. Nevertheless, the study found important aspects of epidemic preparedness in this region while highlighting some opportunities for corrective measures to ensure a timely response to increased diagnostic demand and prevention of large outbreaks.

Conclusion

Despite gaps in capacity and preparedness in laboratories in Guinea, especially the Laboratory of Molecular Biology in N'Zérékoré, overall, the combined level of preparedness in Guinea and Mali is complementary and sufficient to potentially respond to an epidemic of any of the three viral diseases, Ebola, Lassa or Dengue. These efforts clearly need to be sustained and should be routinely re-evaluated to assure capacity and preparedness for future outbreaks. The training capacities in Mali for Dengue should be leveraged to improve capacity in Guinee. Given the current evolution of Ebola in DRC and its significant morbidity and mortality rate in West Africa during the last outbreak, more investment is still needed to assure adequate diagnostic capacity during an outbreak. Furthermore, additional efforts should be undertaken to ensure appropriate capacity and preparedness of regional and district level laboratories, for all three diseases in both Guinea and Mali. In Mali, reliance on only the UCRC could be especially problematic for outbreaks in other parts of the country, given the large size of the country and political instability, which hampers transport in some parts of the country.

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