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Virology & Immunology Journal

The Resurgence of African Viral Haemorrhagic Fevers (AVHFs) in Nigeria

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Mini Review

Volume 1 Issue 5

Received Date: November 08, 2017

Published Date: December 08, 2017

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Abstract

AVHFs are a diverse group of animal and human illnesses that are caused by five distinct families of RNA viruses: the *Arenaviridae, Bunyaviridae, Filoviridae*, *Flaviviridae* and *Togaviridae*. Generally, VHFs are characterized by fever and bleeding disorders and all can progress to high fever, shock, haemorrhage and death in extreme cases. Infections with haemorrhagic fever viruses are an important cause of human illness and a public health problem of global dimension especially in the African continent. VHF agents are all highly infectious via the aerosol route, and most are quite stable as respirable aerosols. This means that they satisfy at least one criterion for being weaponized, and some clearly have the potential to be biological warfare threats. These viruses are found endemic in some areas of Africa, where they depend on animal, insect or natural reservoir for survival; they are usually restricted to the geographical area inhabited by their hosts and vectors. Currently, in Nigeria there are reports of the resurgence of these viral agents such as Lassa fever, Crimean-Congo haemorraghic fevers, Ebola and Rift Valley fever in some parts of the country.

Keywords: Re-emergence; African haemorrhagic fevers; Nigeria

Abbreviations: AVHFs: African Viral Haemorrhagic Fevers; LUJV: Lassa; Lusaka-Johannesburg Virus; CCHF: Crimean-Congo Haemorrhagic Fever; RVF: Rift Valley Fever; YF: Yellow Fever

Introduction

The African viral haemorrhagic fevers (AVHFs) are a diverse group of animal and human illnesses that are caused by five distinct families of RNA viruses: the *Arenaviridae* (Lassa, Lusaka-Johannesburg virus (LUJV) and Lusaka-Namwala (LUNA)-viruses first discovered in Zambia and South Africa) *Bunyaviridae* (Crimean-Congo, Rift Valley fever), *Filoviridae* (Ebola, Marburg), *Flaviviridae* (Dengue, Yellow fever) and Togaviridae (Chikungunya, O'Nyong-nyong) [1,2]. All types of viral haemorrhagic fevers (VHFs) are characterized by fever and bleeding disorders and all can progress to high fever, shock, haemorrhage and death in extreme cases. The viruses cause significant outbreaks of diseases with

person-to-person transmission. Some of the VHF agents cause relatively mild illnesses (Scandinavian Nephropathia epidemica), while others (African Ebola virus), can cause severe, life-threatening disease [3,4]. Infections with haemorrhagic fever viruses are an important cause of human illness and a public health problem of global dimension especially in the African continent. These viruses are found endemic in some areas of Africa (Figure 1), since they depend on their animal, insect or natural reservoir for survival; they are usually restricted to the geographical area inhabited by their hosts and vectors [5].

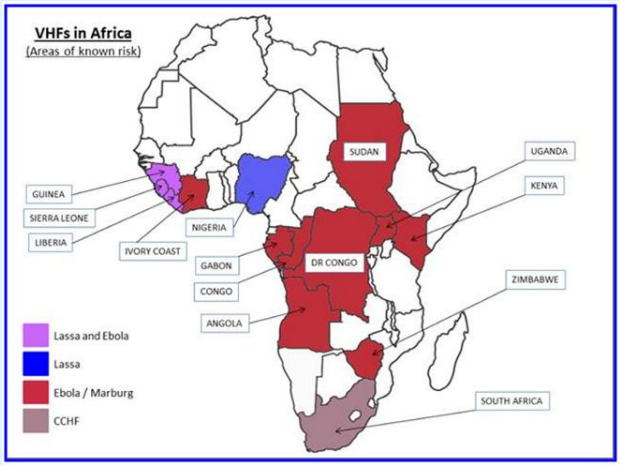

Figure 1: Map of Viral haemorrhagic fevers in Africa showing areas of known risk [6].

The viral haemorrhagic fevers prevalent in Africa (African Haemorrhagic Fevers, AHFs) comprise of:

- The Arboviral (arthropod-borne) infections of Yellow fever (YF), Rift Valley fever (RVF), Crimean-Congo haemorrhagic fever (CCHF); Chikungunya, O'Nyong-nyong and Nairobi Sheep disease virus.
- The Arenaviral (rodent-borne or robovirus) infection of Lassa fever (LASV)
- The Filoviral infections of Ebola (EBO) and Marburg virus disease (MARBV) haemorrhagic fevers.

Each of these groups of VHFs has specific geographic patterns with vector and animal reservoirs (usually asymptomatic viraemic carriers). Although the individual disease pattern may differ for each virus, the VHFs may share many common features. They may be transmitted to humans through contact with infected animal, rodent or arthropod vectors [3,4].

The distribution of the VHF viruses is generally limited and is endemic in certain areas of the world. Their geographical ranges may be highly circumscribed. Changing social, economic and climatic conditions such as the advent of jet travel resulting into increasing international travel, bioterrorism and ecological disruption coupled with human demographics increase the opportunity for humans to contact these infections and for introduction of VHF-associated viruses into new areas or increase the incidence in endemic areas [7-9]. The potential danger of transmission and importation of non-endemic VHFs has also been the focus of intense media attention and public concern [3]. The VHF agents are all highly infectious via the aerosol route, and most are quite stable as respirable aerosols. This means that they satisfy at least one criterion for being weaponized, and some clearly have the potential to be biological warfare threats. In Africa, AHFs usually do not cause major epidemics; however, localized outbreaks do occur and may have devastating effects on the local community and cause widespread concern. In addition to having high fatality rates, some also cause permanent disability, such as hearing loss following Lassa fever, or blindness after Rift Valley fever [10]. In Nigeria, there are reports from literature of serological and virological evidence of AHF virus activity in certain parts of the country among humans and animals [11-20]. Previous virological and serological surveys in Nigeria have revealed the presence of human and animal infections by some of the viruses associated with haemorrhagic fevers [21]. These include YF Dengue 1 and 2 Congo of the Crimean-Congo haemorrhagic fever group RVFV LASV, Ebola and Marburg viruses [22-37]. Also since the first case of LF was reported in 1969, there have been reports of several outbreaks in many parts of the country [35,36]. In 2017, between weeks 1 and 41, 569 suspected cases of Lassa fever with 120 Laboratory confirmed cases and 65 deaths (case-fatality rate, 11.4%) were reported from 86 Local Government Areas (LGAs) in 26 States compared with 87 Laboratory confirmed and 102 deaths (CFR,11.9%) from 138 LGAs of 28 States during the same period in 2016 [37].

Serologic and virological studies on some of the viral aetiologic agents of the AHFs indicate increasing prevalence and activities in recent years. RVFV antibodies have been found in sheep, goats, cattle, horses and camels in the northern States of Kaduna and Sokoto [38] and in the plateau area [15] suggesting that the virus may be enzootic in Nigeria. In addition, serological studies conducted on human sera have confirmed the existence of the disease in Nigeria [16,19]. In one of these studies, conducted by Bukbuk et al. in 2014 among the human

population in Borno Nigeria, RVFV antibodies (14.1%) were found to be more prevalent relative to antibodies against Lassa virus (7.4%) and CCHF virus (2.4%). The first report of CCHF in Nigeria occurred in 1970, when it was identified in various tick species, including Hyalomma spp. collected from market animals, and hedgehogs [19,26]. However, very few cases of CCHF have been reported in Africa [39]; the majority are described from South Africa [40]. The risk of CCHF in several African countries is poorly defined and infection with the virus is often undiagnosed in these regions [41]. Of importance, CCHFV is a known to be a notorious cause of nosocomial infections especially when undiagnosed, and the virus presents a significant risk to health care workers [42-46].

However, despite several studies on the seroprevalence of antibodies against CCHFV from humans and animals in Nigeria, detailed investigation demonstrating the presence of IgG and IgM antibodies to the virus have not been reported until recently [20]. This study reported prevalence rates of IgG and IgM antibodies to be 10.6% and 3.5% respectively. This is also coupled with the fact that there have been no virological confirmations of human infection reported from Nigeria. The first virological or genomic analysis of CCHFV from sera of a 15-year-old female patient who presented with an undiagnosed febrile illness consistent with a case of VHF provided the first published evidence of a human case of CCHFV in Nigeria and its phylogenetic context [20]. CCHFV RNA obtained from this case (N428) was characterized by next generation sequencing (NGS) resulting in complete S.M. and L segment sequences. Phylogenetic analysis clustered the S segment in the Africa 3 phylogenetic group (Figure 2). The S segment open-reading frame showed close homology with a previous isolate of CCHFV from Nigeria (IbAr10200), as well as isolates from Mauritania (ArD39554) and South Africa (SPU415/85 and SPU128/61/7). The M and L clustered closely with the Sudan ABI-2009 isolate and the Nigeria IbAr10200 isolates (Figure 3).

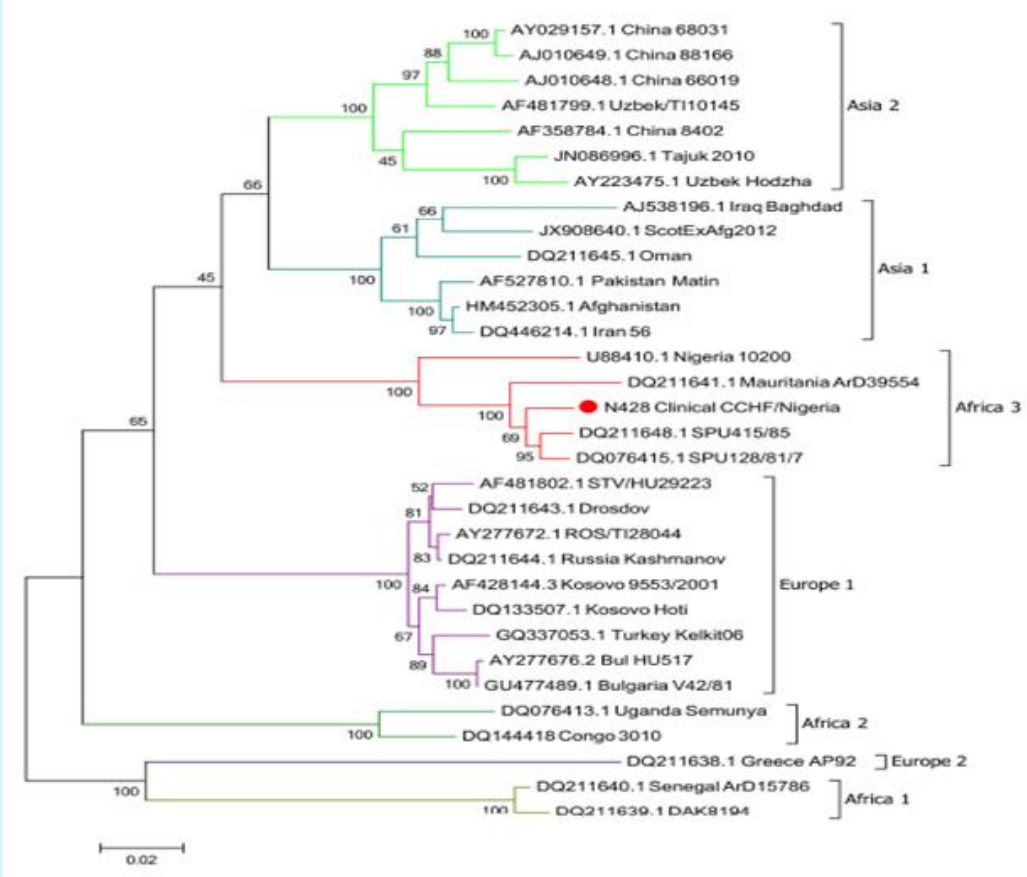

Figure 2: Maximum-Likelihood phylogenetic tree showing relationship distances obtained by comparing CCHFV S segment open-reading frames. Different CCHFV cladws are indicated by coloured lines [20].

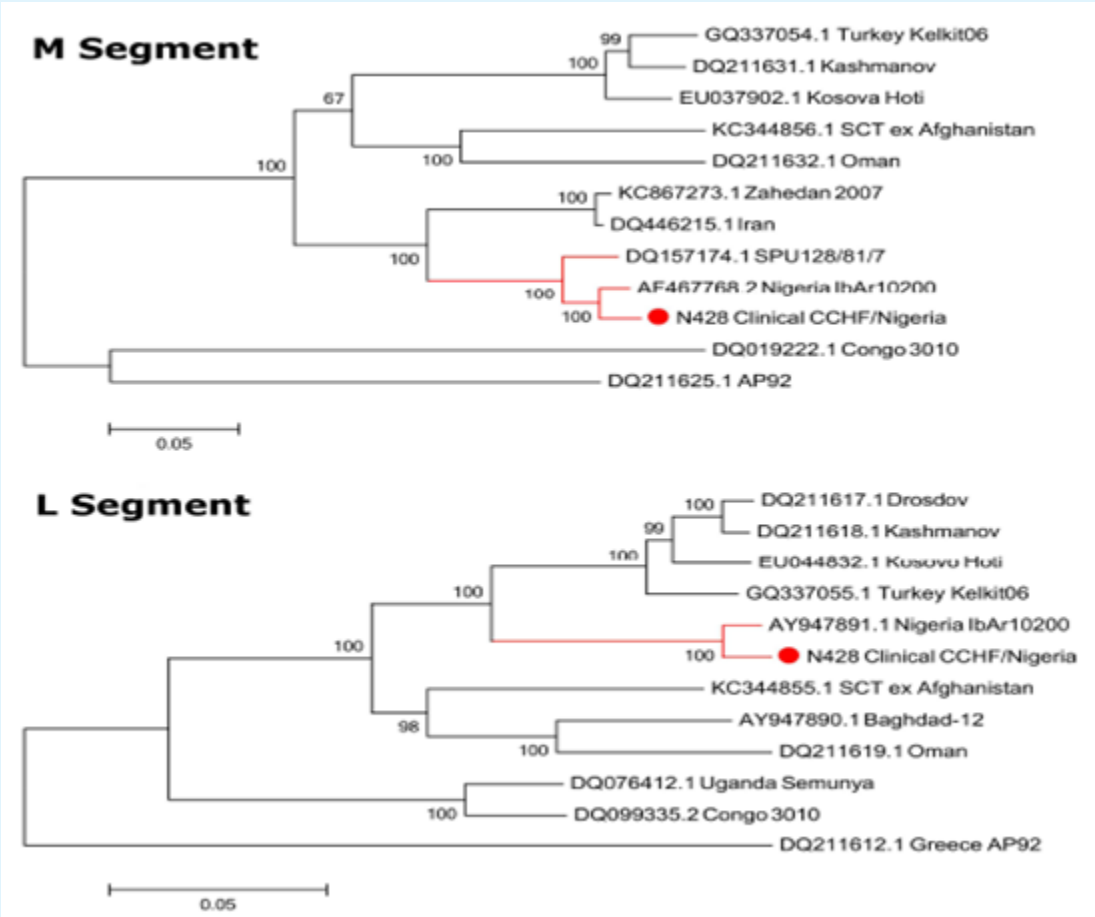

Figure 3: Maximum-Likelihood phylogenetic tree showing relationship distances obtained by comparing CCHFV M-and L-segment open-reading frames [20].

The specific geographical location of Borno State in northeastern Nigeria, which shares international borders with three other African countries of Cameroun, Chad and Niger, makes it vulnerable to the transboundary spread of various diseases, including VHFs. In addition, Borno State has been reported as the ecologic niche for Lassa fever virus and possibly other VHFs.

These reports indicate the active circulation and endemicity of some AHFVs and the changing epidemiology with renewed and increasing activity of AHFs in Nigeria.

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