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THE SUDDEN OUTBREAK OF VIRAL HEMORRHAGIC FEVER IN NIGERIA: WHAT RADIOGRAPHERS AND OTHER HEALTHCARE PROVIDERS MUST KNOW

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ABSTRACT

Background: Viral Hemorrhagic Fevers (VHF) are a group of infectious and life-threatening diseases that are vector-borne and zoonotic. This narrative review aims to highlight and reinforce the knowledge of VHFs to Radiographers and other healthcare professionals. An extensive literature search was conducted from 1969-2024, using the Google search engine, MEDLINE, PUBMED, EMBASE, POPLINE and Scopus for original, systematic reviews and grey literature on VHFs in English language, and Boolean operators like "AND" and "OR", and keywords like, Viral Hemorrhagic Fever, Hemorrhagic Fever, Filoviridae, Arenaviridae, Bunyaviridae, and Flaviviridae. The search was extended by scrutinizing the selected articles' reference lists to ensure that much relevant literature was extracted on the subject. The literature synthesis is presented in a flow chart and emerging themes are summarized and discussed.

Introduction

Viral Hemorrhagic Fevers (VHF) are a group of infectious and life-threatening epidemic-prone diseases that are primarily caused by viruses [1]. Viral Hemorrhagic Fever is both a vector-borne and zoonotic disease. It is transmitted by vectors and insects like mosquitoes, ticks, sandflies, and animals such as porcupines, rats, goats, sheep, cows and bats [1]. VHF is a multi-systemic syndrome (affecting multiple organs and systems) disease that is spread by contact with infected animals, persons or insects. VHF is caused by several families of viruses like.

The Filoviridae (Ebola and Marburg viruses).
Arenaviridae (Lassa fever and New World Hemorrhagic fever).
Bunyaviridae (Rift Valley fever, Crimean-Congo fever and agent of hemorrhagic fever with renal syndrome).

Flaviviridae (Yellow fever, Omsk hemorrhagic fever, Kyasanur Forest disease and Dengue) [2]

Most of the VHF viruses are virulent, some are very infectious like the filoviruses and arenaviruses with transmission from person to person due to direct contact with blood and body secretions. Strict precautionary measures and early detection are the only sure means of protection as there are no effective therapies and prophylaxis, even if there are, they are extremely limited, except for Yellow fever [2]. VHF are all ribonucleic acid (RNA) viruses, they are enveloped in a lipid coating and their survival is highly dependent on their natural reservoir (animal or insect host) [3]. The first Arenavirus was isolated during the St. Louis Encephalitis virus outbreak in 1933, followed by the Junin virus isolated in the plains of Argentina in Agricultural workers in 1958, it was one of the first Arenavirus to cause hemorrhagic fever. Machupo virus was isolated in Bolivia in 1963 and Lassa virus in Nigeria in 1969. Other new Arenavirus strains have been discovered but not all may cause hemorrhagic fever [3]. This narrative review aims to highlight and reinforce to the front-line healthcare providers the knowledge of VHFs, their clinical presentation, diagnoses, risk assessment and patient triaging and some recommended treatment options for VHFs.

Methods:

An extensive literature search was conducted from 1969 to 2024 using the Google search engine, MEDLINE, PUBMED, EMBASE, POPLINE and Scopus for original, systematic reviews and grey literature on VHFs in English language retrieved from the World Health Organization (WHO) reports, governmental and nongovernmental agencies among others, using Boolean operators like "AND" and "OR", and keywords like, Viral Hemorrhagic Fever, Hemorrhagic Fever, Filoviridae, Arenaviridae, Bunyaviridae, and Flaviviridae. The search was extended by scrutinizing the selected articles' reference lists to ensure that much relevant literature was extracted on the subject. The result of the literature synthesis is presented in a flow chart Fig. 1, and emerging themes are summarized in Table 1 and discussed accordingly.

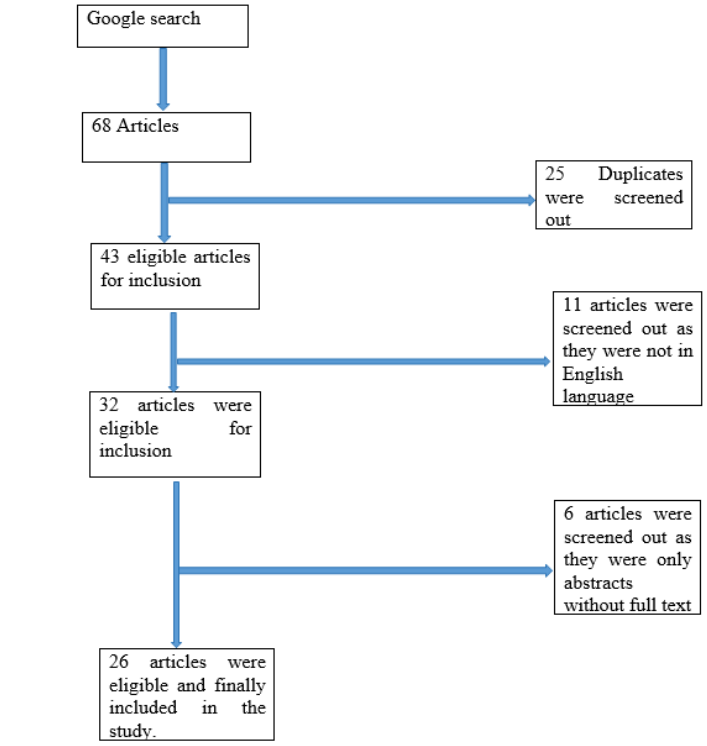

Fig 1: Showing Flow Chart of Articles included in the Study

Table 1: Emerging themes from reviewed literature

Authors	Themes
Snow et al[3], Fhogartaigh and Aarons[5], Bente et al[9], Ansari[11], Mangat and Louie[12], Feldmann and Geisbert[13], Mehedi et al[14]	Clinical presentation of VHF
Fhogartaigh and Aarons[5], Bente et al[9], Mehedi et al[14], ACDP[15], Rollin et al[16], Cummings et al[17], Asogun et al[18]	Risk Assessment of VHF
Snow et al[3], Mangat and Louie[12]	Diagnosis of VHF
Snow et al[3], Mangat and Louie[12], Asogun et al[18], Iannetta et al[19], Rougeron et al[20], Saphire et al[21], Kularatne[22], Gubler and Halstead[23]	Recommended Treatment Options for VHF
Snow et al[3], Cummings et al[17], Guimard et al[24], Chandak and Kumar[25], Donald et al[26]	Control and Prevention of VHF during Outbreaks

Results/Discussion

A Concise Epidemiology of Viral Hemorrhagic Fever (VHF)

Filoviruses like Ebola and Marburg viruses are filamentous enveloped virions with RNA-encoded genomes. Ebola was discovered in 1976, during the simultaneous outbreaks of febrile illness with shock and hemorrhage in Sudan and former Zaire [4,5]. There are up to five different species of the Ebola Virus with different degrees of Virulence. Marburg virus was first discovered among handlers of African green monkeys in Marburg Germany in 1967 [6]. Several cases have also been reported in Zimbabwe, Uganda, the Democratic Republic of Congo, Kenya and Angola. The mortality rates from these viruses are very high and their outbreaks can be traced back to an index human or animal infection [5].

Lassa virus is an Arenavirus with pleiomorphic virions enveloped with RNA-encoded segmented genomes. The virus was first discovered in 1969 in Northern Nigeria, in a town called Lassa [7]. Lassa virus fever is endemic in West African countries like Sierra Leone, Liberia, Guinea and Nigeria with an estimated 100,000-500,000 cases each year [8]. The natural reservoir is the multimammate rat that inhabits both homes and fields in rural areas. Infection occurs from inhalation of contaminated dust with infected rat urine or close contact with rodents and infected persons [5].

The Crimean-Congo Hemorrhagic fever (CCHF) is a Bunyavirus of the genus *Nairovirus* having spherical virions enveloped with segmented RNA genomes [9]. It is believed to be carried by the *Hyaomma spp* tick scattered across Africa, Asia, the Middle East and Eastern Europe. The reservoir of the infection includes cattle, sheep, goats, and rodents. Infection may be contracted through an infected tick bite when crushing a tick or removing a tick with bare hands, or through contact with blood and body fluids of infected persons or animals [9]

1.3: Clinical Presentation of Viral Hemorrhagic Fever.

The initial clinical syndrome may be non-specific, with flu-like symptoms like fever, myalgia, and generalized malaise. These are followed by nausea, vomiting, diarrhea, and rashes progressing to petechiae, conjunctival hemorrhage, epistaxis, melena, hematemesis, shock and encephalopathy in severe cases [11]. Bleeding may also occur in internal organs and from orifices like the nose, eyes, or mouth [3]. Specific signs and symptoms may vary by the type of VHF, but the initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength and exhaustion [3]. Clinical features that are common for VHFs include retro-orbital pain, joint pains, eye redness, abdominal pain, diarrhea and vomiting. There may also be complaints of bleeding gums, and epistaxis, where a physical examination may be notable for petechiae [12]. Pathogenesis of Viral hemorrhagic fever is not clear, however, the viruses target cells like the monocytes, macrophages, dendritic cells and vascular endothelial cells which enable dissemination through the lymphatics to several organs and parts of the body [13]. For example, Ebola virus disease, a viral protein, VP35, inhibits interferon (IFN)-regulatory factor 3 that is necessary for the induction of IFN α/β and an antiviral immune response [13]. There is also an extensive activation of cytokine with the release of tissue factor that results in endothelial damage, oedema, coagulopathy, shock, tissue necrosis and multiorgan failure [5].

VHFs are similar in their clinical presentations, although Lassa fever may present with a high rate of asymptomatic and sub-clinical infections, this is however, in contrast with Filoviruses infections which are symptomatic with high rates of mortality. In high endemic areas sub-clinical Crimean-Congo Hemorrhagic fever may be more frequent [9].

Generally, there are three phases of the illness.

The generalization phase (First Week)

The early organ phase (Second Week)

The late organ phase (Third Week) [9,13,14]

The generalization phase is non-specific, as the presentation is often with fever, chills, myalgia, malaise, headache, gastrointestinal symptoms and sore throat. Severe watery diarrhea is a common clinical feature in the current Ebola virus disease outbreak.

Cough and chest pain are also common. There is a more abrupt onset with Ebola virus, Marburg Virus and Crimean-Congo Hemorrhagic fever. Conjunctivitis and maculopapular rash may also be seen [5,9,13,14].

During the early organ phase, the complications of the endothelial damages manifest as petechiae, ecchymoses, conjunctival injection, oedema, mucosal hemorrhage, bloody diarrhea, melaena, hematemesis, dyspnea due to pulmonary oedema and irritability. In the late organ phase, illness may progress to disseminated intravascular coagulation, shock, liver and renal dysfunction, seizures, coma and death [5,9,13,14].

Crimean-Congo Hemorrhagic fever (CCHF) has a shorter course with the appearance of hemorrhagic features around 3-5 days in most cases. However, hemorrhagic features may be absent in other viral hemorrhagic fevers [10]. Patients that recover, defervesce, may also run a protracted convalescence, hearing loss, visual impairment, psychological disturbance and social isolation [13,14].

Differential Diagnosis

Acute human immunodeficiency virus (HIV) infection.
Chikungunya virus.
Leptospirosis.
Malaria.
Malignancy.
Systemic lupus erythematosus
Typhoid fever [10,13,14]

1.4: Risk Assessment and Patient Triaging of Viral Hemorrhagic Fever

Based on the recommended algorithm for risk stratification of patients with the possibility of Viral Hemorrhagic Fever (VHF), the Advisory Committee for Dangerous Pathogens (ACDP) (ACDP, 2014), proposed that when there is an uncertainty if a patient should be designated as an either low or high possibility of VHF, and if there is no previous contact with a sick or death person, or exposure to an environment where VHF is endemic, an alternative diagnosis should be most likely considered[5,17].

The "CALM" algorithm which is used by emergency healthcare providers in examining a patient suspected with signs and symptoms of VHF. This algorithm covers the common VHF seen around the globe, like the Ebola virus, Marburg virus, Lassa virus and Crimean-Congo Hemorrhagic Fever (CCHF) virus among others. It is noteworthy that this algorithm may not be a comprehensive guideline and should be used in conjunction with the local institution's established guidelines for managing suspected and confirmed cases of VHFs [15-17].

The "CALM" acronym stands for.

Consider risk factors for VHF.

Act.

Laboratory examinations.

Monitor contacts.

i. Consider Risk Factors for VHF

Risk factors like exposure history, if the patient has experienced any of the following.

- If a patient had travelled to geographical areas where VHF is endemic or areas currently experiencing outbreaks.
- Have had close contact with any sick person(s) who has been to regions experiencing VHF outbreaks recently. Has come in contact with bats, rodents, livestock or ticks in regions where VHF is endemic or experiencing VHF outbreaks currently.

If the patient does not have any risk factor for VHF, it is advisable to continue with the usual triage and investigate other possible causes of fever, especially among returning travelers. The tour algorithm can be of great assistance. Travel notices are designed to provide information on the current health issues related to specific destinations [17].

ii. Act

The patient must be isolated; the Patient should be isolated in a private room or a separate enclosed designated area with a private bathroom, or a covered bedside commode. Such an exclusion must not be open to visitors and only essential healthcare personnel with designated roles to examine the patient and provide care to limit the risk of nosocomial infection. Each precautionary measure should be taken on a case-by-case basis, in collaboration with local, state and federal healthcare authorities [17].

The appropriate personnel protective gear should be worn by all healthcare personnel having anything to do with/for the patient. Immediately, the health institution's infection control management team should be informed, and the local, state and federal healthcare authorities should also be notified. Dedicated medical equipment, preferably, disposable ones should be used where available, and if non-dedicated and non-disposable equipment is used in providing care for patients with VHF, such equipment should be cleaned properly, and disinfection should be based on manufacturers' guidelines and the hospital's best practices [17].

iii. Laboratory Examinations

Inform the laboratory; that the bio-samples collected from patients must be managed according to the laboratory protocols for handling potential VHF samples. Leucopenia, thrombocytopenia and transaminitis (aspartate transaminase (AST>alanine transaminase)) are suggestive of VHF in a patient with compatible clinical history, most especially within 21 days of confirmed epidemiological exposure and when malaria film is negative [5]. Standard precautions are to be adhered to in handling bio-samples from suspected cases of VHF. Varaemia occurs from the first day and persist through out illness. IgM and IgG appear from the third to the seventh day respectively, although there may be delays in the production of antibodies and this may result in poor prognosis[5,9,14,16,17]. The reverse transcription polymerase chain reaction (RT-PCR) is very sensitive and also specific and can be used to run blood, urine, saliva and throat swabs samples. Enzyme-linked immunosorbent serologic assay (ELISA) which can detect IgM and IgG antibodies. Viral culture can be done, but this should only be carried out in high containment laboratory with very good laboratory practices in place. Immuno-chemistry can be performed on formalin-fixed tissue specimens for post mortem diagnosis[18].

iv. Monitor Contacts

A contact tracing log should be maintained; health facilities should maintain a log record of all the persons entering the patient's room, with full details of their contact addresses. Healthcare personnel providing care for the patient should also be monitored including the environmental services, ancillary staff among others[17].

Limit visitors

It is very important to avoid unnecessary access to the patient's room, with the exception of only those offering essential services for the patient's well-being. Based on a case-by-case basis, a procedure for monitoring and managing visitors and also for monitoring healthcare providers managing the patients as well. Healthcare providers should be on regular shift duties, and given sick leave when necessary and this information should be communicated to the patients and their relations[3,17]. Inter-professional team approach whenever viral hemorrhagic fevers are suspected provides a better health outcome. Effective communication between clinicians, nurses, radiographers, epidemiologists, virologists and environmental health experts is necessary to help prevent any further spread of disease[19]. Patients should also be educated regarding the geographical distribution of these viruses and practice infection prevention measures when travelling to areas where these diseases are endemic.

1.5: How is Viral Hemorrhagic Fever Diagnosed:

Clinically, most of our laboratories in the developing worlds are not equipped to make rapid diagnoses of viral hemorrhagic fever viruses, bio-samples are usually sent to designated laboratories with the capacity to run the necessary tests like serology, PCR, Immunohistochemistry, viral isolation and electron microscopy of VHFs[3].

The clinical evaluation for VHFs includes complete blood count with differential, comprehensive metabolic panel, type and cross, coagulation studies, liver function tests, as well as evaluation for bacterial infections with urinalysis, urine culture, Chest X-ray, and blood cultures. Serological testing for virus-specific IgM and IgG can be helpful but it is not as sensitive or specific as molecular-based testing. Reverse transcriptase-polymerase chain reaction and

virus isolation through cell culture are the methods that can be used for the diagnosis of VHF [12]

1.7: Some Recommended Treatment Options for VHF

Generally, patients diagnosed with VHF received supportive therapy, with special attention to maintaining fluid and electrolyte balance, circulatory volume, and blood pressure and treating for any complications [3]. There are no established treatment options. Vaccines like Ribavirin have been effective in treating some patients with Arenaviridae and Bunyaviridae but have not been successful in treating Filoviridae or Flaviviridae infections. Treatment with convalescent-phase plasma has been successful in some patients with Junín, Machupo and Ebola [3]. If an infection with VHF is suspected, such a case should be immediately reported to the healthcare authorities and strict isolation of the patient is also advised [3].

Appropriate care and management of individuals suspected of having viral hemorrhagic fever include early diagnosis to increase the chances of survival and prevent nosocomial infections[12]. It is very important to note the patient's travel history, especially patients presenting with symptoms suggestive of VHFs should immediately be isolated. All the healthcare personnel caring for such a patient must wear appropriate protective gear (viral hemorrhagic fever isolation precaution) [12]. The main thrust for the treatment of VHFs is supportive care. Some specific treatment regimens for the treatment of VHFs include; Ribavirin has been shown to improve treatment outcomes for Lassa fever when administered at an early stage of the disease course, although, there is limited empirical pieces of evidence [12,18]. Newer drugs like Favipiravir and LASV-specific monoclonal antibodies are currently being evaluated. There is currently a lack of effective vaccines for Lassa fever. For Crimean-Congo hemorrhagic fever, the treatment largely remains supportive. Ribavirin has demonstrated an antiviral effect against this virus in vitro, there are also no effective vaccines for humans[19]. Ebola virus disease and Marburg Hemorrhagic fever treatment involve mainly supportive care. There are also no current effective vaccines for the Marburg virus. Currently, the Food and Drug Administration has approved one vaccine for the Ebola vaccine against the Zaire Ebola virus[12,19-21]. Dengue fever also has no effective antiviral regimes available for treatment, thus, the management involves supportive. There is currently one vaccine that is available for Latin America and Southeast Asia, however, the WHO has recommended that it only be given to individuals who have a previous history of dengue infection[12,22,23].

1.8: Outbreak Control and Prevention of VHF

Prevention of VHF is first by avoiding contact with the host species. Most of the VHF host are rodents, controlling the rodent populations, discouraging their entry into homes and safe clean-up of nesting areas and droppings. For the VHFs that are spread by arthropods, prevention should involve a community-wide insect and arthropod control. The use of insect repellent, proper clothing, use of treated bed nets, window screens, and other insect barriers to avoid being bitten[3].

The only licensed vaccine is for yellow fever, which is a live vaccine that is safe and effective against yellow fever and gives immunity that lasts for up to 10 years or more. Other vaccines are still under study for other hemorrhagic fevers like the Junin virus which also protects against the Machupo virus. Other vaccines are also being developed for Rift Valley fever, Hantavirus and Dengue. One of the reliable ways of controlling an outbreak is the isolation of infected persons to prevent person-to-person transmission using protective apparel is also very essential to reduce transmission between people[3]. The World Health Organization (WHO) and the Centre for Disease Control (CDC) document for Infection Control for Viral Hemorrhagic Fevers in African Healthcare Settings, which is a practical hospital-based guideline is also a reliable document that can help healthcare facilities recognize cases and prevent further transmission of other hospital-based diseases using the locally available resource at their disposal. Other recommendations include the proper use of disinfectants, and proper disposal of instruments and equipment used in treating or caring for VHF. All disposables including linens should be placed in a

double plastic bag and saturate with 0.5% sodium hypochlorite (1:10 dilution bleach). all sharps should be carefully placed in the sharp container and saturated with 0.5% solution wipe the containers with 0.5% solution and send them to be incinerated [2,3].

To prevent transmission of the VHF pathogens to the healthcare professionals involves three tiers of hierarchy of controls [17]. the standard approach to controlling workplace hazards involves using physical engineering controls that can remove or reduce exposure to the hazards; secondly, administrative controls that involve management policy and work practice training; then, the personnel protective equipment (PPE), a supplementary method when engineering and administrative controls alone cannot provide sufficient protection. The effective use of PPE requires comprehensive supporting programs for medical evaluation and training of employees and proper selection, fit, maintenance and storage of equipment [17,24].

Several radiological investigations are carried out for patients with VHFs, among them are ultrasonography of the abdomen and the thorax, Computed Tomography (CT) scan of the head, chest or abdomen, plain chest radiography, or a combination of the above radiologic investigation [25]. For the sonographic examinations, the thoracic scanning is usually perfumed with the patient either sitting erect or in a supine position, using the inter-costal and the sub-costal approach to evaluate both the pleural spaces, using both the convex and linear probes for proper assessment not to miss out on any pleural effusion. Abdominal ultrasound scans are done after 4-6 hours of fasting for proper distension of the gall bladder. Patients with gall bladder wall thickness of greater than 3mm as measured on the ultrasound are positive for gall bladder wall oedema [25]. Computed Tomography scans are carried out with the patient supine on the CT couch. Plain chest radiographs are routinely requested by clinicians to monitor the progress and involvement of thoracic organs like the heart, lungs and vessels [25,26].

Conclusion

Radiographers as front-line health care workers who have primary contacts with patients in radiology even in events of infectious disease outbreaks such as viral hemorrhagic fevers as highlighted in this piece or the recent global pandemic COVID-19 as recently witnessed around the globe. Thus, a need to ensure strict compliance with infectionn prevention and control measures and radiation protection principles in our care for patients during health emergencies.

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