

**SCHOOL OF PUBLIC HEALTH
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA, LEGON**



**DETERMINANTS OF EBOLA VIRUS DISEASE INFECTION
AMONG HEALTHCARE WORKERS, MONTSERRADO COUNTY,
LIBERIA**

BY

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**THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF
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APPLIED EPIDMIOLOGY AND DISEASE CONTROL**

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DECLARATION

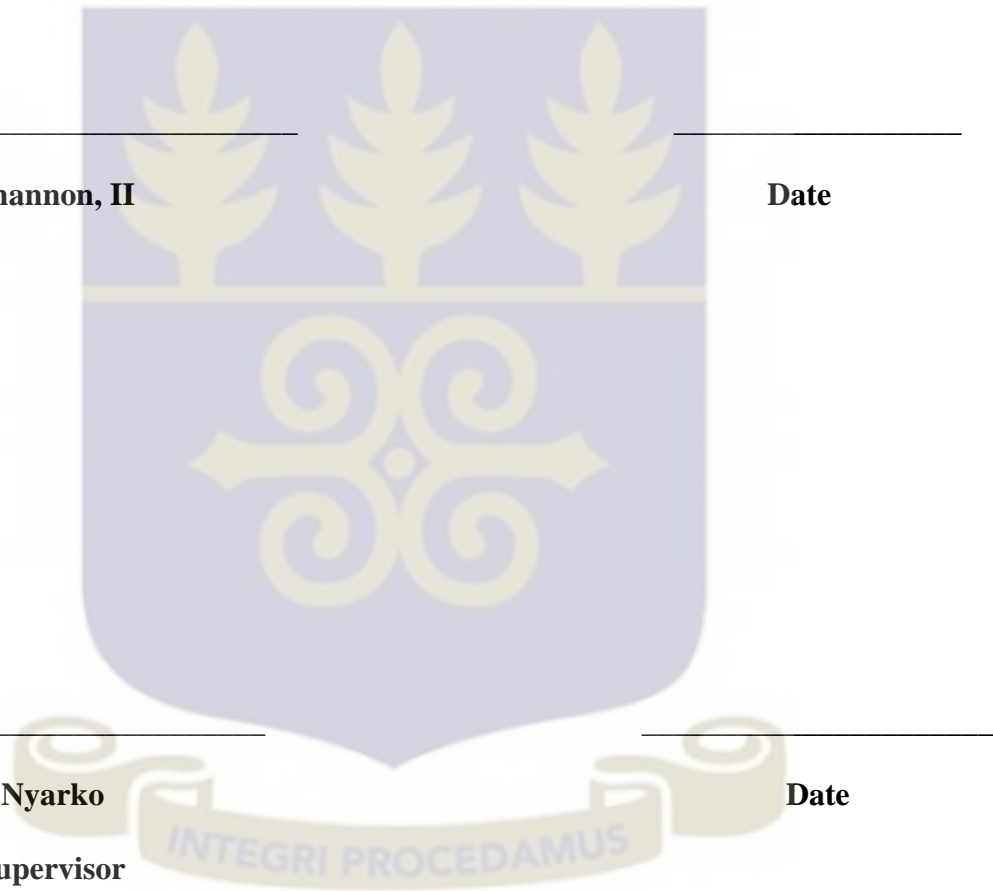
I, Fulton Q. Shannon, II hereby declare that apart from the references to other people's works, which have been duly acknowledged, this dissertation is a result of my independent work. I further declare that this dissertation has not been submitted for award of a degree in this institution and other universities elsewhere.

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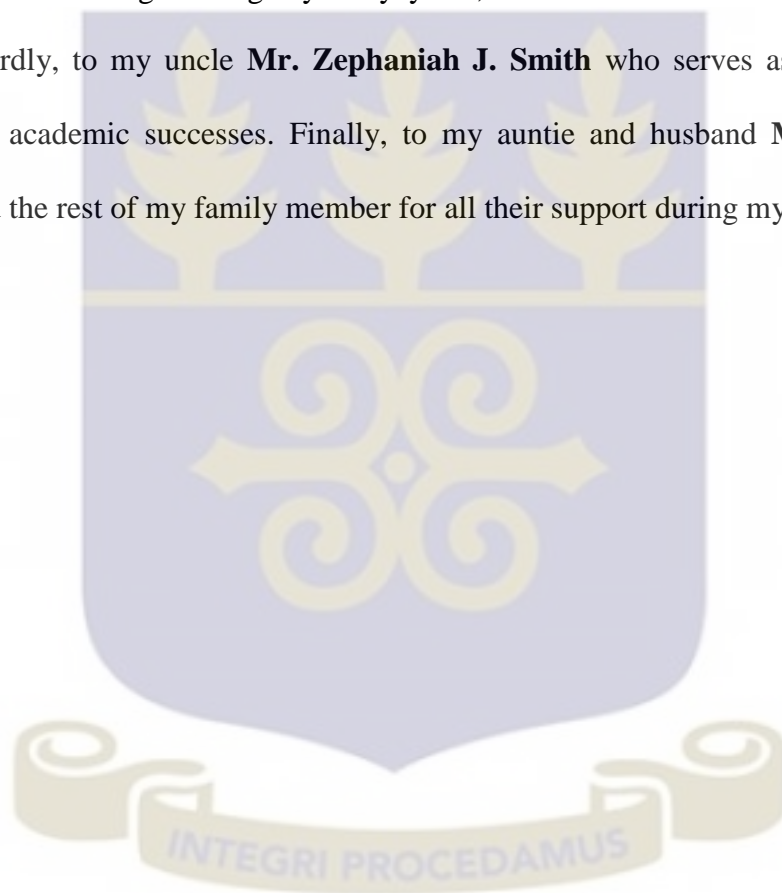
Dr. Kofi M. Nyarko
Academic Supervisor

Date



DEDICATION

I want to firstly dedicate this paper to my wife, Mrs. **Marnijina M. Shannon** and daughter, **Quennell N. Shannon** who I left home to pursue this degree; especially to my wife who tirelessly supported me even in some of our most challenging moments. Secondly, to my mother, **Ms. Tete Smith** for her endless support going back to my early school years, up to this level and also to my grandparents, **Mr. & Mrs. John W. Smith**, for their sound teachings during my early years, to which I can attribute my desire to succeed. Thirdly, to my uncle **Mr. Zephaniah J. Smith** who serves as a yard-stick to measure my academic successes. Finally, to my auntie and husband **Mr. & Mrs Lee Samuels** and the rest of my family member for all their support during my studies.



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ABSTRACT

Background: Ebola Virus Disease (EVD) is a zoonotic and fatal illness. The fatality rates in outbreaks have ranged from 25% to 90%. An outbreak of EVD hit West Africa in 2014, especially Guinea, Liberia and Sierra Leone; claiming more than 2000 lives, including 881 health care workers. EVD caused about 378 cases and 192 deaths among healthcare workers in Liberia; Montserrado County was the hardest hit with over 90 cases and about 60 deaths. This research determined risk factors associated with Ebola Virus Disease infection among health workers in Montserrado County.

Method: An unmatched case control study design was employed. It involved 168 participants (42 cases, and 126 controls). The study covered the period from May 2014 to May 2015. Cases (selected from health workers survivor database) included all healthcare workers reported as confirmed EVD cases in the Epi-surveillance and survivor database within the period of the outbreak. Controls included healthcare workers working (within the same one year period) in the same health facility or environment as the case subjects but did not have EVD. Self-administered questionnaires were employed. Data entry and analysis was conducted using Epi Info version 3.4.5.

Result: Mean age of the study participants was 31.6 years (std. dev 7.1). The odds of being exposed to EVD in a health facility was 5.3 (CI 2.2-12.9) times higher in the cases compared to the controls. Maternity ward (OR 6.6, CI 2.1-21.0) and inpatient room/ward (OR 5.2, CI 1.9-14.1) were the places with the highest and significant odds of exposure to EVD in cases compared to their controls. Functions which had very high and significant odds of exposure among the cases compared to their controls included providing injection (OR 29.4, CI 3.5-243.4), placing intravascular device (OR 18.4, CI 4.9-68.7), providing medication (OR 16.9, CI 3.5-82.1), and emptying bedpan (OR 12.4, CI 2.5-62.4). Hand hygiene and wearing of Personal Protective Equipment (PPE) was relatively poor.

Conclusion & Recommendations: Health care workers were at high risk for EVD infection during service provision especially when providing injection, placing intravascular device, providing medication, and emptying bed pan. Therefore, the need to address these risks and others cannot be overemphasized, as measures to prevent and manage future outbreaks and consequences that come along. Thus health authorities at all levels must ensure heightened vigilance and improved occupational safety measures, especially in the health facilities to prevent and manage EVD infection among health care workers.



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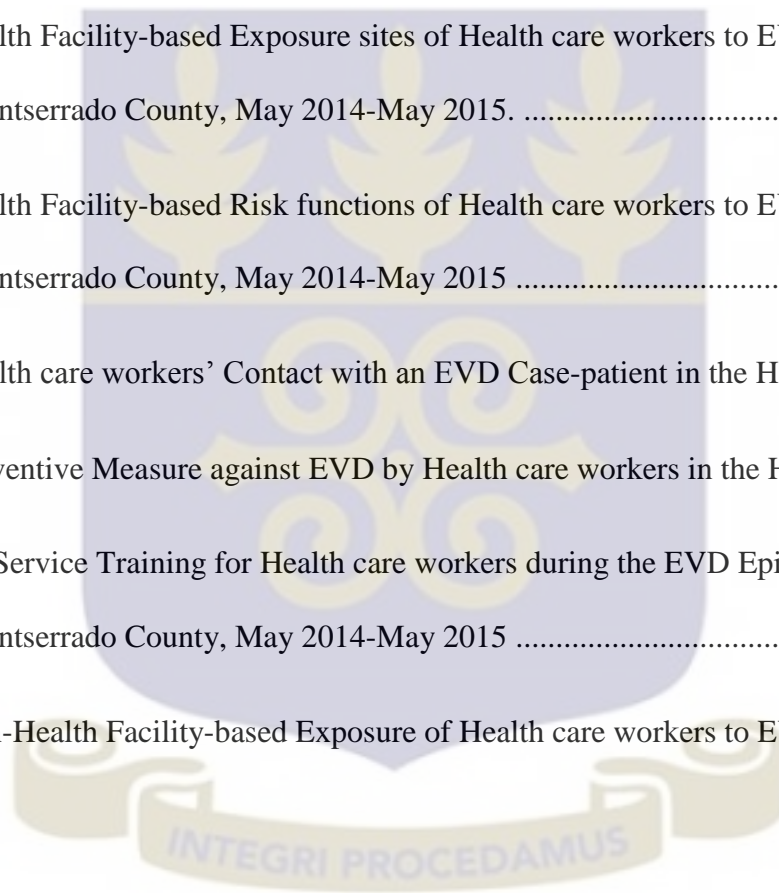
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LIST OF ABBREVIATIONS

CDC	Center of Disease Control and Prevention
EVD	Ebola Virus Disease
IPC	Infection Prevention and Control
OR	Odds Ratio
UL-PIRE	University of Liberia- Pacific Institute for Research and Evaluation
WHO	World Health Organization

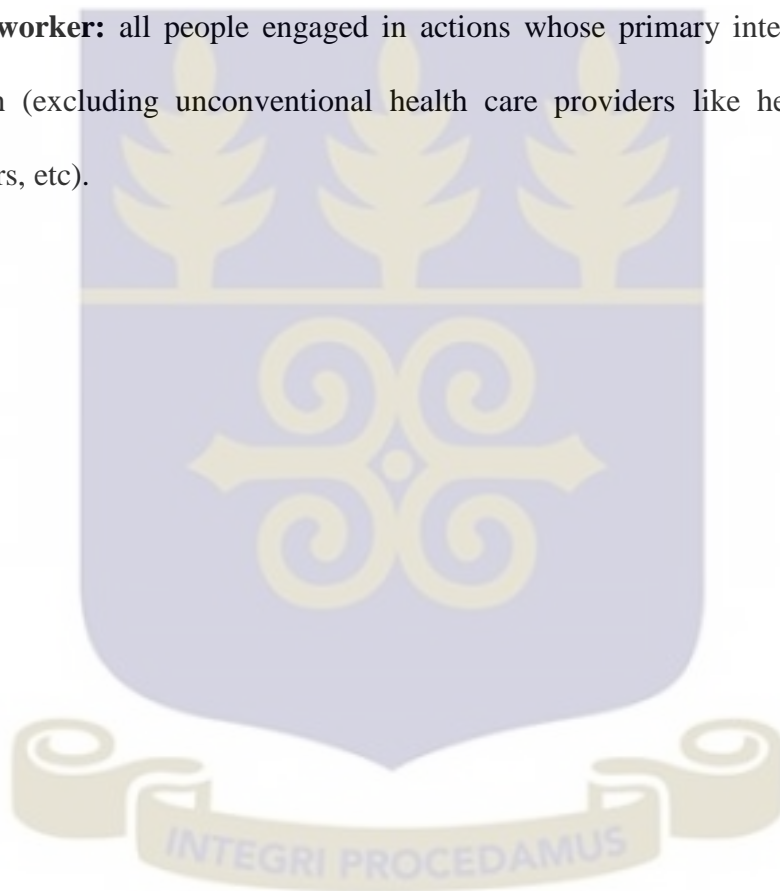


DEFINITION OF TERMS

Case: all healthcare workers in the study areas with history of confirmed Ebola Virus Disease infection.

Control: all healthcare workers in the study areas who work in a health facility where a case is selected and was working during the period of the outbreak and are negative for EVD.

Healthcare worker: all people engaged in actions whose primary intent is to enhance health (excluding unconventional health care providers like herbalist, spiritual healers, etc).



CHAPTER ONE

INTRODUCTION

1.1 Background

Ebola virus disease (EVD) is a fatal disease caused by the Ebola virus and belongs to the family Filoviridae and genus Ebolavirus. The first known human outbreak of EVD occurred simultaneously in northern Democratic Republic of Congo (formerly Zaire) and southern Sudan in 1976. The reservoir for the virus has not been clearly established although investigations conducted by researchers over time gives a suspicion that bats are potential reservoirs. (Oduyayo, 2015). The name ebola originated from the Ebola River in Zaire where the virus was first identified.

The most recent EVD epidemic started in December 2013 where nine countries (Liberia, Guinea, Sierra Leone, Nigeria, Mali, Senegal, United States, United Kingdom, & Spain) in three (3) continents (Africa, Europe, & North America) were affected. The three main countries that were greatly affected are Liberia, Guinea and Sierra Leone. In Guinea, Liberia and Sierra Leone, about 28,000 cases including suspected, probable and confirmed cases with over 11,000 deaths were recorded by August 26, 2015 (WHO 2015).

Since the Ebola epidemic started in Guinea, Liberia and Sierra Leone, healthcare workers have died at a higher rate compared to any other population group, worsening the shortage of skilled personnel in countries that already had inadequate trained health personnel. As of May 2015, 0.11% of Liberia's entire general population had died due to Ebola, as compared with 8.07% of its health workers, defined in the study as doctors, nurses and midwives. In Sierra Leone, the loss was 0.06% of the general population compared with

6.85% of the health workers, while 0.02% of Guinea's overall population had died compared with 1.45% of all health workers (World Bank, 2015).

The recent epidemic has a caustic nature and can be attributed to several interconnecting causes, including infection and death of health workers, traditional funeral practices, fear, poverty, and international indifference (Odotayo et.al, 2015).

Transmissions of EVD among health care workers do occur when appropriate precautions, like proper protection (e.g. wearing PPEs), are not taken while providing health care services to infected person(s) (Olowookere et al., 2015).

The disease spread so fast among health workers that it greatly hindered the control of the outbreak. Liberia, Guinea and Sierra Leone recorded 840 confirmed cases and 491 deaths related to EVD among health workers (World Health Organization et.al, 2015). Due to the high risk of infection among health workers, it was challenging for World Health Organization to recruit adequate number of medical practitioners to work in areas highly affected by the outbreak.(World Health Organization et.al, 2015)

This research determined risk factors associated with Ebola Virus Disease infection among health workers in Montserrado County during the EVD epidemic in Liberia.

1.2 Problem statement

Healthcare workers are usually at high risk of being infected whether working in or outside a health facility. Consequently, working in an EVD outbreak setting amplifies the

risks of health care workers being infected. In August 2014, over 240 health workers in Guinea, Liberia, Nigeria, and Sierra Leone contracted EVD and more than 120 died as the result of the disease (World Health Organization & others, 2015).

In Liberia, EVD infection among healthcare workers in Montserrado County was also unprecedented with over 90 confirmed cases and more than 60 deaths, according to the EVD database at the Montserrado County Health Team Office.

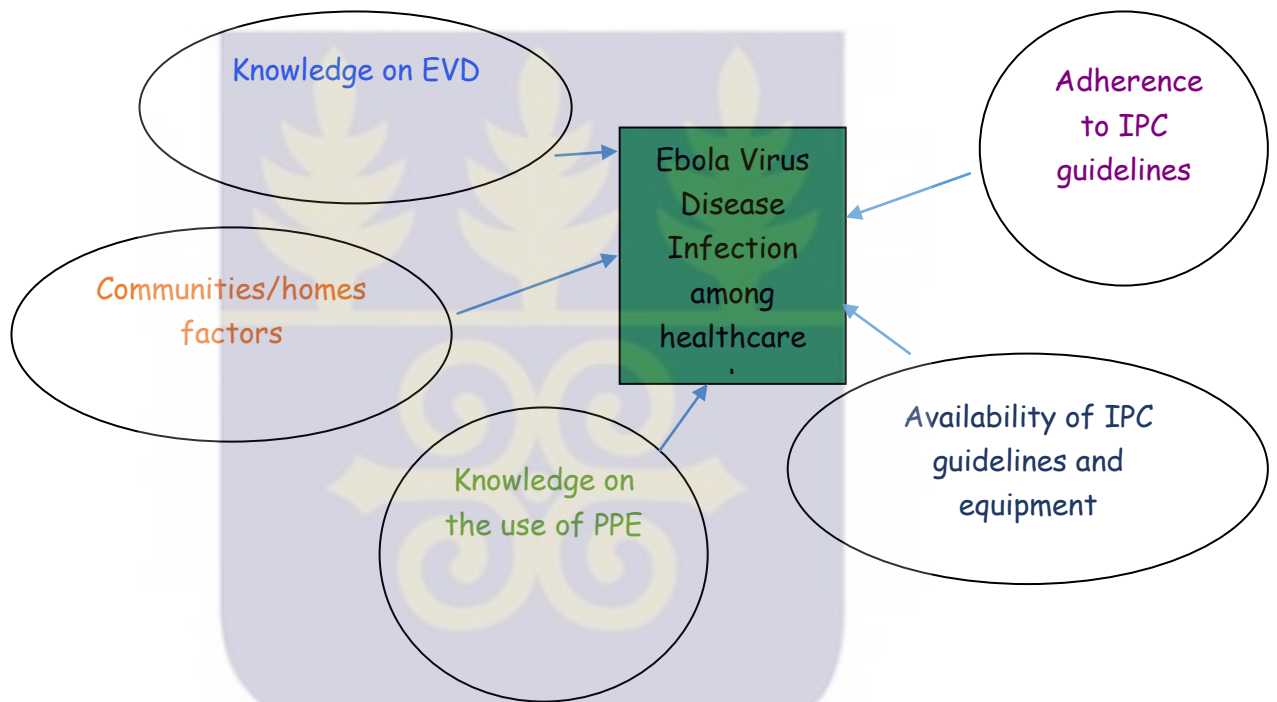
Gaps in knowledge, and failure of healthcare workers to practice “good” occupational safety measures as well as poor implementation of infection prevention and control guidelines and equipment predisposed them to being infected with EVD (Olowookere et al., 2015). Additionally, the lack of training in infection prevention and control might also influence healthcare workers’ infection with diseases including EVD.

Prior to the 2014–2015 Ebola outbreaks, infection prevention and control (IPC) activities in Liberian healthcare facilities were basic. There was no national IPC guideline, nor dedicated staff at any level of government or private healthcare facility to ensure the implementation of best practices. Efforts to improve IPC early in the outbreak were ad hoc and messaging was inconsistent. At the height of the outbreak, a national IPC Task Force was established with a mandate to coordinate IPC response activities; including standardized messaging and IPC training (Cooper, Fisher, Gupta, MaCauley, & Pessoa-Silva, 2016).

If the factors responsible for the infection of healthcare workers are not addressed properly, the risk of them being infected with EVD, especially during an outbreak remains very high.

1.3 Conceptual Framework on Determinants of Ebola Virus Disease

Figure 1: Conceptual Framework on Determinants of Ebola Virus Disease



This Conceptual Framework attempts to explain factors that influence health workers exposure to the Ebola Virus Disease. The factors, as display above, include availability of IPC guidelines and equipment, Knowledge on the use of PPE, adherence to IPC guidelines, Community/home factors, and Knowledge on EVD.

The frame work points out that the lack of IPC guidelines and equipment for healthcare workers when providing service for EVD patients predisposes them to EVD infection. These guidelines and equipment enforce the practice of standard precaution at the job site. Standard precautions require that health care workers assume that the blood and body

substances of all patients are potential sources of infection, regardless of the diagnosis, or presumed infectious status. Additional precautions are needed for diseases transmitted by droplets and contact. The guidelines are usually developed to assist infection control practitioners in the integrated management of health facility based infections prevention and control as well as outside of the health facility during an outreach exercise and/or during an outbreak, like in this case, EVD outbreak and to ensure that health care administrators understand the significance of infection control programmes. The need to have IPC guidelines and equipment available to healthcare worker at all time during service provision cannot be overemphasized as their absence lead to exposure to infections such as EVD. Personal protective equipment includes: gloves; protective eye wear (goggles); mask; apron; gown; boots/shoe covers; and cap/hair cover.

The framework explains that knowledge on the proper use of PPEs is very crucial. Using personal protective equipment provides a physical barrier between micro-organisms and the wearer. It offers protection by helping to prevent micro-organisms from: contaminating hands, eyes, clothing, hair and shoes; being transmitted to other patients and staff. However, if healthcare personnel lack the knowledge on how to properly use PPEs, they still remain exposed despite their use of the equipment. Example, a healthcare worker may put on a glove for a procedure and after use, he/she takes off the glove in the wrong way, thereby contacting substances from an infected patient. This leads to infection in that healthcare worker. Personal protective equipment should be used by healthcare workers who provide direct care to patients and who work in situations where they may have contact with blood, body fluids, excretions or secretions; support staff including medical aides, cleaners, and laundry staff in situations where they may have contact with

blood, body fluids, secretions and excretions; laboratory staff, who handle patient specimens.

Even with the availability of IPC guidelines and equipment, and knowledge on the use of PPEs, healthcare worker sometimes tend not to adhere to these guidelines. Therefore the lack of adherence to infection prevention and control guidelines among health care workers has a number of consequences including increased exposure to and infection with diseases such as Ebola. Nosocomial infections, such as EVD present a serious cause for concern due to attendant morbidity and potential mortality, therefore preventing it among patients and even healthcare workers themselves is of critical importance.

The framework also shows that lack knowledge on EVD plays a role in healthcare workers being exposed to EVD infection. Knowledge on EVD is very crucial for healthcare workers in the line of work to manage and treat patients especially in an outbreak setting. In order to properly do their job and avoid being infected with EVD, healthcare worker must know the clinical signs and symptoms, as well as the media of transmission of EVD to accomplish the aforementioned. Ebola was not a familiar disease to many healthcare workers in West Africa prior to the epidemic. Some of the clinical signs and symptoms are similar to some of the endemic disease in West Africa; hence it put healthcare workers in massive danger during the early days of the epidemic. Without a good knowledge on EVD, one may easily mistake EVD for malaria or cholera, thereby not following the necessary precautionary measures unique to EVD prevention, thereby possibly resulting into infection.

Communities/homes are some of the major exposure sites for EVD infection. This is because in the community and at home, there is little or no attention given to IPC. At this level, there usually no IPC guidelines and equipment, thus services are provided mostly without protective barriers. Therefore, the framework points out that healthcare workers who provide healthcare services at home (a breach of policy and regulations) are exposed to EVD infection in communities/homes.

1.4 Justification

Understanding the determinants of EVD among healthcare workers is crucial for its prevention and control while they are providing health care services. Therefore, the need to understand the nature of EVD cannot be overemphasized as healthcare workers are faced with risks while providing health care services at all times, especially during outbreak without the necessary precautionary safety measures.

However, very little is known about EVD risk factors among healthcare workers in Liberia and the magnitude of their contribution to the overwhelming infection of EVD among healthcare workers in Montserrado County.

Findings from this study may help to identify risk factors for EVD infection among health workers in Liberia which may be used to advocate for the alleviation of these risks while providing health care services at all times, through the development and implementation of policies, strategies and guidelines at all levels of the health system.

1.5 Objectives

1.5.1 General objective

- To determine risk factors associated with the infection of Ebola Virus Disease among healthcare workers in Montserrado County

1.5.2 Specific objectives

- To determine healthcare workers' behavioral risk factors for EVD infection
- To determine health facility-based risk factors for EVD infection
- To determine non-health facility based risk factors for EVD infection
- To determine healthcare worker functions that are predictors of high risk for EVD infection



CHAPTER TWO

LITERATURE REVIEW

2.1 The Ebola Virus

The Ebola Virus Disease is a severe and mostly deadly zoonotic infection especially in humans. EVD is part of a group of diseases known as viral haemorrhagic fevers. There are five species of the Ebola Virus Disease: Zaire ebolavirus, Sudan ebolavirus, Tai Forest ebolavirus, Bundibugyo ebolavirus, and Reston ebolavirus. The species responsible for the epidemic in West Africa is the Zaire ebolavirus. This was the largest outbreak of Ebola since its discovery in 1976. One of the most common ways that Ebola can be transmitted is by close contact with body fluids of infected persons or animal. The incubation period after infection with EVD is usually 5-9 days, but a person infected usually gets infectious and develop symptoms between 1-21 days. Initially it is non-specific, which makes early clinical diagnosis complicated. Case fatality of EVD in human is usually high depending on the species of Ebola virus and quality of supportive care available (Beeching, Fenech, & Houlihan, 2014).

EVD was initially thought to be acquired by exposure to body fluids or tissue from infected animals, such as bats and non-human primates; nevertheless, the natural reservoir and mode of transmission to humans has not been confirmed. Testing of reservoir competence in laboratory shows that successful infection is possible in bats and rodents, but not in plants or arthropods (Beeching et al., 2014).

Since the first outbreak of EVD in 1976, there has been over twenty (25) different outbreaks involving different species with case fatality rate ranging from 0% to 100% (CDC, 2016)

Over the years, a total of five species of Ebola have been isolated. With the exception of Ebola Reston, all other species are known to cause Ebola Hemorrhagic fever in humans. (CDC, 2015).

Since Ebola virus was first identified more than 30 years ago, tremendous progress has been made in understanding the molecular biology and pathogenesis of this virus. However, the means by which Ebola virus is maintained and transmitted in nature remains unclear despite dedicated efforts to answer these questions. Recent work has provided new evidence that fruit bats might have a role as a reservoir species, but it is not clear whether other species are also involved or how transmission to humans or apes takes place (Groseth, Feldmann, & Strong, 2007). Two opposing hypotheses for Ebola emergence has surfaced; one of long-term local persistence in a cryptic and infrequently contacted reservoir, versus another of a more recent introduction of the virus and directional spread through susceptible populations. Nevertheless, with the increasing frequency of human filovirus outbreaks and the tremendous impact of infection on the already threatened great ape populations, there is an urgent need to better understand the ecology of Ebola virus in nature (Groseth et al., 2007).

2.2 Structure and replication cycle of Ebola Virus

Ebola virus is a negative-sense RNA virus (NSV) and it causes a severe hemorrhagic fever in humans and nonhuman primates. The virus is classified as a biosafety level 4 (BSL4) agent, hence working with infectious Ebola virus is therefore restricted to a few recognized maximum-containment laboratories (Watt et al., 2014)

The Ebola virus genome consists of a single 19 kb strand of negative sense RNA consisting seven viral genes which are transcribed by the presence of the viral RNA polymerase in the virion. The single strand of RNA is covered by helically arranged viral nucleoproteins NP and VP30, which are linked by matrix proteins VP24 and VP4 to the lipid bilayer that coats the virion (Beeching et al., 2014).

Replication of the RNA genome starts with the fusion of a positive-sense replicative intermediate, the antigenome, which is the reverse complement of the RNA genome. The antigenome, in turn, serves as a template for the generation of new genomes. Both the genomes and the antigenomes are encapsidated by the nucleocapsid proteins. The replication and transcription processes of EVD have been investigated using reconstituted replication and transcription systems based on the simultaneous expression of the nucleocapsid protein genes and a virus-specific minireplicon in transfected cells (Mühlberger, 2007).

Tissue invasion occurs through infected fluid coming into contact with breaks in the mucosa or skin. This can occur with animal to human or human to human transmission. Monocytes, macrophages, and dendritic cells are the preferred replication sites for filoviruses on initial infection. Infected cells migrate to the regional lymph nodes, liver, and spleen, thereby disseminating the infection. (Beeching et al., 2014).

2.3 Diagnostic methods for EVD

In outbreaks of EVD, infections are confirmed by various laboratory diagnostic methods. These include virus isolation, reverse transcription-PCR (RT-PCR), including real-time quantitative RT-PCR, antigen-capture enzyme-linked immunosorbent assay (ELISA),

antigen detection by immunostaining, and IgG- and IgM-ELISA using authentic virus antigens. Histological techniques, including antigen detection by immunohistochemical analyses, are sensitive methods, particularly for postmortem diagnosis. Diagnosis by detection of virus antigens is suitable for patients in the early stage of illness, while serological diagnosis by the detection of specific IgM and IgG antibodies is suitable for patients in a relatively late stage of illness. The former is especially suitable for patients who die before an antibody response is mounted (Saijo et al., 2006). Diagnostics for viral hemorrhagic fevers, including EVD, must be sensitive, specific, and reliable because misdiagnosis of viral hemorrhagic fevers may bring huge turmoil to society. Therefore, the diagnosis of EVD must not rely on any single diagnostic method. The risk of misdiagnosis must be extremely minimized. In actual EVD outbreak areas, patients with EVD must be isolated. This indicates that a false-positive result will put an individual at unnecessary risk of infection by making the person be placed in a high-risk environment such as an isolation ward (Saijo et al., 2006).

A false-negative result will allow persons who are infected with EVD to be released into the community with the understanding that they do not have viral hemorrhagic fever, when in fact they have the potential to become highly contagious and cause person-to-person transmission of these viruses in the community. In Africa, Lassa fever is also endemic. Therefore, the diagnosis of viral hemorrhagic fevers must rely on multiple diagnostic assays for viral hemorrhagic fevers in a comprehensive manner (Saijo et al., 2006).

Laboratory diagnosis of Ebola Virus Disease is currently performed by virus isolation and serology and can be done only in a few high-containment laboratories worldwide. In 1995,

during the EVD outbreak in the Democratic Republic of Congo, the possibility of using immunohistochemistry (IHC) testing of formalin-fixed postmortem skin specimens was investigated as an alternative diagnostic method for EVD. Fourteen of 19 suspected cases of EVD met the surveillance definition for EVD and were positive by IHC. IHC, serologic, and virus isolation results were concordant for all EVD and non- EVD cases. IHC and electron microscopic examination showed that endothelial cells, mononuclear phagocytes, and hepatocytes are main targets of infection, and IHC showed an association of cellular damage with viral infection (Zaki et al., 1999). The finding of abundant viral antigens and particles in the skin of EVD patients suggests an epidemiologic role for contact transmission. IHC testing of formalin-fixed skin specimens is a safe, sensitive, and specific method for laboratory diagnosis of EVD and is useful for EVD surveillance and prevention (Zaki et al., 1999).

EVD patients treated at Kikwit General Hospital during the 1995 outbreak were tested for viral antigen, IgG and IgM antibody, and infectious virus. Viral antigen could be detected in virtually all patients during the acute phase of illness, while antibody was not always detectable before death (Ksiazek et al., 1999a). Virus was also isolated from patients during the course of their febrile illness, but attempts to quantify virus in Vero E6 cells by standard plaque assay were often unsuccessful. IgG and IgM antibody appeared at approximately the same time after disease onset (8–10 days), but IgM persisted for a much shorter period among the surviving convalescent patients. IgG antibody was detectable in surviving patients through about 2 years after onset, the latest time that samples were obtained. Detection of Ebola virus antigens or virus isolation appears to be the most reliable means of diagnosis for patients with suspected acute EVD, since patients with this

often-fatal disease (80% mortality) may not develop detectable antibodies before death (Ksiazek et al., 1999b).

During the 2 EVD outbreaks in the Republic of Congo in 2003, Formentry et al in 2006 assessed the use of oral fluid specimens versus serum samples for laboratory confirmation of cases of EVD. Serum and oral fluid specimens were obtained from 24 patients with suspected Ebola and 10 healthy control subjects. Specimens were analyzed for immunoglobulin G antibodies by enzyme-linked immunosorbent assay (ELISA) and for Ebola virus by antigen detection ELISA and reverse transcriptase polymerase chain reaction (RT-PCR). Oral fluid specimens were collected with a commercially available collection device.

The study failed to detect antibodies against Ebola in the oral fluid specimens obtained from patients whose serum samples were seropositive. All patients with positive serum RT-PCR results also had positive results for their oral fluid specimens (Formentry et al., 2006).

In November 2007, hemorrhagic fever cases were reported in Bundibugyo District, Western Uganda. Laboratory investigation of the initial 29 suspect-case blood specimens by classic methods (antigen capture, IgM and IgG ELISA) and a recently developed randomprimed pyrosequencing approach quickly identified it to be an EVD outbreak associated with a newly discovered Ebola virus species (Bundibugyo Ebola virus) distantly related to the Côte d'Ivoire Ebola virus found in western Africa. Due to the sequence divergence of this new virus relative to all previously recognized Ebola viruses, these findings have important implications for design of future diagnostic assays to

monitor EVD in humans and animals, and ongoing efforts to develop effective antivirals and vaccines (Towner et al., 2008).

During what was yet the largest outbreak on record of EVD in Uganda from August 2000 to January 2001, the laboratory used antigen capture and reverse transcription-PCR (RT-PCR) to diagnose the string of EVD which caused the infection in suspect patients. The RT-PCR and antigen-capture diagnostic assays proved very effective for detecting EVD in patient serum, plasma, and whole blood. In samples collected very early in the course of infection, the RT-PCR assay could detect ebolavirus 24 to 48 hours prior to detection by antigen capture. More than 1,000 blood samples were collected, with multiple samples obtained from many patients throughout the course of infection. Real-time quantitative RT-PCR was used to determine the viral load in multiple samples from patients with fatal and nonfatal cases, and these data were correlated with the disease outcome. RNA copy levels in patients who died averaged 2 log₁₀ higher than those in patients who survived. Using clinical material from multiple EVD patients, the variable region of the glycoprotein was sequenced. Both sequence and epidemiologic data were consistent with the outbreak having originated from a single introduction into the human population (Towner et al., 2004).

In Sierra Leone, a convenience sample of 100 male survivors of EVD, at different times after their recovery from EVD, and recorded self-reported information about socio-demographic characteristics, the EVD episode, and health status were enrolled in a study. Semen specimens were obtained at baseline and were tested by means of a quantitative reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay with the use of the target-gene sequences of NP and VP40. A total of 93 participants provided an initial

semen specimen for analysis, of whom 46 (49%) had positive results on quantitative RT-PCR. Ebola virus RNA was detected in the semen of all 9 men who had a specimen obtained 2 to 3 months after the onset of EVD, in the semen of 26 of 40 (65%) who had a specimen obtained 4 to 6 months after onset, and in the semen of 11 of 43 (26%) who had a specimen obtained 7 to 9 months after onset; the results for 1 participant who had a specimen obtained at 10 months were indeterminate. The median cycle-threshold values (for which higher values indicate lower RNA levels) were 32.0 with the NP gene target and 31.1 with the VP40 gene target for specimens obtained at 2 to 3 months, 34.5 and 32.3, respectively, for specimens obtained at 4 to 6 months, and 37.0 and 35.6, respectively, for specimens obtained at 7 to 9 months (Deen et al., 2015).

At present, diagnosis of Ebola virus disease requires transport of venepuncture blood to field biocontainment laboratories for testing by real-time RT-PCR, resulting in delays that complicate patient care and infection control efforts. Braodhust et al conducted a field validation of the Corgenix ReEBOV Antigen Rapid Test kit. They performed the rapid diagnostic test on fingerstick blood samples from 106 individuals with suspected Ebola virus disease presenting at two clinical centres in Sierra Leone. They excluded patients with haemodynamic instability and those who were unable to cooperate with fingerstick or venous blood draw. Two independent readers scored each rapid diagnostic test, with any disagreements resolved by a third. They also compared point-of-care rapid diagnostic test results with clinical real-time RT-PCR results (RealStar Filovirus Screen RT-PCR kit 1.0; Altona Diagnostics GmbH, Hamburg, Germany) for venepuncture plasma samples tested in a Public Health England field reference laboratory (Port Loko, Sierra Leone). Separately, a rapid diagnostic test performed (on whole blood) and real-time RT-PCR (on plasma) on 284 specimens (Broadhurst et al., 2015).

In point-of-care testing, all 28 patients who tested positive for Ebola virus disease by RT-PCR were also positive by fingerstick rapid diagnostic test (sensitivity 100% [95% CI 87.7–100]), and 71 of 77 patients who tested negative by RT-PCR were also negative by the rapid diagnostic test (specificity 92.2% [95% CI 83.8–97.1]). In laboratory testing, all 45 specimens that tested positive by RT-PCR were also positive by the rapid diagnostic test (sensitivity 100% [95% CI 92.1–100]), and 214 of 232 specimens that tested negative by RT-PCR were also negative by the rapid diagnostic test (specificity 92.2% [88.0–95.3]). The two independent readers agreed about 95.2% of point-of-care and 98.6% of reference laboratory rapid diagnostic test results. Cycle threshold values ranged from 15.9 to 26.3 for the PCR-positive point-of-care cohort and from 17.5 to 26.3 for the reference laboratory cohort. Six of 16 banked plasma samples from rapid diagnostic test-positive and altona-negative patients were positive by an alternative real-time RT-PCR assay (the Trombley assay); three (17%) of 18 samples from individuals who were negative by both the rapid diagnostic test and altona test were also positive by Trombley (Broadhurst et al., 2015).

The study found that ReEBOV rapid diagnostic test had 100% sensitivity and 92% specificity in both point-of-care and reference laboratory testing in this population (maximum cycle threshold 26.3). With two independent readers, the test detected all patients who were positive for Ebola virus by altona real-time RT-PCR; however, this benchmark itself had imperfect sensitivity (Broadhurst et al., 2015).

A blood sample collected at the hospital before the patient's death was transported to the US Centers for Disease Control/Uganda Virus Research Institute (CDC/UVRI) laboratory

in Entebbe for diagnostic testing by reverse transcription PCR (RT-PCR), antigen-detection ELISA, and IgM for filoviruses as described. Evidence of infection with an Ebola virus of the genus and species *Ebolavirus Sudan ebolavirus* (SEBOV) was detected by RT-PCR and confirmed by antigen-detection ELISA. Results of ELISA IgM against Ebola viruses and all tests for Marburg virus were negative. SEBOV was also isolated from blood on Vero E6 cells at the Viral Special Pathogens Branch, CDC, Atlanta, GA, USA. Overlapping PCR fragment copies of the complete virus genome were amplified, and the nucleotide sequence was obtained as described. Maximum-likelihood phylogenetic analysis confirmed SEBOV and demonstrated that the isolate (Nakisamata isolate, JN638998) was closely related (99.3% identical) to the Gulu SEBOV strain obtained from northern Uganda in 2000. A postmortem diagnosis indicated EVD caused by SEBOV as the cause of the patient's death (Shoemaker et al., 2012).

A study was conducted in the Public Health England EVD diagnostic laboratory in Port Loko, Sierra Leone, using residual diagnostic specimens remaining after clinical testing. EDTA-WB specimens (n = 218) were collected from suspected or confirmed EVD patients between April 1 and July 20, 2015. Buccal swab specimens (n = 71) were collected as part of a national postmortem screening program between March 7 and July 20, 2015. EDTA-WB and buccal swab specimens were tested with Xpert (targets: glycoprotein [GP] and nucleoprotein [NP] genes) and Trombley (target: NP gene) assays in parallel. All whole blood specimens were fresh; 84/218 were tested in duplicate on Xpert to compare whole blood sampling methods (pipette versus swab); 43/71 buccal swab specimens had been previously frozen. In all, 7/218 (3.2%) whole blood and 7/71 (9.9%) buccal swab samples had Xpert results that were reported as “invalid” or “error” and were excluded, leaving 211 whole blood and 64 buccal swab samples with valid

Trombley and Xpert results. For whole blood, 22/22 Trombley-positive samples were Xpert-positive (sensitivity 100%, 95% CI 84.6%–100%), and 181/189 Trombley-negative samples were Xpert-negative (specificity 95.8%, 95% confidence interval (CI) 91.8%–98.2%) (Semper et al., 2016).

The result also showed that seven of the eight Trombley-negative, Xpert-positive (Xpert cycle threshold [Ct] range 37.7–43.4) whole blood samples were confirmed to be follow-up submissions from previously Trombley-positive EVD patients, suggesting a revised Xpert specificity of 99.5% (95% CI 97.0%–100%). For Xpert-positive whole blood samples (n = 22), Xpert NP Ct values were consistently lower than GP Ct values (mean difference –4.06, 95% limits of agreement –6.09, –2.03); Trombley (NP) Ct values closely matched Xpert NP Ct values (mean difference –0.04, 95% limits of agreement –2.93, 2.84). Xpert results (positive/negative) for whole blood sampled by pipette versus swab were concordant for 78/79 (98.7%) whole blood samples, with comparable Ct values for positive results. For buccal swab specimens, 20/20 Trombley-positive samples were Xpert-positive (sensitivity 100%, 95% CI 83.2%–100%), and 44/44 Trombley-negative samples were Xpert-negative (specificity 100%, 95% CI 92.0%–100%) (Semper et al., 2016).

2.4 Clinical signs and symptoms of Ebola Virus Disease

Patients infected with EVD show a nonspecific febrile illness associated with myalgia, which progresses to gastrointestinal symptoms (abdominal pain, nausea, vomiting, and diarrhea). Additionally, in the second week of illness, hemorrhagic symptoms and sepsis may develop in patients (Lyon et al., 2014).

A retrospective, observational study conducted of all patients with suspected or confirmed EVD who were admitted for care in Guinea Conakry shows the common clinical features

presented by patients were nonspecific and included fever, fatigue in patients, and gastrointestinal symptoms with diarrhea and vomiting, headache in patients who were evaluated, and anorexia in patients. The result also showed that at admission, patients had mild tachycardia with a mean systolic blood pressure of 125 ± 25 mm Hg. Hiccups occurred in 28% of patients during the period of hospitalization. The median time from symptom onset to presentation was 5 days (interquartile range, 3 to 7), and the median time from symptom onset to death was 8 days (interquartile range, 7 to 11) (Bah et al., 2014).

Humans are only infectious when they have developed symptoms. Usually, the first symptoms are the sudden onset of fever fatigue, muscle pain, headache and sore throat. They are followed by vomiting, diarrhoea, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding (e.g. oozing from the gums, blood in the stools). Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes (WHO, 2016a).

A systematic review and meta-analysis was conducted to assess the utility of clinical signs, symptoms, and laboratory data in predicting mortality in EVD and found bleeding events, abdominal pain, vomiting, diarrhea, cough, sore throat, and conjunctivitis were more often present in pooled proportion of fatal cases as compared to EVD survivors (Moole et al., 2015).

2.5 Global Burden of Ebola Virus Disease

Emerging infectious diseases (EIDs) are a significant burden on global economies and public health. Their emergence is thought to be driven largely by socio-economic, environmental and ecological factors, but no comparative study has explicitly analyzed

these linkages to understand global temporal and spatial patterns of EIDs. About 335 databases of EID ‘events’ (origins of EIDs) between 1940 and 2004, were analyzed and demonstrated non-random global patterns. EID events have risen significantly over time after controlling for reporting bias, with their peak incidence (in the 1980s) concomitant with the HIV pandemic. EID events are dominated by zoonoses (60.3% of EIDs): the majority of these originate in wildlife (for example, severe acute respiratory virus, Ebola virus), and are increasing significantly over time (Jones et al., 2008).

The EVD outbreak in West Africa was the largest since Ebola virus was first identified in 1976, spreading beyond East and Central Africa to Europe and North America. On August 8, 33 weeks into what was now the longest, largest, and most widespread Ebola outbreak on record, the World Health Organization (WHO) declared the epidemic to be a Public Health Emergency of International Concern (PHEIC). This was based on concerns that the continuing transmission of Ebola in West African communities and health facilities, the high case fatality rate of Ebola virus disease (EVD), and the weak health services of Guinea, Liberia, Sierra Leone, Nigeria, and other neighboring countries at risk for infection (Frieden et al, 2014) .

Given the extensive mobility and air travel in West Africa, EVD could have reached many other countries in the region and beyond. Every day that disease transmission remained uncontrolled, the likelihood of spread to unaffected countries increased (Frieden et al., 2014).

In order to prevent Ebola from crossing borders, travelers leaving West Africa were screened at airports. More than 339,000 people were screened before leaving Guinea, Liberia and Sierra Leone. Exit screening helped to identify those at risk for Ebola and prevent disease transmission to other countries (CDC, 2016).

Over 28,600 cases and 11,300 deaths (including suspected, probable and confirmed) of EVD was reported as of March 2016. However, the International Health Regulations (2005) Emergency Committee regarding Ebola virus disease (EVD) in West Africa met on 29 March 2016 for a ninth time. In that meeting, the WHO Director-General declared the end of the Public Health Emergency of International Concern regarding the Ebola virus disease outbreak in West Africa on the basis of the Committee's advice and her own assessment of the situation. The Committee also noted that since its last meeting Guinea, Liberia, and Sierra Leone have all met the criteria for confirming interruption of their original chains of Ebola virus transmission. It was also noted although new clusters of EVD cases continue to occur as expected, including a recent and ongoing cluster in Guinea, all clusters to date have been detected and responded to rapidly (WHO, 2016).

2.6 Ebola Virus Disease Outbreak in West Africa

The complex and unprecedented Ebola epidemic which occurred in West Africa has highlighted the need to review the epidemiological characteristics of Ebola Virus Disease (EVD) as well as our current understanding of the transmission dynamics and the effect of control interventions against Ebola transmission. A review of key epidemiological data from past Ebola outbreaks and carry out a comparative review of mathematical models of the spread and control of Ebola in the context of past outbreaks and the epidemic in West

Africa, it was shown that mathematical modeling offers useful insights into the risk of a major epidemic of EVD and the assessment of the impact of basic public health measures on disease spread. It was also discussed the critical need to collect detailed epidemiological data in real-time during the course of an ongoing epidemic, carry out further studies to estimate the effectiveness of interventions during past outbreaks and the ongoing epidemic, and develop large-scale modeling studies to study the spread and control of viral hemorrhagic fevers in the context of the highly heterogeneous economic reality of African countries (Chowell & Nishiura, 2014).

The outbreak of Ebola Virus Disease (EVD) in West Africa (Guinea Conakry, Liberia and Sierra Leone) caused anxiety, fear and panic for communities in these three countries, the deadliest in years with the majority of deaths occurring in Guinea and Sierra Leone. It was spreading faster than health services could cope, with many people hiding from services, refusing to turn bodies over to burial teams and government systems failing to respond when called upon. People fled to areas they deem safe, carrying the virus and its consequences with them. In addition, deeply rooted cultural practices, such as those around death and burial, contributed to transmission. The WHO was leading the response to the outbreak, including addressing areas of social mobilization and risk communication (Omidian, Tehoungue, & Monger, 2014).

Phylogenetic analyses indicate that the virus strain in the current outbreak likely originated from Central Africa around 2004. In Sierra Leone, the outbreak is believed to have started from the introduction of two genetically different viruses from Guinea, where people were attending a funeral. These two viruses diverged in Guinea in late April, before they were discovered in Sierra Leone a month later. These sequencing efforts identified 396 genetic

mutations that have occurred over time, including 50 nonsynonymous mutations since separation from the Central African lineage. During this current outbreak, the frequency of nucleotide substitution rates has been approximately two times higher than that observed across all previous Ebola outbreaks from which sequence data were available. Substitutions have been more commonly nonsynonymous, which change the amino acid sequence of the virus and could potentially be correlated with phenotypic changes that might influence outbreak dynamics and virus behavior. While more research is required to understand the effect of increased nonsynonymous mutation rates in the West Africa EVD population, the sustained nature of the outbreak increases the opportunity for further change in the virus, with uncertain consequences. However, as yet, similarity in outbreak characteristics (including R_0 , symptoms, incubation time, serial time) between the West Africa 2014 outbreak and previous Ebola outbreaks suggests that there has not been any significant change in the virus affecting transmissibility. Rather, outbreak progression appears to be more strongly influenced by the urban setting of the outbreak and other socioeconomic features (Alexander et al., 2015).

Guinea notified the World Health Organization on March 23, 2014, of an outbreak of Ebola virus disease (EVD), although it is said the epidemic began in December 2013. Nine months later (by mid-September), after the first case had occurred, the numbers of reported cases and deaths had grown from week to week despite multinational and multisectoral efforts to control the spread of infection. The epidemic became so large that the three most-affected countries (Guinea, Liberia, and Sierra Leone) were faced with enormous challenges in implementing control measures at the scale required to stop transmission and to provide clinical care for all persons with EVD (WHO, 2014).

On December 18, 2014, the Guinea Ministry of Health was notified by local public health authorities in Kissidougou, a prefecture in southeastern Guinea (pop. 284,000), that the number of cases of Ebola virus disease (Ebola) had increased from one case reported during December 8-14, 2014, to 62 cases reported during December 15-21. Kissidougou is one of the four Guinea prefectures (the others are Macenta, Gueckedou, and Conakry) where Ebola was first reported in West Africa in March 2014, and the mid-December increase was the largest documented by any prefecture in Guinea in a single week since the beginning of the epidemic. The Guinea Ministry of Health requested assistance from CDC and the World Health Organization to investigate the local outbreak, identify and isolate persons with suspected Ebola, assess transmission chains, and implement control measures. The investigation found that 85 confirmed Ebola cases were linked to one traditional funeral ceremony, including 62 (73%) cases reported during December 15-21. No additional cases related to this funeral ceremony were reported after January 10, 2015. After the outbreak was identified, rapid implementation of interventions limited additional Ebola virus transmission. Improved training for prompt reporting of cases, investigation, and contact tracing, and community acceptance of safe burial methods can reduce the risk for Ebola transmission in rural communities (Victory et al., 2015).

According to Dr. Margaret Chan, Director General of the World Health Organization, the single answer for why the outbreak of Ebola virus disease in West Africa was so large, so severe, and so difficult to contain was “*poverty*”. The three countries hardest-hit are among the poorest in the world. “*They have only recently emerged from years of conflict and civil war that have left their health systems largely destroyed or severely disabled and, in some areas, left a generation of children without education. In these countries, only one or two doctors are available for every 100,000 people, and these doctors are*

heavily concentrated in urban areas. Isolation wards and even hospital capacity for infection control are virtually nonexistent". Additionally, fear was the most difficult barrier to overcome. It caused people who have had contact with infected persons to escape from the surveillance system to relatives to hide symptomatic family members or take them to traditional healers, and patients to flee treatment centers (Chan, 2014).

EVD also spread to other West African countries like Nigeria, Senegal, and Mali.

In July 2014, Nigeria reported its first case of EVD. The Nigerian index case had visited and cared for a sibling in Liberia who died from the disease on 8 July 2014. Despite being aware of his exposure to Ebola virus in Liberia, the index case flew from Liberia to Lagos, Nigeria, on a commercial airplane on 20 July 2014, with a stopover in Lome, Togo. The case became symptomatic while flying and collapsed at Lagos airport upon landing, which prompted him to seek medical attention and led to a number of people being exposed to Ebola virus. A total of 20 EVD cases (19 laboratory confirmed, one probable) were reported in Nigeria, with no new cases reported since 5 September 2014. All 20 cases stemmed from a single importation from a traveler returning from Liberia on 20 July 2014. Epidemiological investigation revealed that the index case had contracted Ebola virus in Liberia; the patient died on 25 July 2014 (Fasina et al., 2014).

On 30 August 2014, Senegal's Ministry of Public Health and Social Affairs provided WHO with details about a case of Ebola virus disease (EVD) announced in that country on 29 August. WHO also received details of the emergency investigation immediately launched by the Government. Testing and confirmation of Ebola were undertaken by a laboratory at the Institut Pasteur in Dakar. The case was a 21-year-old male native of

Guinea, who arrived in Dakar, by road, on 20 August and stayed with relatives at a home in the outskirts of the city.

On 27 August, authorities in Conakry, Guinea, issued an alert, informing medical services in Guinea and neighbouring countries, that a person, who was a close contact of a confirmed EVD patient, had escaped the surveillance system. That alert prompted testing at the Dakar laboratory, launched an investigation, and triggered urgent contact tracing (WHO, 2014).

In the “Low Ebola” scenario, according to a World Bank report, lost GDP for West Africa as a whole is estimated at \$2.2 billion in 2014 and \$1.6 billion in 2015 (The World Bank Group, 2014). In the case of “High Ebola”, estimates suggest \$7.4 billion in lost GDP for 2014 and \$25.2 billion in 2015 (The World Bank Group, 2014). Both cases assume at least some spread to other countries. Factors contributing to the growing cost of Ebola include direct costs of the illness (government spending on health care) and indirect costs, such as lower labor productivity as a result of workers being ill, dying or caring for the sick. But the majority of the costs stem from the higher costs of doing business within countries or across borders. These are largely due to “aversion behavior”, or changes in the behavior of individuals due to fear of contracting the disease, which has also left many businesses without workers, disrupted transportation and led to restrictions on travel for citizens from the afflicted countries (The World Bank Group, 2014).

2.7 Ebola Virus Disease in Liberia

Ebola Virus Disease (EVD) outbreak was confirmed in Liberia on March 31st 2014. A response comprising of diverse expertise was mobilized and deployed to the country to

contain transmission of Ebola and give relief to people already impoverished from protracted civil war (Kouadio et al., 2015).

In Liberia, for virtually all model parameters, EVD deaths exceeded the expected number of deaths due to the leading non-EVD cause of death (Helleringer & Noymer, 2015). A total of 10,666 cases and 4,806 deaths (including suspected, probable, & confirmed) occurred in Liberia (WHO, 2016).

The President of the Republic of Liberia declared the EVD epidemic a national health emergency on 26th July 2014. A National Response Plan was launched and a National Task force, which included an Incident Management System (IMS), was established to manage all aspects of the response and to coordinate all technical sub-committees as well as County task force. An Ebola Response Team mechanism was adapted from the National Response Team structure, and established. The components included: (1) Case Management teams; (2) Infection Control and Health Promotion teams; (3) Epidemiology/Surveillance teams; (4) Case Investigation teams (5) Contact Tracing teams; (6) Social Mobilization teams; (7) Burial teams; (8) Media and Communication teams; (9) Logistics teams and (9) Security teams (Kouadio et al., 2015).

Montserrado County was the hardest-hit of all the fifteen counties in Liberia. The county is mostly urban. Since Ebola virus spreads through bodily fluid contact from infected persons, overcrowded urban areas may present exceptionally high risk for disease transmission. Over one million individuals and more than 90% of Montserrado County residents live in Monrovia, the nation's capital. Reducing transmission is particularly challenging in Monrovia's West Point slum where over 75,000 people live without

running water, making it impossible to implement WHO-recommended hand-washing when caring for sick household members. The current outbreak posed a mounting threat internationally as witnessed by infected individuals traveling from Monrovia to the United States and to Nigeria, causing an outbreak of at least 19 cases in the latter. The study revealed that for Montserrado, the estimated basic reproductive number (R_0) of 2.49 (Lewnard et al., 2014). This value defines the expected number of cases caused by an infected person in an otherwise susceptible population in the absence of any public health or clinical interventions. This estimate showed that as of 5 October 2014, 7,260 total cases and 2,941 total deaths had occurred, of which the study predicted that 1,975 of the cases and 1,315 of deaths would be reported, respectively. The Liberian Ministry of Health and Social Welfare data reported 1,635 cumulative cases and 1,081 cumulative deaths as of that time. Without expanded control effort beyond levels of 23 September 2014, the model projected 170,996 total cases and 90,122 total deaths by 15 December 2014. Of these, it estimated 42,669 cases and 27,175 deaths will have been reported (Lewnard et al., 2014).

A cohort of inhabitants of a small village and an Ebola hot zone in Sinoe County of Liberia was followed on a day-by-day basis to search for new cases and to minimize the spread of Ebola to the other community members or to other regions. Technical, clinical, and humanistic aspects of the response are discussed in this report. Of the 22 confirmed Ebola cases in Sinoe County since the beginning of outbreak (June 16, 2014), 7 cases were inhabitants of Polay Town, a small village 5.5 miles east of Greenville, the Sinoe County capital. After the last wave of outbreak at the beginning of December, enhanced response activity provided essential coordination and mobilized the resources to stop the epidemic. Despite unprotected contacts in crowded houses, no new cases were detected among the contact families, or in the surrounding houses or communities (Williams et al., 2015).

2.8 Associated risk factors and risk group

Although Ebola virus is transmitted by unprotected physical contact with infected persons, few data exist on which specific bodily fluids are infected or on the risk of fomite transmission (Bausch et al., 2007).

Virus invasion in humans appears to occur through mucosal surfaces, breaks and abrasions in the skin, or parenteral introduction. Route of exposure is important in determining the course of disease. During the 1976 outbreak in the DRC, the incubation period in humans exposed to EVD through injection (in association with unsterilized needle reuse) was shorter than individuals exposed through known contacts (5–9 days, in respect of virus strains circulating in that outbreak). Case fatality rates also differed by exposure route, with 100% mortality among those exposed through injection (85 out of 85) and 80% among cases with known contact (119 of 149). In laboratory studies of EVD infection in nonhuman primates, the disease course was more rapid with exposure through intramuscular or intraperitoneal injection than through aerosol droplets. Aerosol transmission has been identified only in laboratory settings and is thought to be rare or absent in natural outbreaks. Oral and conjunctival EBOV exposure was found to be extremely lethal in experimentally infected rhesus macaques. Additionally, organs from laboratory-infected, nonhuman primates had extremely high infectivity titers (5.5–8.6 log₁₀ pfu/g), indicating that exposure to high infectious doses might occur with consumption (Alexander et al., 2015).

A study was conducted in the Democratic Republic of Congo, with surviving members of 27 households in which someone had been infected with Ebola virus were interviewed in order to define the modes of transmission of EVD.

Of 173 household contacts of the primary cases, 16% developed EVD. All secondary cases had direct physical contact with the ill person, and among those with direct contact, exposure to body fluids conferred additional risk. After adjusting for direct contact and exposure to body fluids, adult family members, those who touched the cadaver, and those who were exposed during the late hospital phase were at additional risk. None of the 78 household members who had no physical contact with the case during the clinical illness were infected. EVD is transmitted principally by direct physical contact with an ill person or their body fluids during the later stages of illness (Dowell et al., 1999).

There is a specific risk for healthcare workers and volunteers, especially if involved in caring for Ebola viral disease patients. However, if the recommended level of precaution for such settings is observed, it should effectively prevent the transmission of the disease (Read, 2014).

An Ebola assessment done in Guinea, Liberia, Nigeria and Sierra Leone revealed that some factors responsible for the high infection rate among health included scarcities of personal protective equipment or/and its incorrect use, as well as limited number of medical staff to manage a huge number of cases. Additionally, the desire of some medical staff to work in “*isolation wards*” beyond the recommended safety hours was also a major factor for infection with EVD (“EVD Situation Assessment.pdf,” 2014).

In Liberia, due to the EVD outbreak, the Ministry of Health (MOH) has heighten vigilance on Infection Prevention and Control (IPC) as a means of preventing and controlling the infection of EVD and other infectious diseases.

Knowledge, like “good” IPC practices and training in IPC plays integral roles in the management and response to outbreaks. A study conducted in Nigeria showed that even with high knowledge of Ebola, health workers who showed “good” practices of IPC were very low (4.5%). The study also revealed that training was a very good predictor of “good” practices. During the Ebola outbreak in West Africa and other continents, Nigeria was a success story in the prevention and control of the outbreak (Oladimeji et al, 2014).

2.9 Infection of Ebola Virus Disease among healthcare workers

Infections among health care workers have played a major role in outbreaks of Ebola virus disease since the virus was discovered in 1976. Available data from past outbreaks show that the deaths of health care workers were the canary in the coal mine signaling that an outbreak of a viral hemorrhagic fever had begun. The Ebola outbreak devastated West Africa is unfortunately no different. In addition to an unprecedented number of total infections and deaths, this outbreak surpassed all previous ones with respect to the number of health care workers infected (Fischer, Hynes, & Perl, 2014).

A study of EVD in healthcare workers was conducted in Guinea. The findings revealed that little could be ascertained about risks factor among health workers (Grinnell et al., 2015). This was due to poor data reporting; a lot of information on exposure was missing from the database. However, health workers were less likely to report funeral attendance and contact with an EVD patient, when compared with the general population. Meanwhile in 2014, the cumulative incidence among health workers aged 15 years and above was reported to be 42.2 times higher than the general population (Grinnell et al., 2015).

In Sierra Leone, funeral attendance, and contact with “*known or suspected Ebola or an ill person*” accounted for 13.8% and 18.2% of EVD infection among health workers respectively (Kilmarx et al., 2014). Furthermore, the study revealed that a broad spectrum of factors were also responsible for EVD infection among health workers in Sierra Leone. They included the lack of Standard Operating Procedures (SOP) as well as clearly assigned responsibilities for infection prevention and control and specialist for infection prevention; inadequate staff and appropriate transport vehicles for patients and corpses. The study further found that improper triage for identifying probable Ebola in patients and corpses, no reexamination of admitted patients to identify new symptoms of Ebola (mostly in children aged <5 years) and delayed lab diagnostic report of cases due to poor turn-around time were responsible for infection with EVD among health workers. In addition, inadequate control of Ebola patient and health workers movement within health facilities, lack of delineation between high-risk and low-risk Ebola zones and limited availability of appropriate personal protective equipment were also mentioned as risk factors for EVD infection. Others included limited hand washing facilities; lack of water and sufficient chlorine supplies; no or inadequate training about and monitoring of personal protective equipment use as well as lack of equipment and materials. Moreover, no or inadequate training about and monitoring of decontamination of transport vehicles and care facility spaces; limited capacity and no or inadequate training about safe management of contaminated waste; and limited capacity and no or inadequate training about safe management and burial of corpses were risk factors for EVD infection in Sierra Leone (Kilmarx et al., 2014).

A Similar study was conducted in Liberia between June-August 2014 among health workers not working in Ebola Treatment Units. The study revealed that the major

determinant for EVD infection among health workers included spill of infected patient blood onto the exposed skin of a phlebotomist, and medical care provided by health workers not using adequate PPE due to initial differential diagnosis. Additionally, inadequate infection control infrastructure, including inadequate protocols, training, materials, and setup contributed to EVD exposure in the non-ETU health care facilities (Matanock et al., 2014).

2.10 Global health security Agenda on Ebola Virus Disease

Emerging diseases such as Ebola pose a growing threat to the global population. A lot of efforts have been put in place to forge new solutions to these emerging global disease threats. Though the International Health Regulations (2005) exists and has kept countries aware of public health risks, and to guide countries to build capacity to help detect, report, and respond to public health events. Unfortunately, countries still struggle with meeting these capacities, fewer than 20% of countries reported in 2012 that they have fully achieved compliance with the International Health Regulations (IHR) and are fully prepared to detect and respond to disease threats, hence the creation of the Global Health Security Agenda, which aims to close this gap (Nussbaum, 2015).

One of the most important non-traditional security issues is health security. When the Ebola virus crossed national borders, it was a clear understanding that the outbreaks in west Africa were a threat to the health security of humanity everywhere around the world as people with infection have travelled across borders within Africa and to Europe and to North America where they have unintentionally caused small chains of transmission far from the epicenter of the outbreak. The Ebola crisis brought under the spotlight, the importance of reducing the vulnerability of societies to infectious disease threats that

spread across national borders. This aspect of health security is collective and has been the focus of attention and the commonly understood conceptualization of health security for centuries. The paradigm today is rapid detection of these events, and rapid response (Heymann et al., 2015).

The Global Health Security Agenda (GHSA) was developed on the 13th of February 2014, with the intents to improve a country's ability to detect, prevent and respond to emerging health threats. The GHSA has eleven (11) action packages under detection, prevention, and response. The detection action package included antimicrobial resistance, zoonotic diseases, national biosafety/biosecurity and immunization. The prevention action package included establishing a national laboratory system, strengthening real-time biosurveillance, advancing timely and accurate disease reporting and establishing a trained global health security workforce. The response action package focused on establishing emergency operation centers, linking public health and law enforcement and enhancing medical countermeasures/personnel deployment (Nussbaum, 2015).

Although the worst is perhaps over, the improving situation cannot hide the public health, governance, and political failures that occurred 1979 during the epidemic (Fidler, 2014). The failures are epic because actions taken nationally and internationally deviated from the strategy that the international community designed, built, and implemented over 20 years to manage threats to global health security. The behavior of states and international organizations damaged virtually every element of this strategy and revealed how fragile progress has been since global health security emerged as a policy objective in the latter half of the 1990s (Fidler, 2014).

2.11 Management and Treatment of EVD

Clinicians providing care for patients infected with Ebola virus must also be familiar with management of severe disease not only with screening and infection control measures. Fever, fatigue, vomiting, diarrhea, and anorexia were the most common symptoms of the 2014 West African outbreak. Massive fluid losses from the gastrointestinal tract result in volume reduction, metabolic abnormalities (including hyponatremia, hypokalemia, and hypocalcemia), shock, and organ failure. Unconcealed hemorrhage occurred rarely. As of yet, there is no proven antiviral agent to treat Ebola virus disease, although several experimental treatments may be considered. Even in the absence of antiviral therapies, intensive supportive care has the potential to markedly blunt the high case fatality rate reported to date. Optimal treatment requires conscientious correction of fluid and electrolyte losses (West & Arnim, 2014).

Additional management considerations include searching for coinfection or superinfection; treatment of shock (with intravenous fluids and vasoactive agents), acute kidney injury (with renal replacement therapy), and respiratory failure (with invasive mechanical ventilation); provision of nutrition support, pain and anxiety control, and psychosocial support; and the use of strategies to reduce complications of critical illness. Cardiopulmonary resuscitation may be appropriate in certain circumstances, but extracorporeal life support is not advised. Among other ethical issues, patients' medical needs must be carefully weighed against healthcare worker safety and infection control concerns. However, meticulous attention to the use of personal protective equipment and strict adherence to infection control protocols should permit the safe provision of intensive treatment to severely ill patients with Ebola virus disease (West & Arnim, 2014).

Uyeki et al studied the clinical management of EVD among patients in the United States and Europe. The findings revealed that all patients received oral or intravenous electrolyte-replacement fluids to correct metabolic abnormalities. All but 1 patient received intravenous fluids, and 15 patients (56%) received total parenteral nutrition. A total of 11 patients (41%) had a peripherally inserted central catheter, and 18 (67%) had a central venous catheter placed. Fluids were administered intravenously in 18 of 20 medically evacuated patients before their arrival in the United States or Europe, either initiated in West Africa or initiated during the evacuation flight. Antiemetics were given to most patients, but few received antidiarrheal medications. A total of 22 patients (81%) received empirical antibiotic treatment with a median of 2 antibiotics (range, 0 to 7), the most common of which was a third-generation cephalosporin (Uyeki et al., 2016).

The study also highlighted that of 24 patients with EVD who had been in West Africa, 17 received antimalarial prophylaxis or treatment (or both) during their illness; of 14 patients who received antimalarial prophylaxis or treatment in West Africa, 1 had confirmed malaria. Of 8 patients who were treated for malaria in the United States or Europe, 2 had malaria that was confirmed by parasitologic testing. A total of 11 patients with EVD (41%) received nonconvalescent blood products, including nonconvalescent whole blood in 4 patients, fresh-frozen plasma in 6 patients, and platelets in 5 patients. Respiratory supportive care was provided frequently; 19 patients (70%) received supplemental oxygen, of whom 9 (47%) had respiratory failure. The median time from illness onset to respiratory failure was 9 days (range, 4 to 18). Four patients (15%) received noninvasive ventilation, of which 2 also received invasive mechanical ventilation after noninvasive failed ventilation (Uyeki et al., 2016).

Two patients with EVD were treated at Emory University Hospital after been infected with EVD in Liberia. They both had hypovolemia, hypokalemia, hypocalcemia, and hypoalbuminemia. Patient 1 also had hyponatremia. Both patients had thrombocytopenia without evidence of coagulopathy. With aggressive fluid and electrolyte replacement, the condition of both patients improved. The two patients were observed to have subjective and objective improvement shortly after receiving the first dose of the antibody cocktail, but this improvement occurred in the context of receiving other care as well. Malaria had also been diagnosed in one patient, who was treated for it early in the course of EVD. As the patients' condition improved clinically, there was a concomitant decline in the amount of virus detected in plasma (Lyon et al., 2014).

A study done by Lidell et al to describe the clinical characteristics and management of a cluster of patients with EVD, including the first cases of Ebola virus (EVD) infection acquired in the United States. The result showed that the index patient had high EBOV RNA levels, developed respiratory and renal failure requiring critical care support, and died. Both patients with secondary EBOV infection had nonspecific signs and symptoms and developed moderate illness; EBOV RNA levels were moderate, and both patients recovered. Patient 1 was given electrolyte replacement continued per routine ICU protocol. Levofloxacin was replaced with ertapenem. A peripherally inserted central catheter was placed for hydration and blood collection. Serum aminotransferase levels increased sharply, with a peak serum AST level of 1308 U/L. Diarrhea remained copious, up to an estimated 8 L/d (Liddell et al., 2015).

For patient 2, multiple investigational therapies were administered with the patient's informed consent after approval of an eIND request by the FDA and the hospital's

institutional review board. She received oral brincidofovir in a 200-mg loading dose on illness day 3 and a 100-mg dose on illness day 6. Two 500-mL infusions of convalescent plasma (matched by blood type) from a recovered patient with onset of EVD 81 days earlier were administered on illness days 3 and 4 and were well-tolerated. On illness day 4, elevated serum aminotransferase levels were observed. The small interfering RNA molecule TKM-Ebola (Tekmira Pharmaceuticals) was administered intravenously at 0.3 mg/kg of body weight on illness day 4 after premedication with acetaminophen and diphenhydramine. Approximately 6 hours after the infusion started, the patient developed high fever (40.0 °C), rigors, and chills consistent with cytokine release syndrome from TKM-Ebola, and acetaminophen and meperidine were administered. She also developed tachycardia and systolic hypotension for several hours that responded to a 25% albumin infusion. On illness days 5 and 6, a reduced dosage of TKM-Ebola (0.24 mg/kg) was well-tolerated. On illness day 5, one 44.8-mg/kg (recommended dose, 50 mg/kg) intravenous dose of ZMapp was administered without adverse effects (Liddell et al., 2015).

A trial was done in Guinea by Sisoko et al to experiment favipiravir on EVD positive patients. The results of the study indicate that monotherapy with favipiravir is unlikely to be effective in patients with very high viremia and merits further investigation in patients with intermediate to high viremia. This conclusion was based on two findings, namely, the observed mortality rates and the dynamics of EVD RNA load on treatment. In Group A Ct < 20, mortality was 7% higher than the target value and viral loads did not decrease. This suggests that any future trial is unlikely to demonstrate any benefit of favipiravir in these patients. In Group A Ct greater than or equal to 20, mortality was 33% lower than the target value and viremia decreased rapidly on treatment. However, the trial was non-randomized, the statistical power was low, and the 95% CI of mortality included the target

value. Therefore, the finding does not prove that favipiravir was effective in these patients but only suggests that the question remains open and gives some indication on how to better address it (Sissoko et al., 2016).

The same study came up with a third set of findings related to biological markers of organ damage also supports the pertinence of stratification of patients according to viral load. Patients with very high viremia had levels of creatinine, transaminases, and CK that suggested established organ failures requiring intensive care, while patients with a medium to high viral load had less frequent and, when present, reversible organ failures. In the context of limited resource availability, the former type of patients is unlikely to benefit from any specific monotherapy, while the latter is more likely to benefit from specific interventions (Sissoko et al., 2016).

Epidemiological data from UNICEF Guinea showed that children have accounted for a substantial proportion of patients admitted to West African medical centres for Ebola. 390 (22%) of 1744 reported patients infected with Ebola virus from the present outbreak in Guinea were children (Bouazza et al., 2015). The overall case fatality proportion in the outbreak tends to be higher in children (73.4%) than in adults aged 15–44 years (70.8%). In the context of an urgent need to assess potential specific interventions for Ebola in children, favipiravir is an interesting drug candidate because of its efficacy against Ebola virus in vitro and animal models, good tolerance profile in adults, immediate availability, and ability to be used in the paediatric population because pills can be crushed and mixed with food and liquid (Bouazza et al., 2015).

A trial in Sierra Leone involved 14 patients enrolled into the TKM-130803 cohort. They received between one and seven infusions of TKM-130803. Of these 14 patients, three

survived to day 14 and were discharged from the ETC, and 11 died. Two patients died within 48 h of admission and were excluded from the primary outcome analysis (and the ongoing futility plot). Two patients died on 15 June 2015, at which point enrolment to the trial was stopped since the futility boundary had been reached, with only three of the twelve patients eligible for inclusion in the primary outcome analysis surviving to day 14. All deaths were considered to be consistent with severe EVD. In participants who died, viral loads were high at admission and remained high over time; correspondingly, EBOV PCR Ct values were low at admission and remained low over time (Ct values are inversely proportional to viral load). Serial viral load and Ct data were available for two patients in the observational cohort; viral load steadily decreased in the survivor, whereas viral load increased in the patient who died. The final point estimate of the probability that a patient receiving TKM-130803 who survives for 48 h will subsequently survive to day 14 was 0.27 (95% CI 0.06, 0.58). Two of the three patients in the observational cohort died (Dunning et al., 2016).

Ebola virus disease (EVD) developed in a patient who contracted the disease in Sierra Leone and was airlifted to an isolation facility in Hamburg, Germany, for treatment. During the course of the illness, he had numerous complications, including septicemia, respiratory failure, and encephalopathy. Intensive supportive treatment consisting of high-volume fluid resuscitation (approximately 10 liters per day in the first 72 hours), broad-spectrum antibiotic therapy, and ventilatory support resulted in full recovery without the use of experimental therapies. Discharge was delayed owing to the detection of viral RNA in urine (day 30) and sweat (at the last assessment on day 40) by means of polymerase-chain-reaction (PCR) assay, but the last positive culture was identified in plasma on day 14 and in urine on day 26. This case shows the challenges in the management of EVD and

suggests that even severe EVD can be treated effectively with routine intensive care (Kreuels et al., 2014).

Use of antidiarrheal agents for the management of EVD-mediated diarrhea is infrequently reported, and no safety and efficacy data to guide use in EVD exist. Although the mechanism of EVD mediated diarrhea has not yet been characterized, the large volume of watery stool suggests a secretory process. Tolerance of enteral feeding when gastrointestinal symptoms are adequately controlled suggests that the small intestine structure and function remain intact. Autopsy studies of patients with EVD who died showed mild inflammation of small intestinal lamina propria, suggesting the possibility of an inflammatory component to a secretory form of diarrhea, as well. Clinically significant gastrointestinal bleeding observed in a small subset of patients with EVD, estimated to be <5%, raises the possibility that gastrointestinal inflammation may contribute to disease pathogenesis. Loperamide is a potent antidiarrheal agent with antiperistaltic and antisecretory effects. It was administered to reduce EVD diarrheal losses by allowing for correction of negative fluid balance, reduce hypovolemic shock, limit electrolyte losses, and consequently improve survival (Chertow et al, 2015).

CHAPTER THREE

METHODS

3.1 Study Design

The study used a 1:3 unmatched Case-control study design to collect data on the determinants of EVD infection among health care workers in Montserrado County from May 2014 to May 2015 in Liberia.

3.2 Study Area

The study was conducted in Montserrado County in Liberia. Montserrado County is the oldest of the fifteen (15) counties in Liberia, almost as old as the Republic itself. The county has an approximated

population of 1,646,421 with about 70% of the people living in Monrovia and its environs, while 30% live in rural areas. The average population density in Montserrado is about 36% per square kilometer. Like the rest of

Map showing Montserrado Health Districts, Liberia, June 2016



the other counties, Montserrado County has a three tier health care system, county, district and community levels. Health services in the county are administrated by a County Health Team. There are seven (7) health districts: Greater Monrovia, Somalia Drive, Bushrod, St. Paul, Commonwealth, Todee and Careysburg Districts and over 270 health facilities, mostly private. Liberia was the hardest hit of the three countries (Sierra Leone, Guinea and Liberia; Montserrado was the hardest hit county in Liberia. More than two thousand confirmed EVD cases were reported in Montserrado County, including health care

workers. Majority of the health care workers infected with EVD in Liberia came from Montserrado County. More than 90 confirmed cases of EVD among healthcare workers were reported in Montserrado County; the highest infection burden among healthcare workers compared to the rest of the fifteen counties.

3.3 Variables

Table 1: Variables

Variables	Definition	Scale of measurement
Socio-demographic factors		
Sex	Male and Female healthcare workers	Nominal
Age	Health care workers 18 years old and above	Interval
Profession/Occupation	Qualification of Healthcare workers providing health services (e.g. Nurse, Doctor, Student, etc)	Nominal
Place of work	Job site of healthcare workers during the epidemic (e.g. Hospital, Clinic, community, etc)	Nominal
Institutional/Organizational factors		
Availability of IPC guidelines & equipment	Infection Prevention & Control guidelines and equipment (gloves, mask) available at site of service provision	Nominal
Behavioral factors		
Hand hygiene	Hand washing using soap & water and hand sanitizers	Nominal
Extra-occupational activities (e.g. funeral attendance)	Any activities outside of a healthcare worker's work	Nominal
Wearing of PPEs (including gloves, mask, ect)	Wearing of Personal Protective Equipment during management and care of patients	Nominal
Exposure of healthcare workers to Ebola Virus Disease	Healthcare workers reporting being exposed to a suspected, probable or confirmed case of EVD during service provision	Nominal

3.4 Study Population

The study population includes all health care workers who were working during the EVD epidemic in Montserrado County, from May 2014 to May 2015. Cases (selected from health workers survivor database) included all healthcare workers reported as confirmed EVD cases in the Epi-surveillance database within the period of the outbreak (May 2014-May 2015).

Controls included healthcare workers working (from May 2014-May 2015) in the same health facility or environment as the case subjects but negative of EVD.

3.5 Sample size

The study targets healthcare workers who worked during the EVD outbreak in Montserrado County. Minimum sample size for this study is **156** participants, including **39** cases and **117** controls; using Epi Info (version 7): two sided confidence level = 95%, power = 80%, ratio of 3 controls to a case, assuming a minimum detectable odds of 3.0. However, the study involved 168 participants, including **42** Case and **126** Controls

3.6 Sampling method

The research involved a census of all confirmed EVD cases in the Epi-Surveillance database. The controls were randomly selected from the same health facilities where the cases (healthcare workers who survived EVD infection) worked during the epidemic. A sampling frame specific to healthcare workers qualification was developed. Based on the required number of controls to be selected from a health facility (based on 1 Case: 3 Controls), a sampling interval was calculated. Then, a random number was selected using a Random Number Table. A number between 1 and the sampling interval was selected, which became the first control selected. That number selected was added to the sampling

interval to select the next control. This process was repeated until the desired samples were acquired.

3.7 Data Collection Techniques and tools

Data was collected using a structured questionnaire, with close ended questions. Questionnaires were self-administered, prior to consent of each study participant. Each respondent took a maximum of 15 minutes on the average to complete a set of questionnaires.

3.7.1 Pretesting

The study questionnaire was pretested among health care workers who were not part of the study. Changes and modifications were made where necessary, after the pretest.

3.7.2 Data collection

3.7.2.1 Inclusion criteria

Cases (selected from health workers survivor database) included all healthcare workers reported as confirmed EVD cases in the Epi-surveillance database within the period of the outbreak.

Controls included healthcare workers working (within the same one year period) in the same health facility or environment as the case subjects but did not have EVD.

3.7.2.2 Exclusion criteria

Generally, the research excluded all healthcare workers in Montserrado County who were not working during the epidemic from the study.

3.7.3 Quality Control

Prior to data collection, the data collection questionnaires were pilot tested outside the study setting to verify and validate its applicability to yield quality data. Codes were assigned to each set of questionnaires according to study group type and a unique identification number of the respondent. Additionally, sets of instructions were attached on how to respond to each question, along with definition of key terms used, to every set of questionnaires. Questionnaire completion was ensured upon retrieval of questionnaires from respondents as well as ensuring that respondents answered every question appropriately and to minimize data entry errors.

3.8 Data processing and Analysis

Upon collection of data, the completed questionnaires were arranged according to study group type and unique identification number. Data entry was completed using Epi Info version 3.5.4. Data cleaning and validation was done to ensure data quality. The data was exported the database to SPSS version 23 for data analysis. The data analysis included descriptive statistics (frequencies & proportions), cross tabulations and odds ratios. Data was analyzed by person, place and time, using frequency and proportion. Independent variables were tabulated against the dependent variable (Exposure) and their odds ratios and confidence intervals calculated.

3.9 Permission/Ethical Consideration

Ethical approval was obtained from University of Liberia-Pacific Institute for Research and Evaluation (UL-PIRE) Ethics Committee, with an approval number before this study commenced. The sole purpose of this approval was to ensure Human-Subject Protection

for participants of the study, as it relates confidentiality, data security, and use of information.

3.9.1 Voluntary Written Inform Consent

Each study participant received a detailed inform consent form in plain language with no ambiguity for their perusal before consenting to participate in the study. This inform consent included the title and purpose of the study, the possible benefit(s) of the study as well as ensure participants' confidentiality and data security and information use.

3.9.1.1 Potential risk

This study posed no minimum risk because there could be breach in confidentiality as well as psychological issues related to participants being a case of EVD. There was no taking of blood and other biological specimen.



CHAPTER FOUR

RESULTS

The Epi-Surveillance database reported over 90 confirmed cases of EVD among health care workers in Montserrado County and approximately 60 deaths. After working with the EVD Survivor Network in Montserrado County, about 42 healthcare worker survivors were found.

An equal proportion of male and female was interviewed as cases, while there were more females (65, 51.6%) among the controls compared to their male counterpart. Mean age was 31.6 years (std. dev 7.1); with the highest proportions of participants between ages 24-28 for both case and control (Table 2).

Nurses accounted for the highest number of study participants interviewed, considering both cases (12) and controls (36), hence the most affected cadre of healthcare workers in Montserrado County were nurses, followed by healthcare students (9) and auxiliary health workers (e.g. Cleaners) (8).

Meanwhile, most of the infections occurred in clinics compared to other health facility types (Table 2).



Table 2: **Demographic Characteristics of Health care workers (Case and Controls) in Montserrado County**

Categories	Case (42)		Control (126)	
	N	%	N	%
Sex				
Male	21	50	61	48.4
Female	21	50	65	51.6
Age (in completed years)				
19-23	0	0	14	11.1
24-28	11	26.2	44	34.9
29-33	7	16.7	36	28.6
34-38	9	21.4	17	13.5
39-43	6	14.3	12	9.5
44 and Above	9	21.4	3	2.4
Occupation				
Doctor	1	2.4	3	2.4
Health care student	9	21.4	27	21.4
Nurse	12	28.6	36	28.6
Laboratory technician	2	4.8	6	4.8
Ambulance staff	2	4.8	6	4.8
Admissions clerk	1	2.4	3	2.4
Auxiliary health worker	8	19.0	24	19.0
Midwife	1	2.4	3	2.4
Physician Assistant	6	14.3	18	14.3
Health Facility Type				
Clinic	24	57.1	72	57.1
Hospital	17	40.5	51	40.5
Ebola Treatment Unit	1	2.4	3	2.4

Both health facility and non-health facility based exposures were assessed in the study participants. The odds of being exposed to EVD in a health facility were 5.3 times higher in the cases compared to the controls. Meanwhile, the odds of being exposed in both a health facility and outside a health facility was 5.7 times higher in the cases compared to their controls (Table 3).

Table 3: Place of Exposure to EVD of Health care workers in Montserrado County

Categories	Case		Control		Odds Ratio (OR, CI)
	N	%	N	%	
Health Facility (Exposure)					
Yes	35	83.3	61	48.4	5.3
No	7	16.7	65	51.6	(2.2-12.9)
Outside Health Facility (Exposure)					
Yes	26	61.9	37	29.4	3.9
No	16	38.1	89	70.6	(1.9-8.1)
Both Health facility & Outside facility (Exposure)					
Yes	20	76.9	16	43.2	5.7
No	6	23.1	21	56.8	(1.9-17.1)

Cases and controls reported that they were exposed to EVD patients while providing health care services. Table 4 shows places where study participants' exposure to EVD patient(s) occurred. Meanwhile maternity ward (OR 6.6), inpatient room/ward (OR 5.2), the laboratory (OR 3.2) and patient transport (ambulance) (OR 3.2) were the places with the highest odds of exposure to EVD in cases compared to their controls (Table 4). Though laboratory and ambulance had high odds of exposure to EVD, their corresponding confidence intervals shows those exposures were not significant. However, the intensive care unit and recovery room were the places least likely for exposure to EVD, comparing cases to control.

Table 4: Health Facility-based Exposure sites of Health care workers to EVD in Montserrado County, May 2014-May 2015.

Categories	Case		Control		Odds Ratio (OR, CI)
	N	%	N	%	
Reception area	8	19.0	21	16.7	1.2 (0.5-2.9)
Emergency ward	16	38.1	40	31.7	1.3 (0.6-2.7)
Intensive care unit	5	11.9	18	14.3	0.8 (0.3-2.3)
Inpatient room/ward	11	26.2	8	6.3	5.2 (1.9-14.1)
Surgical suite/theatre (operating room)	3	7.1	0	0.0	–
Maternity ward	9	21.4	5	4.0	6.6 (2.1-21.0)
Laboratory	3	7.1	3	2.4	3.2 (0.6-16.3)
Outpatient facility/clinic	5	11.9	0	0.0	–
Transport patient (Ambulance)	3	7.1	3	2.4	3.2 (0.6-16.3)
Recovery room	3	7.1	14	11.1	0.6 (0.2-2.3)

Health facility based functions that predispose health care workers to EVD infection in a health facility are listed in Table 5. Table 5 also shows the odds of a case being exposed to EVD infection while performing a function compared to the controls. Functions which had very high odds among the cases compared to their controls included providing injection (OR=29.4, 3.5-243.4) placing intravascular device (OR=18.4, 4.9-68.7), Feeding (OR=9.5, 2.8-32.4), providing medication (OR=16.9, 3.5-82.1), and emptying bedpan (OR=12.4, 2.5-62.4) (Table 5).

Table 5: **Health Facility-based Risk functions of Health care workers to EVD in Montserrado County, May 2014-May 2015**

Categories	Case		Control		Odds Ratio (OR, CI)
	N	%	N	%	
Taking vital signs	24	57.1	38	30.2	3.1 (1.5-6.3)
Performing physical exam	12	28.6	24	19	1.7 (0.8-3.8)
Conducting medical procedures	8	19	19	15.1	1.3 (0.5-3.3)
Placing intravascular device	13	31	3	2.4	18.4 (4.9-68.7)
Placing urinary catheter	2	4.8	13	10.3	0.4 (0.1-2.0)
Drawing blood	4	9.5	5	4	2.5 (0.7-9.9)
Collecting blood specimens for lab	4	9.5	3	2.4	4.3 (0.9-20.1)
Changing linen	6	14.3	7	5.6	2.8 (0.9-8.9)
Bathing	9	21.4	4	3.2	8.3 (2.4-28.7)
Feeding	10	23.8	4	3.2	9.5 (2.8-32.4)
Lifting, positioning	7	16.7	8	6.3	2.9 (0.9-8.7)
Emptying bedpan	7	16.7	2	1.6	12.4 (2.5-62.4)
Providing medication	9	21.4	2	1.6	16.9 (3.5-82.1)
Providing injection	8	19	1	0.8	29.4 (3.5-243.4)
Conducting surgery	1	2.4	1	0.8	2.8 (0.2-48.8)
Haemodialysis	1	2.4	0	0	–
Processing clinical specimens	2	4.8	0	0	–
Taking medical history	2	4.8	3	2.4	2.1 (0.3-12.7)
Caring for body after death	1	2.4	1	0.8	2.8 (0.2-48.8)

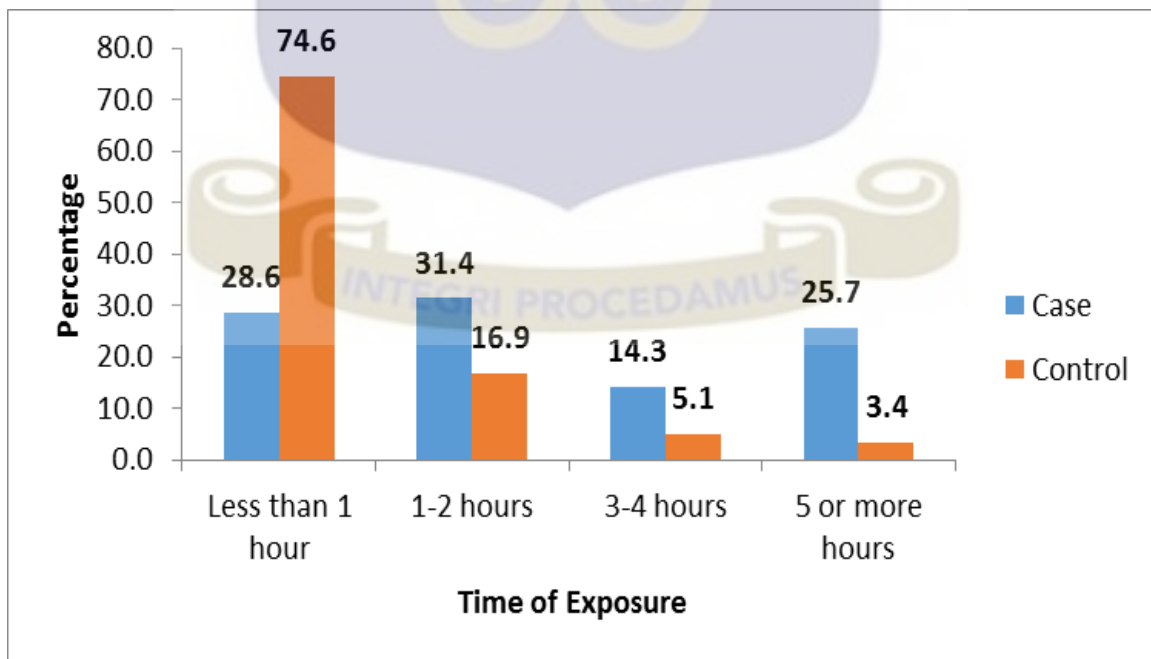
Figure 2: **Estimated time (longest) health care workers spent with a Case-patient of EVD**

Figure 3 shows that generally, controls stayed less time being exposed to a case-patient of EVD compared to cases. More than 70% (95) of the controls spent less than 1 hour with a case of EVD while just 3.4% (5) spent 5 hours or more. However, more than 30% (13) of cases spent 1-2 hours being exposed to an EVD patient and 25% (10) spent 5 or more hours.

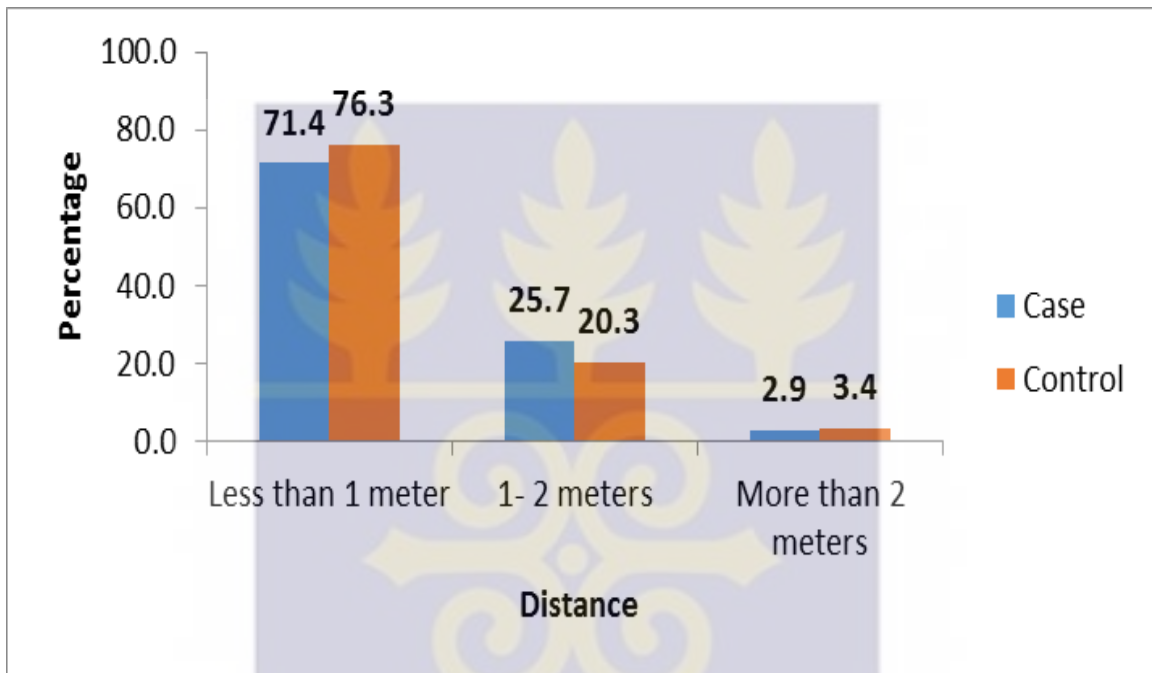


Figure 3: Closest distance health care workers stood to an EVD Case-patient while providing Services

There was little difference between cases and their controls as it relates to distance from an EVD patient when providing health care services. More controls (76.3%, 96) reported to have been less than 1 meter away from an EVD case than cases (71.4%, 30). The converse of this situation was reported by cases (25.7%, 11 and 2.9%, 1), who were 1-2 meters and more than 2 meters respectively, compared to their control (20.3%, 26 and 3.4%, 4).

About 88% (31) of the cases and 71% (42) of controls reported to have had contact with body fluids and excretions of an EVD patient (Table 6). Blood was the most reported body fluid that both cases (58.6%, 17) and controls (79.5%, 31) came in contact with. Similarly, urine was the most common excretion that both cases (31.0%, 9) and controls (7.7%, 3)

reported to have had contact with (Table 6). About 62% (20) of cases reported that the nature of contact with either body fluid or excretion was a touch with the bare skin, compared to about 33% (14) of controls. Meanwhile, 25% (8) of cases reported the nature of contact with either a body fluid or an excretion was on their clothing or PPE, while 66.7% (28) of their control reported the same nature of contact (Table 6).

Table 6: Health care workers' Contact with an EVD Case-patient in the Health Facility

Categories	Case		Control	
	N	%	N	%
Contact with body fluid, excretions, etc of EVD Patient				
Yes	31	88.6	42	71.2
No	3	8.6	17	28.8
Don't know	1	2.9	0.0	0.0
Type of body fluid, excretions, etc				
Blood	17	58.6	31	79.5
Sputum	0	0.0	4	10.3
Urine	9	31.0	3	7.7
Feces	3	10.3	1	2.6
Nature of contact				
Touched bare skin	20	62.5	14	33.3
Got in eye	2	6.3	0	0.0
Penetrating injury	2	6.3	0	0.0
On clothing or PPE	8	25.0	28	66.7

Hand hygiene following the “5 moments of WHO”, a standard hand washing procedure promoted by the WHO, is a very crucial basic preventive measures while providing health care services whether in or outside the health facility. This practice was low among the cases as only 25% (5) of them followed hand hygiene as described by the “5 moments of WHO”, while 65% (13) were unsure of doing so. However, more of the controls (77.8%, 42) reported to have practiced hand hygiene following the “5 moments of WHO” (Table 7).

Meanwhile, 65.0% (13) of the cases reported to have washed their hands properly 100% of the time after removing their PPE and 57.1% (72) of their controls “Never” washed their hands at all, after removing their PPEs (Table 7).

Wearing of PPEs such as gloves, gown, eye protection and medical masks before entry to a patient’s room was very low among cases and controls, especially among the cases. However, more cases (64.3%, 27) reported that they wore gloves when in close contact with a patient compared to their controls (38.1%, 48) (Table 7).

Table 7: Preventive Measure against EVD by Health care workers in the Health Facility

Categories	Case		Control	
	N	%	N	%
Hand hygiene (WHO 5 moments)				
Always (100% of time)	5	25	42	77.8
Often (>50% of time)	0	0	5	9.3
Infrequent (<50% of time)	2	10	0	0
Unsure	13	65	7	13.0
Hand hygiene (after removing PPE)				
Always (100% of time)	13	65.0	49	38.9
Not always	7	35.0	4	3.2
Never	0	0	72	57.1
Close contact with Patients				
Gloves	27	64.3	48	38.1
Gown	19	45.2	45	35.7
Eye protection	16	38.1	30	23.8
Medical mask	18	42.9	29	23.0
For patients' room entry				
Gloves	7	16.7	36	28.6
Gown	3	7.1	34	27.0
Eye protection	3	7.1	21	16.7
Medical mask	4	9.5	20	15.9

About 64% (28) of cases and 82% (104) of their controls reported to have been trained during the EVD epidemic in Liberia (Table 8). However, approximately half of the

number of cases and their controls reported that those training s came around the middle of the epidemic. Meanwhile, 96.2% (100) of the controls and 89.3% (25) of the cases reported that IPC information on the prevention of EVD was an integral part of the training (Table 8).

Table 8: In-Service Training for Health care workers during the EVD Epidemic in Montserrado County, May 2014-May 2015

Categories	Case		Control	
	N	%	N	%
Received any Training during outbreak				
Yes	28	64.3	104	82.5
No	14	35.7	22	17.5
Time of the training				
1-4 months	13	46.4	29	27.9
5-8 months	15	53.6	52	50.0
9-12 months	0	0.0	23	22.1
IPC information on EVD Prevention				
Yes	25	89.3	100	96.2
No	3	10.7	4	3.8

The odds of health care workers being exposed to EVD infection was 2.0 times higher in the cases than their controls (Table 9). However, exposure during funeral attendance was not significant, similar to participation in burial rites and having a confirmed EVD family member and close neighbor.

Table 9: Non-Health Facility-based Exposure of Health care workers to EVD

Categories	Case		Control		Odds Ratio
	N	%	N	%	
Funeral Attendance	8	19.0	13	10.3	2.0 (0.8-5.3)
Participation in burial rites	9	21.4	18	14.3	1.6 (0.7-3.9)
Confirmed EVD family member	16	38.1	33	26.2	1.7 (0.8-3.6)
Confirmed EVD close neighbor	21	50.0	51	40.5	1.5 (0.7-2.9)

CHAPTER FIVE

DISCUSSION

Forty-two health care workers who survived EVD (Cases) were interviewed, along with 126 Controls.

There was an equal proportion, 50% each, of male and female as cases, while there were more females among the controls compared to their male counterpart. A study conducted in Sierra Leone showed that males were less prone to being infected with EVD than their female counterpart with an odds of 0.62 (Fang et al., 2016). The apparent reason for females being more prone to EVD infection compared to their male counterpart points to their responsibilities as caregivers for family member when they get sick.

Mean age was 31.6 years (std. dev 7.1), with the highest proportions of participants between ages 24-28 among both cases and controls. Age doesn't seem to be a significant factor for exposure to EVD. A study conducted in Sierra Leone by Fang et al showed that children were more prone to being infected with EVD than adults in the household. They found that the proportion of children confirmed EVD cases was 26%, similar to 25% of all confirmed cases in Sierra Leone (Fang et al., 2016).

This study shows that health care workers' behavior during health care service provision predisposed them to infection with Ebola. Preventive measures, including hand hygiene and wearing of PPE, against EVD especially in the health facility were relatively fair, less than 70% of healthcare workers reported to have practice these measures while providing services. Meanwhile, certain preventive measures were poorly practiced. For example, a health care worker must wear PPEs before entering an isolation ward or even before

attending to a patient, however, less than 30% of either cases or controls reported wearing any form of PPE before entering patients' room.

Additionally, there was a huge disparity between health care workers wearing a PPE while in close contact with a patient and wearing a PPE before entering a room where the patient is admitted, with the former practiced more than the latter. This could explain the increased infection of EVD among healthcare workers, especially in the health facility. It is evident that wearing protective barriers while providing services mitigates transmission of EVD in health facilities. During the early days of the epidemic in Liberia, there were shortages of PPEs in the country, thereby causing huge exposures to EVD by healthcare workers and patients alike.

Early in the outbreak in Liberia, several clusters of EVD were reported in healthcare facilities throughout the country. These clusters of infection among healthcare workers occurred in part because of poor knowledge and adherence to basic infection prevention and control (IPC) practices, and contributed to EVD transmission among patients and healthcare workers (HCWs) within the healthcare facility and surrounding communities (Cooper et al., 2016).

Shears & O'Dempsey conducted a study on the evolution of EVD in 2015. Their finding pointed out that nosocomial transmission of Ebola to health care workers can easily be mitigated with vigilance and the institution of barrier protection. Two large outbreaks have occurred which were linked to regional hospitals, in DRC in 1995 and in Uganda, in 2000. The outbreak in DRC occurred in Kikwit, a 350-bed regional hospital, resulting in infection in 80 healthcare workers (though some may have been infected in the

community), and subsequent spread to other hospitals following patient transfer. The Uganda outbreak, in Gulu district, was centred on two hospitals, and the surrounding communities. There were 425 cases and 224 deaths, including 17 hospital staff. The lack of resources for infection control and personal protective equipment were the main reasons for nosocomial transmission. (Shears & O'Dempsey, 2015).

This study reveals that the odds of cases being exposed in a health facility compared to controls were **5.3 (2.2-12.9)**. According to Shears & O'Dempsey 2015, healthcare facilities play the amplifying role of healthcare facilities in the evolution of Ebola outbreaks. They analyzed data from the 1976 Sudan outbreak and they demonstrated that unprotected nursing of a patient had an attack rate of 81%, limited physical contact (not described in detail) an attack rate of 23%, and no transmission occurred in visiting a room with a symptomatic case and having no physical contact (Shears & O'Dempsey, 2015). This study found that health facility based risks included both sites or ward and functions executed by health care workers. Service provision points in the health facilities that served as exposure to EVD included maternity ward, inpatient room/ward, laboratory, and transport patient (Ambulance). Meanwhile, risky functions in the health facility included providing injection, feeding patient, providing medication, emptying bedpan, and placing intravascular device.

Others include bathing patient, collecting blood specimens for laboratory, changing linen, drawing blood, taking vital signs, as well as lifting, positioning, taking medical history, caring for body after death, and lifting, positioning of patient.

Having protective kits may avert transmission of Ebola in the health facility. A mathematical modeling analysis conducted with data of the EVD outbreak in Montserrado County, Liberia confirms this; given the projection that incidence in Montserrado was likely to exceed Ebola Treatment Center capacity under current international commitments; protective kits may supplement hospital-based case isolation. For instance, if kits halve transmission, it was expected that allocating kits while increasing case ascertainment would avert 46,123 to 78,623 cases if 600 new beds were concurrently allocated over the span of two weeks. With the delivery of 4,800 new beds in mid-November 2014, the averted cases would have increased to the range of 65,228 to 97,940, compared to 58,529 to 77,312 without kits (Lewnard et al., 2014).

These health facility based exposures are coherent with the nature of human to human transmission of EVD, contact with an infected person by direct body contact and contact with body fluid.

Meanwhile, a huge proportion of cases and their controls reported to have had contact with a body fluid or excretion of a person infected with EVD while providing health care services in the health facility. Ebola is transmitted through direct or indirect contact between bodily fluids from an infected patient and breaks in the skin or exposed mucous membranes of an uninfected person (Fischer et al., 2014).

This study reveals that blood is the most common body fluid reported by both cases and controls. Meanwhile, the most common nature of contact among cases was touched bare skin while for the controls is on clothing or PPE. Direct contact with an infected patient's body fluids or contact with the patient's bare skin is a major transmission medium for

EVD. Compared to controls which had their most common contact on clothing or PPE, it is logical to assume that cases were more exposed than their controls. This is because ideally, PPEs should provide protective barriers against infections.

Hand washing practices were generally poor among Cases compared to Controls. This could partially explain infection of EVD in the former compared to the latter. More than 60% of the Cases were unsure of washing hands at any time during service provision. Hand washing is a very simple practice, when done properly (with soap and running water) can prevent infection of EVD. Hand washing improved among cases after removal of PPEs but declined among controls. However, this study did not find a correlation between hand washing and wearing of PPEs as protective factors against EVD infection.

Health care workers' functions that posed a high risk for EVD infection among the study participants include providing injection, placing intravascular device, providing medications and emptying of bedpan. These health service provision functions had odds of exposure of more than 10 times higher in the cases compared to controls. This means that the possibility of Cases being infected versus the possibility of not being with EVD while providing injection, placing intravascular device, providing medications and emptying of bedpan was more than 10 times higher than controls performing the same functions. This is reasonably correct because these functions require direct contact with the patient or body fluids of the patient, which have been proven to be a major medium for EVD transmission from human to human at home as well as in the health facility.

Non-health facility based risks among the study participants include funeral attendance, participation in burial rites, having a confirmed EVD family member and a confirmed EVD close neighbor. But it was funeral attendance that shows the highest odds in exposing study participant outside the health facility with an odds ratio of 2.0.

Funeral attendance has proven to be a major medium through which EVD is spread outside the health care facility. In Guinea, the Ministry of Health was notified by local public health authorities in Kissidougou, a prefecture in southeastern Guinea (pop. 284,000), that the number of cases of Ebola virus disease (Ebola) had increased from one case reported between December 8-14, 2014, to 62 cases reported between December 15-21, 2014. With assistance from CDC and WHO, the Guinea Ministry investigated the local outbreak. The investigation found that 85 confirmed Ebola cases were linked to one traditional funeral ceremony, including 62 (73%) cases reported during December 15-21 (Victory et al., 2015).

The limitations of this study include the following:

- This study did not investigate the correlations between attending funeral and hand washing after the ceremony.
- The study did not cover any other practice or use of PPEs in the community or at home.
- Due to poor management of EVD data, especially during the early stages of the epidemic, the study must have missed out on some cases either because they were not recorded in the database or wrongly recorded in the database

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

The following functions pose very high risk for EVD infection among health care workers in Montserrado County: Providing injection [**OR 29.4 (CI: 3.5-243.4)**], placing intravascular device [**OR 18.4 (CI: 4.9-68.7)**], providing medications [**OR 16.9 (CI: 3.5-82.1)**] and emptying bedpan [**OR 12.4 (CI: 2.5-62.4)**]

The most significant non-health facility based risk factor for EVD infection was funeral attendance.

Based on the aforementioned, the following recommendations were made:

- Ministry of Health of Liberia must strengthen infection prevention and control intervention in all health facilities
- Health facility administrations must ensure that infection prevention and control interventions are properly implemented
- Health care authorities at the Ministry of Health and health facility levels ensure the provision of regular in-service training for health care workers, especially in detection of infectious diseases like EVD and infection prevention and control
- Health care workers must adhere to preventive measures against infectious diseases both in the health facility and at home or in the community

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INFORMED CONSENT

Title: Determinants of Ebola Virus Disease infection among Health workers in Montserrado County

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General Information about Research

The main objective of this study is to determine the risks factors responsible for Ebola Virus Disease (EVD) infection among health workers in Bong and Montserrado Counties. This study involves research to help us understand how health workers providing health care services in the two counties during the EVD outbreak, were exposed to being infected with Ebola. As a participant, your expected time for participating in this study is no more than 24 hour, though there will be follow-ups on your responses for possible clarifications. However, you are expected to answer all questions appropriately.

Possible Risks and Discomforts

There is no potential risk to participating in this study, as there will not be any taking of blood and other biological specimen.

Possible Benefits

There are no direct benefits to you as a participant of this study. However, data collected will help improve infection prevention and control in health facilities and guide efforts to prevent further spread of Ebola Virus Disease to health workers in the unforeseeable future.

Confidentiality

The Researcher will ensure that your identity and responses are confidential. They will not be shared with anyone not involved with this study. You will not be name in the report; hence, no one can trace your response back to you.

Compensation

At the end of this interview, you will be given Five United States Dollars (\$ 5.00) or equivalent in Liberian Dollars according to the daily exchange rates. This amount will serve compensation for participating in the study.

Voluntary Participation and Right to Leave the Research

Your participation in this study is voluntary. You can decide to discontinue your participation at any time during the study and there will not be any penalties for your action.

Contacts for Additional Information

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Determinants of Ebola Virus Disease infection among Healthcare workers, Montserrado County

Study ID Number |____|____|____|____|____|____|

Sex: Male [] Female []

Status: 0. Case [] 1. Control []

Date of interview (dd/mm/yyyy): ____/____/____

Section 1: General questions

1. Place of primary residence (address): _____
2. Do you have homes elsewhere?
 1. Yes []
 2. No []
 3. If yes, please specify where: _____
3. How old are you as of your last birthday? ____ / ____

General occupational questions

4. What is your occupation?
 1. [] Doctor
 2. [] Health care student
 3. [] Nurse
 4. [] Respiratory therapist
 5. [] Laboratory technician
 6. [] Phlebotomist
 7. [] Radiologist
 8. [] X-ray technician
 9. [] Physical/occupational therapist
 10. [] Morgue staff
 11. [] Ambulance staff
 12. [] Admissions clerk
 13. [] Ward clerk

- 14. Auxiliary health worker
- 15. Patient transport
- 16. Catering staff
- 17. Housekeeping staff/cleaner
- 18. Midwife
- 19. Physician Assistance
- 88. _____] Other,
specify _____

- 5. Health facility of work during EVD epidemics: _____
5a. Health facility type: _____
- 6. Did you work in other health facility (ies)?
 - 1. Yes
 - 2. No
 - 3. If yes, in which facility (ies) did you work? _____

SECTION 2: HEALTH FACILITY EXPOSURE QUESTIONS

- 7. Were you exposed to any confirmed EVD case during service provision in the health facility?
 - 1. Yes
 - 2. No (Do Not Answer Q 8, 9, 10, 14-20)
- 8. Kindly circle all specific health care settings where your exposure to a confirmed EVD patient occurred or may have occurred:
 - A. reception area
 - B. emergency ward
 - C. intensive care unit
 - D. inpatient room/ward
 - E. surgical suite/theatre (operating room)
 - F. maternity ward
 - G. radiology/imaging
 - H. laboratory
 - I. morgue
 - J. outpatient facility/clinic
 - K. transport patient

- L. recovery room
- X. other (specify) _____
9. Circle all specific exposures that you have had with a confirmed EVD patient at any time:
- A. Taking vital signs
- B. Performing physical exam
- C. Conducting medical procedures
- D. Placing intravascular device
- E. Placing urinary catheter
- F. Drawing blood
- G. Collecting blood specimens for lab
- H. Changing linen
- I. Bathing
- J. Feeding
- K. Lifting, positioning
- L. Emptying bedpan
- M. Providing medication
- N. Providing injection
- O. Conducting surgery
- P. Haemodialysis
- Q. Processing clinical specimens
- R. Taking medical history
- S. Caring for body after death
- T. Other, specify _____
10. At time of exposure(s), were hand hygiene facilities and supplies available and accessible?
1. Yes
2. No (skip to Q14)
3. Unknown
11. If yes, which facilities and supplies (Tick all that apply):
1. Running (tap) water

2. Soap
3. Paper towels
4. Hand antiseptic
5. Other, (specify) _____

12. Was hand hygiene performed according to the WHO 5 moments?

1. Always (100% of time)
2. Often (>50% of time)
3. Infrequent (<50% of time)
4. Unsure

13. Was hand hygiene performed after removing PPE?

1. Always (100% of time)
2. Not always
3. Never

14. What is the longest total amount of time that you were exposed to the case-patient on any one shift (include time in the patient's room or checking patient or handling patient's bedding/equipment/fluids) (check one):

1. less than 1 hour
2. 1-2 hours
3. 3-4 hours
4. 5 or more hours

15. During the course of the EVD patient's stay in this health facility, estimate the total duration of time spent in the patient's room or checking patient or handling patient's bedding/equipment/fluids? (check one):

1. Less than 1 hour
2. 1-2 hours
3. 3-4 hours
4. 5 or more hours

16. What was the closest distance on any one shift from the EVD patient?

1. Less than 1 meter
2. 1- 2 meters
3. More than 2 meters

17. Was there a direct contact with blood, body fluids, excretions, secretions of the patient?

1. Yes
2. No (skip to Q20)
3. Unknown

18. With what body fluid or excretion did you come into contact?

1. Blood
2. Sputum
3. Urine
4. Feces
5. Other (specify)_____

19. What was the nature of contact?

1. Touched bare skin
2. Got in eye
3. Got in mouth
4. Penetrating injury (e.g. needle stick or scalpel cut)
5. On clothing or PPE
6. Other (Describe: _____)

20. When in contact with patient during the outbreak, how often did you use the following at time of exposure?

- 1=always
- 2=not always
- 3=never
- 4=not relevant

	Close direct contact	For room entry
Gloves		
Gown		
Eye protection		
Medical mask		
Particulate respirator		
Other1 (specify here: _____)		
Other2 (specify here: _____)		
Other3 (specify here: _____)		

21. Did you receive any training during the outbreak?

1. Yes []
2. No [] (skip to Q24, section 3)

22. What point during the outbreak was the training conducted?

1. [] 1-4 months
2. [] 5-8 months
3. [] 9-12 months

23. Was IPC information on EVD infection provided to you during the outbreak?

1. [] Yes
2. [] No
3. [] Unknown

SECTION 3: NON-HEALTH FACILITY RELATED EXPOSURE QUESTIONS

24. During the EVD outbreak, did you have contact *outside the health facility setting* with a sick person experiencing EVD symptoms?

1. Yes
2. No (skip to Q27)

25. What was the nature of the contact?

1. Direct contact with bare skin
2. Contact with clothing
3. Contact with body fluid

26. What setting did this exposure occur (e.g. home, place of worship, other)?

27. Did you attend funeral(s) of anyone suspected to have died from EVD?

1. Yes
2. No

28. Did you participate directly in any burial rites?

1. Yes
2. No

29. Were any of your family members a confirmed case of EVD?

1. Yes
2. No

30. Were any of you closed neighbors a confirmed case of EVD?

1. Yes
2. No