Project on
A review on Ebola virus disease: its outbreak, Current status and management

A dissertation submitted to the Department of Pharmacy, Daffodil International University, slightly fulfils the needs for the Bachelor of Pharmacy degree (B. Pharm).

Submitted To

The Department of Pharmacy

Faculty of Allied Health Sciences

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In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

Submitted By

Student ID: 191-29-1468

Batch: 21 (B)

Department of Pharmacy

Faculty of Allied Health Science

Daffodil International University

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APPROVAL

This project The Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University has accepted **a review on the Ebola virus disease: its outbreak, current status, and management** as meeting the requirements for the degree of Bachelor of Pharmacy and has given it the positive reaction for both its style and content.

Board of Examiners

Professor Dr. Muniruddin Ahmed

Head of the Department

Department of Pharmacy

Faculty of Allied Health Science

Daffodil International University

Internal Examiner 1

Internal Examiner 2

External Examiner 3

CERTIFICATION

DISSERTATION ACCEPTANCE FORM DAFFODIL INTERNATIONAL UNIVERSITY, DEPARTMENT OF PHARMACY.

This is to confirm that the investigation results for the project work are unique and have never been presented to the university previously. The complete project has been approved as meeting Bachelor of Pharmacy criteria.

Project Supervisor

Sadman Hasib Antu
Lecturer
Department of Pharmacy
Faculty of Allied Health Sciences
Daffodil International University

DECLARATION

I now state that I completed the project report titled "A review on Ebola virus disease: its outbreak, current status, and management" under the guidance of lecturer Sadman Hasib Antu. I also state that this project is entirely unique to me. I further declare that neither this project nor any of its components have been submitted to any institution for the award of a bachelor's degree or any other degree.

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Student ID: 191-29-1468

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Faculty of Allied Health Sciences

Daffodil International University

Acknowledgement

In order to meet the criteria for the Bachelor of Pharmacy degree, I must first express my sincere thankfulness to the Almighty God for providing me the opportunity to study this topic, the capacity to finish my project work, and ultimately the ability to write up the project work & findings. To my esteemed supervisor, Sadman Hasib Antu, Lecturer in the Department of Pharmacy at Daffodil International University, I would like to convey my sincere gratitude and respect.

Also, I want to send my friends, who have helped me finish the project and supported me in my work in the lab, my deepest affection. The head of the pharmacy department of Daffodil International University, Professor Dr. Muniruddin Ahamed, has my heartiest welcomes. The people that helped me complete my research, write my dissertation, and put this project together in whatever way are all deserving of my appreciation.

DEDICATION

DEDICATED TO

ALL OF MY RESPECTED TEACHERS AND MY FAMILY MEMBERS WHO HAVE ALWAYS SUPPORTED AND ENCOURGED ME

Abstract

In humans and other primates, the very pathogenic Ebola virus causes severe hemorrhagic fever. The virus is spread by direct contact with contaminated body fluids, and it has a high death rate. The current Ebola epidemics throughout West Africa have brought attention to the critical need for better Ebola diagnostic equipment, vaccines, and therapies. This research report gives an in-depth analysis of the history, epidemiology, pathophysiology, clinical symptoms, diagnosis, and treatment of the Ebola virus. The report also addresses the ongoing research being done to create efficient Ebola vaccines and treatments. In-depth literature reviews, data analysis, and interviews with subject-matter experts were all part of the research. According to the findings, there is still more to be done to tackle the persistent threat of Ebola, even though tremendous progress was made in studying the genetics of the virus and creating viable therapeutics. The paper closes with suggestions for further study and policy initiatives, including more financing for Ebola study and development, expanded public awareness and education campaigns, and improved monitoring and epidemic response. This project's overarching objective is to support international efforts to stop and contain Ebola.

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Introduction

1.0 GENERAL INTRODUCTION:

The severe and sometimes deadly hemorrhagic disease that the Ebola virus inflicts upon humans and other primates belongs to the family of viruses known as the Filoviridae. When outbreaks occurred in Sudan and the Democratic Republic of the Congo in 1976, it was first discovered. The only known viral family about which we know so little is Filoviridae. We don't even fully comprehend the maintenance tactics used by the agents in nature, let alone the illnesses they cause, their pathophysiology, or their intricate virology [1]. The Ebola viruses are the primary cause of Ebola hemorrhagic fever (EHF) in humans and other primates, often known as the severe Ebola virus disease (EVD) [2]. EVD is one of the most prevalent illnesses in the world because it spreads through contact with bodily fluids from infected people or animals [2]. The seven filoviruses that have been identified in humans are either members of the genus Marburgvirus (Marburg virus (MARV) and Ravn virus (RAVV)) or the genus Ebolavirus (Bundibugyo virus (BDBV), Ebola virus (EBOV), Reston virus (RESTV), Sudan virus (SUDV), and Ta Forest virus (TAFV) [3]. It is a serious, frequently deadly zoonotic filovirus illness known as the Ebola virus disease (EVD) [4]. Five different types of the Ebola virus (EBOV) have been identified since it was first found in central Africa in 1976: the Zaire ebolavirus (ZEBOV), Sudan ebolavirus (SEBOV), Ta Forest ebolavirus, Bundibugyo ebolavirus (BEBOV), and Reston ebolavirus [4]. There are presently no licensed treatments or vaccines for these two species, ZEBOV and SEBOV, which cause viral hemorrhagic fever with case fatality rates as high as 90% in both humans and nonhuman primates [5]. Zaire ebolavirus is to blame for the current outbreak in West Africa (2013–2016), which has resulted in a total of 28,616 confirmed, probable, or suspected cases in Guinea, Liberia, and Sierra Leone, including, 310 reported deaths. This outbreak is the largest one to be documented since the virus was first identified in 1976 [4].

Ebola virus was discovered during two outbreaks in the Democratic Republic of the Congo (DRC) and Sudan about 30 years ago, while Marburg virus, the first member of the filovirus family to be recognized, was found nearly 40 years ago [6]. When the Marburg virus first appeared in 1967, biomedical research first learned about the viral family Filoviridae [1] Commercial laboratory employees were being treated in a Marburg, Germany, hospital at the time for a serious and uncommon illness [1]. As a condition exclusively brought on by EBOV, Ebola virus disease (EVD) is defined [3]. This subcategorization of FVD is primarily based on mounting evidence that ebolaviruses and Marburg viruses have different molecular properties that might affect the tropism of the virus-host reservoir, the pathogenesis, and the disease manifestation in unintentional primate hosts [3]. The discovery of the Ebola virus as the primary cause of significant outbreaks of hemorrhagic fever in the Democratic Republic of the Congo (DRC) and Sudan astonished the world community once more in the late 1970s [1]. As international scientific teams came to deal with these extremely contagious infections, they discovered that transmission had mostly stopped, but they were still able to reconstitute a lot of information from the survivors [1]. The latter was in a community close to the Ebola River,

which is where the illness got its name [2]. Most cases of Ebola are found in isolated settlements in Central and West Africa that are close to tropical rainforests [2].

The discovery of a new member of the filovirus family in 1990, this one occurring in Reston, Virginia, infected cynomolgous monkeys from the Philippines, shocked the scientific community [6]. Epidemiologic investigations into both epidemics successfully linked the viral introductions to a single Filipino exporter but were unable to identify the virus's true source [1].

Figure 1: A Patient with Ebola virus

In Guinea, Liberia, and Sierra Leone, the WHO proclaimed the end of Ebola transmission on December 29, 2015, January 14, 2016, and March 17, 2016, respectively [4]. The creation of a long-lasting and potent Ebola vaccine, however, should be a top priority in order to both end the current outbreak and stop and contain any future outbreaks [4]. On the other hand, up until 2013, SUDV produced the largest epidemic, which included 425 cases and 224 fatalities (CFR 52.7%) [3]. The total low number of FVD cases (1967–2013: 2,886 cases with 1,982 fatalities) The comprehensive investigation of clinical FVD in humans has been hindered by the characteristic distant and rural sites of outbreaks and the sometimes-delayed reporting of new outbreaks to the worldwide community [3].

In December 2013, in the sleepy village of Meliandou in the Guéckédou Prefecture, Guinea, human contact with an animal reservoir of the Ebola virus (EBOV) seems to have triggered the 2013–2016 Ebola virus disease (EVD) pandemic in West Africa [7]. The first verified case of the Ebola virus illness (Ebola) was discovered in Sierra Leone on May 25, 2014 [8]. All of Sierra

Leone's districts had confirmed Ebola cases as of September 20, 2014, except for Koinadugu district [8]. At the time, the district task force and a well-known private donor who constructed checkpoints for temperature monitoring and a pass system to restrict travel into and out of the area were considered as having contributed to Koinadugu's status as an Ebola success story [8]. The World Health Organization (WHO) declared a new Ebola epidemic on March 23, 2014, which had its beginnings in December 2013 in the Gueckedou district in the Republic of Guinea's southeast [9]. Reports of the sickness in patients from Liberia, Sierra Leone, and Nigeria were then made [9].

Figure 2: Ebola virus hit countries.

1.1 EPIDEMOLOGY OF EBOLA VIRUS:

When two distinct outbreaks in the DRC and South Sudan were found, EVD was first diagnosed in 1976 [10]. At the time, it was believed that these epidemics were the result of a single incident involving a traveler who was sick in both places [10]. Further research, however, showed that the 2 viruses, Sudan EBOV and Zaire EBOV, which originated from different origins and propagated independently in each of the afflicted countries, were genetically unique from one another [10]. Consuming contaminated bush meat might result in transmission [11]. It has been proposed that chimpanzees, gorillas, and duikers (a small to medium-sized antelope) act as intermediary hosts for transmission to humans [11]. Although concrete proof has not been provided, bats may serve as reservoirs. Secondary human-to-human transmission of the Ebola virus occurs as a result of exposure to the bodily fluids as well as semen, perspiration, and breast milk [11]. According to historical records, EBOV may have only been able to spread from its natural reservoir host(s) to humans 20–30 times, however it's likely that a few small EVD outbreaks may have gone unnoticed or unreported [3]. The distribution of reservoir species, along with governance, communications, isolation, infrastructure, health care, and global connection, have all been considered when estimating the likelihood that an index case may become infected and then spread locally and worldwide [3].

On August 22, 1976, the first instance was reported [10]. The patient, the principal of the Yambuku Mission School in the Equateur District, was 42 years old and had just returned from a two-week road trip to northern Zaire, where he had bought antelope and smoked monkey meat [10]. Studies of monkey and human infections have shown for decades that viruses may infect and remain in immune-privileged organs like the testes [11]. The inquiry into the 1976 EVD epidemics in the Sudan and Zaire led to the well-documented case of laboratory acquired EVD, which demonstrated that EBOV could be recovered from semen up to 61 days after commencement [11]. Prospective examinations of EVD convalescent patients conducted in the wake of the 1995 Kikwit Ebola epidemic revealed that four of five semen donors had positive quantitative reverse transcriptase polymerase chain reaction samples, with post onset times ranging from 47 to 91 days [11]. Antigen levels in the semen of these survivors proved negative, and virus isolation failed. Indirect evidence of EBOV transmission from one of the survivors to a household contact through sexual interaction via semen was found during the screening of household contacts for this research [11].

1.2 A MODEL OF EBOLA VIRUS DISEASE PATHOGENESIS:

Human index cases infected EBOV outbreaks are typically started by spillover incidents that happen when hunting wild animals, coming into touch with animal corpses discovered in the forest, or meeting bats, the putative viral reservoir [12]. The following human-to-human transmissions brought on by these initial infections account for 99% of all occurrences of EVD in humans [12]. Human EVD symptoms typically appear 2 to 21 days following the start of the incubation period [12]. Even though EVD has claimed the lives of thousands of individuals, very few autopsies or biopsies have been carried out, and those that have mostly focused on cases from the first outbreaks [13]. Petechiae and ecchymoses in the mucous membranes and parenchymatous organs, bleeding in the gastrointestinal tract lumen, congestion of abdominal organs, hepatomegaly, and splenomegaly are among the lesions found at autopsy [13]. There are normally three stages to an illness; the first is a brief period of nonspecific fever, headache, and myalgia; the second is the gastrointestinal stage, which is characterized by diarrhea and vomiting, stomach pain, and dehydration [12]. As the major histologic finding in the liver, hepatocellular necrosis with minor inflammation may also be accompanied with mild periportal inflammation, Kupffer cell hypertrophy and hyperplasia, microvascular lipidosis, mild cholestasis, and the development of Councilman bodies [13]. Hepatocytes typically show eosinophilic intracytoplasmic viral inclusions, while hepatocytes, Kupffer cells, and portal tracts frequently show viral antigen [13]. By 16 days of the onset of symptoms, the disease has progressed to its most severe and fatal stage, when liver and kidney function decrease frequently results in acute metabolic compromise, convulsion, shock, and death owing to mucosal bleeding, bloody diarrhea, and multi-organ failure [12].

Monocytes/macrophages, DCs, fibroblasts, hepatocytes, adrenal cells, and epithelial cells can all be productively infected by this virus, according to analyses of human samples taken from

individuals who had passed away or from experimentally infected animal models [14]. Additionally, several studies revealed that the early replication sites for EBOV infection include DC and monocytes/macrophages [14]. On the other hand, the study of the pathogenic processes behind EHF has made great strides in recent years [15]. Unfortunately, due to the incidence of outbreaks in remote locations and the absence of facilities that permit safe and complete studies during an outbreak, there are only a few data available addressing the pathophysiology of EHF in people [15]. As a result, the creation of EHF animal models has greatly contributed to our understanding of EBOV pathogenesis [15]. By moving from the spleen and lymph nodes to other organs, these cells play important roles in the virus's ability to spread [14]. Mice are the most often used animal model in the EBOV field for a variety of reasons, including their ease of handling in the Animal Biosafety Level 4 laboratory, the availability of transgenic and knockout strains for study, and the abundance of instruments for analyzing host reactions [12]. Yet, in adult immunocompetent mice, wildtype EBOV isolates do not result in any clinical symptoms of illness [12]. NHPs are currently the best species to replicate EHF in, however mice and guinea pigs can also be used [15]. Importantly, wild-type EBOV can become lethal by viral passaging even if it is not lethal in these rodent models [15]. Mutations in NP and VP24 have been linked to enhanced virulence in both mouse and guinea pig models [15]. Even though these animal models have greatly advanced our understanding of EBOV pathogenesis, several characteristics of the human form of the illness have not been accurately modeled [15].

As a result, researchers have employed immunodeficient mouse strains, primarily those without a functioning type I IFN system, to examine illness, such as STAT1 or interferon receptor mice or severely combined immunodeficient mice [12]. Since a little dosage of WT-EBOV is sufficient to largely produce fatal illness 1 week after infection, these immunodeficient mice are particularly sensitive to infection [12]. It is important to remember that the immunology of rodents and humans differs significantly [15]. Both mouse and guinea pig models lack the distinct hemorrhagic symptoms that characterize EBOV infection in humans [15]. Moreover, rats do not exhibit a lot of the bystander lymphocyte apoptosis that is seen in humans [15]. It's interesting to note that the virus mostly replicates in the liver and spleen, which are crucial organs for EBOV infection in NHPs and humans [12]. These results also show that mice's susceptibility to EBOV infection is strongly influenced by the type I IFN response [12].

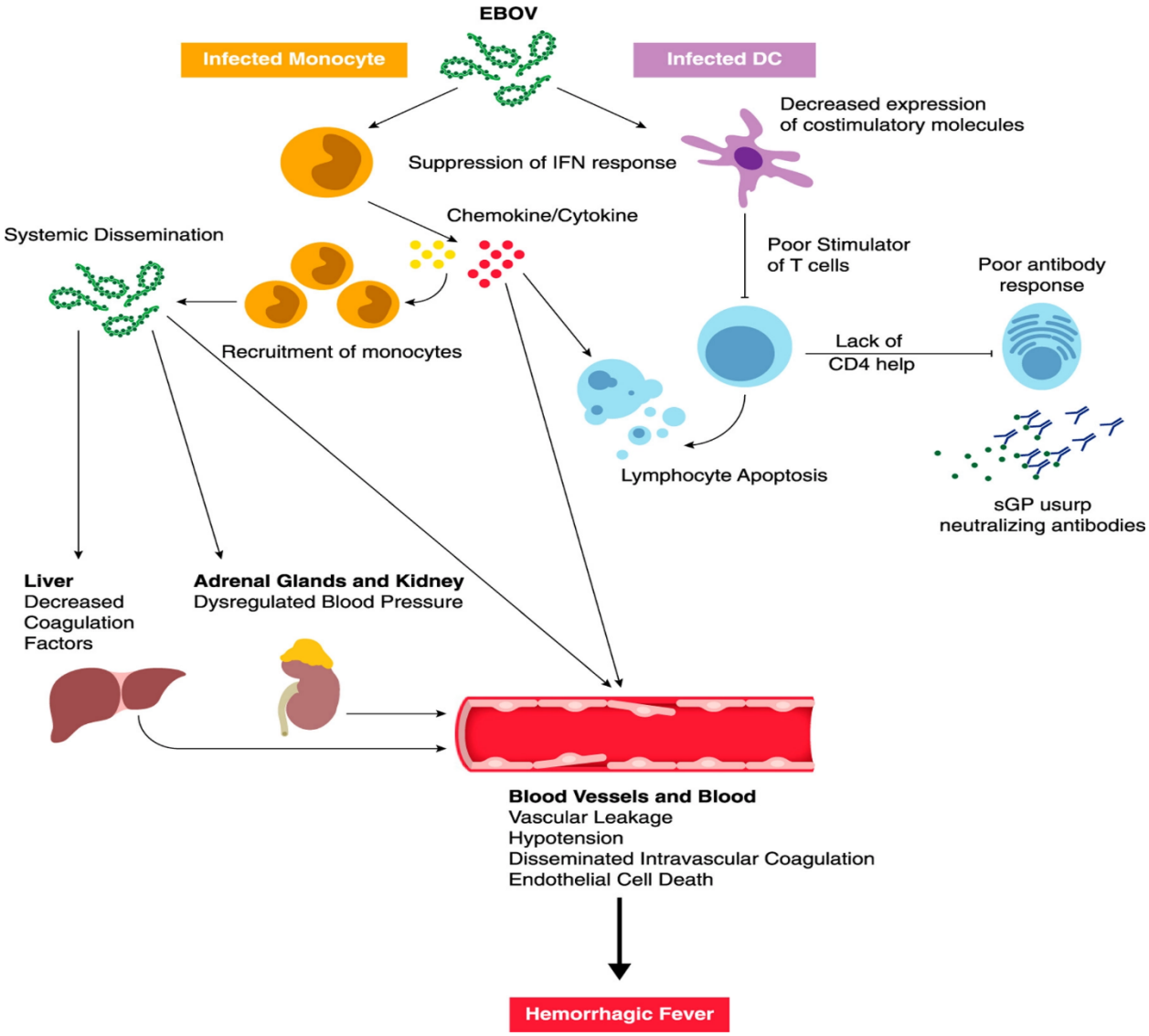

Figure 3: Ebola virus disease pathogenesis

1.3 POST EBOLA VIRUS SYNDROME:

The greatest outbreak of the ebolavirus disease (EVD) ever, which is now raging in West Africa's Zaire region, has resulted in a sizable amount of mortality and morbidity [16]. Since the epidemic began at the end of 2013, there have been more than 27,740 cases, primarily in Guinea, Liberia, and Sierra Leone [16]. Around 28,000 people had EVD suspected or diagnosed, and 11,000 people passed away during the West Africa pandemic between 2014 and 2016 [17]. In the middle of 2018, a brand-new EVD hotspot appeared in the Democratic Republic of the Congo, and it is most probable that further outbreaks will happen in the future [17]. Patients are deterred from seeking treatment due to the low survival probability, and healthcare workers are deterred from caring for patients who are highly contagious due to the occupational danger [17].

A significant number of survivors, known as PES patients, report having ongoing symptoms such arthralgias and ocular issues [17]. Studies on PEVDS are few, and the long-term implications of Ebolavirus infection are poorly known [16]. Several symptoms, including reduced vision and hearing, headaches, pains in the muscles and joints, weariness, disorientation, stomach discomfort, and weight loss, have been recorded by EVD survivors [16]. Several people have now survived the Ebola virus sickness (EVD). Focus has been placed on reducing infection transmission and enhancing survival during the current EbolaZaire outbreak. In a recently released research, after the 2007 Uganda EVD outbreak, 157 controls and 49 Bundibugyo ebolavirus survivors were matched [16].

Both arthritis and uveitis, which can cause blindness, may be impacted by inflammation [17]. The availability of an effective supplementary therapy medicine would reduce mortality, boost treatment attendance, and bolster HCWs' desire to provide care for patients [17]. A successful PES adjunctive medication might lessen the morbidity endured by survivors [17]. During the convalescence phase, reports of blurred vision, retro-orbital discomfort, hearing loss, neurological symptoms, exhaustion, sleep difficulties, big joint arthralgias, poor mood, and memory loss were made [16]. After EVD, the long-term sequel continued for more than two years [16].

1.4 DIAGNOSIS OF EBOLA VIRUS DISEASE:

Etiological testing and serological testing are the two main types of conventional laboratory tests determine whether or not EBOV infections have occurred [18]. Reverse transcription polymerase chain reaction (RT-PCR), which enables the detection of the viral genome, enzyme-linked immunosorbent assay (ELISA), which enables the identification of viral antigenemia, as well as the culture and identification of live virus are some etiological testing techniques [18]. The Ebola virus may be found quickly and accurately using the RT-PCR method that targets viral nucleic acids [19]. There are several in-house and commercial PCR assays available for the detection of the Ebola virus with various targets [19]. The WHO advises sending tests conducted elsewhere to a WHO Supporting Center for secondary confirmation, such as the Centre Pasteur de Lyon (France) or an institute founded by Bernhard-Nocht for Tropical Medicine (Germany) [19]. Patients might test negative during the first three days of the beginning of symptoms, hence the WHO advises repeat testing within 72 hours [20]. In real-world settings, reporting times are frequently several days and factors like specimen transport, human resources, and supply chain are more significant reasons for delays than hands-on analysis time [20]. RT-qPCR tests generally require cold-chain reagents but also take 1-3 hours, depending on throughput and batching [20]. When opposed to obtaining mouth swabs and other non-invasive specimens, the demand for intravenous blood poses a danger for healthcare workers to transmit the infection [20]. A WHO emergency process has been developed to evaluate in vitro diagnostics [19]. An only item, the RealStar Filovirus Screens RT-PCR kit 1.0, had received approval as of December 11th, 2014 [19]. The US Food and Drug Administration (FDA) has granted an Emergency Use

Authorization for a real-time RT-PCR assay for the Ebola virus nucleoprotein [19]. According to retrospective modeling research, Sierra Leone's epidemic might have been cut in half by adopting dual screening that included an extremely sensitive RDT accompanied by an extremely specific PCR test [20]. Nevertheless, as was the case of the initial outbreak of BDBV, when there was a nucleotide variation of 32% among BDBV & TAFV, it is possible that there are undiscovered filovirus species that cannot be diagnosed by the present molecular diagnostics [20]. This was not the situation for the recently found BOMV, it is important to mention [20].

1.5 TREATMENT OF EBOLA VIRUS DISEASE:

The current protocol for sick people with suspicious or proved EVD is lockdown, symptomatic control and supportive therapy, including rehydration, recovery of electrolyte deficiencies, initial care of further bacterial infections, empiric dengue diagnosis, and vital organ function help in case of disease progression; mostly restricted to settings that allow for maximal care [21]. As of this writing, there are no accepted vaccines or treatment options available for human use [21]. Supportive care is the current course of treatment for EVD [22]. The progression of gastrointestinal symptoms, including vomiting and diarrhea, that result in intravascular volume depletion, severe electrolyte abnormalities, and shock have been the most noticeable EVD hallmark in this epidemic [22]. Bleeding is a later symptom that only a small percentage of people experience. Hence, maintaining intravascular volume through intravenous fluids or mouth rehydration and electrolyte-containing solutions is the most crucial component of supportive treatment [22]. Despite the ethical, logistical, organizational, and technical challenges that typically prevent the design and execution of clinical trials in outbreak situations, a great deal of progress has been made during the most recent outbreak in West Africa beyond these limited prevention and treatment options [21]. The prompt approval of numerous clinical vaccination experiments represented a significant advancement in this regard [21]. Effective therapy development has advanced more slowly than other areas [21]. Blood transfusions and evidence-based suitable sepsis care might also be considered [22]. Together with empiric antibiotic for enteric infections, treatment of other concurrent disorders like malaria infection is advised, particularly during the gastrointestinal phase of sickness [22]. The potential impact of supportive treatment is significant for an illness that has a high baseline mortality [22]. But it's important to remember that supportive therapy may not be sufficient [22]. Also, conventional hyperimmune globulin derived in Ebola animal models, short interfering RNAs targeting certain proteins of Ebola viruses, monoclonal antibodies, & morpholino oligomers. In nations where EVD is prevalent, several medicinal drugs are currently undergoing expedited human studies [23]. Postexposure prevention and EVD treatment are objectives of therapeutic agent development [23]. More treatment techniques will probably be created as our understanding of the virology and pathophysiology of the Ebola virus expands [23]. Controlling epidemics requires preventing the transmission of the Ebola virus. This entails taking precautions including utilizing personal protective equipment, separating sick people from others, and maintaining excellent hygiene. Moreover, vaccines that have demonstrated promising outcomes in preventing Ebola virus infection have been created.

1.5.0 Nucleoside Analog Candidate Therapies (favipiravir):

In 2014, antiviral studies and developments were concentrated on finding secure and effective treatments that could be used postexposure [26]. One of these drugs, T-705, has undergone tests on animals to see how effective it is against EBOV [26]. It has been demonstrated that the pyrazine carboxamide derivative favipiravir is effective against ZEBOV both in vitro and in vivo [26]. Favipiravir is successful in treating animals infected with the EBOV aerosolized E718 strain, according to research conducted on animals [26]. Recent research suggests that favipiravir causes viral mutagenesis, which decreases viral replication and infectivity [26]. The substance was first created as an agent versus influenza viruses and has wide antiviral properties [26].

It has been demonstrated that the related pyrazine carboxamide compounds T-1105 and T-1106 are efficient against a variety of viruses [27]. Among T-705, T-1105, and T-1106, T-1105 had the strongest antiviral activity against the foot-and-mouth disease virus, with an EC50 value of 12 lM [27]. Even though anti-antibody was found, no clinical symptoms of FMD were seen in the T-1105-treated pigs during the whole investigation [27]. T-1105 was shown by Leen Delang et al. to prevent the multiplication of several laboratory strains, clinical isolates, and other investigated alphaviruses [27]. T1106 surprised researchers by demonstrating unexpected therapeutic efficiency in a hamster yellow fever model while having very moderate in vitro activity against by the virus (EC50 > 369 lM) [27]. Both tissue culture and small mammal models of the Ebola virus infection response to favipiravir look promising [28]. Favipiravir should be administered for 14 days at a dosage of 300 mg/kg/d in two split doses for influenza [28]. Yet, this treatment led to a chance of survival of 1/6 in early investigations using monkey models of the Ebola virus [28]. In monkey models, higher-dose regimens are now being tested [28]. It is noteworthy that a French nurse who had the Ebola virus appeared to have responded well to an oral favipiravir treatment [28]. Because favipiravir is already in later phase research, it should be widely available, which is one benefit of using it in the present outbreak [28].

1.5.1 Nucleoside Analog Candidate Therapies (Brincidofovir):

Brincidofovir (BCV), an antiviral for double-stranded viruses, is a lipid conjugation of the acyclic nucleotide phosphonate cidofovir [26]. The US FDA has accorded BCV investigational new drug designation as a possible therapy for EBOV due to BCV's documented in vitro activity towards EBOV, even though clinical trials to examine BCV's effectiveness versus human cytomegalovirus (CMV), pox, and adenovirus illnesses are continuing. In order to investigate BCV's effectiveness and safety during the treatment of EBOV infection, an open-label, multinational trial in humans is now being considered [26]. There shouldn't be any significant production problems since brincidofovir had previously entered phase 3 studies for other purposes [28]. Some information on the pharmacokinetics and safe profile of brincidofovir is provided by a current phase safe and acceptability trial where it was investigated for preventing

CMV infection in recipients of hematopoietic cell transplants [28]. Adult participants in this trial received oral brincidofovir at various dosages for nine to eleven weeks [28]. With the dosages given once weekly, trough concentrations of brincidofovir & cidofovir were almost undetectable [28]. In both groups receiving doses twice weekly, higher nadir levels were observed [28]. As the dosage was increased, the plasma levels three hours after delivery rose linearly [28].

1.5.2 Nucleoside Analog Candidate Therapies (BCX4430):

A new broad spectrum nucleoside analog named BCX-4430 has shown promise in treating the Marburg and Ebola viruses [28]. Adenosine analog BCX-3340 is phosphorylated intracellularly into a triphosphate form. Mammal RNA or DNA do not include BCX-3340 [28]. Transcription is terminated because viral RNA replication occurs as a result of BCX-3340's indirect inhibition of RNA polymerase activity with nonobligate RNA chain termination [28]. Early animal studies showed that BCX-3340 provided protection from Ebola infection for 96 hours after a lethal dosage was administered to a mouse model [28]. When administered 1 hour, 24 hours, and 48 hours and after delivery of a fatal dose of the virus, BCX-3340 proved protective in macaques infected with the Marburg virus [28]. Although BCX4430 is still up for debate, high-risk or possibly exposed individuals may benefit from early treatment. While pharmacokinetics findings show that the intramuscular method may produce more favorable therapeutic levels, administration of BCX4430 via the oral route may be viable [26].

In the recent time for the ebola virus drug isn’t established perfectly. Some of them are on clinical trial or animal trial and some of them are investigated. So here the list of some drug which used of the ebola virus patient right now.

Medication	Mechanism of Action	Route	Dosing
ZMapp	Three monoclonal antibodies combined	IV	People: unknown Macaque: three dosages of 50 mg/kg every three days.
Brincidofovir (Chimerix)	Ebola: unknown CMV:Incorporated into DNA chain, inhibiting DNA synthesis	Oral	200 mg Once, then 100 mg twice weekly for 2 weeks
Favipiravir (Fuji Film/ Toyama Chemical)	Nucleotide analog that, when incorporated into viral RNA, inhibits RNA polymerase and results in deadly mutagenesis3333	Oral	150 mg/kg Twice daily for 14 days
TKM-Ebola (Tekmira)	siRNA; interferes with proteins L, VP24, and VP35	IV	Human: 2.4 mg/kg/ dose Macaque: 2 mg/kg/ dose daily for 4-7 doses
AVI-7537 (Sarepta)	PMO, which inhibits protein VP24	IV	Human: 16 mg/kg (estimated effective dose) Macaque:~30 mg/kg daily
cAd3 (GSK/ USNAIAD)	Stimulates immune. response to Ebola glycoprotein using chimpanzee adenovirus	IM	Single dose

rVSV-Ebola (Newlink Genetics/PHAC)	Stimulates immune. response to Ebola glycoprotein using rVSV	Oral and IM	Single dose; could be affected for postexposure prophylaxis

Table 1: Overview of Ebola Therapeutics

1.5.3 Small Interfering RNA Agents:

To aid in cellular transport, lipid nanoparticles are used to contain one formulation of short interfering RNAs that specifically targets EBOV. SiRNAs force messenger RNAs to cleave, which stops the EBOV from producing three essential viral proteins [29]. A technique for controlling gene expression known as RNA silencing also controls cell differentiation & development [26]. Insects, nematodes, and plants all use RNAi as an intrinsic antiviral defense. Viruses in mammals encode suppressors of RNA silencing, allowing for larger titers of viral replication [26]. Within 30 minutes after receiving a fatal dose of EBOV, two groups of macaques were given intramuscular injections of TKM-Ebola [29]. On days 1, 3, and 5 after exposure, one group received TKM-Ebola treatment, whereas the opposing group received post-exposure care every day for six days. The second regimen offered 100% protection while the first one offered 66% [29]. Moreover, research is also being done to assess the lipid nanoparticle/siRNA known as TKMEbola [26]. TKM-Ebola phase I studies have started. The U.S. Food and Drug Administration granted fast-track approval for TKM-Ebola in March 2014 [26]. Moreover, TKM-Ebola is currently undergoing human clinical assessment in Guinea for use in the urgent treatment of EBOV patients in association with a consortium headed by the WHO. The ZEBOV species' Guinea variation is the target of the TKM-Ebola chemical that is currently being tested [26].

1.5.4 Immunotherapy:

When there are no safe and effective treatments or vaccines available and a condition has the potential to be severe or have major effects, convalescent whole blood, plasma, and hyperimmune serum have historically been used [29]. In the Kikwit, DRC epidemic in 1995, patients with EVD were treated therapeutically with passive immunotherapy and convalescent immune plasma [29]. Passive immune therapy and convalescent immune plasma have been used to treat EVD outbreaks in the past, such the one that hit Kikwit, Zaire, in 1995 [26]. Passive immunity treatment was used on eight individuals who fit the case criteria for EVD; seven of these patients recovered [26]. In this study, 8 patients received the blood of recovering patients, of whom 7/8 (87.5%) recovered from the illness [26]. Nevertheless, there are currently no conclusive results from human clinical trials demonstrating the efficacy of CWB or CP in lowering the severity or duration of EVD [26].

1.5.5 Ebola virus vaccines:

The two types of ebolavirus vaccines nonreplicating and replicating can be generally classified, with the former further subdivided into inactivated, subunit, and vector-based vaccines [30]. Unlike vector-based vaccinations, which use DNA or viral vectors to produce the immunogen in the vaccinee, subunit vaccines deliver the immunogen in the form of purified proteins or virus-like particles [30]. The 1980s saw the start of the development of an ebola vaccine [26]. Rodents and NHPs have been used to evaluate a variety of vaccine candidates, including vaccines based on recombinant viral vectors, DNA vaccines, virus-like particles, and inactivated virus [26]. Genes necessary for the viral vector's life cycle are deleted in non-replicating viral vectors [30]. As these vectors can only survive for one infectious cycle and must be created while delivering the proteins encoded by the erased genes in trans, many safety worries regarding vaccines are dispelled [30]. Nevertheless, greater dosages and/or repeated injections are frequently necessary for these vaccines to really be effective [30]. The fact that the control group's mortality rate in this study was only 29% should be noted as an extra phenomenon, since it raised questions about validity of the study [31]. After being challenged with 10 PFU of the Ebola virus that had been modified for use in mice, it was later demonstrated that the inactivated vaccination can offer 100% protection [31]. However, the continued study has been put on hold since 2002 due to the biological safety risk and the fact that this inactivated vaccine did not shield NHPs from exposure to 1000 PFU of EBOV [31].

1.5.5.0 DNA vaccines:

In order to immunize guinea pigs, Xu et al. created a DNA vaccine that expressed the GP or NP gene in the early months of 1998 [31]. The findings revealed full protection [31]. Another study showed that immunizing animals with 4 doses of GP DNA vaccine resulted in 100% protection against challenge with 30LD of mouse-adapted EBOV [31]. The combination of DNA vaccinations and a boost with a replication-deficient recombinant adenovirus encoding ZEBOV GP was evaluated in NHPs, and this was the first method to successfully protect 100% of NHPs against a challenge that would otherwise be fatal [30]. It is unclear, however, how much the DNA element of this strategy contributed to this achievement considering that recombinant adenovirus alone may produce 100% protection [30]. A mega DNA vaccine expressing the GP genes of EBOV, SUDV, and MARV was later shown to be extremely efficacious in mice in 2012 without showing any signs of interference [31]. Moreover, it has been demonstrated that protecting NHPs against a deadly EBOV challenge involves priming with a DNA vaccine and bootstring with adenoviral vectors [31]. A most promising and efficient method of preventing the spread of the Ebola virus is first thought to be the DNA vaccine, which causes robust CD4 responses and long-lasting protection [31].

1.6 FUTURE DIRECTIONS:

Several EVD outbreaks since the 1970s have produced evidence that EVD may be classified as a deadly virus that has evolved and spread when human interaction with wild species of animals has grown [26]. Further ecological, epidemiologic, and clinical disease surveillance will remain crucial across all Ebola-endemic nations in order to investigate potential initiators and predictors of fresh outbreaks in the future [26]. The fast development of the West Africa outbreak in 2014 and 2015 brought to light the necessity for more investigation into the systems and technologies that quicken local, national, and international health organizations' response to the containment of EBOV transmission and epidemics [26]. The development of an Ebola vaccine has significantly advanced over the past two years, and several vaccine candidates have done remarkably well in phase I or II clinical trials [31]. Phase III trials on Ebola vaccines are continuing [31]. Although though the frequency of Ebola outbreaks had decreased and there had only been a few rare cases of the disease recorded in recent months, the Ebola virus continued to garner a lot of interest on a global scale [31]. The first vaccination to effectively exhibit a high level of protection against Ebola illness in a phase III study is the rVSV-EBOV vaccine, which may become first Ebola vaccine to be approved by the FDA [31].

Chapter 2
Purpose of the study

2.0 Purpose of the study:

The precise research topic being addressed will determine the project's objectives for an Ebola virus investigation. However, a study on the Ebola virus can have the following objectives:

1. Knowing the Ebola virus's biology and discovering potential targets for vaccines or antiviral medications.
2. Examining the epidemiology of the Ebola virus and detecting danger signs for infection and the spread of an epidemic.
3. Developing and testing diagnostic instruments for quick Ebola virus infection detection.
4. Comparing the efficacy of various treatment modalities for Ebola virus infection.
5. Identifying methods for containing and avoiding Ebola virus epidemics, including as vaccination drives, public health awareness initiatives, and outbreak response preparation.

The overall objective of an Ebola virus research would be to further our knowledge of the disease and create tactics for halting and controlling its transmission, thereby enhancing the public medical conditions of individuals and impacted by Ebola virus epidemics.

Chapter 3
Methodology

3.0 Data collection procedure:

The review's search technique was created in conjunction with a few web articles. The primary search, which comprised the major database: bibliographic databases, PubMed, Research Gate, Google scholar, and Medline, was finished in February 2023 after many trial searches. It provides a description of the instructional setting. The study sample, study population, research instruments, methodology, and data analysis are just a few of the numerous factors to consider. This is an overview of prior studies on the symptoms of the Ebola virus disease. Because of its extraordinary scope, an Ebola virus outbreak is the main subject of this review. I collected data from paper registers at each site using standardized data abstraction forms. Data gatherers had received training and were not connected to the facilities. research on the origins, symptoms, and treatments for Ebola virus. While some of the material was gathered by reading past study publications directly, some of it also came via searching the internet for relevant information. All the data imported was numerically coded from earlier study papers.

3.1 Data analysis strategy:

Data analysis techniques encompass the generally exclusive to the actions including data assembling, purification, and organizing. To prepare the data for commercial use, data needs to undergo various processes, which often require the use of data research tools. Data analytics, a different term for data gathering, is understood to be the discipline of looking at raw data to draw reasonable conclusions from it.

Chapter 4
Literature Review

4.0 Ebola Virus disease:

Ebolaviruses are single stranded RNA virus that really are native to parts of western and equatorial Africa and are members of the Filoviridae family [24]. These public health infections, which cause severe and acute systemic illness with a high fatality rate, are largely spread through human-to-human contact with contaminated bodily fluids and corpses [24]. This 2013–16 west African epidemic demonstrated the significant pandemic potential of ebolaviruses [24]. With much more than 28000 cases reported and 11000 fatalities, this outbreak had a size never seen. It had a catastrophic economic effect on west Africa [24]. This epidemic also shown the potential for a quick shift from the urban districts of major cities to the predominantly impacted rural communities when there is a lack of public infrastructural resources [24]. The pandemic was eventually contained because to strong international cooperation and efforts from the afflicted nations [24]. This outbreak was especially exceptional because it sparked the development and implementation of extensive research programs into the pathophysiology associated with the ebolavirus, which resulted in significant discoveries in science [24]. The information on epidemiology, illness manifestation, pathophysiology, case treatment, and community control of various diseases is reviewed in this seminar [24].

4.1 Ebola Virus Disease: Reproductive, Maternal, and Child Health:

It was also observed that prenatal, postnatal, and reproductive services were used differently [25]. ANC & PNC visits declined throughout Sierra Leone: during the final 6 months in 2014, visitation considerably reduced in six out of fourteen districts, as well as the number of women receiving their fourth ANC visit plummeted by 27% [25]. In May and July 2014, prenatal attendance at a hospital in Moyamba district plummeted by more than 50%, while in Kenema region, the number of the first ANC visits fell by 29% and the frequency of PNC trips in the first 48 hours following delivery fell by 21% [25]. Despite a drop in services for family planning of 50–75% during the length of the epidemic, study of routine health care data in three different regions in the last three months of 2014 did show this [25].

The decrease in use also affected children's health services. Throughout the course of 2014, Guinea's hospitals and health facilities saw fewer young children under the age of five for ARI and diarrhea [25]. Regarding vaccination, there was an 18 to 32% decrease in the distribution of tetravalent vaccine dosing frequency 1 and 3 at healthcare centres in Guinea, a 21% drop in the number of kids receiving dose 3 of the vaccine across Sierra Leone, and a 26% drop in the number of young kids who were fully immunized in a hospital in the Moyamba district [25].

Modeling research for all three nations looked at how a 6-, 12-, or 18-month interruption in the delivery of health services might alter children's measles risk. Before the EVD outbreak, a

projected 778,000 children in these nations between the ages of nine months and 5 were unvaccinated [25]. By 18 months, there would be 1.5 million unvaccinated children, or an additional 20,000 for every additional month of health care interruption. In this circumstance, 200,000 cases of measles during an epidemic would be more likely than 100,000 [25].

Chapter 5
Results & Discussion

5.0 RESULT:

The Ebola virus may cause severe viral disease in both humans and quasi primates. It is a highly contagious and frequently fatal infection. In 1976, two outbreaks of the Ebola virus occurred simultaneously, one was in Sudan and one in the DR Congo. Ever since, there have been an increasing number of Ebola outbreaks in African, including the most recent one occurring in Guinea in 2021.

Contact with body fluids from infected people, like blood, saliva, urine, and feces, is how the Ebola virus is spread. Fever, headache, muscular aches, weakness, exhaustion, nausea, vomiting, stomach pain, and bleeding are among the symptoms of an Ebola virus infection.

Blood or other body fluids are tested in a lab to determine whether someone has the Ebola virus. The primary form of therapy for an Ebola virus infection at this time is supportive care. Nonetheless, a number of investigational therapies are being created and examined.

5*.1 DISCUSSION:*

Due to the Ebola virus's high fatality rate, quick dissemination, and potential for worldwide transmission, it poses a serious threat to public health. With almost 28,000 cases & 11,000 confirmed fatalities, the Ebola outbreak that occurred in West Africa between 2014 and 2016 was the biggest in recorded history.

Local, national, & international health institutions must act swiftly and in unison to contain Ebola epidemics. The spread of the virus can be stopped by taking steps including contact tracing, isolating sick people, and using personal protective equipment. To create efficient cures and vaccines against Ebola virus infection, research is continuing. The U.S. Food and Drug Administration authorized an Ebola vaccine in 2019, and clinical trials for several experimental therapies have yielded encouraging results.

In summary, the Ebola is indeed a severe and highly contagious disease that poses a serious risk to the public's health. For outbreaks to be contained, control methods include quick action, contact tracking, and isolation of affected people are essential. To stop further outbreaks and lessen the virus' impact on world health, research of efficient treatments and vaccinations is crucial.

Chapter 6
Conclusion

6.1 Conclusion:

In summary, the Ebola virus represents a dangerous danger to the general population since it is extremely infectious and frequently fatal. The most recent epidemic in Africa to be caused by the Ebola virus was in Guinea in 2021. Regional, national, & international health institutions must act swiftly and in unison to contain Ebola epidemics. The spread of the virus can be stopped by taking steps including contact tracing, isolating sick people, and using personal protective equipment.

The Ebola virus infection does not presently have a particular therapy; however, a number of investigational drugs are being created and evaluated. To stop further outbreaks and lessen the virus' impact on world health, research of efficient treatments and vaccinations is crucial. The creation of the Eb vaccine represents a huge advance in the battle against the illness.

It is critical to keep spreading knowledge about the Ebola and the need of precautions and controls. Those who contract the virus may have a better chance of surviving with early discovery and timely treatment. Global action and cooperation across several stakeholders, including authorities, health organizations, and communities, are necessary to control and prevent Ebola epidemics.

Chapter 7
Reference

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