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ABSTRACT

Monkeypox is an uncommon virus that is mostly found in Central and West Africa and can be transmitted to humans from animals. The treatment of monkeypox requires the prompt isolation of potential cases, strict infection prevention protocols for healthcare workers, and placing close contacts under quarantine. It is essential to have surveillance systems in place to monitor the spread, while public health education is crucial in order to increase awareness and encourage the adoption of preventative measures. While there is no targeted antiviral treatment, smallpox vaccination has proven to be effective in preventing the disease, and scientists are currently working on developing vaccines specifically for monkeypox. Control tactics concentrate on identifying and controlling animal reservoirs, imposing travel limitations, and managing possible vectors. It is crucial to make efforts to minimize the interaction between humans and animals in areas where diseases are prevalent. Supportive care is the main component of treatment, focused on easing symptoms, addressing secondary bacterial infections with antibiotics, managing pain, and maintaining fluid levels. It is crucial for local health authorities to work together with international organizations in order to effectively implement control measures and prevent outbreaks. As our understanding of monkeypox grows ongoing research and monitoring play a key role in improving methods for managing, controlling, and treating the disease. This highlights the necessity of a comprehensive and well-coordinated approach to addressing this public health issue.

Keywords: Monkeypox; Zoonotic virus; Surveillance; Vaccination; Supportive care

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INTRODUCTION

Monkeypox (MPX) is an emerging zoonotic viral infection. The causative agent of this disease is a DNA virus of the genus Orthopoxvirus. MPXV is a member of the Poxviridae family and subfamily of Chordopoxvirinae. It is a double-stranded DNA virus that multiplies in the cytoplasm of infected cells. It is wrapped and lump-shaped (Karagoz et al. 2023).

The first case of MPXV infection was reported in 1958 in Denmark (A small Scandinavian country), where the monkeys were kept for study purposes (Brown and Leggat 2016). The term "Monkeypox virus" is used for the pathogen that was first discovered in monkeys in 1958. However, the name is misrepresentative because monkeys are incidental hosts, not natural hosts, of viruses. This viral disease was found to be prevalent in animals other than monkeys, like rodents, squirrels, rats, and mice. The disease is endemic to Africa and caused by MPXV. The virus exists naturally in the woody regions of central and West Africa (Chomel 2016).

Evolution of monkeypox The origin, evolutionary history, genetic diversity, and phenotypic traits of the accessible MPXV genomes must be determined in order to inform diagnosis, prevention, and research. OPVs typically change their gene composition to adapt in the hosts. Furthermore, whereas pathogenicity and genome-sequence length are inversely correlated, they pragmatically correlate with a wide spectrum of hosts (Isidro et al. 2022). Larger genomes and content in the WA clade of MPXV than in the CB clade (196,850-196,959 bp) may be a factor in the WA clade's decreased pathogenicity. Additionally, a phylogenetic study of the MPXV viral classifications linked to multicounty outburst in 2022 showed that the virus belongs to a third recently formed clade: (Within the earlier named "WA" clade, which also includes Clade two). The hMPXV-1A clade and the 4 recently identified lineages A.1, A.1.1, A.2, and B.1, with heredity B.1 having all MPXV genomes from the 2022 epidemic, However Clade 3 has a reduced disease-fatality rate. The three clades' principal distinctions are connected to coding areas. In comparison to the related viruses, the 2022 MPXV differs from 50 single-nucleotide polymorphisms (SNPs) by an average. This divergent branch, which separates the current epidemic virus from the sequence, might point to faster evolution (Luna et al. 2022).

2. MPXV STRUCTURE GENOME AND MORPHOLOGY

According to morphological studies, MPXV is an ovoid or brick-shaped particle covered in an outer lipoprotein membrane with geometric corrugations. Its virions are physically identical to those of other orthopoxviruses. MPXV is expected to be between 200 and 250 nm in size. (Khattak et al. 2023). The DNA genome, enzymes, and transcription factors of viruses are all shielded by the outer membrane. Due to an anomaly in electron microscopy, the core is described as being biconcave and having an adjacent body on either side (Manoj et al. 2020). A linear double-stranded DNA molecule with a length of 197 kb makes up the structure of the MPXV genome and contains a lot of open-reading frames (ORF). The structure of viruses contains palindromic hairpins with inverted terminal repeats (TTRs), simultaneous repeats, and hairpin looping, which are inextricably linked at both ends (Ghosh et al. 2023). DNA viruses, including MPXV, Complete their full life cycle inside the infected cells. All of the proteins required for viral DNA replication and transcription are encoded by the MPXV genome. Orthopoxvirus (OPV) species share a set of constitutive genes in the genome's central region. Genes that regulate virus-host communication are found in the terminal region and are less conserved (Senkevich et al. 2021). MPXV produces two different types of infectious virions: EEV (extracellular-enveloped virus) and IVM (intracellular mature virus). In contrast to IMV, when cell lysis starts, IMV is released. EEV is formed when actin tails come into contact with cells, allowing the virus to easily spread in the host body (Khattak et al. 2023).

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Inner encapsulated viruses (IEVs) that reach the cell's edge and fuse with the plasma membrane form cell-associated virions (CEVs). CEVs are fundamentally in control of cell-to-cell communication. IEV is formed when IMV is encircled by a double membrane produced by the trans-Golgi network (TGN) (Khatif 2017). Orthopoxvirus (OPV) species share a set of housekeeping function genes in the genome's central region. Through the plasma membrane is another method for EEV synthesis in addition to IEV exocytosis. A-type inclusions (ATIs) include neither ATIs nor IMVs because MPXV truncates the gene for the A-type inclusion body protein (Khattak et al. 2023).

3. IMMUNITY TO MONKEYPOX VIRUS

There is a scarcity of knowledge about human immunity to MPXV infection. However, the virus has been recognized and known for years. The research studies related to members orthopoxviruses group are often considered to suppose how MPXV interacts with the immune system of the host.

4. INNATE IMMUNE RESPONSES TO MPXV

Innate immune cells of the body are usually considered as the first line of defense, When a virus attacks the individual with active viral infection, though some viruses also consider these immune cells as their targets. Among these cells, monocytes are the first cells that target poxviruses. According to several *in-vitro* and *in-vivo* studies, it has been proposed that early identification of poxvirus antigens in neutrophils and monocytes is a powerful aspect to predict against MPXV. Monocytes causing monkeypox are aggressively drawn to infection sites, and viral pneumonia is caused by MPXV infection. It causes a substantial increase of CD14+ monocytes in the lungs of cynomolgus macaques. Inflammatory monocytes have been revealed to be permissive to replication of VACV and may be possible carriers of the virus. Moreover, it was revealed that M2 human primary macrophages promoted VACV replication and spread (Davies et al. 2017). These primary macrophages developed actin tails, cell connections, and branching structures linked with the VACV virions after becoming infected, suggesting that these cells may help in the transmission of the virus. It was also noted that phagocytic cell depletion did not completely stop the spread of VACV72, indicating that other immune cells are also capable of promoting virus spread. Ly6G+ innate immune cells, were in charge of invading and regulating virus-infected cells, hence reducing viral tissue damage. These findings were indirectly supported by a study that discovered a link between sickness in MPXV-infected animals and low blood neutrophil extents. It is highly essential to consider that immune cells reach to the infection site to stop fleshy tissue pathology. However, immune cells don't play any role in stopping the transmission of the virus. Systemic immune response is required for recovery from widespread infection. Natural killer cells are an essential part of innate immunity and may involve directing the course of the response of adaptive immunity.

5. EPIDEMIOLOGY

MPX infection was identified when a smallpox-like disease broke out in colonies of monkeys in a research institution in 1958. The virus-causing MPX infection was isolated and characterized for the first time in 1958 when monkeys with vesicular illness were brought from Singapore to Denmark. However, the first case of MPX disease in humans was detected in a 9-month-old child in the year 1970 in the Democratic Republic of Congo. The Democratic Republic of the Congo recorded 485 MPX cases, of which 25 were deaths, from 2001 to 2002 (Iqbal and Jaffri 2022). From the years 2017 to 2018, in Nigeria, 122 cases of MPX infection were reported, in which seven people died due to the

disease. However, the outbreak of MPX disease outside of Central and West Africa was considered to be rare (Yinka-Ogunleye et al. 2019). By May 23, 2022, Pakistan had challenged two sporadic occurrences of the zoonotic MPX disease, which had already spread to 12 other nations. According to the medical staff of Lahore Services Hospital (LSH), two cases of MPX were found in Lahore Jinnah Hospital, Pakistan. The patients were isolated and given good care in different isolated wards. After the detection of these cases, the National Institutes of Health (NIH) advised the nation's healthcare facilities to treat the illness with caution. 8 Moreover, the MPX disease outbreak was declared a Global Health Emergency on July 23, 2022, and 18597 cases of MPX were reported worldwide. According to the latest WHO data (January 3, 2023), a total of 25,736 MPX cases have been detected in 45 countries and regions in the European Region. The CDC's most recent data show that there are 84,471 cases overall in the world as of January 10, 2023. 1,200 of them are from areas where MPX cases have previously been found; the remaining are from areas where MPX has never been reported historically (Doganay and Aydin 2023).

6. TRANSMISSION

It was stated that the transmission began when rats were imported from Ghana to the United States. These rodents are thought to be responsible for causing MPX infection among prairie dog species that were being sold as pets (Simpson et al. 2020). The disease may also be caused by close physical contact, lesion exposure, and direct and indirect contact with infected animals. However, it is still under inquiry whether the virus is spread via rodent invasions or by eating wild animal meat. Exposure to animal excrement can be a serious risk factor in common regions of Africa due to insufficient resources and basic structure (Kaler et al. 2022). Many people live near or travel to forests where infected animals are more prevalent, sleep outside, or sleep on the ground. Hunting is the only option available in places where there are not enough resources or necessities like food, which raises the danger of exposure to MPX. It was also observed that the rate of animal transmission to animals is higher than that of human transmission to humans in the case of this disease. The transmission of viral infection may involve respiratory droplet exposure and face-to-face or lesion contact between infected individuals (Anwar et al. 2023).

6.1. TRANSMISSION BETWEEN ANIMALS AND HUMAN

The MPX virus has a variety of host species, so there are chances for better transmission modes to humans. Squirrels, Gambian pouched rats, dormice, and non-human primates are the natural reservoirs of MPXV (Cohen 2022). Exposure to the stools, saliva, and meat of infected prairie dogs In 200, 47 cases were documented in the United States because the infected people were in contact with these prairie dogs (Siegrist and Sassine 2023). An epidemiologic study shows that prairie dogs and imported rodents from Ghana have a long history of close interaction. Likewise, five cases were confirmed by patients who had contact with infected wild animals and reported. Transmission from people to pets has also been noted. Animal lovers are in danger of spreading the MPX infection to their pets (Seang et al. 2022). Fig. 1 shows the potential sources of infection transmission from animals to humans.

6.2. TRANSMISSION BETWEEN HUMAN AND HUMAN

Previously, it was thought that outbreaks were caused by human-to-human transmission; however, long-term transmission between humans was thought to be limited. Currently, it is thought that a significant factor in MPXV transmission is sexual transmission. For example, according to a report, four

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individuals had insecure sex. MPXV was detected in their seminal fluids (Antinori et al. 2022). In addition, 86 cases of MPX were reported, all of which involved sexual activities like bisexual, homosexual, or (men sex with men) MSM (Vivancos et al. 2022). MSM was the cause of all 54 occurrences at one UK health Centre (Girometti et al. 2022). Evidence shows that close physical contact is also a major cause of the transmission of MPX. According to the information that is available today, males having sex with other males (MSM) account for increasing the cases of MPX (Russo et al. 2021).

6.3. TRANSMISSION BETWEEN HUMANS AND ENVIRONMENT

Direct contact with items such as sheets, clothing, or towels that have been used by an infected person's body fluids, lesion fluid, or scab may serve as a transmission medium. In general, OPXVs have a high level of environmental stability and are more resistant to environmental stress. Depending on the parameters of the room. However, information on environmental transmission is currently scarce. There is no information available right now about MPXV contamination of wastewater.

7. MANAGEMENT OF MPXV

7.1. CLINICAL EFFECTS AND SYMPTOMS

MPXV infections have two stages. First, the invasion phase, which lasts 2 to 13 days. The second rash phase, which lasts 7 to 24 days. After an MPXV infection, symptoms may take 6–10 days to manifest. Monkeypox is a self-limiting illness with symptoms that last between two and four weeks. Severe headache (27%), Fever (62%), myalgia (31%), and lymphadenopathy (56%) (WHO 2022). During a fever, the patient will develop skin lesions that primarily affect the face (95%), as well as the palms, feet, oral mucosa, genitals, and conjunctiva (20%) (Thornhill et al. 2022).

8. HOSPITAL MANAGEMENT AND PRECAUTION

Patients who are exposed to the primary infection of monkeypox may be at risk of secondary infection at the lesion stage of MPX. The patient should be encouraged to wear fully covered clothing and a full-sleeve shirt to prevent secondary infection. A disposal sheet should be used to cover the lesions. So that exposure will be reduced. Medical staff should inform the patients of the importance of surgical masks, which play a vital role in the prevention of spreading respiratory droplets. Moreover, after every 8 hours, the temperature, pulse rate, blood pressure, and respiratory rate should be monitored (Bryer et al. 2022). Patients with primary infections should be treated with medications including analgesics, antipyretics, anti-allergics and a wide range of antibodies. The lesions of the patients should be managed with analgesic ointment, saline compresses, and soft paraffin massages. All the isolation ward common rooms and washrooms should be washed with hypochlorite solution. Additionally, all healthcare workers have to design the proper duty schedule. They must use personal protective equipment, including a cover nail, N95 mask, face shield, and double gloves, for patient care activities (Relhan et al. 2023).

9. DIAGNOSTIC TECHNIQUES

9.1. LABORATORY TEST

Currently available diagnostic methods for MPXV detection include enzyme-linked immunosorbent assay (ELISA). Polymerase chain reaction (PCR), immunohistochemistry, electron microscopy cell culture,

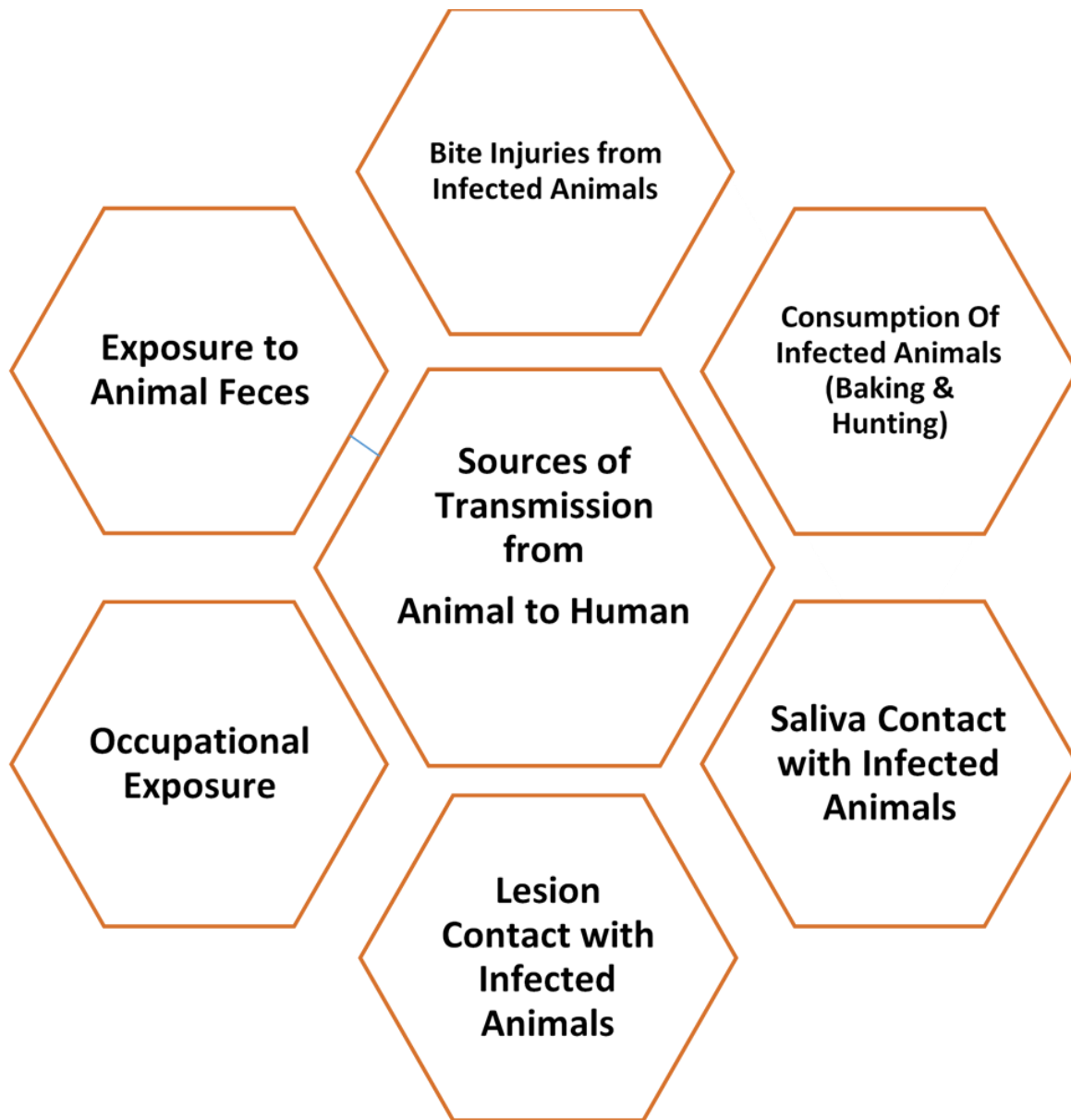


Fig. 1: Potential sources of infection transmission from animals to humans.

Western blot examination, or sequencing, with PCR being utilized for conclusive diagnosis. Laboratory diagnosis calls for the collection of lesion roof, scab, tonsillar tissue, nasopharyngeal parts swabs, punch biopsy kits, and whole blood. The lesion sections must be kept in a dry, cool, and disinfected tube. Typical contact and droplet precautions must be used when collecting specimens, and any sections that may be contaminated with the MPXV must be handled.

10. REAL-TIME PCR

After 5 and 8 days of infection, immunosorbent assays (ELISA) are used to identify specific IgG and IgM antibodies in individuals' serum who had monkeypox. For serological testing. Both the acute and

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convalescent stages of MPX infection can be identified using a four-fold increase in blood antibodies. The technique, which is often used in epidemiologic studies, is ineffective at identifying monkeypox virions. Because virions cannot be discriminated morphologically (Sterlin et al. 2021). Monkeypox can be found using the real-time polymer chain reaction (RT-PCR) genomic test. When a brick-shaped particle is discernible after negative staining in viral cultures, scab material, vesicular fluid, or biopsy specimens. The virus can be visually identified by using electron microscopy to find the viral particles. A main laboratory with trained staff and an electron microscope is required to conduct the test (Anwar et al. 2023).

11. SEROLOGIC TEST

Orthopoxvirus antibodies can be measured by immunofluorescence in serology tests (anti-orthopoxvirus IgG and IgM). WHO does not advise using antibody testing alone to diagnose MPXV (Altindis et al. 2022).

12. ELECTRON MICROSCOPE

Viral cultures, vesicular fluid, blood samples, and biopsy samples from lymph nodes can all be examined using electron microscopy with negative staining. Under an electron microscope, 24 MPXV is seen as an intracytoplasmic brick-shaped particle with lateral bodies and a central core that are 200-300 nm in size. Because OPXV species cannot be identified morphologically, this approach does not offer a conclusive diagnosis; however, it does show that the virus is a member of the Poxviridae family, which helps to identify it from Herpes and Parapox viruses (Petersen et al. 2019; Alakunle et al. 2020).

13. TREATMENT

13.1. SUPPORTIVE CARE

The majority of MPX patients heal without any medical assistance. Those who experience gastrointestinal symptoms (such as vomiting or diarrhea) will need oral or intravenous rehydration (Reynolds et al. 2017).

14. ANTIVIRALS

MPX infections may be successfully treated with several antivirals. The animal models were used to support the approval of these medications for the treatment of smallpox. Human dose studies for these medications have been carried out, although their effectiveness has not been fully investigated.

15. VACCINATION

Vaccination has traditionally been a powerful tool for preventing or dissipating viruses. There isn't yet a specialized vaccine to prevent MPXV infection. Vaccination against smallpox offers 85% protection against MPXV (Nasir et al. 2018) (Petersen et al. 2019). The older smallpox vaccine generations are no longer used in normal immunization programs. Modified smallpox vaccinations have undergone several advancements in recent years, including second-generation vaccines like ACAM200025, which was advised for post-exposure prophylaxis (PEP). Seven guidelines recommended the third-generation vaccination, also known as Imvanex or Jynneos, for PEP. Only two guiding lines offered suggestions for when PEP should be administered.

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The PEP recommendations for various at-risk populations were scarce. A smallpox vaccination may be contraindicated by pregnancy, age, and a history of eczema in the pre-event setting, but it can be given with caution in the event of exposure, according to one of the two guidelines published on PEP in children and pregnant women.⁴⁷

A different recommendation urged against immunizing newborns and expectant mothers.⁴⁵ Two recommendations particularly advise against administering the smallpox vaccine to immunosuppressed individuals (i.e., those with HIV and CD4 counts below 200 or those receiving chemotherapy).

The instructions for using VIG were unclear. Three recommendations suggested taking into account VIG in people with weakened immune systems⁴⁷. While the two guidelines did not make any recommendations about its use, they did state that there is a dearth of information regarding its efficacy for PEP and therapy. Six guidelines advised immunizing those who might be exposed to MPX, such as healthcare professionals.

16. PREVENTION MEASURES AND CONTROL

Epidemiology studies in high-risk areas strengthened laboratory-based surveillance capabilities, laboratory diagnostics, the development of regional capacities to put effective local solutions into action, and increased research activities. Animal outbreaks can be prevented by control techniques such as routine screening and isolation of newly affected animals. By keeping in mind the following, people can prevent the spread of MPX. A patient with a suspected or confirmed infection should stay at home and minimize contact with others; an immunocompetent person who has mild MPX symptoms should avoid contact with others for three to four weeks; and clinical and other healthcare workers face greater challenges in preventing MPX infection because they come into contact with patients who are sick. Follow-up advice like avoiding direct contact with skin lesions or items used by MPX patients can help reduce the risk of infection. An individual should avoid intimate contact, including sexual contact, with someone infected with or exposed to the MPX virus. The individual should maintain good hand hygiene and respiratory etiquette, such as wearing a fitted mask and covering coughs and sneezes with a bent arm, piece of tissue, or cloth. After having visitors at home, proper cleaning and disinfection of high-touch areas are recommended. Any interaction with diseased people or animals should be avoided. It's crucial to observe sick people and to practice self-quarantine. Healthcare professionals should use protective clothes, eye protection, gloves, and protective cloth during the treatment of infected patients (Marshall et al. 2022). They should provide hand sanitizer and masks to travelers during travel. People should take the necessary safety measures to minimize the danger of infection (Sotomayor-Castillo et al. 2021). Maintaining healthy sexual performance is crucial, particularly for MSM people. By supplying fundamental knowledge, it is essential to increase public awareness of viral infection and MPVX transmission. Additionally, global efforts should be promoted. Monkeypox is a complicated infection that is caused by MPXV. The disease can be transmitted from animals to humans or from humans to humans. The disease can also be transmitted through physical contact, such as taking a bite from, through lesion exposure, the saliva of infected animals and humans, and also from cockroaches and unlocking food from infected animals. Due to large outbreaks all over the world, a global health emergency was declared on July 23, 2022. MPX disease spreads all over the world, even in those countries in which MPXV is not endemic. In Pakistan, some cases were reported. Some specific parameters have been measured to prevent the disease. All over the world, medical staff were trying to treat the infection. Proper management is necessary for the cure of patients. Treatment like antivirals, vaccination, and some supportive parameters used. At first, patients are treated with supportive measures, and then antivirals are given to patients to treat the infection. Vaccination is also a good way

to prevent the disease. Hospital management plays an important role in the prevention of disease. For the prevention of disease, proper treatment is necessary, and patients have to stay in isolated wards. The use of masks must increase. Wear full-sleeved dresses and contact lenses. Visitors must be at a minimum. People should be aware of all of the prevention measures that can help reduce diseases.

17. CONCLUSION

Monkeypox is a complicated infection that is caused by the MPXV. The MPX disease was first recognized in 1958 during the monkeys' research study in humans. The disease is endemic to the central and West Africa. The disease can be transferred from animals to humans or also from man to men. The disease also can be transmitted through the physical contact, taking a bite from, lesion exposure, saliva, of infected animals and humans, and also from cock and unlock food from infected animals. Due to large outbreaks in all over the world, Global health emergency was declared on 23 July,2022. MPX disease spread all over the world even in those countries in which the MPXV is not endemic. In Pakistan some cases were seen. Due to some specific parameters have been measured to prevent the disease. all over the world medical staff were trying to treat the infection. Proper management is necessary to for the cure of patients Treatments like Antiviral, vaccination, and some supportive parameters used. At the start, patients are treated with supportive measures then Antiviral are given to patients to treat the infection. Vaccination is also a good parameter to prevent the disease. Hospital management plays a vital role in the prevention of disease. For the prevention of disease, proper treatment is necessary, patients have to stay in the isolated wards. The use of mask must be increased. Wear full-sleeved dresses and contact. With visitors must be minimum. People should be aware of all of the prevention measures that can help to reduce the diseases.

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