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COMPREHENSIVE REVIEW ON MONKEYPOXVIRUS

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Abstract : Healthcare-association transmission of Monkeypox has been observed on multiple occasion in areas where the disease is endemic. Outside Africa, MPXV was reported in the United Kingdom, the USA, Israel and Singapore .In 2022 in Europe and elsewhere posed a potential threat to humans of world. Monkey pox, a vesiculo-pustular rash illness, was initially discovered by world health organization (WHO).The first human MPXV case in medical history was recognized on 1 September 1970, a nine-month-old child was admitted to the Hospital in the Democratic republic of Congo. Monkeypox virus is an Orthopoxvirus belongs to poxviridae family. MPXV required host cell to regulate and integrate within themself. In order to survive within the host cell these virus acts on some proteins and those proteins are responsible for the modulatory action against the host immune response. Those who had been previously vaccinated against smallpox were identified to have 85% protection against MPXV. When it was taken into the consciousness, the national level response measure had not always been undertaken because of limited resources. Now MPXV is endemic to the other countries like Europe, America, Austria and also in India. Till august 2022, 10 cases were confirmed in India

Keywords: Monkeypox virus (MPXV) ,Orthopoxvirus, Smallpox vaccine, Antiviral drugs.

INTRODUCTION

Monkeypox is a zoonotic illness that is related to the smallpox virus and causes rashes. The camelpox, cowpox, vaccinia, and variola viruses are all members of the poxviridae family, which also includes the orthopoxvirus known as monkeypox[2]. It was initially identified in 1958, at a period when monkeys and their tissues were increasingly used for safety evaluations and early development of both the inactivated and live attenuated poliovirus vaccines [14]. WHO reports that on September 1, 1970, a nine-month-old baby was admitted to the Basankusu Hospital in the Democratic Republic of the Congo, marking the first human MPXV case in recorded medical history [3]. Human-human transmission and animal-human transmission are the two potential routes by which MPXV can spread. It has been discovered that respiratory droplets, contact with bodily fluids, contaminated patient possessions or surroundings, and skin lesions of an infected individual are connected with inter-human transmission [3]. It is still unclear how MPXV is transmitted to people. It is believed that handling monkeypox-infected animals can lead to primary animal to human infection by direct (touch, bite, or scratch) or indirect contact [1]. MPXV first had signs like the "smallpox virus." It includes a headache, a fever, bodily aches, tiredness, enlarged nodes, herpes on the skin, scarring following scabs, and other symptoms. Studies have demonstrated that smallpox immunisation offers cross-protection against other orthopoxvirus species, such as MPXV. It was found that people who had previously received the smallpox vaccine had 85% protection against MPXV. PCR-SWAB is used to diagnose MPXV (polymerase chain reaction). MPXV-specific treatments are not yet available or licenced. Between April 27 and June 24 in 2022, 43 sites in 16 countries have reported 528 cases.

1. AN EMERGE OF MONKEYPOX VIRUS IN NORTHERN HEMISPHERE OF EARTH (INDIA).

1.1. KERALA ON SIGHT OF MONKEYPOX VIRUS

India's **first ever case** was reported from kerala on July 14,2022. A rare illness arrived in kollam district of keralaby 35 years old man. Who have arrived from middle east earlier. He was treated by thiruvanandhapuram government medical college hospital. At the time it is not serious, on next Saturday he discharged by the hospital[38]. On July 18, the **second case** is arrived from Kannur district from kerala, India on alert. He was 31, who is migrant from dubai. On continuous, the cases are started to emerge[39]. On July 22, who returned to mallapuram from UAE has confirmed as third case of india[40].

1.2. ON CAPITAL OF INDIA

No history of foreign travel, tested positive for the monkeypox virus on delhi. He was 34 year old man and confirmed as fourth case of India. He was visited to himachalpradesh with four friends. So, the thought infection may by climatic changes. After a while, lesions are developed and it shows the threat[41]. In same district, india confirmed its fifth case of MPVX. She

is 22 year old African women has tested positive in loknayak jai Prakash Narayanan (LNJP) hospital. She travelled a month ago from Nigeria. Except them other 2 are reported positive by august 2022[42].

TOTAL CASES IN INDIA

10 cases are confirmed till august 2022. Five from kerala and five from delhi. Because of the limited resources available, not always a reaction is taken when alarms are transmitted to the national level. In most endemic nations, case definition are not defined, and healthcare staff' training is insufficient. However, India has already experienced numerous pandemics. It has undergone a number of measures, such as small pox immunisation, and is a significant
defence against MPVX[18]

State / Union Territory	District	Confirmed Cases	Suspected Cases	Total Cases
Bihar	Patna	-	1	1
	Nalanda	-	1	1
Delhi	New Delhi	-	1	1
	West Delhi	1	-	1
Kerala	Kannur	1	-	1
	Kollam	1	-	1
	Malappuram	1	-	1
Telangana	Khammam	-	1	1
Uttar Pradesh	Auraiya	-	1	1
	Ghaziabad	-	2	2
	Gautam Buddha nagar	-	1	1
India (total cases)		**4**	**8**	**12**

Table 1: cases and statistics [48]

1.3 INITIATION OF STROM IN AFRICA:

A group of monkeys in a Danish laboratory were the first to exhibit symptoms of the MPXV in 1958. During the vigorous hunt for smallpox cases in the Democratic Republic of the Congo (formerly known as Zaire) in 1970, the first human case was discovered in a 9 month old child[43]. The mother of the four-year-old girl was the second instance. The mother was said to have contracted the disease through her child. The affected people were residents of IhieUmduru, which is in the current state of Abia. Similar to the second instance, the third MPXV case in Nigeria happened in 1978 in a 35-year-old man residing in Omifunfun (Oyo state)[3]. Between 2000 and 2009, cases of monkeypox were documented in the DRC, Republic of the Congo, and South Sudan. However, between 2010 and 2019, cases were discovered in seven different African nations, including Cameroon, the Central African Republic, the Democratic Republic of the Congo, Liberia, Nigeria, Sierra Leone, and the Republic of the Congo. As of the year 2000, outbreaks had more cases overall and fewer single case reports than the final three decades of the 20th century. In Africa, 139 instances were documented between 2000 and 2009. There were 280 recorded instances between 2009 and 2019[13].

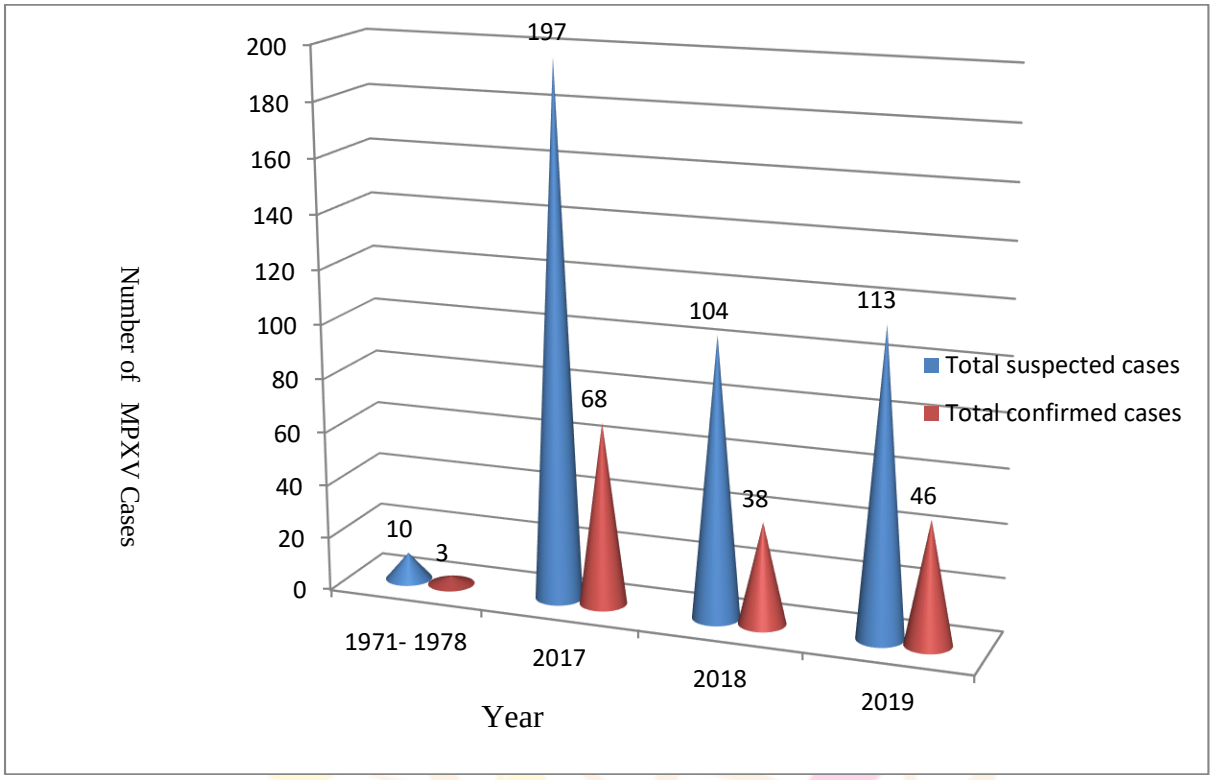

Fig 1: **All human MPXV cases in Nigeria over the year[3]**

1.4 IN EUROPE:

The United Kingdom (UK) reported an imported case of monkeypox (MPX) in a traveller from Nigeria on May 7, 2022. The subject reported exhibiting a rash-like sickness on April 29, 2022, and travelled from Lagos to London on May 3–4. The UK Health Security Agency (UKHSA) Rare and Imported Pathogens Laboratory performed a monkeypox virus (MPXV) PCR on a vesicular swab to confirm the diagnosis on May 6. The UK reported two additional MPX cases on May 13, 2022. These cases are from the same family and are unrelated to the one imported case from Nigeria that was made known on May 7. The instances were verified using PCR analysis of vesicle swabs. A third family member had previously experienced a rash but totally recovered. None of the individuals in this cluster had ever travelled or interacted with somebody who had. Four further MPX cases from the UK were reported on May 15, 2022, and were PCR-confirmed. The imported case from Nigeria (notified on 7 May) and the family cluster do not have any known epidemiological connections with any of these patients (notified on 13 May). In the four cases, the vesicular rash-like disease was evident in men who have sex with men (MSM). Their presence at genitourinary medicine (GUM) clinics allowed for their identification. The cases are being managed in high consequence infectious diseases centres in the UK. Two other cases (both MSM) were reported on May 18, one each in London and the South-East of England. Twenty MPX cases have been confirmed in England as of May 20, 2022, according to the UKHSA, who also reported 11 further cases. The MPXV West African clade has been identified as the cause of every case reported in the UK. Since May 18, numerous EU/EEA Member States have reported new suspected or verified cases. In the Lisbon and Tagus River Valley Region, Portugal reported 14 cases of MPXV on May 18. The clinical symptoms in all cases—rash, some of it ulcerative in nature, fever, myalgia, and asthenia—were present in men. None of the instances required hospitalisation. Nine further confirmed cases were announced on May 20 increasing the total to 23 confirmed cases. The west African clade was recognised in two instances. On May 19, Spain reported seven MPX cases that were confirmed and 23 cases that were suspected to be men only. There were 16 more confirmed cases reported on May 20. 39 new suspected cases are being looked at as of May 22, and seven more instances were confirmed. On May 19, Belgium announced a confirmed case in a guy who had previously visited Lisbon, Portugal. His girlfriend experienced similar symptoms and was diagnosed on May 20. A total of four confirmed cases has been reported as of May 22. On May 19, Germany announced the discovery of its first case in a man who had previously visited Spain and Portugal. Two additional confirmed instances were reported on May 20. With three other cases being investigated, France reported its first confirmed case on May 20 in a guy who had no prior history of travel. On May 20, Italy reported one confirmed incidence of MPX in a hospitalised male who had previously visited Spain. Two additional confirmed cases were reported on May 21. Sweden announced a man's confirmed case on May 18. The Netherlands reported one confirmed case on May 20th, involving a male who had previously visited Belgium. Austria announced its first case of confirmation on May 22. In nine EU/EEA Member States, 67 verified cases have been recorded as of May 23, 2022, and at least an additional 42 suspected cases were being investigated. Outside of Europe, cases have also been recorded. On May 18, 2022, Canada reported two verified and 20 suspected cases that were all male, examined at STI clinics, and are currently undergoing testing. On May 19, 2022, Australia announced two confirmed cases, one of which involved a male who had previously visited the UK. Israel announced a verified case on May 20, 2022, along with additional suspected cases. Switzerland reported a confirmed case with a history of travelling to Europe on May 22[44].There were 4 cases found in the UK from 2010 to 2019. 47 instances between 2000 and 2009 were found. 1 instances were found between 2020 and 2021[17].

1.5 OUTBREAK OF MPVX IN AMERICA:

In 2003, around 70 cases or confirmed cases of the first MPXV outbreak outside of endemic nations occurred in the USA. This outbreak was connected to the importation of large Gambian rats and squirrels from Ghana, which had infected prairie dogs before being sold and brought to the USA as pets and spreading the virus to them. There were no instances of person-to-person transmission that were verified. Human cases of imported monkeypox infections following travel have been documented in the UK, Israel, and Singapore in 2018–19, and then the US once again in 2021[43]. The West African lineage of the monkeypox virus is responsible for the greater outbreak of human monkeypox that will affect the world in 2022, which will also affect the United States. In 2022, an outbreak of monkeypox occurred in the United States, which was the fourth nation outside of those in Africa with endemic monkeypox. On May 19, 2022, Boston, Massachusetts, recorded the first case. By August 22, all 50 states in the US had been affected by the monkeypox epidemic. The majority of monkeypox cases worldwide are in the United States. In the US, California has the most incidences of monkeypox[45].

1.6 2022 MONKEYPOX OUTBREAK IN AUSTRIA :

The West African clade of the monkeypox virus is responsible for the bigger human monkeypox outbreak, which includes the outbreak of 2022 in Austria. Austria is the sixteenth nation outside of Africa to have an ongoing outbreak of monkeypox. On May 22, 2022, the first case was reported in Vienna, Austria[46]. As of 6 December 2022, 36 mpox cases had been recorded from 10 EU/EEA countries since the last update on November 22, 2022.41 instances were recorded in week 45, excluding the possibly incomplete data from the previous three weeks (7–13 November 2022). This represents a decrease of 34.1% from week 44. (31 October–6 November 2022).The number of newly reported cases during week 44 has decreased by 98.8% when compared to the peak of reported cases (2, 164 instances during week 29; 18–24 July 2022).[17]Nations have not reported an MPXV cases for longer than 21 days as of December 6,2022.As of 6 december 2022, 20 934 confirmed cases of MPXV had been reported from29 EU/EEA nation since the outbreak began, and 62 cases had been recorded from three Western Balkan countries and Turkey .[47]

2 THE PATHOGENESIS

2.1TRANSMISSION ABOUT MPV VIRUS:

Transmission of the monkey pox virus is still unknown. There exact mode of transmission is from animals to humans are not identified.[7]. Monkeypox is described as those are enveloped, slightly pleomorphic, with a dumbbell-shaped core with lateral bodies"""""". Aerosol transmission has been demonstrated after the nosocomial outbreak in central African. These has the two modes of transmission that includes direct or indirect. The direct mode includes touch, bite, scratch[1]. Serological survey suggests that many animals that are infected with MPV under normal condition[2]. This monkey pox virus was first reported in 1970, there was a massive outbreak of the pox like disease[3]. A clear and consistent transmissibility and mortality of the of MPV has been hampered by various epidemiological data[2]. And the first case of the MPV has been identified when 1 September 1970, for nine-year-old child in the democratic republic of congo[3].

2.3 PATHOGENISIS OF MPV:

Most of the excretion and secretions, as well as the skin lesions, have been discovered to contain the MPV (eg: feces, oral, nasal and urine). The three main methods of transmission are inhalation, direct injection into skin breaches, and ingestion of infected tissues[37]. Some Vero cells demonstrate cytopathic consequences within 24 hours of infection, including typical monolayer separation and cell rounding[5]. The viral DNA that is present in the tissue from the lesion is stable for a very long time[6].

Animal bites, close contact aerosols, or direct contact with lesions, blood, or bodily fluids can all cause human infection[37]. Infected prairie dogs used in experiments can shed MPV in 21 days[15]. To detect the presence of the orthopox virus, real-time polymerase chain reaction is used[6]. This virus's incubation time was discovered to be between 5 and 21 days, whilst the onset of symptoms was seen to be between 2 and 5 weeks.

Fever and rashes of various sizes may appear five days after the virus has begun to manifest in the body. These rashes move through a number of stages in their development, starting with macules, papules, vesicles, pustules, etc[1]. The mpvx infection process can be broadly divided into two phases: the prodromal phase, which lasts for about 0–2 days and is characterised by symptoms including fever, faituge, severe headache, lymphadenopathy, muscle pains, etc., and the rash phase, which lasts for about7–12 days.

There may be a feverish component to the rashes' appearance, which first start on the face before spreading to other areas like the palms and soles of the feet, etc[7]. This virus is a self-limiting illness; the severity of the case depends on the virus' exposure level, the patient's health, and the type of sequelae. Young children may experience severe cases that result in death, with a fatality rate of roughly 1-10%[7]. Severe cases can also result from vaginal, conjunctival, and pharyngeal inflammation.

2.3.1 POXVIRIDE:

At least 9 or 10 envelope proteins are involved in the entrance mechanism used by poxviruses to enter cells through endocytosis or direct fusion at the plasma membrane. This entry mechanism is followed by a carefully controlled series of processes that enable viral multiplication. There are still many unidentified processes in the virus life cycle, and this research on the activity of silver nanoparticles istoo early to attempt to provide a satisfactory explanation of how they work.

It is likely that the silver nanoparticles will interfere with the initial steps of molecular binding and penetration by physically obstructing the attachment of the virus to the host cell or, if internalised, by obstructing intracellular pathways vital for viral multiplication. They also mentioned that AgNO3 was a potent MPV inhibitor, but at a concentration of 100 g/mL, Vero cells were toxic, making it difficult to assess AgNO3's antiviral effectiveness. At the highest doses, an increase in the average number of MPV plaques may consolidate and subsequently produce on cells regions open for higher interactions between viral particles and the cell membrane, enhancing internalisation and plaque formation[9,2,6].

The virus particles measure between 200 and 250 nm and have an oval or brick form (Cho and Wenner, 1973). During replication, the poxvirus creates the extracellular enveloped virus (EV) and the intracellular mature virus (MV), both of which are contagious viral particles . The viral core and lateral body, which include certain proteins, are enclosed by a lipoprotein envelope on the surface of the MV. Upon cell lysis, MV is liberated, and it is comparatively stable in the outside environment. It mostly serves to spread among animals. Exocytosis causes EV to be released, and it is made of MVs and a lipid membrane. It comes from endosomes or the Golgi transport system . Inverted terminal repeats (ITRs) are located at the ends of the linear, double-stranded MPXV genome, which is about 197 kb in size[7].

Poxviruses differ from other viruses in that they significantly rely on virus-encoded proteins to facilitate cytoplasmic replication[28]. Genes involved in crucial processes like transcription and virus assembly are found in the genome's core region, whereas those near the genome's termini are responsible for virus-host interactions[26,29]. Out of the more than 150 genes that poxviruses encode, 49 are shared by all sequenced members of this family and 90 are shared by the chordopoxvirussubfamily[30]. The majority of these conserved genes are essential for viral function and make up the genome's core[26].

It is more difficult for viruses like monkeypox to get past host defences by passing through gap junctions because poxviruses are larger in size. Orthopoxviruses require a more elaborate approach to live inside the host because of the bigger size of the virus, which also hinders the virus's ability to replicate quickly[31]. The bigger size of the orthopoxviruses causes the immune system of the individual to become aware very early on and quickly triggers an immunological response[31,32]. Orthopoxviruses have a series of chemicals expressed by their virulence genes that are directed towards the host's immune system's components and serve as modulators, enabling them to elude the host immune system[31]. These proteins are in charge of controlling host immune system modulation.

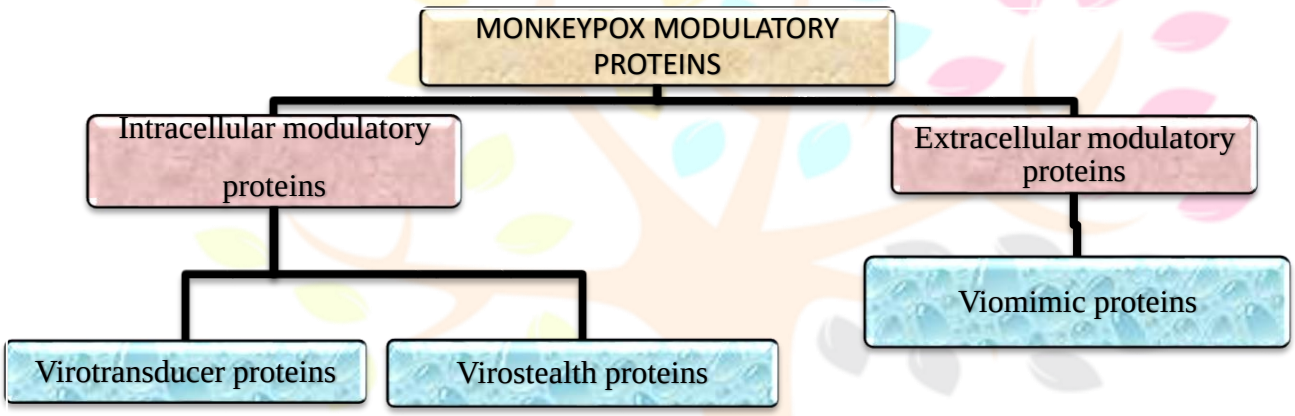

Fig 2: Intracellular and Extracellular modulatory proteins of monkeypox virus.

As shown in Figure 2, there are two classes of proteins that are in charge of modulatory effects against the host's immune response. Virotransducer proteins and virostealth proteins are examples of intracellular proteins. The ability of the cell to respond to the infection, including the oxidative burst and apoptotic pathways, is interfered with by the virotransducerproteins[31,32]. The major histocompatibility complex class 1 (MHC 1) and CD+4 are immune recognition molecules that the virostealth proteins, which also operate intracellularly, downregulate in order to decrease the possibility that the virus would be recognised by the host's immune system[37,20,21].

There is just one form of external protein, viromimic proteins, however there are two different types of intracellular modulatory proteins that help monkeypox evade the host's immune response. Viromimic proteins fall into two categories, as depicted in Figure 2, and both have the ability to control how the immune system reacts. The host cytokines and chemokines are competitively bound by the viroreceptors, which prevent them from performing their functions[31,32]. The viroreceptors are either produced or present as cell surface glycoproteins.

As a result, virokines develop viral mimics of host cytokines, chemokines, and growth factors that are successful in both obstructing host responses that are harmful for virus survival and in encouraging responses appropriate for viral replication and dissemination[15,16]. These modulatory proteins function in concert to circumvent the host's immune system and promote viral multiplication. Monkeypox and other orthopoxviruses would be unable to subvert the immune system in the absence of these proteins.

The replication cycle of poxviruses offers information about how the monkeypox virus replicates. like other viruses, poxvirus also have proteins that allow and facilitate the virus's attachment to a cell, fusion with a cell's membrane, and entry into the host cell. The mature virion (MV), which has a single membrane, and the extracellular enveloped virion (EV), which has a second outer membrane, are both broken before the fusion in the case of the poxvirus[27]. The four viral proteins that are connected to the MV work together to help the virus attach to a host cell by attaching to laminin or glycosaminoglycans on the cell surface[27,28].

Regardless of whether the MV or EV mediate infection, 11 to 12 non-glycosylated, transmembrane proteins with sizes ranging from 4 to 43 kDa 27 are required for the fusion of the virus to the host cell. While EVs have a fragile outer membrane and are particularly tailored for departing the intact cell and spreading within the host, MVs are relatively durable and are hypothesised to mediate transmission across host mammals[35,22].

Guarnieri bodies, now more popularly known as factories, are cytoplasmic structures where pxv DNA replication takes place[19]. Each factory originates from a single infectious particle, and in the initial stages of infection, they are small DNA-containing structures surrounded by membranes that appear to originate from the rough endoplasmic reticulum (RER) of the cell[19,33]. As DNA synthesis continues, these factories will get larger and gradually start to take on an irregular shape as cavities filled with viral mRNA and host translation factors develop[19,35].

As DNA synthesis continues, these factories will get larger and gradually start to take on an irregular shape as cavities filled with viral mRNA and host translation factors develop[19,35]. In the later stages of the replication cycle, a group of viral membrane assembly proteins and a complex of late gene products work together to disrupt the endoplasmic reticulum membranes in the area and create crescent-shaped structures that serve as substrates for the assembly of the immature virions (IV)[35]. The most prevalent infectious species, MV, are created from the IV. These MV will fuse with the cytoplasmic membrane and leave the cell that way.

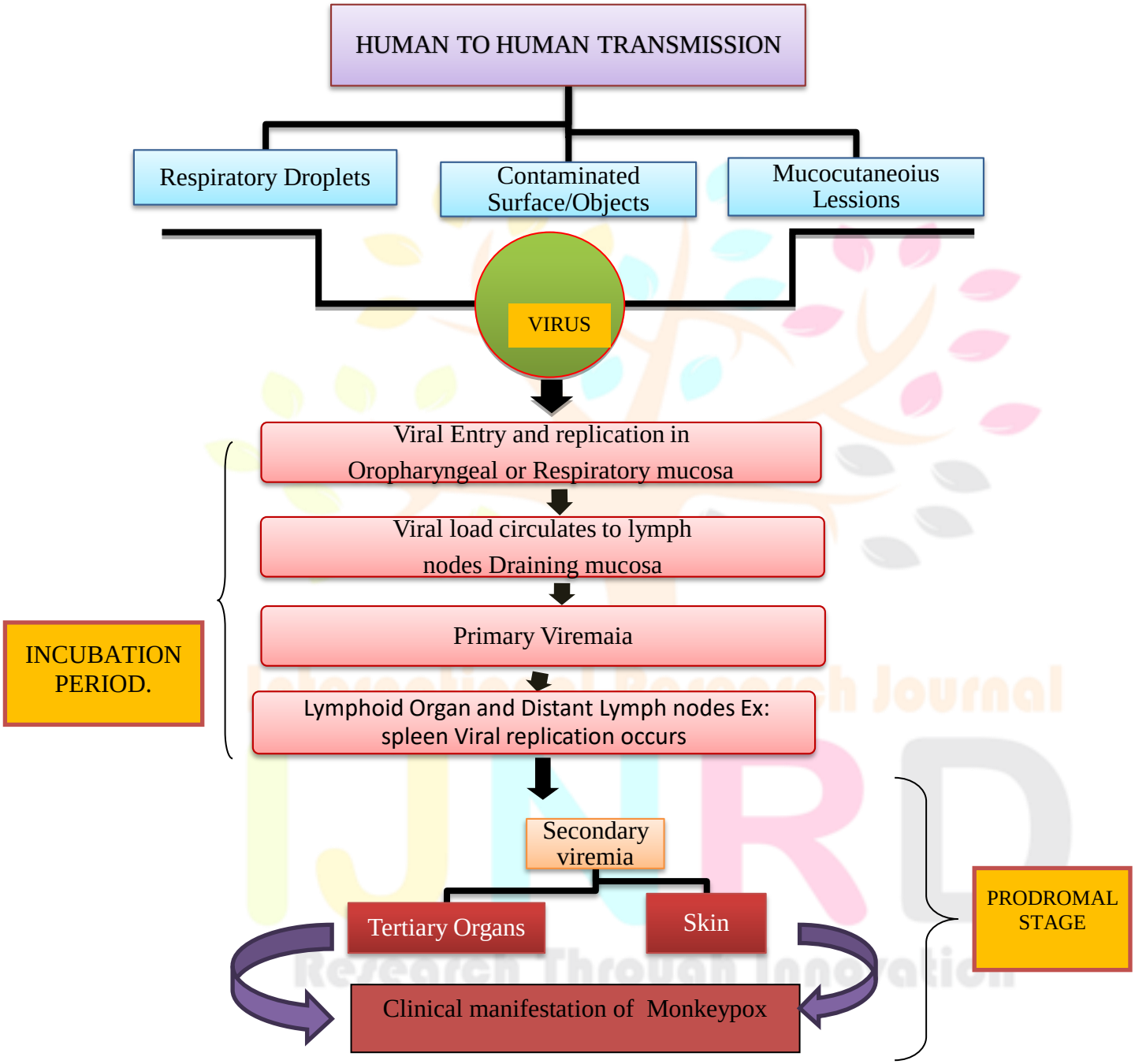

Fig 3: Overview of pathogenesis.

2. PHENOTYPE OF MPXV

A phenotype is a trait that can be seen in an individual and includes things like physical features, behaviours, physiological or developmental processes, chemicals, and network emergent properties. Molecular phenotypes have a poorly defined genotype-to-phenotype transition, making it difficult to identify and measure virus phenotypes. It also helps that virions are small and can only be seen with sophisticated equipment.

The Orthopoxvirus genus of the Poxviridae family contains the enclosed double-stranded DNA virus known as the monkeypox virus. The central African (Congo Basin) clade and the west African clade are two separate genetic clades of

the monkeypox virus. In the past, the Congo Basin clade was thought to be more contagious and to produce more severe illness. The only nation where both viral clades have been discovered is Cameroon, which serves as the geographic boundary between the two groups.

The monkeypox virus has been found to be susceptible to several animal species. This comprises non-human primates, dormice, rope and tree squirrels, Gambian pouched rats, and other species. There is still uncertainty about the monkeypox virus's natural history, and further research is required to pinpoint the precise reservoir or reservoirs and understand how the virus circulates in the wild.

The 3-Dimensional structure of the monkeypox virus was discovered to be composed of the mRNA capping, ubiquitine, poxin-schlafen, RNA polymerase, immunomodulator A46, transcript, chemokine inhibitor, TNF receptor, and ankyrin. This structure was created using homology modelling using the SwissModel web-based server (https://swissmodel.expasy.org/interactive), while TMHMMPred Estimates of the stability of possible mutations have been made using the online servers CUPSAT [16] and Dynamut2 [17].

3. GENOTYPE OF MPXV

These viruses have genomes that are around 200 kb long, highly conserved middle regions that code for replication and assembly machinery, and more variable terminal ends that carry genes implicated in pathogenicity and host range selection. Although antigenically and genetically similar, orthopoxviruses differ in their host range and virulent characteristics[24].

MPXV has a linear DNA genome of around 197 kb and about 190 nonoverlapping ORFs that are longer than 180 nt (1,7,26). The central coding region sequence (CRS) at MPXV nucleotide locations 56000-120000 is highly conserved, like that of all orthopoxviruses, and is flanked by variable ends that have ITRs (inverted terminal repeats)[36].

A database of 196694 base pairs from 106 high coverage MPXV sequences has been created. Following manual alignment and editing of all the sequences, all missense mutations in various proteins were examined. The sequences were compared to the reference MPVX West Africa sequences during the manual editing stage. We discovered five missense mutations in all of the MPXV isolates from the year 2022 that had never been seen in any other MPXV sequences before, and one mutation that had only ever been seen in sequences isolated from Israel and Singapore in the years 2018 and 2019, respectively. The 2022 MPXV outbreak, which was influenced by host-human contact, altered the immunomodulation and replication pathways, which are essential for viral fitness, either favourably or unfavourably.

4. SIGN AND SYMPTOMS

The three distinct phases of MPVX are the incubation, prodrome, and rash. Its symptoms last for two to four weeks. Incubation lasts 7–14 days, with a prodromal stage characterised by fever, malaise, a diffused vesicular or pustular rash, and lymphadenopathy (lymph node swelling). Nodes enlarge) and the principal consequence is followed by 2 to 5 mm-wide skin rashes.Thepapular vesicular pustular stage is where rashes develop before collapsing and dropping off.These lesions can be found on the face, trunk, genitalia, and other areas. It has contagious viruses that can spread among people. Within one to two weeks, the lesions disappear. Secondary problems start to emerge after threediscrete phases. Bacterial skin infection, gastroenteritis (inflammation of the stomach and intestine), sepsis, bronchoeumonia, encephalitis (inflammation of the brain due to infection), keratitis (corneal inflammation), hyper- and hypopigmented atrophic scars, patchy alopecia (patchy hair loss), hypertrophic skin scars, contractile or deformity of facial muscles, and death in severe cases are examples of secondary complications HIV patients have a significant mortality rate when exposed to MPVX. According to the WHO, those under the age of 40 to 50 may be more susceptible to monkeypox[20].

5. DIAGNOSIS

RT-PCR (a genetic method), electron microscopy, immunological testing, phenotypic testing, and antibody tests (anti-orthopoxvirus IgG, anti-orthopoxvirus IgM, and tetracoreorthopox biothreat alert) are all used to detect MPVX.

1.RT-PCR(real time - polymerase chain reaction) (real time - polymerase chain reaction)

Using a patient's lesion material, it is possible to diagnose an active case. Viral DNA is used in the experiment, and it can remain stable if a material is stored in a cool, dark environment. Specifically made to target the monkeypox virus.

highly sensitive assays where contamination worries are justified. These tests need for pricey supplies and equipment. Must be carried out by trained technicians at a significant laboratory. RTPCR, which targets conserved areas of the extracellular-envelope protein gene, DNA polymerase gene, DNA dependent RNA polymerase subunit, and F3L gene, is regularly used to identify MPXV DNA from clinical and veterinary materials, as well as from MPXV-infected cell cultures. In order to detect MPXV DNA, restriction length fragment polymorphism (RFLP) of PCR-amplified genes or gene fragments is also utilised; however, RFLP is time-consuming and necessitates viral culture. When speed, sensitivity, and specificity of the procedure are crucial, RFLP of PCR products that also need enzyme digestion is the best approach. The gold standard for characterising MPXV and other OPVs continues to be whole-genome sequencing using next-generation sequencing (NGS) technologies, however the technique is expensive and downstream processing of sequencing data needs a lot of computer power[3,10].

Therefore, NGS might not be the best tool for characterization, especially in sub-Saharan African nations with limited resources. Even while RT-PCR is still the preferred technique for diagnosing MPXV on a regular basis, it must be supplemented by field genome sequencing technology, such as Oxford Nanopore Minion[10,3].

6.1. MMUNOLOGICAL TECHNIQUES:

Tests for the presence of orthopoxvirus-specific antigen are performed using immunohistochemistry (viral antigen detection).Antigens in biopsy specimens can be found using this technique.Although not specifically for MPVX, these strategies can be applied to eliminate or identify other suspicious agents.It distinguishes between the herpes virus and the pox virus[3]

B) Test for the existence of orthopoxvirus antibodies using anti-orthopoxvirus IgG. It can be used to determine whether a pathogen or small pox immunisation has previously exposed a person to an orthopoxvirus. A cold chain and the collection of blood (serum) are necessary. This method uses polyclonal or monoclonal antibodies against all orthopoxviruses to distinguish between viruses.

C)Anti-Orthopoxvirus IgM: Examines the body for antibodies to the orthopoxvirus.can be used to determine whether a disease or smallpox vaccination recently exposed someone to an orthopoxvirus. This test might be utilised as a diagnostic tool for people having a history of smallpox immunisation who may have the orthopoxvirus. requires a cold chain and the collection of blood (serum).The monkeypox virus cannot be detected with this test. It is known that T-cell responses and antiviral antibodies both rise at the beginning of a disease. IgM and IgG, however, are seen in serum five and more days, respectively, after the commencement of the rash. Orthopoxvirus antigens are checked for using the TetracoreOrthopoxBioThreat Alert test.A point-of-care diagnostic test can quickly diagnose an active case utilising lesion material from a patient. can be done with little expertise at room temperature. less accurate than PCR[3].

6.2.ELECTRON MICROSCOPY:

Negative staining results in an image of a brick-shaped particle that is clear and allows for the visual classification of poxviruses other than parapoxvirus. In a biopsy specimen, scab material, vesicular fluid, or viral culture, it can be utilised to identify viral particles. can distinguish between Herpesviruses and Orthopoxviruses. Under an electron microscope, MPXV has an intracytoplasmic brick-like appearance with lateral bodies and a central core that is between 200 and 300 nm in size. OPV species cannot be distinguished morphologically, hence this method cannot provide a conclusive diagnosis, but it does provide a hint that the virus is a member of the Poxviridae family.gel electrophoresis, and might not belong to the poxviridae family.Due of this, PCR is still more commonly utilised[3].

6.3.PHENOTYPING TECHNIQUES

According to clinical diagnosis, MPXV has an incubation period of 4–21 days, and it is typically followed by a prodromal sickness with a number of symptoms such lymph node enlargement, headache, fever, back pain, myalgia, strong asthenia, severe headache, pharyngitis, drenching sweats, and malaise. Following the prodromal phase, the exanthema phase is characterised by vesiculopustular rashes that start on the face and extend across the body between 1 to 10 days.

Lesions in MPXV patients resemble smallpox in appearance and are monomorphic, pea-sized, and rigid. Smallpox cannot be confused with MPXV lesion because of its crop-like appearance and weak centrifugal spread. The key clinical characteristic that sets MPXV apart from smallpox is the presence of lymphadenopathy[3].

6. TREATMENT

MPVX is not specifically treated. It started off and kept on like smallpox treatment. The current solutions are vaccination, antiviral medications, and neutralising antibodies.

7.1.VACCINATION

Numerous vaccines are extensively used to prevent smallpox, but only a few are effective against monkeypox. FDA-approved vaccines like ACAM2000 and IMVAMUNE are frequently utilised. In addition to that, MVA-BN JYNNEOS (modified vaccinia ankara-bavarian Nordic), Dryvax, and Lister are employed. LiveFDA vaccinia virus, ACAM2000 a single dose of medication. A lesion at the injection site indicates a successful immunisation. prepared for long-term storage in lyophilized form. Live viral vaccination with the potential for mammalian cell replication; hazards include contact transmission and autoinoculation. However, it shows a contraindication with people who have immune-compromising illnesses, eczema or atopic dermatitis history, or pregnant women. In order to prevent cardiac episodes after vaccination, dryvax is utilised. It granted vaccine approval in the US. presently accessible to particular populations from Strategic National Stockpile, IMVAMUNE, and modified vaccinia AnkaraAttenuated vaccinia virus (US); IMVANEX (Europe).In mammalian cells, the virus can only replicate in small amounts. The immunisation site did not result in any lesions. injections administered in two doses. The marketing of vaccines for the broader adult population, including those who are immunocompromised, has been approved by the European Commission. kept in the Strategic National Stockpile of the United States. Use in people with immune weaknesses such AIDS and atopic dermatitis is not contradicted.Attenuated vaccine virus, single-dose injection, *LC16m8.demonstrates a safer profile and fewer adverse effects in both human and animal vaccines than ACAM2000. virus that has been weakened but can still reproduce in mammalian cells. It is legal to use in Japan. Some immunisations have been linked to myopericarditis[20,21,22,3,25].

7.2.ANTIVIRAL AGENT

Brincidofovir and ST-246 (Tecovirimat) are two antivirals that have received U.S. approval for the treatment of smallpox. The orthopoxvirus envelope protein (F13L) is the target of ST-246, which prevents virion release.Brincidofovir is an orally accessible lipid compound of cidofovir, an approved drug for the treatment of human cytomegalovirus infection. Cidofovir is an acyclic nucleoside analogue. The inhibition of poxvirus DNA replication is the mechanism of action of cidofovir. The medications' efficacy in a small number of instances of human monkeypox suggests that tecovirimat is effective whereas brincidofovir is not. Brincidofovir has more selective index due to its improved efficacy, which was at least 25-fold higher, while having higher cellular toxicity and better antiviral activity than cidofovir against varialovirus, monkey pox virus, and cowpox virus in vitro. Brincidofovir has superior efficacy because it is taken up by cells more readily and is better converted by intracellular enzymes into the active form.Cidofovir is a monophosphate nucleotide analogue that becomes an inhibitor of viral DNA polymerase when cellular kinases add a second phosphate group, which is equivalent to Brincidofovir action inhibiting viral DNA synthesis. After Brincidofovir has entered the cells by the endogenous liquid absorption channels, it is liberated by cleavage and is then converted by intracellular kinases into phosphorylated cidofovir. These medications decrease the symptoms of MPVX while also preventing its spread[20,3,25].

7. CONCLUSION

We would like to draw the conclusion that they are the virus-causing agents, spreading extensively and quickly as compared to the small pox virus. As a result, the numerous smallpox vaccinations are also fairly effective in protecting against the monkeypox virus. Since these are human-to-human diseases, everyone should always practise good hygiene.

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