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A REVIEW ARTICLE ON MONKEYPOX

Muhammad Zaman Khetran[1], Rahman Gul[1,2]*, Ghulam Farooq[1], Safia Mengal[1], Imran Lashari, Kashmala Khan[3], Falsafa Jamal[1] and Nighat Saleh[1]

[1]Institute of Public Health Balochistan, Pakistan.
[2]Faculty of Pharmacy and Health Sciences University of Balochistan, Pakistan.
[3]Fatima Jinnah Medical College Lahore, Pakistan.

***Corresponding Author: Rahman Gul**

Institute of Public Health Balochistan, Pakistan.

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ABSTRACT

Monkey pox outbreak in 2022 brought innovative public health danger from the summit of continuing corona virus disease 2019 (COVID-19) pandemic in the entire countries of world. Monkey pox disease spread whole six continents of the world including 104 Countries by means of maximum encumber in (North America) and Europe. Since 1959 isolated infected monkeys and its etiological agent identified virulence between humans reported ever-since 1970s typically in endemic countries of Central and West Africa. Therefore disease re-emerged in 2022 at surprising tempo in ‘’(human to human)’’ transmission capability and community spread in non endemic region. The entire world needs to mitigate-effort from health care workers, public health workers and policy makers should update the communities regarding the neglected viral diseases. The responsibilities of health care providers should update the communities about the monkey pox overview such as etiology, epidemiology, clinical features, pathogenesis, diagnosis and management. Therefore world declared ‘’public health emergency of international concern’’ (PHEIC) to discuss or apply preventive control measures and latest vaccines development to handle the re-emerging viral disease. This literature review provides a general knowledge to the whole world communities regarding the current outbreak.

KEYWORDS: Public health, PHEIC, Prevention, Emergency, Pandemic, Epidemic, Endemic, Vaccination.

INTRODUCTION

Monkey-pox outbreak 2022 world health organization (WHO) reported many cases in entire countries of the world. During Out-break an accumulative sum of (64,290) lab confirmed cases reported in entire countries of world. During 21 September 2022 20 deaths resulted across the 106 countries of the world.[1]

Rapid Outbreak build a public health threat that rise a new viral pandemic.[2] Duration of monkey pox causative agent needs more than 60 years.[3] Monkey pox virus first discovered during an outbreak among monkeys at laboratory in1958 in Denmark.[4] Therefore several monkey-pox outbreaks identified disease monkey-pox virus in laboratories or zoos between imprisoned monkeys.[5] Human infection of monkey pox first identified in 9 month old child in democratic republic of Congo since 1970.[6] At that time monkey-pox was reported as zoonotic/endemic in central or western Africa.[7.8.9]

The endemic countries of Central Africa reported the current 2022_ out- break transmission of (Mpox-v) in human-to-human,[10] Additionally monkey-pox outbreaks an outstanding example reported non endemic countries which frequently associated through imported animals from endemic region during 2003 outbreak in united-states of America.[11]

The global emerging zoonotic monkey-pox out-breaks highlighted the earlier experiences significance.[12] Several factors regarding the rise in frequency of monkey-pox outbreak surveillance during past 40 years. Factors consist of increased susceptibility of monkey-pox infection followed the termination of smallpox vaccination.[13] 85% effectiveness of vaccination against smallpox incorrigible for the prevention of monkey-pox.[14]

Additional factors involved widespread consumption of animal such as (protein source) with. probable Mpox-v reservoirs commonly in regions like poverty and social-crises during civil war[15] Additional factor directly associated with the appearance of monkey-pox outbreak include enlarged population density, no difficulty for travel, ecological and environmental factors (e.g clearance of tropical rain forests) among enlarged risk of exposure to reservoir animals.[15.16.17]

Literature-review intention (desired outcome) to deliver comprehensive up-to-date impression of monkey-pox including laboratory findings, etiology, pathogenesis, epidemiology and clinical features, complication, sequelae management and preventive (vaccination) procedures.

EPIDEMIOLOGY

Danish virologist Preben von Magnus identified the naturally occurring pox infection in '' crab-eating macaques'' from Singapore. The disease known as monkey-pox due to first identified in colonies of monkeys kept for research in 1958 history when two outbreaks resulted.[18]

Monkey- pox was detected in human in 1971.[19]
1st September 1970: First human case diagnosed in 9 month baby boy admitted to the Basankusu Hospital in Zaire (now called Democratic Republic of Congo) during intensive search for smallpox cases after its elimination in 1968. Cases reported as.

- From 1970-to-1979 as
- D.R. CONGO_38, LIBERIA_4, NIGERIA_3, CAMROON_1, SIERRA LEONE_1, Cote d'lvoire_1.
- From 1980-to- 1989;
- D.R.CONGO_343, CAMROON_1, Cote d'lvoire_1, GABON_4, CENTRAL AFRICAN REPUBLIC_8.
- From 1990-to -1999;
- D.R.CONGO_511, GABON_4.
- From 2000-to-2009;
- From 2010-to-2019;
- In 2020 eight (8) cases in Nigeria
- In 2021 34 cases in Nigeria, 3 cases in UK and 1 case from USA

Now current situation from 3rd May 2023 as total confirmed cases are 87, 301from 111 countries and still 130 deaths reported. As earlier monkey-pox was declared as PHEIC from 23rd jully 2022.

VIROLOGY CLASSIFICATION

Monkey-pox virus belong to similar group as variola, cow-pox and pox-virus classify within genus ortho-poxvirus, (Pox-viridae family)[20] Distinctive traits of Mpox-v along with other poxviruses with wide range of host species tropism from rope squirrel (sooty mangabey) which permit the extended zoonotic circulation of MPOX-v in world.[21]

Monkey pox name first isolated during 1958 from infected cynomolgus monkeys. On the other hand this name might be a misnomer or (incorrect use of name) as (1) because animal samples shows serological evidence appearance of rodent as primary natural reservoirs while infections in primate purely spill-over events and two direct-transmission may occur among spill-over host and monkey e.g most recent Global outbreak during 2022 within human to human etc.[22]

Recent cases phylogenetic analyses really point out genomic division of new isolates from unique monkey-infected Mpox-v strains. The current discussion favored the reasons from new name Mpox-v.[23.24] However , introduction of Mpox-v into non-human primates proved an perfect animal infection model of pox-virus having similar symptoms to smallpox infection in human beings.[25] Minor animal models also investigated including Bagg and Albino (BALB /c mice) basis for monoclonal antibodies.[26]

Morphologically Mpox-v exhibit an ovoid (rectangular) brick shape appearance in pox-virus measuring (200-250 nm) embellishment through surface tubule or filament which show biconcave core constituent on electron micrograph.[27,28] Virion specially immature distinguish by spherical shapes while mature virion via harmful staining into two forms mulberry (M) smaller with short (10 nm) on surface tubules or capsular (c) which somewhat larger and penetrated through staining.

The life cycle of pox-viruses shows special between DNA viruses. Virus-replication entirely restricted in cytoplasm without interfering host genome. Monkey-pox virus genome structurally linear double stranded DNA with massive length more than 197 kb consisting of about 200 genes explain important challenge during de novo genome assembly.[29] Every single protein essential for replication and structurally encoded inside viral genome blocked at both end covalently by two inverted (opposite) terminal repeats (ITRs) just about each one (10 kb). Distinctive ortho-poxviruses succession conservation elevated in middle region of Mpox-v genome but decreases toward terminal ITRs. At that time gene responsible for house-keeping located in central region and particularly preserved between ortho-poxviruses while genes encoding proteins act together with host factors just because of lesser series uniqueness and located toward termini region.[30.31] The residual coded-genes properly named virulence factors appear not necessary for vitro replication in cell culture but lack attenuates in vivo-pathogenesis.[32]

All strains succession identity alonely from African continent Mpox-v that differentiate into two clades such as strain isolated from Congo Basin (or Central Africa) and West Africa showing inter-clade series homology about 95% while intra-clade homology move toward 99% .[33] On the other hand geographic allocation of two clades differentiated into clinical appearance, severity and communication.[34]

West african clade mortalities during 2017–2018 Nigeria Outbreak appeared milder whereas case fatality ratio of congo basin clade was reported as about 10% . Investigation of pre-liminary-phylogenetic revealed the recent 2022 outbreak that mostly correlated to west-africa-clade.[35]

Nomenclature system shows changes in Mpox-v clades that have been considered to keep away from discriminatory geographical identification.

Whereas isolated source from the Congo-Basin known as Mpox-v clade 1 and those rooted as west- African well-known as clade 2 and 3. Generally virulence differs among clades: clade 2 and 3 shows less virulent and not contagious in human and non-human primates (NHPs) than clade 1. Such findings may clarify the zero-case fatality in 2003 outbreak in U.S.

Approximately 90% reported cases hailed from congo-basin rather than outer surface shows analogous non-vaccinated sero-prevalence between both regions.[36, 37]

Outbreak of 2022 shows original two clades signs of separation from other predominantly throughout spread effectiveness between humans and sub-clade divided from clade 2 and now at present as clade 3 or human MPox-v (h Mpox-v).

Highest diversity between clade 1,2 (and 3) become visible clustered in terminal regions toward ITRs containing proteins known as genes encoded host-response modifier (HRM). One of these known as pox-viral inhibitors that show monkey-pox ortholog of the complement-enzymes (PICEs) or monkey-pox inhibitor of complement enzymes (MOPICE) protein which measured as degree of difference virulence factor between clade 1 and 2 For example in clade 2 lack of MOPICE contributes its slighter pathogenicity.[38] However Rhesus Macaques (Robust Study) showed opposite increased (MOPICE) deletion in vivo replication that destabilized adaptive immune response.[39] Virulence willpower differentiate into two clades showing numerous genetic factor inside immense genome of Mpox-v as well as open analysis frames of D10L (host range protein), B10R (apoptotic regulator), B14R (interleukin (IL)-1β binding protein) and B19R (serine protease inhibitor like protein).[40]

The 2022 outbreak indicated the former correctness because the entire universal isolates phylo-genetically resulting from clade 2 and till up to date just 20 death reported among 60,000 laboratory qualified tests.[41]

PATHOPHYSIOLOGY

There are several entry routes of Monkey Pox Virus Mpox-v penetrate the human body such as oro-pharyngeal, naso-pharyngeal or intra-dermal routes etc.[42]

By significance it establish that Mpox-v get entrance into body through sexual transmission.[43.44] Mode of entrance occurs between humans through direct contact or by droplets like breathing, infected skin lesion or mucosa etc.[45] Therefore direct-contact with contaminated belongings like furniture clothes, utensils considered. Durining entrance virus replicates within the location and spread directly to confined (local) lymph nodes . After incubation period (1–3 weeks) several symptom appeared for example sore throat, shortness of breath, fever, chills, backache, malaise, headache and enlarged lymph nodes.[46,47] During 1–3 days after appearance of fever and lymph-adenopathy patient enter into infectious stage showed development of rash that often appears at facial area then spreads to other parts of body.[48] It is earlier discussed that ortho-pox viruses be capable to disturb pattern recognition receptors (PRRs) articulated by innate immune cells. These types of protein consist some sub-families includes NOD like receptors (NLRs), Toll like receptor (TLRs), RIG-1-like receptor (RLR), and C type lectin receptor (CLRs) etc. These proteins exhibit the major responsibilities such as distinguish different microbe-related molecules or molecules released by impaired cells.[49] At start Pattern Recognition Receptors (PRRs) binds to microbial ligands with successive cascades occur like activation of inflammation-related transcription factor such as interferon regulatory factor (IRFs), nuclear factor kappa B (NF-_B) and activating protein-1 (AP-1) etc.[50] Durining signal transduction of TLRs involves numerous types of intracellular adaptors proteins such as MAL, TRAM, TRIF, MyD88 and SARM are essential for triggering intracellular immunologic reactions.[51] Several disturbances within the adaptor protein may cause problems that exert (show) adequate immunological response toward viral infections.

Sometimes adaptor protein show disturbed physiological functions resulting inhibition of transcription factors that linked with inflammation i.e (NF-B).[52]

Finally condition shows failure of innate immune systems distinguishes viruses. Inhibitory action might be mediated by numerous viral proteins e.g (B12R and C7L) usually in Mpox-v strain Zaire-I-96 test. Additionally like other ortho-pox viruses Mpox-v contain gene that encodes protein mimicking activity of Bcl-2 proteins that play a critical role in regulating apoptosis.[53,54,55] It exposed that b-cell lymphoma-2 (Bcl-2) include activity similar to viral protein (P1L) like proteins in Mpox-v strain Zaire-1-96. At molecular level the viral protein interact with I-KB kinase (IKK) complex that provides critical role to facilitate the activation of NF-_KB.[56.57]

In addition to above mentioned mechanisms ortho-pox viruses have many several genes encoding proteins that valid to disturb various stages of host's inflammatory cascade. The main disturb function on the production of chemokines and cytokines and activity of ubiquitin proteasome pathway, the activity of the complement system and numerous targets.[58] According to recent records the clinical manifestations of monkey-pox surprisingly similar with the smallpox. However by means of these infectious diseases to allocate the much consistency in their signs and symptom several manifestation apply to distinguish smallpox and monkey-

pox e.g lymph-adenopathy directly associated with monkey-pox but not a trait of smallpox. Enlargement of lymph nodes point out immune response activated by host trail Mpox-v infection that further effective than infection caused by further ortho-pox viruses.

CLINICAL CHARACTERISTICS

- Clinical features of monkey-pox that are similar to the small-pox infection and presence of symptoms might vary endemic or non-endemic situation as well as depending on the virus Clades.[59]
- Incubation period estimated 5 to 21 days and symptoms & signs duration as 2 - 5 weeks. Sickness begin with imprecise signs and symptoms comprise headaches, fever, chill, lethargy, asthenia, back pain, lymph node swellings and myalgia (muscle ache) thus appeared with fever before rashes appear.
- Onset of fever after 1 to 5 days rashes of different size emerge,, first on face then across the entire body like hands, legs and feet etc.
- Rash undergo numerous stages of development from macules, vesicles (fluid-filled blisters) papules and pustules followed by time into crust and scab which drop off after recovery.
- Different types of rashes seen at same time in areas of erythema or skin hyper-pigmentation frequently seen around discrete lesions.
- Inflammation of conjunctival, pharyngeal and genital mucosa may also be seen.[60]

Common symptoms of mpox are

- Fever
- Rash
- Sore throat
- Muscle ache
- Headache
- Back pain
- Swollen lymph nodes.

COMPLICATIONS

- Most monkey-pox cases completely determined within 2–4 week. However various complications may result infection.
- Retropharyngeal abscess and Encephalopathy reported severe complication. Other complication reported includes as bronchopneumonia, encephalitis, sepsis, secondary-skin infection, corneal infection and deep abscess pitted scar frequently reported.
- Some cases shows vision loss due to orbital infection.
- Severe complications like sequelae which more obvious in non-vaccinated as compared to vaccinated patients.[61]
- Mpox affecting the heart (myocarditis), lungs (pneumonia) or brain (encephalitis) and eye problems.

INVESTIGATIONS

- Optimal clinical specimens for laboratory analysis like skin lesion such as swab of vesicular lesion exudate or crusts stored in dry sterile tube (no viral transport media) that kept cold.
- Viral culture ought to obtain by pharyngeal or naso pharyngeal swab.
- Polymerase chain reaction (PCR) by testing from skin lesions, chosen diagnostic test due to elevated sensitivity in presence of bacterial infection of patient's specimen. Gene expert usually in-conclusive due to non verification.[62].
- Best recommended laboratory test for the diagnosis of Mpox is nucleic acid amplification (NAA) frequently as PCR. Detection of Mpox DNA by PCR or NAA based techniques is considered as diagnostic.
- Mpox is diagnosed by (PCR test) for monkey pox virus (Mpox- virus) on a viral swab taken from one or more vesicles or ulcers.

DIAGNOSIS

- Evaluation of monkey-pox depends upon taking exact medical history and clinical manifestation.
- Traveling history interrelate with endemic area either undomesticated (wild) animal from infected areas or take care from contaminated patients must be calculated.
- Therefore ultimate diagnosis must be justified by laboratory findings. Diagnosis shows differential diagnoses such as acute rash as chief complain.[63,64]
- Therefore situation must be measured varicella (chickenpox) molluscum contagiosum, cutaneous bacterial infection and measles, drug allergies, syphilis and scabies.[65,66]

TREATMENT

- Treatment of monkey-pox disease commonly by management and long term prevention. Fluid and sufficient nutrition be essential to improve overall-recovery.
- A drug named tecovirimat, initially researched and developed for smallpox and accepted for Mpox-v from early 2022. However yet widely not available.
- Two supplementary antiviral-drugs cidofovir and brincidofovir may also developed to treat smallpox and can inhibit viral DNA polymerase that be able to use in monkey-pox.[67]

MILD OR UNCOMPLICATED MONKEY-POX MANAGEMENT

- Symptomatic relievers can be prescribed according to the patient's condition (situation),, for example,,
- Antipyretics, analgesics, or antiemetic medication. Adequate hydration, vaccination review, and nutritional assessment should be performed,, particularly in pediatric patients.

- Supplementing vitamin A, which has demonstrated (confirmed) an essential role in wound healing,, may benefit deficient patients
- Mild skin rashes can be given supportive treatment to. quell irritation and promote healing. Antimicrobial agents to eradicate Streptococcus pyogenes or Staphylococcus aureus are recommended if a secondary bacterial infection is suspected.
- Complications such as cellulitis,, necrotizing soft tissue infection, or abscess should be monitored and treated appropriately.
- Mental health should also be followed up in patients with monkey-pox. Long-term isolation can cause anxiety and depression which should be helped with psychological-support

PREVENTION

Direct contact control from secretion of infected (unhygienic) person or animal that may be the key means of viral transmission. These secretion may through respiratory droplet or skin, mucus membrane lesions or bodily fluid.

Durining 2022 outbreak (epidemic) in (Europe and North America) exposed mostly affected men who contain sex with men (MSM) that generate proposal that monkey-pox be able to sexually transmitted in fact earlier unknown.[68] Current study from Italy originate that viral DNA of semen enlighten contaminated patient persisting at least nine days after onset of symptoms while evidence of contamination residue indistinguishable.[69] During and after birth transmission of virus through placenta is frequently reported.[70]

VACCINATION

Eradication of smallpox showed the important activities of modern medicine which skillful through effective vaccination program.[71] Successive smallpox eradication since1980 general population vaccination discontinued after vigilant consideration of risk and benefits.[72]

Therefore new vaccines developed for monkey-pox to conduct prohibited clinical-trial to evaluate the exploit of smallpox vaccines against deterrence of monkey-pox.

Modern studies show rate benefit population based immunization and analysis of substitute vaccination strategies such as target vaccination in exaggerated areas, health care worker, contact with wider geographic area. Centers for disease control (CDC) recommend preexposure small-pox vaccination (immunization) for countryside investigators and animal control workers, contacts of monkey-pox patients, health care employees, veterinarians, researchers-carrying for such patients.[73]

CONCLUSION

Monkey-pox spread across west-africa during past decade and long-lasting out-break in Nigeria. Viral-zoonotic disease happens mostly in inaccessible part of innermost and west-africa in front of tropical rain-forest. This spread potential increased regionally and internationally remains chief concern. The clinical characteristics illustrate ecological, zoonotic, epidemiologic & public health aspect of monkey-pox stay incorrectly.[74] Initial production of live attenuated vaccinia-virus (variant of cowpox virus) vaccines stored for emergency purpose at several countries that neglected just because of severe adverse reaction. Dis-continuing smallpox vaccination program produced ecological gap where as by increased quantity of population either waning or non-existent protection to mpox-virus. The expansion forced to extra increase in risk of both animal to human and human to human due to spread (expend) of virus.[75]

As a result major concern on research and surveillance should create single-human animal environmental health efforts (hard work) across the middle, west-africa and entire world.

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