REVIEW ARTICLE

OPEN ACCESS

Has Monkey Pox Got Viral: Is it time to Worry?

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Received: June 05. 2023 Revised: July 17, 2023
Accepted: November 24. 2023 Published: January 05, 2024
DOI: https://doi.org/10.70394/jhbsmdc.v3i2.24

Abstract

The world has seen a worldwide rise of Monkey pox infection since May 2022 and now has reached an endemic status in Africa. This situation has spurred concerns about the risk for another viral pandemic especially after experience of COVID 19. Though only 3 cases of Mpox have been detected in Pakistan so far ,but we need to be vigilant for any future outbreak as transmission and pathogenicity of this virus is increasing day by day. By this scoping review we would like to create an awareness for public and health workers regarding etiology, routes of transmission and susceptibility. Current clinical presentations, methods for diagnosis, available treatments and active immune prophylaxis are also considered. Readiness of health authorities in Pakistan to deal with any emerging epidemic, documented as set guidelines by National Institute of Health (NIH) will be discussed briefly and few recommendations are put forward. Different search engines (Google Scholar, PubMed) and databases like SCOPUS are used for extracting relevant information. The need of this narrative review is to compile worldwide guidelines and strategies on dealing with Mpox virus as a proactive approach.

Keywords: Monkey Pox, Mpox, Transmission, Prophylaxis

Conflict of Interest: None **Funding Source**: None

Introduction

Monkeypox (Mpox) is a viral zoonotic disease by infection of “Monkey pox virus” (MPXV). It is a DNA virus, classified in genus Orthopoxvirus (Poxviridae family), same as of Variola virus implicated in small pox.[1] This virus was first detected during a vaccine trial in monkeys, in 1958, in Denmark so named as ‘monkey pox’.[2] Later on it was found to be pathogenic in both animals and humans.[3] Human monkeypox was initially endemic in African countries by animal human transmission. In 2003 first case of human monkey pox was detected in United States (US) resulting through same route.[4]

In 2022 Mpox outbreak in non-endemic areas and number of rising cases forced World Health Organization (WHO) to announce a “global health emergency of moderate nature[(5)]. Its nomenclature was changed to "Mpox" instead of "monkeypox" for a non-discriminatory and non-stigmatizing reason.[6] Till January 16th 2023 WHO reported 110 countries, areas, or territories having cases of Mpox and eighty deaths, while United states(US) having the highest number of cases.[7]

This is a serious concern firstly because, though global cases have declined after achieving their highest peak in August 2022 but Mpox virus has potential for mutation hence relaxation of safety measures can lead to more waves of international outbreaks. Secondly, due to globalization, social and population exchange has increased manifold so as the risk. In recent years due to extensive international travels the disease shows rapid spread across multiple countries and control has become a global challenge. Mpox outbreaks the past, especially in non-endemic countries a clear transmission chain could be traced. The infected patients exhibited a clear history of animal exposure with recent travel to area with outbreak , and/or exposure to imported cases.[8] But in current episode of rapidly spreading international outbreak a new human to human (social) transmissions predominantly among men, was the main source.[9]

In recent epidemic a concern and alarm was raised due to fact that 10% of cases of Mpox have proved fatal [(10)] unlike smallpox infections and more so, its spread from endemic areas to nonendemic regions. Also after eradication of small pox , Mpox is the only naturally

occurring poxvirus infection that poses threat during pregnancy.[11]

SITUATION IN PAKISTAN

Three cases have been detected till May 2023 in Pakistan.[12] Initially (because of lack of diagnostic facilities) it was denied by the Government but then typical history and symptoms raised concern and virus was positively isolated. In Pakistan Mpox virus can become major threat as the population is more susceptible. This occurred, ever since small pox vaccine got discontinued since 1980 from EPI after WHO declared Pakistan small pox free creating a lack of pox virus immunity(13). The objective is to acquaint health care providers and authorities, especially in Pakistan, with Mpox routes of transmission and symptoms as it presents challenges in all three domains: Inadequate capacity to diagnose, Clinical management of patients and accurate identification of exposure. Health system in Pakistan is already overburdened along with worsening economic situation. Hence, if proper actions are not taken such pandemics can prove catastrophic in future.

ETIOLOGY

Mpox virus (DNA) enters host cells by multiple routes through direct contact, mucosal surfaces, body fluids, shedding through feces, intramuscular, subcutaneous or intradermal pathways. Inflammatory immune-mediated phagocytosis is triggered by its replication at the inoculation site which causes virus to spread to the blood, lymph nodes, tonsils, bone marrow, spleen, and other organs.[14, 15]

ROUTES OF TRANSMISSION

Several modes of transmission of Mpox virus are observed: Animal-to-animal, animal-to-human, or human-to-human.[16] In animal-to-human transmission rodents, squirrels and non-human primates are believed to be reservoir hosts. Direct contact with an infected animal (where animal contact is frequent due to rodent infestations) or body fluids like blood, urine, saliva is the commonest mode seen in endemic manifestations .Human-to-human transmission such as exposure to large respiratory droplets, use of contaminated personal items or direct contact with skin lesions are some of the mediators for transmission.[17] In 2018 a health employee in United Kingdom(UK) got infected from a patient contaminated bedding.[18] The 2022 outbreak is different from previous endemics as more sufferers were homosexual or promiscuous men..[19] Center of disease control (CDC) has also identified other routes like kissing, hugging, oral, anal and vaginal sexual intercourse.[20]

In current era more people are exposed to infections due to massive migration and travelling from one place to another either for religious meetings or sports event or forced migration because of natural disasters or wars(16).

SYMPTOMS

Typical symptoms of Mpox (before current outbreak) included fever lasting for few days followed by appearance of well circumscribed vesiculopustular rashes. These rashes are spread over different exposed skin portions of the body, such as face, mouth, and eyes, hands and feet but with maximum intensity on face .The rash progressed as macule then papule, passing to vesicle, pustule and finally crust formation and desquamation occurring 14–24 days after rash onset.[21] Lymphadenopathy is also very discrete symptom where lymph nodes around ear, jaw, and neck or groin region enlarge.[22] Nonspecific features involved headache, muscular pain, back ache associated with extreme tirednesss.[23] The incubation period of varies from five to twenty-one days. The symptoms are very similar to small pox however the incubation period of Mpox is dependent on its route of transmission.[24]

WHO data collected in current outbreak exhibited asynchronous skin lesions. The prodromal symptoms and the appearance of skin lesions had no clear distinction, with only about half of cases having systemic symptoms. The genital rash and perineal lesions were seen in only 37 percent of cases. In Africa harbors a predominance of affected males (>99%) especially in individuals claiming to be homosexual, bisexual, gay, or promiscuous. Most cases in current outbreak had no travel history to endemic countries but do admit having multiple sex partners or were HIV-positive.[25] The current approach of 21 days quarantine (or other methods to avoid infectious contacts) is appropriate. But the different transmission routes can cause transmission hence, continued surveillance in incubation period for Mpox is mandatory.

SUSCEPTIBILITY OF Mpox

M-pox susceptibility is dependent upon age ,gender, ethnicity and medical history. The vaccination status also and exposure history also effect the susceptibility. Vaccination against Orthopoxvirus species and age-related immunity are also important considerations. HIV-positive immunosuppressed individuals, when get coinfection exhibit causes symptoms and also higher mortality.[26] In 2022 outbreak, males were more prone, especially gay and homosexual men, showed worse

symptoms. Those working with animals –farmers, butchers –or any connection with possible animal reservoirs make individuals more susceptible.[27] Since long, there has been absence of vaccination against small pox (since 1971 worldwide and 1980 in Pakistan) in the population. Hence individuals, due to lack of immunity (similar genome of M pos and small pox) have become more vulnerable to M pox [28]. Extremes of age (children and elderly) , pregnant females with a suppressed immune system were included in a vulnerable group[(29).]

VULNERABLE GROUP

PAEDIATRIC Mpox

Children were disproportionately more affected in previous outbreaks, but had higher morbidity with relatively less mortality (up to 10% during the 1980s)(1). The authorities should be prepared to rapidly implement vaccination for them, should outbreaks involve them. Secondly symptoms of viral exanthemas, like in varicella (chicken pox) and hand foot & mouth disease can be quiet similar and confusing[(30)]. Hence very few children are tested for M pox and false positive results could be seen. This can result in an unnecessary and prophylactic vaccination of close contacts[(31)] with over burdening the health care system and unintended social stigma.

PREGNANT WOMEN & Mpox

Pregnant woman can easily contact Mpox. This could result in a high-risk pregnancy loss, maternal morbidity or even mortality along with fetal transmission. Fetal infections lead to poor outcomes, include spontaneous abortion, stillbirth, and congenital infections thereby classifying MPXV as "TORCH" agent.[32] In this outbreak UK, USA, Brazil, the positive cases for Mpox reported at various stages of pregnancy, resulted in one vertical transmission to the neonate. A nine-day-old neonate developed the typical vesicular rash starting from palms and soles, and eventually spreading to face and trunk along with axillary lymphadenopathy. The PCR testing in this case confirmed MPXV.[11]

Symptoms in pregnant woman are more or less same as above -vesiculopustular rash—including rash localized to genital or perianal region- and lymphadenopathy.[33]

Various routes of transmission from mother to fetus, as suggested by researches.[34, 35] include vertical MPXV transmission via antenatal transplacental infection after an episode of maternal viremia, hence the virus reaches placenta through blood in uterine artery. Postnatal environmental exposure is also suggested as an alternate route.

DIAGNOSIS

Diagnosis on the basis of history, symptoms and signs needs to be assisted by tests on patient specimens for case confirmation.

Conventional and real-time C-(PCR) & (RT)-PCR tests for diagnosing suspected Mpox cases is recommended by WHO as it specifically targets MPXV's DNA taken from lesion material from active cases. This is an expensive yet very sensitive method plus needs trained technician with specific equipment.[36]

Serology tests measuring antibodies against Orth poxviruses including ELISA testing is not recommended alone for diagnosing MPXV[37] as this virus being similar to variola virus may show false positive results for Mpox where the antibodies had been developed in suspected case as a result of smallpox immunization so vaccination may interfere with serologic testing.

In Pakistan smallpox vaccination is no longer a regime of EPI program as it has been declared small pox free region in 1980.[38]The diagnostic facilities for M pox are unknown at present. But all health authorities have been advised as effective control and prevention measure to ensure surveillance by isolating suspected cases, providing available lab diagnostics, contact tracing and follow up of contacts to observe any early signs of infection.[39] Rapid identification of suspected cases, determination of source, clusters of infections and identification of risk groups are needed the most.

THERAPEUTIC OPTIONS

all patients with mild symptoms require no treatment and get well without any medical treatment. They just require supportive treatments like pain killers and plenty of fluid to prevent dehydration, and are sufficient. Most of the time the supportive is coupled with symptomatic treatments along with antiviral agents. The common antiviral drugs used, act as an inhibitor for viral DNA synthesis.

The indications of antivirals use are; severe cases, pregnant or breast-feeding women, immuno-compromised patients, extreme of age like pediatric population and elderly. The patients suffering from lesions near mouth, eyes and genitalia can also be prescribed antivirals.[40]

In cases of pregnant women presenting with lymphadenopathy and vesiculopustular rash with suspected MPXV exposure, diagnosis should be confirmed by real time PCR. At the same time varicella (chicken pox), herpes simplex and syphilis should be ruled out. In case mother is found to be positive for

Mpox the fetus should be monitored by periodic ultrasounds for further management. Real-time PCR analysis for specimens, obtained from suspected neonate immediately at delivery, should be the standard protocol.[34, 41]

PREVENTION

Smallpox vaccines such as JYNNEOS™ (live-attenuated, non-replicating vaccine)-are made from weakened vaccine viruses. These vaccines like Imvamune/ Imvanex, can cross-protect humans from MPXV. This is due to similar viral infection, but its use is restricted to prophylaxis. Vaccination after show of Mpox symptoms is not recommended by CDC.2nd Food and Drug Administration (FDA) approved vaccine ACAM2000 (live-attenuated, replicating vaccine) can cause side effects because the virus replicates inside cells. Both are currently available for post exposure prophylaxis and for prevention in high risk populations like health care workers , laboratory researchers, military personnel living in combined facilities(42). International agencies WHO and American agency FDA are planning future vaccination programs. They are also working on provision of vaccine supplies along with adjusting suitable doses and determining correct vaccination intervals.

Conclusion

Current review has shown that Mpox infection has acquired high transmissibility and pathogenicity. There is a increase danger of a pandemic effecting a wider human populations. Strict regulatory measures are required to prevent further Mpox spread, especially among non-endemic regions of the world. Potential factors regarding susceptibility need scientific and thorough investigation. Furthermore, scientific approaches and techniques are needed to clarify the relationship among population genetics, viral genomics, disease susceptibility and public immunity. More research data is required to assess the vaccine efficacy and treatments results for Mpox to develop standard guidelines. Affected countries in partnership with local scientific and public health authorities are best venues for such researches. This report is based on cases but but has tried to acquaint general public and high-risk health workers with recognition of symptoms in general and in specific vulnerable population.

RECOMMENDATIONS[41, 43]

We suggest following in Pakistan for spread of this viral infection, shaking our health care system and preventing this disease,

1. Educating community by awareness programs for:
   - Awareness of symptoms and routes of transmission including sexual practices and promoting vaccination drives.
   - Significance of detecting symptoms and self-quarantining and contact for immediate healthcare consultancy as a precautionary measure.
   - All general Physicians should be educated to be aware of Mpox infectious symptoms so as to limit the spread by identifying the contacts.
2. General precautionary measures especially in suspected areas, like COVID 19, should be implemented as Mpox transmission mode is still not fully comprehended.
3. Better to vaccinate health workers before disease exposure and educate them for all necessary precautions in all health providing facilities.
4. Social media platforms spreading misinformation about case reporting or mortalities should be strictly dealt with for the benefit of public.

In addition, designing or importing diagnostic kits, approving therapeutics against Mpox, improving pre-exposure and post-exposure vaccination are all the practices which needs government support. Pharmaceutical companies and Private sector can prove itself helpful by collaboration with government.

FOR TREATMENTS

Considering symptomatic patients as high-risk groups antiviral treatment should be started. Antivirals against Mpox like Cidofovir, Modified Vaccinia Ankara virus, Tecovirimat and Vaccinia Immune Globulin Intravenous (VIGIV)) should be made available in a proactive way. Proper isolation facilities coupled with nutritional and psychological support for the patients with symptoms should be made.

ACKNOWLEDGEMENT: We are extremely thankful for the efforts put by our two students of 4th year MBBS, HBS Medical college ,Miss Asma Ashraf and Miss Atifa Bibi ,who took out time to do literature review for this article.

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Authors Contribution:

[1,3]Substantial contributions to the conception or design of the work; or the acquisition, analysis, & Final approval of the version to be published.

[1,2] Drafting the work or revising it critically for important intellectual content.