Re-Emerging Trend of Mpox Infection: The Indonesia's Experience and Review

Erni Juwita Nelwan[1], Caroline Tanadi[2], Fegita Beatrix Pajala[2], Maureen Miracle Stella[2], Kevin Tandarto[2], Yehuda Tri Nugroho Supranoto[3], Ayers Gilberth Ivano Kalaij[4], Randy Adiwinata[5], Leonard Nainggolan[1], Lie Khie Chen[1], Sri Masyeni[6], Robert Sinto[1]

[1] Division Tropical and Infectious Disease, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[2] School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia.
[3] Research Assistant, Clinical Epidemiology and Evidence-Based Medicine Department, Dr. Cipto Mangunkusumo, Jakarta, Indonesia.
[4] Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.
[5] Department of Internal Medicine, MRCCC Siloam Hospital Semanggi, Jakarta, Indonesia.
[6] Department of Internal Medicine, Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia.

[*]***Corresponding Author:***
Robert Sinto, MD. Division of Tropical Infection, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia – Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta 10430, Indonesia. Email: robert.sinto01@ui.ac.id.

ABSTRACT

Background: *Since Monkeypox (mpox) had an outbreak on 6th May 2022 in 75 countries, it has been declared by the World Health Organization (WHO) that mpox is a public health of international emergency concern (PHEIC). WHO declared mpox as PHEIC again in August 204. Indonesia was also affected by the mpox outbreak with most of the cases coming from vulnerable populations. This study aimed to give an overview of mpox as well as the recent outbreak situation and management in Indonesia.* ***Methods:*** *In this narrative review (using PubMed, Scopus, and Cochrane databases combined with countries' national official reports and grey literatures), we discussed an overview of mpox including epidemiology, morphology, transmission, symptoms, treatment, and prevention. The management of mpox in Indonesia was specifically reviewed.* ***Results:*** *Mpox is an infectious disease caused by the mpox virus which has infected 79,231 individuals globally. In Indonesia, the first mpox case was detected in August 2022 with 0 deaths and 88 confirmed cases as of August 2024. The virus is transmitted via respiratory droplets or direct contact with contaminated objects, surfaces, or mucocutaneous lesions of an infected individual which could lead to symptoms such as epidermal papules-pustules and clinical characteristics of classical smallpox. Although antivirals such as tecovirimat, cidofovir, and brincidofovir have been raised as potential treatments for mpox, these agents were only considered in severe cases in Indonesia.* ***Conclusion:*** *Mpox is a contagious disease that could cause major health problems if left uncontrolled, especially in specific vulnerable populations due to its high morbidity and mortality. Therefore, particular measures must be performed, especially in Indonesia.*

Keywords**:** *Monkeypox, Mpox, Outbreak, Re-emerging infectious disease, Indonesia.*

INTRODUCTION

Mpox is a zoonotic disease caused by the monkeypox virus (MPXV) from the Poxviridae family.[1] MPXV also shares the same genus, namely Orthopoxvirus, along with other viruses, such as Vaccinia Virus (VACV), Variola Virus (VARV), Camelpox Virus (CMPV), and Cowpox Virus (CPXV).[2] This disease was first reported in a shipment of monkeys delivered from Singapore to Denmark during the year 1958.[3] The first mpox infection in humans was found as early as 1970 in the Democratic Republic of Congo (DRC) in a nine-month-old child.[4] Since the year 1970, mpox has become an endemic disease in Central and West Africa.[5]

On 6th May 2022, mpox had an outbreak in 75 countries which made the World Health Organization (WHO) to declare mpox as a public health of international emergency concern (PHEIC) on 23rd July 2022.[6, 7] During this period, there was only one confirmed case of mpox in Indonesia and no further cases were found throughout the year. However, mpox became a re-emerging disease in Indonesia when multiple cases were reported on 13th October 2023. Ever since, cases of mpox have continued to multiply in Indonesia.[8, 9] Although cases of mpox seemed to slow down in 2023, leading to WHO lifting the PHEIC on May 2023, the situation has worsened ever since with the emergence of a new strain, clade 1b, in DRC. This has led to a resurgence in mpox cases, prompting WHO to declare a second PHEIC in August 2024.[10] According to the recent outbreaks, those who contracted mpox were mainly men who have sex with men (MSM) or people with Human Immunodeficiency Virus (HIV). Greater caution should be exercised in such populations, especially during the current outbreak in Indonesia.[11] Although it has been declared as an outbreak, no review has given an overview of the conditions of mpox in Indonesia. This review aimed to give an overview of mpox as well as the current outbreak situation in Indonesia.

METHODS

This review is a narrative review using PubMed, Scopus, and Cochrane databases combined with national official reports among countries and grey literatures. We searched using the keywords of ”mpox” through databases and grey literatures. As in all narrative reviews, a selection bias could not be excluded. In this review, we discussed an overview of mpox including epidemiology, morphology, transmission, symptoms, treatment, and prevention. The management of mpox in Indonesia is specifically reviewed.

EPIDEMIOLOGY OF MPOX

Mpox is an infectious disease caused by MPXV and was first identified in a Danish primate laboratory among monkeys in 1958.[5] A nine-month-old child in the Democratic Republic of the Congo was the first human mpox case, which was discovered several years later in 1970.[12] For the following 20 years throughout the 1970s and 1980s, mpox was limited to African tropical rainforests, with the Democratic Republic of the Congo accounting for 95% of all cases. Around the same period, the virus spread to other African countries, such as South Sudan, Nigeria, Cameroon, Liberia, Sierra Leone, Gabon, and the Central African Republic. Later, mpox started to spread in 2005, and since diseased animals were being imported, an outbreak occurred in the United States of America. This disease has been endemic in West and Central Africa for the past 15 to 20 years, with brief epidemics occurring in a few neighboring African nations.[13-15]

Globally, the number of mpox cases has reached 79,231. In Africa, from 1970 to September 2022, there have been 57,995 cases of mpox. Since May 2022, the number of newly reported cases each week has dramatically increased, leading the WHO to declare this outbreak as PHEIC.[16, 17] In June 2022, WHO received reports of cases from various regions: Europe (86%), America (11%), Africa (2%), Eastern Mediterranean (<1%), and West Pacific region (<1%).[18-22] Recently in August 2024, WHO has re-declared a second PHEIC for mpox due to the resurgence of mpox cases in Africa. If left uncontrolled, this outbreak could potentially lead to a new pandemic.[10] As of 30th June 2024, WHO had received 99,176 laboratory-confirmed cases of mpox and 208 deaths from 116 countries.[23]

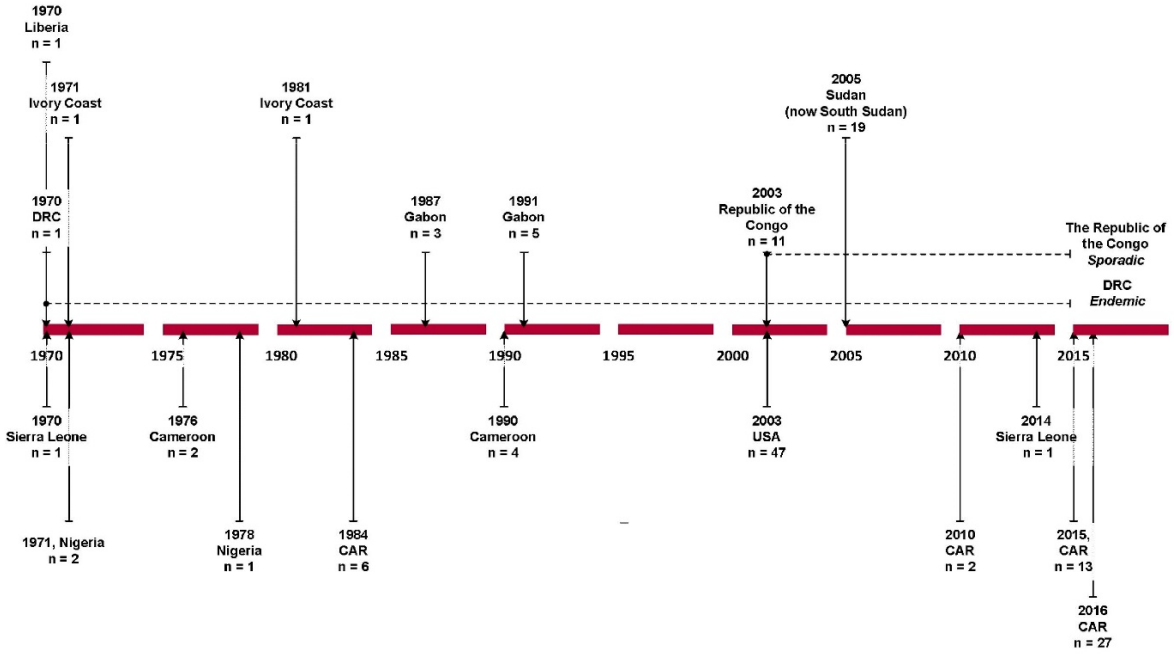

Figure 1. Timeline of human mpox outbreak from 1970 to 2015.
Source: based on data from Centers for Disease Control and Prevention,[24] Formenty et al. (2010),[25] Learned et al. (2005),[26] International Federation of Red Cross and Red Crescent Societies (2016),[27] Damon et al. (2006).[28]

The first mpox case was discovered in Jakarta on 19th August 2022, involving a 27-year-old male patient with a history of travel to several countries. As of 17th August 2024, there have been 0 deaths and 87 recovered cases out of 88 confirmed cases. The number of reported cases in order were 59 cases (67.0%) in DKI Jakarta, 13 cases (14.8%) in West Java, nine cases (10.2%) in Banten, three cases (3.4%) in East Java, three cases (3.4%) in DI Yogyakarta, and one case (1.1%) in Riau Islands.[29]

MORPHOLOGY AND PATHOGENIC MECHANISM

MPXV is a double-stranded DNA (dsDNA) virus that belongs to the *Orthopoxvirus* genus

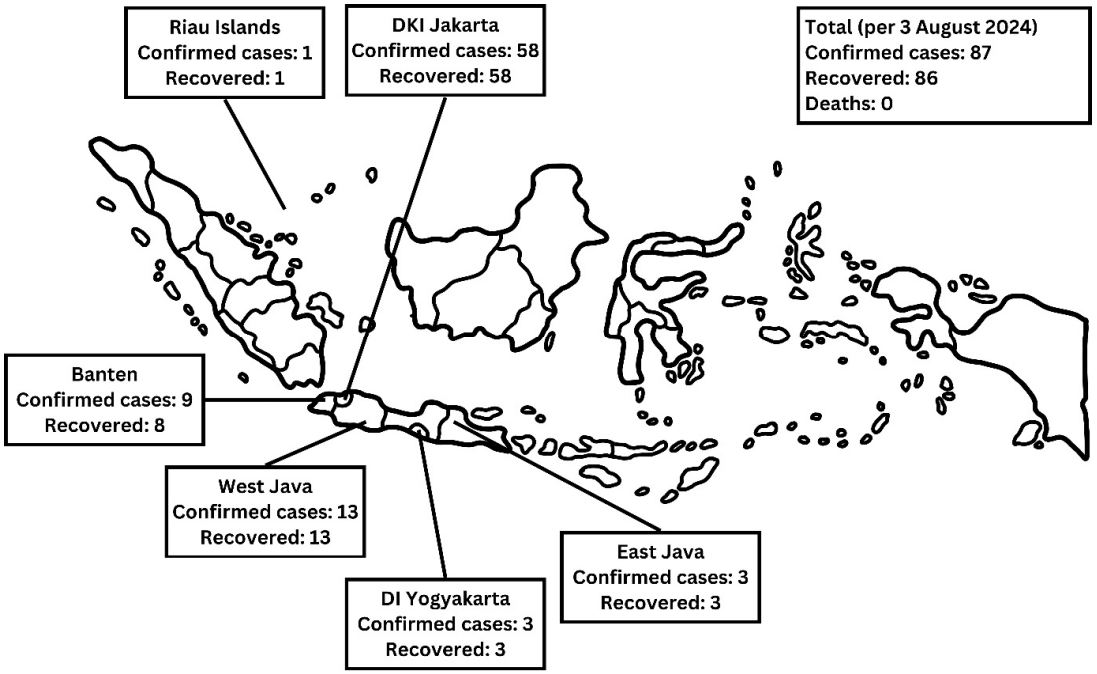

Figure 2. Distribution of mpox cases in Indonesia per 3rd August 2024.[29]

of the *Poxviridae* family. It has an ovoid or rectangular brick shape and is approximately 200-250 nm in diameter. During replication, the virus may produce infectious viral particles, such as intracellular mature virus (MV) and extracellular enveloped virus (EV), which are vital during transmission.[30, 31]

The MPVX genome has a length of 197 kb and has about 190 open reading frames (ORFs). The replication process of MPVX occurs in the cytoplasm. To enter host cells, three steps must take place: adsorption, membrane fusion, and core invasion. Up to now, no specific cell receptors for poxvirus have been identified. However, given its similarity to VACV, it may share similar pathogenic mechanisms. VACV relied on four viral proteins (A26, A27, D8, and H3) to adsorb MV to the host cell. After adsorption to the cell surface, membrane fusion of MV occurs via an entry fusion complex (EFC) formed from 11 viral proteins (A16, A21, A28, F9, G3, G9, H2, J5, L1, L5, and O3). Once the membrane has fused, the viral core will enter the cytoplasm and initiate the viral replication process. This step is mediated with the help of viral proteins, such as A16L, A21L, A28L, F9L, G3L, G9R, H2R, J5L, and L5R.[31]

Up to this point, there are officially three clades for mpox, namely: Central African MPVX (CA-MPVX)/Clade I, West African MPVS (WA-MPVX) detected before 2017/Clade IIa, and WA-MPVX detected after 2017/Clade IIb. Clade I was the first clade of MPVX detected in humans in Congo and was responsible for the subsequent periodic outbreaks in Central Africa. Meanwhile, Clade IIa was responsible for the mpox outbreaks in West Africa. Unlike Clade I, which caused severe disease, Clade IIa had milder symptoms and shorter outbreaks due to the lack of human-to-human transmission. In the years 2017 to 2018, the Clade IIa viruses underwent a mutation and gained the ability for human-to-human transmission, thus creating Clade IIb. Clade IIb can be further classified into A.1 and A.2. A.1 can be subdivided into the lineages A1.1. and B.1. The lineages A, A.1, A.1.1, A.2, and B.1 were classified based on the core single nucleotide polymorphisms (SNPs) and inverted terminal repeat (ITR).

The viruses that triggered the West African outbreak during 2017-2018 formed lineage A or hMPVX-1A. The hMPVX-1A viruses are capable of human-to-human transmission. After the outbreak in West Africa, the hMPVX-1A viruses continued to spread to the United Kingdom, Israel, and Singapore, forming group A.1. MPVX viruses discovered in the United States during the years 2021-2022 formed group A.2. The MPXV/United States/2021/MD (A.1.1) virus was first discovered from a human travelling from Nigeria to United States in 2021. This A.1.1 virus was an evolutionary intermediate to the B.1 viruses that cause the global mpox outbreak in 2022.[32] More recently, a new strain known as clade 1b has been identified as the cause of the new outbreak in DRC and neighboring countries in 2024.[10]

TRANSMISSION

The transmission and subsequent establishment of MPXV within a host involved a sequence of steps that resulted in pathogenesis and pathophysiology. The virus can be transmitted through respiratory droplets in human-to-human transmission, or via direct contact with contaminated objects, surfaces, or mucocutaneous lesions of an infected individual.[33] Upon entering the body, the virus exposed to the oral or respiratory mucosa will undergo replication at the site of infection. The virus then travels to local lymph nodes during the primary viremia stage, and subsequently to distant lymph nodes and organs during the secondary viremia stage via circulation. The incubation period, ranging from 7 to 21 days between exposure and symptom onset, does not exhibit clinical manifestations, and individuals in this stage cannot transmit the virus to others.[34]

In regions where infrastructure and resources are limited, the risk of exposure to the faeces of infected animals constitutes a significant factor. Additionally, many individuals in these areas opt to sleep outside on the ground or reside near forests where infected animals are more prevalent.[34] In settings with insufficient resources and necessities like food, hunting becomes a necessity, further elevating the risk of exposure to mpox. The transmission rate from

animal-to-animal surpasses that of human-to-human transmission, often involving respiratory droplets, face-to-face contact, and contact with lesions among infected individuals.[35]

It is important to note that earlier outbreaks of mpox before 2017 were mainly transmitted from animals to humans and lacked human-to-human transmission. Meanwhile, the clade IIb MPVX, which is responsible for the global pandemic in 2022, has increased human-to-human transmission. In fact, there is currently no known zoonotic link in the 2022 mpox outbreak.[36]

CLINICAL MANIFESTATION

The clinical manifestations of mpox due to clade I infection have been reported to be similar to smallpox. This typically starts with a prodromal period of fever, malaise, and headache, followed by the eruption of synchronous generalized centrifugal rash and cervical or axillary lymphadenopathy. This rash period usually starts 14-28 days post-infection. Clade IIa infections also have similar manifestations to clade I but with a higher degree of severity and less pronounced rashes. Meanwhile, clade IIb infections during the current outbreak differ greatly from infections caused by clade I and clade IIb. Unlike clade I and clade IIa, infections by clade IIb have a less pronounced prodromal phase, followed by the development of asynchronous localized vesiculopustular rash. These rashes are typically concentrated in anogenital areas and may be accompanied by inguinal lymphadenopathy. The presence of anogenital rashes suggests the predominant human-to-human transmission nature of clade IIb. Around 96% of cases have rashes and only 69% have flu-like symptoms. Notably, mpox is frequently mistaken for other sexually transmitted infections (STIs), including granuloma inguinale, molluscum contagiosum, chancre, or herpes simplex infection.[36-38]

It is also important to note that in previous mpox outbreaks, the reported cases that were men was only 53%, with 50% of cases aged 0-17 years. On the other hand, the cases reported during the current outbreak mainly consisted of men (96%), with 84% of them being those who have sex with men and are in their thirties. Furthermore, more than 50% of these cases tested positive for HIV.[36] Mitjà et al found that the most common presentations of mpox in HIV patients are skin rash (95%) and fever (64%). Skin rashes in HIV patients were often more severe, numerous (may reach up to 100 lesions), widespread, and tended to progress from vesiculopustular rash (78%) to ulcerative lesions (22%). Similar to non-HIV patients, the most common location for rash was genital (62%), followed by anal (53%), oral (38%), and ocular (5%). Of note, HIV patients often develop complications, including skin complications (25%) such as necrotizing lesions (22%) and ecchymosis or hemorrhagic lesions (3%). These lesions often present as multiple, large (>2 cm in diameter), round ulcers with necrotic centres and raised borders. Other common organ complications include the lungs (9%), eyes (5%), and brain (3%).[39]

In Indonesia, clade IIb was the most common variant.[29] The most commonly reported manifestations of mpox in Indonesia were skin lesions (100%), fever (86.9%), and lymphadenopathy (57.9%). Similar to the manifestations seen in clade IIb infections, mpox patients in Indonesia also mostly developed asynchronous lesions (59.4%). The skin lesions were often in the range 6-25 (50.7%), followed by 1-5 lesions (24.6%). Unlike the reports of mpox in other countries, the most common location for lesions in Indonesian mpox patients was at the face (60.9%), followed by legs (46.4%), and genital (46.4%). Similar to reports of mpox cases in multiple countries, cases of mpox in Indonesia are also overrepresented by men (98.6%) with the most common age group being 30-39 years (44.4%). Among these reported cases, 63.5% were men who have sex with men (MSM) and 23.6% were bisexual. Nearly all of these cases were deemed to be transmitted sexually (88.9%) with the rest being unknown. In addition, around 73.6% of the mpox cases in Indonesia tested positive for HIV. Overall, most of the mpox infections in Indonesia were mild in severity (70.8%). Meanwhile, around 25% were classified as severe and 4.2% asymptomatic.[40]

In Indonesia, mpox lesions in patients with

HIV may exhibit patterns than differ from those reported in other countries, demonstrating a unique clinical spectrum that requires special attention. For example, two patients reported by Sinto et al have showed variations in the presentation of mpox lesions in Indonesia. Figure 3 showcased a 48-year-old male who originally developed maculopapular lesions on the face, followed by the back and hands. The patient had no genital or mucosal lesions. **Figure 4** was taken from a 28-year-old male patient who had pustular lesions on the face and then spread to other parts of the body. These lesions then grew larger and became pseudo-pustules and ulcers as well as mucosal involvement. These differences suggest that mpox lesions in HIV patients in Indonesia may have characteristics distinct from those abroad, highlighting the importance of clinical vigilance and local understanding in the diagnosis and management of this infection.[41]

TREATMENT

Since there is no specific antiviral treatment for mpox, its management is primarily supportive

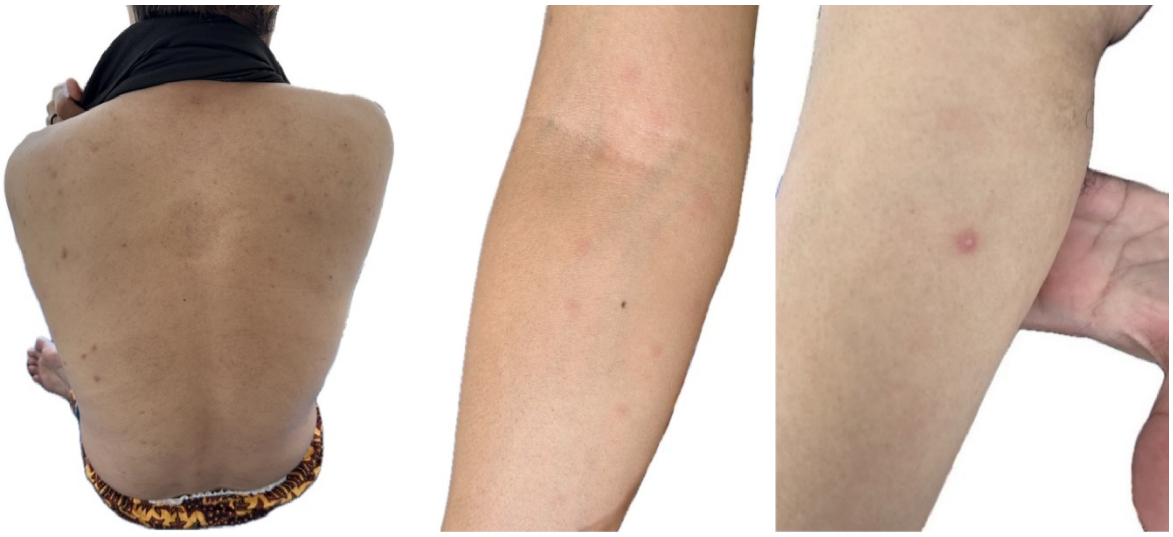

Figure 3. (A-B) A 48-year-old male with mild skin manifestation of mpox.[41]

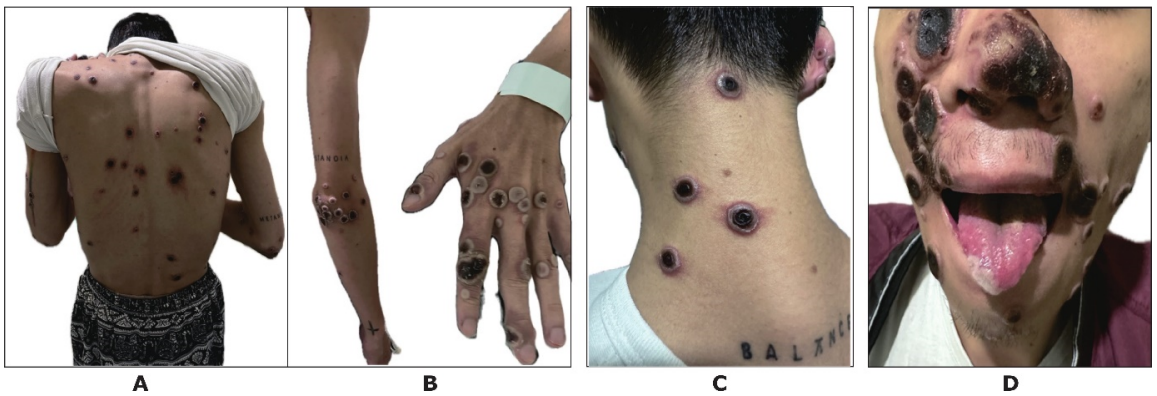

Figure 4. (A-D) A 28-year-old male mpox and severe skin manifestations of mpox with mucosal involvement.[41]

and symptomatic. Most patients develop mild symptoms and recover without medical treatment.[42] Clinical management for mpox must be effective in minimizing symptoms, treating complications, and preventing long-term sequalae.[43] Although there is no specific therapy for mpox, research has showed that the smallpox vaccine has an 85% effectiveness in preventing mpox. Moreover, several antiviral drugs such as tecovirimat (oral and intravenous), cidofovir (intravenous and topical), and brincidofovir (oral) may also be effective in treating mpox.[44,45] According to the Centers for Disease Control and Prevention (CDC)-held expanded access Investigational New Drug EA-IND) protocol, indications for receiving antiviral treatment include the presence of a severe disease or at risk for a severe disease (immunocompromised patients, patients aged < 1 year, pregnant or breastfeeding women, skin diseases), and the presence of lesions in areas that may cause scarring or strictures (pharynx, genitalia, urethra, anorectum).[46]

Tecovirimat (TPOXX or ST-246), an FDA-approved antiviral drug used to treat smallpox infection in children as well as adults has been proposed as a treatment for mpox. This agent works by targeting the F13L gene which produces the membrane protein p37. This membrane protein plays a vital role in the formation of extracellular enveloped virus (EV) that are responsible for transmission between cells and via the bloodstream.[47] Tecovirimat is available as 200 mg oral capsules and 200 mg/20 mL single-dose injection vials. Intravenous (IV) tecovirimat may be considered in patients who are unable to consume the medicine orally or in patients with gastrointestinal dysfunction. However, IV tecovirimat should be used cautiously in individuals with renal impairment and are contraindicated in those with creatinine clearance (CrCl) < 30 mL/min. A fourteen-day course of tecovirimat has proven effective in preventing rebound infection and mortality. In general, tecovirimat is well tolerated with mild side effects such as headache, abdominal pain, nausea, and vomiting. Animal studies have not found any embryo-fetal abnormalities with tecovirimat use during pregnancy. However, tecovirimat appears to be excreted in breast milk six to 24 hours post-consumption and thus breastfeeding patients may consider discarding the breast milk when under treatment.[46] Although tecovirimat has a favourable efficacy against mpox, drug resistance has been reported in clade IIb variant B.1 strain that has amino acid substitutions in the F13 protein. One study reported that 83 out of 130 isolates were found to be tecovirimat-resistant and 16 out of 130 isolates were partially resistant.[44]

Cidofovir (Vistide) has been mainly used to treat cytomegalovirus (CMV)-induced retinal infection in acquired immunodeficiency syndrome (AIDS) patients.[43] Unlike tecovirimat, cidofovir could inhibit viral DNA synthesis via selective inhibition of DNA polymerase. It is only available as 75 mg/mL IV infusions due to its poor gastrointestinal absorption. The recommended dose for cidofovir is 5 mg/kg body weight given once every week consecutively for two weeks, followed by a maintenance dose of 5 mg/kg body weight once every two weeks. Animal studies have shown its efficacy in suppressing disease progression in various orthopoxvirus infections. Furthermore, a study in primates with mpox has also shown that cidofovir could prevent lesion development when given within 48 hours of exposure. Some of the most commonly reported side effects were proteinuria, nausea, fever, and neutropenia. Similar to tecovirimat, cidofovir is also contraindicated in patients with renal impairment (CrCl ≤ 55 mL/min, serum creatinine > 1.5 mg/dL, or urine protein ≥ 100 mg/dL / ≥ +2). Moreover, cidofovir also has dose-dependent nephrotoxicity and thus warrants a prehydration using normal saline infusion along with oral probenecid. It is important to note that cidofovir is not recommended in pregnant and breastfeeding mothers due to its embryotoxic and carcinogenic properties.[47, 48]

Brincidofovir (CMX001 or Tembexa), a prodrug and lipid conjugate of cidofovir, also acts by inhibiting the DNA synthesis process. It is available as 100 mg tablets or 10 mg/mL oral suspension. The typical dose for brincodofovir is 200 mg once every week for two doses. When compared to cidofovir, brincidofovir has shown efficacy against various orthopoxviruses with

a lower half-maximal effective concentration (EC_{50}). In addition, due to the presence of alkoxyalkyl moiety, brincidofovir has better gastrointestinal absorption when compared to cidofovir. Thus, brincidofovir has the advantage of easier administration via oral route compared to cidofovir which can only be administered intravenously. Due to its lipophilicity, brincidofovir can efficiently cross cell membranes and reach higher intracellular concentrations. Another advantage of brincidofovir is its reduced nephrotoxicity when compared to cidofovir. Some common adverse reactions include diarrhoea, nausea, vomiting, and abdominal pain. Of note, brincidofovir has been found to cause elevated hepatic transaminases and bilirubin levels and thus warrants monitoring of liver laboratory parameters before and during treatment. As with cidofovir, brincidofovir is embryotoxic and should be avoided during pregnancy. Although there is no available data for brincidofovir in human breast milk, brincidofovir has been found to be excreted in animal milk.[47, 49]

Overall, the Indonesian guideline for the management of mpox follows the WHO guideline. For mild or uncomplicated cases, patients can be isolated at home with symptomatic treatment (antipyretics, analgesics, antihistamines, etc), adequate nutrition intake and hydration, as well as conservative treatment for skin lesions. For severe or complicated cases, patients should be hospitalized for rigorous monitoring, given supportive treatment according to complications, empirical antibiotics, and antivirals (tenofovir, brincidofovir, and cidofovir).[50, 51]

PREVENTIVE MEASURES

The primary preventative approach for mpox is to improve public knowledge about the risk factors and educate people on steps they may take to lessen their exposure to the virus. The most significant risk factor for contracting mpox is close contact with an infected individual. Healthcare professionals and household members carry a higher risk of infection. Therefore, it is recommended that medical personnel who are caring for the patients or handling mpox specimens follow standard infection control protocols.[43] When in contact with an infected patient, healthcare professionals should wear a face mask and practice hand hygiene. Furthermore, it is important to identify and isolate anyone who has travelled to regions with cases of mpox or who has engaged in sexual activity with an infected individual. It is recommended that preventive measures be continued for 4 to 14 days following exposure.[52]

According to the WHO, it is not yet advised to carry out mass vaccination against mpox. Rather, preventive immunization is recommended for high-risk groups and additional groups at risk of acquiring severe forms, such as immunocompromised individuals, children, and pregnant women, but only when there is a concrete risk of infection.[53] Two licensed vaccines are currently available to prevent smallpox in the United States of America: ACAM2000 (live, replication-competent vaccinia virus) and JYNNEOS (live, replication-incompetent vaccinia virus).[54] JYNNEOS can be given to all groups of people (children, adults, pregnant women) of all ages with a recommended dose of 0.5 mL. In contrast, ACAM2000 is contraindicated in infants and pregnant women, and only recommended in individuals aged ≥ 18 years. The recommended dose for ACAM2000 is 0.0025 mL. In general, JYNNEOS provides superior immunogenicity when compared to ACAM2000 with a higher mean titre of neutralizing antibodies (153.5 vs. 79.3). In addition, JYNNEOS also had milder side effects when compared to ACAM2000.[55] Smallpox vaccines were advised for use in the current mpox outbreak due to the immunological cross-protection among orthopoxviruses.[16] Although the evidence suggests that smallpox vaccination may provide long-term protection against mpox, further research is necessary to determine the duration of protection, particularly in susceptible groups and immunocompromised individuals.[56]

In Indonesia, mpox vaccination has been conducted in four target areas in Jakarta with a total of 495 individuals (142 participants in West Jakarta, 140 participants in Central Jakarta, 120 participants in South Jakarta, and 93 participants in East Jakarta). The vaccine that is currently used for mpox in Indonesia is JYNNEOS

administered twice with an interval of four weeks from the first vaccination. In this trial, Indonesia managed to achieve 100% vaccination rate for the first dose and 86.9% for the second dose.[40]

MANAGEMENT OF MPOX IN INDONESIA

In Indonesia, the management of mpox is based on the guideline constructed by the Ministry of Health Republic of Indonesia. The management option which Indonesia has implemented is epidemiologic surveillance from the local to the nationwide level. Indonesia's surveillance strategy starts from case discovery with the following formulated case definitions:[50, 57]

1. Suspected
   - Individuals who has had contact with a probable or confirmed case within 21 days before the onset of symptoms/ signs, and has one or more of the following symptoms/signs such as fever (>38,5 C), cephalgia, myalgia, or fatigue **OR**
   - Individuals experiencing acute skin rash, mucosal lesions or lymphadenopathy since 1st January 2022. These skin rashes can be single or multiple lesions located in the anogenital area or elsewhere. Mucosal lesions can be solitary or multiple in the mouth, conjunctiva, urethra, penis, vagina, or anorectal. Anorectal lesions may also manifest as anorectal inflammation (proctitis), pain, and/or bleeding. The following common causes of acute rash do not explain the clinical appearance of other skin rashes including varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infection, and other types of commonly relevant causes of vesiculopapular lesions.
2. Probable
   Individuals experiencing unexplained acute skin rash, mucosal lesions, or lymphadenopathy. Skin rashes can be single or multiple lesions in the anogenital area or elsewhere. Mucosal lesions include solitary or multiple lesions in the mouth, conjunctiva, urethra, penis, vagina or anorectal. Anorectal lesions may manifest as anorectal inflammation (proctitis), pain, and/or bleeding **AND**
   That person must have at least one of the following conditions:[50]
   - Having an epidemiological link to a probable or confirmed case within 21 days before symptoms onset.
   - Identified as gay, bisexual, or MSM.
   - Having more than one sexual partner or anonymous sexual partners in the 21 days before symptom onset.
   - IgM antibodies to anti-Orthopoxvirus (OPXV) detected within the period 4-56 days from rash onset; or a 4-fold increase in IgG titre compared to acute phase (up to 5-7 days) and convalescent period (day 21 and above); provided there is no history of smallpox/mpox vaccination or exposure to OPXV.
   - Having a positive result for Orthopoxvirus infection (PCR for OPXV-specific without MPXV-specific or sequencing results).
3. Confirmed
   Suspected or probable cases that are defined as positive for MPXV infection by polymerase chain reaction (PCR) laboratory examination and/or sequencing.
4. Discarded
   Suspected or probable cases with negative PCR results taken from lesion fluid, skin or crust specimens and/or negative mpox results from sequencing examination. However, there are things that must be considered in determining discarded cases.
   - Probable cases obtained retrospectively where it is not possible to take specimens from skin/mucosal lesions and no other specimens detected positive by PCR are still classified as probable cases.
   - Suspected or probable cases should not be included as discarded cases if they are based only on negative results from oropharyngeal, anal or rectal specimens,

or from blood/serum examination only.

5. Close contact
   Individuals who have a history of contact with a probable case or confirmed case (from the start of symptoms until the crust peels off/ disappears) of mpox and meets at least one of the following criteria:
   - Direct skin-to-skin physical contact (e.g., touching, hugging, kissing, and intimate or sexual contact);
   - Contact with contaminated objects such as clothing or bed during the washing or room cleaning process;
   - Prolonged face-to-face respiratory exposure at close range; And
   - Respiratory exposure (possible inhalation) or exposure of the ocular mucosa to lesion material (e.g., crusts) from an infected person.
   - Healthworkers without using appropriate PPE.
6. Death
   Death with convincing clinical manifestations for probable or confirmed cases unless there is another cause unrelated to mpox (e.g. trauma).

The clinical care of mpox depends on the degree of severity. After the case-finding process, patients need to be categorized based on the degree of severity. This categorization ideally needs to be done when patients are still in the triage station. In Indonesia, suspected or probable cases need to be identified whether the patients require immediate medical intervention (severe case) or not (mild case), based on the following criteria:[50]

1. Patients who are at high risk including children under eight years old, pregnant women, uncontrolled immunocompromised patients, patients who have chronic skin disease or patients who have an acute skin disease but potentially develop a bacterial infection.
2. Patients who are having at least one complication including vomiting, lymphadenopathy, visual impairment, hepatomegaly, sepsis, dehydration, or respiratory impairment with or without alteration of consciousness.
3. Patients who have at least three abnormal laboratory findings including leucocytosis, elevated liver enzymes, decreased renal function, hypoalbuminemia, or thrombocytopenia.
4. Patients who have severe skin lesions (more than 100 skin lesions).

A suspected or probable or confirmed case with at least one criterion above is defined as a severe condition. Patients with severe conditions can be considered to be given antiviral agents following symptomatic treatments. Although there is currently no antiviral specifically approved for mpox infections, the use of antivirals in Indonesia can be considered for some patients' conditions including severe clinical symptoms (sepsis, encephalitis, bleeding, and other types of conditions that needs to be observed and treated in the hospital) or high risks to progress to severe clinical symptoms (immunocompromised, progressive severe mpox infection in children, history of atopic dermatitis, pregnant and breastfeeding woman).

The smallpox vaccine has not been administered in many years. Consequently, a large number of people have little to no protection from mpox. To discover more effective treatments and management strategies for this viral infection, additional worldwide efforts, in-depth disease examinations, and exploratory research studies are required.[58] Evidence-based medicine must be implemented in the management of mpox and ought to direct future therapeutic choices. The antiviral medications, immunotherapy, and vaccines for mpox that are currently on the market are not widely accessible. Lots of work to make these reachable worldwide, particularly for the countries that have reported outbreaks including Indonesia. The prognosis for mpox is reliant upon multiple factors, such as prior vaccination history, initial health level upon onset of illness, and other illnesses or comorbidities. Therefore, the most sensible course of action is to customize treatment to each patient's specific risk of contracting a life-threatening illness. In order to treat this disease successfully, more thorough research

is needed to identify antiviral medications that work, advanced multidisciplinary fields of immunology and biotechnology.[59] Proactive identification of high-risk individuals and appropriate measurement should be employed.

CONCLUSION

Mpox is a contagious disease that could cause major health problems if left uncontrolled, especially in specific vulnerable populations because of its high morbidity and mortality. Thus, particular measures have to be conducted in Indonesia. The first mpox case in Indonesia was discovered in August 2022 and as of 17th August 2024, there have been 0 deaths and 87 out of 88 cases have recovered. The virus is transmitted through respiratory droplets or via direct contact with contaminated objects, surfaces, or mucocutaneous lesions of an infected individual which could lead to symptoms resembling classical smallpox. Tecovirimat, cidofovir, and brincidofovir have been raised as potential treatments for mpox. In Indonesia, antiviral agents are only administered in severe conditions. Prevention of transmission is the key to countering the outbreak. Further studies regarding treatments for mpox are still needed to more effectively counter the outbreak, including in Indonesia.

COMPETING INTEREST

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