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REVIEW ARTICLE

Mpox in Neonates and Children: A Review Article

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ABSTRACT

Mpox, caused by the monkeypox virus, has expanded beyond its historical African boundaries, with significant global outbreaks, including a 2022 surge. While traditionally affecting adults, recent cases in neonates and children show more severe complications, including respiratory failure, encephalitis, and sepsis. Children are more vulnerable due to an immature immune system and at higher risk for multi-organ involvement. Prevention focuses on vaccination, personal hygiene, and safe sexual practices, with JYNNEOS® and ACAM2000® vaccines recommended for high-risk groups. Early diagnosis, supportive care, and antiviral treatment are crucial in managing severe cases. This review highlights differences in disease severity between adults and children and outlines key prevention and treatment strategies.

Keywords: children, monkeypox, Mpox, neonate, transmission

INTRODUCTION

Mpox, formerly known as monkeypox, is caused by the monkeypox virus (MPXV), an enveloped double-stranded deoxyribonucleic acid (DNA) virus belonging to the Orthopoxvirus genus in the Poxviridae family. First identified in 1958, Mpox's initial human case was reported in a 9-month-old boy in the Democratic Republic of the Congo.[1] Historically, Mpox outbreaks were sporadic and largely confined to Central and West Africa until the 21st century. In these settings, infections were reported predominantly among children, accounting for up to 90% of cases, with case fatality rates of approximately 11%, particularly among unvaccinated group.[2] However, the virus has demonstrated its ability to cause significant outbreaks outside Africa, such as the 2003 U.S. outbreak and the global outbreak in 2022.[3] The virus comprises two distinct clades: Clade I (with subclades Ia and Ib) and Clade II (with subclades IIa and IIb), which differ in various aspects, as summarized in Table 1.[4-7]

In 2022, a global outbreak of Clade IIb began and persists, including in several African countries. Concurrently, there have been increasing outbreaks of Clades Ia and Ib, particularly impacting the Democratic Republic of the Congo and other African nations.[8] By August 2024, Clade Ib had also been detected outside Africa. World Health Organization (WHO) Director-General Dr. Tedros Adhanom Ghebreyesus has declared Mpox a Public Health Emergency of International Concern (PHEIC) on two occasions: first in May 2022 and again in August 2024.[3] Among the 2022-2024 cases, the majority (61.8%, 691) were reported in the WHO Region of the Americas, followed by the African Region (30.3%, 339), the European Region (7.5%, 84), the Eastern Mediterranean Region (< 1%, 3), and the Western Pacific Region (< 1%, 1).[9]

Table 1 Comparison of Clade I and Clade II of Mpox[4-7]

	Clade I	Clade II
Distribution	Central Africa, especially in the Congo Basin region	West Africa, with notable outbreaks in Nigeria, Sierra Leone, and Liberia and Global spread in 2022
Virulence	More severe disease, estimated 10% mortality	Milder disease, estimated 3% mortality
Transmission	More efficient human-to-human transmission and larger outbreak potential	Less efficient transmission, especially in close contact group

Between January 2022 and August 2024, more than 120 countries reported cases of Clade II Mpox, with over 100,000 laboratory-confirmed infections and more than 220 associated deaths. Clade II Mpox continues to primarily spread through sexual and intimate contact, with men who have sex with men at the highest risk. Cases in children remain rare, accounting for just 0.3% of cases in the United States.

In 2024, the WHO declared a PHEIC due to the spread of Clade Ib in Africa. In some African regions, Mpox transmission among children has been notably high, with 30% of cases in the Democratic Republic of Congo—rising to over 50% in children under 5 years in certain areas—and 47% of cases in Burundi. More than 50% of Mpox-related deaths have occurred in children under 15 years old, underscoring the need for focused pediatric epidemiological attention.[10] The increased transmission in children may be due to household contact, a weaker immune response, and a lack of prior smallpox vaccination. Additionally, Clade I may be more severe, contributing to the higher fatality rate in the pediatric population.

Nowadays, the number of Mpox cases in neonates and children is increasing. The differences in symptoms, severity, and transmission methods compared to adults are interesting topics, which we review to improve knowledge and develop the best prevention strategies.

CONTENT OF REVIEW

WHO Case Definition for Mpox Outbreak[11]

1. Suspected case: an individual with clinical features compatible with Mpox, including

1.1 Fever or systemic symptoms (e.g., fever > 38.5°C, headache, myalgia, back pain, or marked fatigue) occurring within 21 days of contact with a probable or confirmed case, or

1.2 An unexplained acute rash, mucosal lesions, or lymphadenopathy since January 2022. Lesions may be single or multiple and involve the ano-genital region, oral cavity, conjunctiva, or other body sites, and may present with proctitis, pain, or bleeding.

2. Probable case: an individual with an unexplained acute rash, mucosal lesions, or lymphadenopathy and at least one of the following:

2.1 An epidemiologic link to a probable or confirmed Mpox case within 21 days before symptom onset.

2.2 High-risk exposure, including multiple or casual sexual partners within 21 days prior to symptom onset.

2.3 Gay, bisexual or other cis or trans man who has sex with men.

2.4 Serologic evidence of orthopoxvirus infection (antibody against orthopoxvirus immunoglobulin M during 4-56 days after rash onset or a fourfold rising in immunoglobulin G) in the absence of recent orthopoxvirus vaccination.

2.5 A positive orthopoxvirus test without MPXV-specific confirmation.

3. Confirmed case: an individual with laboratory-confirmed Mpox, demonstrated by detection of MPXV-specific DNA using real-time polymerase chain reaction (PCR) and/or genomic sequencing.

Transmission[12-14]

Incubation period is between 3-21 days, sometimes noted as 6-13 days. Mpox can be transmitted from 4 days before symptoms appear until all lesions are fully healed (infectious period). There are four main methods of transmission:

1. Close contact: Mpox is transmitted primarily

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through direct contact with an infected person's skin lesions, scabs, or bodily fluids. Infection can also occur via contact with contaminated objects, such as clothing, bedding, or towels used by an infected individual. Sexual contact and intimate activities, including kissing, are recognized routes of transmission. In addition, close contact with lesions may result in transmission during specific situations, such as vaginal delivery. Regarding breastfeeding, data on transmission through breast milk remain limited. Nevertheless, breastfeeding should be temporarily deferred if the mother has active Mpox infection or lesions involving the breast, to reduce the risk of transmission to the infant.

2. Droplet transmission: The virus can spread through respiratory droplets from coughing or sneezing.

3. Maternal-to-child transmission (in utero): Mpox can be transmitted from a mother to the fetus, with reported outcomes including miscarriage of fetal death, congenital anomalies, and chorioamnionitis.

4. Animal-to-human transmission of Mpox is rare in children and neonates. When it does occur, infection may result from scratches or bites from infected animals, consumption of undercooked meat from infected animals, or direct exposure during activities such as hunting or trapping infected animals.

Diagnosis

Diagnosis is based on compatible clinical manifestations with laboratory confirmation.

Clinical Manifestations in Children[15-17]

In children, Mpox commonly presents with skin rash, which is reported in nearly all cases (100%). The rash typically follows a chronological progression, beginning as maculopapular lesions and evolving into vesicles, pustules, lesions with umbilication, and eventually scab formation. In children younger than 12 years, the rash is most frequently distributed on the face and trunk, whereas in adolescents it is more commonly localized to the anogenital region. In some cases, lesions on the tongue or within the oral cavity may be the earliest clinical manifestation. Systemic symptoms are also common. Fever occurs in approximately 73% of pediatric patients, and lymphadenopathy or adenitis is observed in about 47%. Other clinical features include pharyngotonsillitis (17%) and conjunctivitis (10%). Less frequent manifestations, reported in fewer than 10% of cases, include myalgia, headache, hepatosplenomegaly, nausea and vomiting, facial edema, cough, and abdominal pain.

Clinical Manifestations in Neonates[16-19]

There are similar to older children, including fever and axillary lymphadenitis; however, the rash pattern differs. Neonatal disease typically presents with vesicular eruption beginning on the palms and soles, followed by spread to the face and trunk, with subsequent progression to pustular lesions. Additional reported features include irritability and respiratory failure, and affected neonates frequently have a history of maternal or parental rash occurring within 3 weeks prior to delivery.

Furthermore, 3 cases of congenital Mpox have been reported, all confirmed by MPXV PCR from placental, oropharyngeal, and/or skin swabs. In all cases, maternal Mpox infection was documented one to four weeks before delivery. Two cases resulted in fetal death: one at 8 weeks' gestation due to spontaneous abortion, and another at 18 weeks' gestation with intrauterine fetal death, accompanied by macular lesions with small vesicles on the face, chest, abdomen, and upper limbs. The third case survived after birth and presented with 17 ulcerative lesions distributed over the face, upper and lower limbs, abdomen, and dorsum, while other findings were unremarkable; the skin lesions resolved within 7 days.[19]

Laboratory Investigation for Diagnosis[1,14,20]

Mpox is confirmed by detecting the virus using PCR from a vigorous swab of a rash, crust, or fluid. If no lesions are present, swab the throat or anus. It is recommended to swab more than one lesion for accurate results. Blood tests for Mpox antigen and antibody are not recommended.

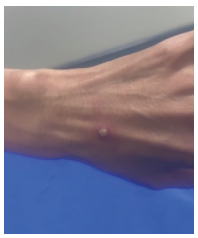
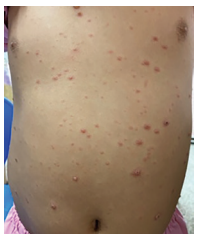
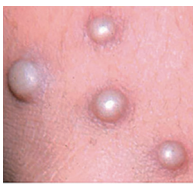
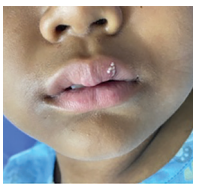
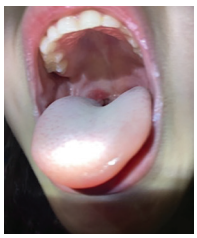
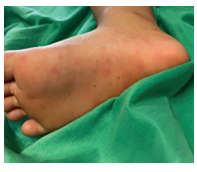
Differential Diagnosis[21-22]

Mpox in children should be differentiated with other infectious diseases such as chicken pox, smallpox, herpes simplex virus (HSV) infection, hand-foot-mouth disease (HFMD) as shown in the **Table 2**.

Complication in Children and Neonates[15,21,23-26]

In neonates and children, the complications tend to be more severe, encompassing extensive skin infections, respiratory distress, neurological problems such as encephalitis, dehydration, malnutrition, septicemia,

Table 2 Differential Diagnosis of Mpox

	Mpox	Chicken Pox	Smallpox*	HSV	HFMD
Common age	Adolescents and adults	2-10 years old	Children and young adults	HSV-1: toddlers and school-aged HSV-2: adolescents and young adults	1-5 years old
Clinical manifestations	Fever Malaise precede rash	Fever Fatigue	High fever Toxemia precede rash	Fever Stomatitis	Fever Sore throat Malaise
Lymphadenopathy	Common	Rare	None	Possible	None
Incubation	5-21 days	10-21 days	7-19 days	2-12 days	3-6 days
Rash	Deep, umbilicated pustules Synchronous in area	Superficial, pruritic vesicles Multiple stages	Deep, firm pustules Synchronous in area	Painful vesicles	Vesicles, flat spots Same stage
Distribution	Palms, soles, face, body	Trunk → face, limbs	Face → extremities → trunk	Localized	Palms, soles, mouth
Example					  

Abbreviations: HFMD, hand-foot-mouth disease; HSV, herpes simplex virus

* Smallpox was declared eradicated in 1980

ophthalmologic issues, multi-organ involvement, and deaths as summarized in **Figure 1**.

Treatment[21-24,27-32]

The treatment for Mpox includes both supportive and specific care **(Table 3)**.

1. Supportive care include hydration, nutrition, avoidance of eye contact with lesions, and wound care, with gentle cleaning and protective dressings. Patients with ocular involvement should be consulted ophthalmologist. Pain management is addressed with acetaminophen (paracetamol), non-steroidal anti-inflammatory drugs, and for severe pain, opioids or gabapentin. Indications for hospital admission in

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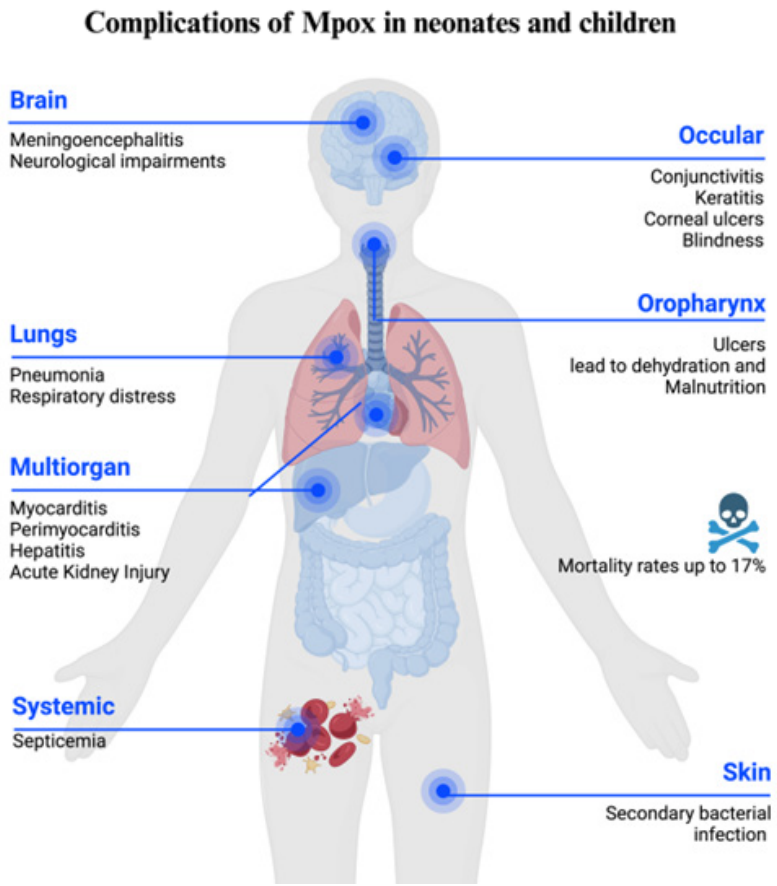

Figure 1 Complication of Mpox in Neonate and Children

Table 3 Treatment of Mpox in Adults, Children, and Neonates

Treatment	Details
Supportive care	1. Ensure proper hydration and nutrition 2. Cleansing wounds with gentle soap and water or an antimicrobial soak 3. Creating a moist wound healing environment 4. Applying a protective coating, such as white petrolatum, zinc oxide paste, or a silicone film
Pain control	1. NSAIDs for mild to moderate pain 2. Opioids and gabapentin for severe pain 3. Topical steroids and anesthetics
Antiviral for 1. Severe disease: ocular, neurological, myocarditis, multi organ involvement, sepsis, and disseminated rash 2. High risk group: infants, immunocompromised hosts, pregnant, breastfeeding, skin integrity	1. Tecovirimat: The drug of choice for severe Mpox or in high-risk groups (body weight 13-25 kg: 200 mg every 12 hours, 25-40 kg: 400 mg every 12 hours, 40-120 kg: 600 mg every 12 hours) for 14 days 2. Brincidofovir / Cidofovir: consider in cases of significant disease progression while on tecovirimat. Use if there are contraindications to tecovirimat. 3. Maybe used in combination with tecovirimat for severely immunocompromised hosts.
Vaccinia immune globulin intravenous	1. Considered in severe cases

Abbreviations: kg, kilogram; mg, milligram; NSAIDs, non-steroidal anti-inflammatory drugs

children and neonates with Mpox are not clearly defined and largely depend on the clinical judgment of the pediatrician. Admission is generally recommended for patients with severe clinical manifestations.

2. Specific antiviral treatment is recommended for severe cases including hemorrhagic disease, confluent lesions, secondary bacterial infections, sepsis, encephalitis, lesions on the penile or strictures involving the urethral meatus, severe involvement of other anatomic sites, such as anorectal disease impairing bowel movements or significant dysphagia, conditions requiring hospitalization and antiviral drugs indicated for high-risk groups, including infants, immunocompromised hosts, and pregnant or breast-feeding women.

2.1 Tecovirimat is the preferred antiviral agent, it acts by inhibiting the viral p37 protein, thereby interfering with viral maturation and preventing release of virions from infected cells. Clinical data suggest that tecovirimat is associated with reduced mortality and fewer severe outcomes, particularly when initiated early in the course of illness, although the time to lesion resolution has not been shown to differ significantly from placebo. Oral tecovirimat is approved for patients weighing ≥ 13 kg and should be administered with moderate- to high-fat meals, while the intravenous formulation is approved for patients weighing ≥ 3 kg. Tecovirimat is not recommended during pregnancy or breastfeeding. Common adverse effects include headache, dizziness, and gastrointestinal symptoms.[32]

2.2 Brincidofovir and cidofovir may be considered as alternative options when tecovirimat is contraindicated or ineffective; however, evidence supporting their effectiveness remains limited.

2.3 Vaccinia Immune Globulin Intravenous (VIGIV) may be used for severe cases, although data on its effectiveness is limited.

Infection Control[23-24, 32-33]

Infection control measures for Mpox include standard, droplet, and contact precautions, with airborne precautions required during aerosol-generating procedures, which the patient should be placed in a negative-pressure ventilation room. Isolation duration for Mpox patients depends on their case status. For suspected cases, isolation is required until Mpox is excluded as a differential diagnosis. For confirmed cases, isolation should continue until all lesions have crusted and no new lesions appear. Confirmed or suspected cases should be reported to the local Public Health Department. Patients diagnosed with Mpox who do not require hospital admission should follow home isolation measures. These include staying in a separate room, using a separate bathroom if available, avoiding the sharing of dishes or towels, and minimizing close physical contact with others. Shared surfaces and common areas should be cleaned and disinfected after use by the patient. When close contact is unavoidable, the patient should wear a surgical mask. These measures reflect the core principles of contact and droplet precautions.

For individuals who have had contact with Mpox patients, asymptomatic contacts do not need isolation. Healthcare personnel may continue working but should monitor for symptoms of Mpox daily for 21 days after the last exposure. Symptomatic contacts should undergo empirical isolation precautions until test results confirm or exclude Mpox. If no rash is present, isolation should continue for at least 5 days, and isolation can be discontinued if no new symptoms or lesions develop.[32-33]

Post-exposure prophylaxis (PEP) with the Mpox vaccine should be administered as soon as possible, ideally within 4 days of exposure. Vaccination within 4–14 days after exposure may still offer protection, and after 14 days, vaccination may be considered on a case-by-case basis. Monitoring and PEP recommendations depend on the risk level of exposure.[33] **(Table 4)**

For neonates born to individuals with suspected, probable, or confirmed Mpox, they should be bathed promptly with soap and water after birth. PEP is recommended for newborns exposed to Mpox, and they should be closely monitored for symptoms for 21 days after birth or their last exposure. Routine care can be provided by caregivers or family members who are not infected with Mpox.[23]

Prevention[1,34-36]

1. Vaccination

Vaccination is prioritised for individuals with occupational exposure (such as laboratory personnel and healthcare workers), travellers spending time in areas of sustained high Mpox transmission and those with sexual practices that predispose to higher rates of transmission:

1. People with multiple sexual partners in areas of ongoing Mpox transmission.

2. Gay, bisexual, and other men who have sex

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Table 4 Monitoring and PEP Recommendations Based on Risk Level[33]

	Definition	Monitoring	PEP
High risk	Unprotected contact with lesions or fluids of a Mpox patient involving broken skin or mucous membranes.	Yes	Yes
Intermediate risk	Unprotected contact with lesions or fluids of a Mpox patient involving intact skin or clothing. Or Not wear PPE while inside a Mpox patient's room. Or Examining the oral or laryngeal cavity of a Mpox patient without appropriate PPE.	Yes	+/-
Low risk	Unprotected contact with a fully covered Mpox patient with no contact with skin, fluids, or contaminated equipment.	+/-	No
No risk	No contact with a Mpox patient, and only transient time spent in their vicinity.	No	No

Abbreviations: PEP, post-exposure prophylaxis; PPE, personal protective equipment

with men.

3. Transgender or nonbinary individuals who, in the past 6 months, have had:

3.1 A new diagnosis of ≥ 1 sexually transmitted infection.

3.2 More than one sexual partner.

3.3 Sex at a commercial sex venue.

3.4 Sex associated with a large public event in a geographic area where Mpox transmission is occurring.

There are two licensed vaccines for the prevention of Mpox infection:

a) JYNNEOS® is a live, attenuated orthopoxvirus vaccine that is non-replicating in humans.

JYNNEOS® is licensed for the prevention of both smallpox and Mpox and is recommended by the Advisory Committee on Immunization Practices (ACIP). Because of its favorable safety profile, it is considered the preferred vaccine for Mpox prevention. The vaccine is administered as a two-dose series, with doses given 28 days (4 weeks) apart. Subcutaneous administration is preferred, while intradermal injection is approved only for individuals 18 years of age and older.

JYNNEOS® is authorized for PEP in children following potential exposure. However, in infants younger than 6 months, VIGIV should be considered as an alternative to vaccination. The vaccine may also be considered for pregnant or breastfeeding individuals, with decisions guided by shared clinical decision-making that carefully balances potential risks and benefits.

In terms of effectiveness, vaccine efficacy is estimated to be approximately 75% after a single dose and 86% after completion of the two-dose series. The most commonly reported adverse events are local injection-site reactions, including pain, erythema, swelling, and induration. Serious adverse events are rare, occurring in about 1% of vaccine recipients.

b) ACAM2000® vaccine is a live, attenuated vaccine capable of replication in the human host.

ACAM2000® is licensed for the prevention of smallpox and is recommended by the ACIP for individuals at risk of exposure to orthopoxvirus infections. It is considered an alternative to JYNNEOS®; however, its use is limited by a higher risk of adverse events and it is not recommended for infants.

Vaccine effectiveness has been reported to be approximately 95%. Common adverse events include local reactions at the inoculation site, lymphadenitis, and systemic (constitutional) symptoms. More serious adverse events have also been reported, including myocarditis and pericarditis (approximately 5.7 per 1,000 persons), encephalitis, encephalopathy, and ocular vaccinia. Because of these safety concerns, ACAM2000® is not recommended for use in pregnant or lactating individuals, or in children, particularly those younger than 12 months of age.

2. Personal Hygiene

Prevention of Mpox relies on avoiding direct contact with the skin, lesions, or bodily fluids of infected individuals. It is also important to refrain from sharing personal items, such as towels, bedding, or clothing, that may be contaminated. In addition, good hand hygiene should be practiced consistently, including frequent handwashing with soap and water or the use of alcohol-based hand sanitizers.

3. Safe Sexual Practices

Sexual transmission of Mpox can be reduced by using barrier protection methods, such as condoms, and by avoiding sexual contact with individuals who have symptoms suggestive of Mpox, particularly those with active rashes or lesions.

4. Community Awareness and Education

Public health measures should focus on educating the public about Mpox transmission, clinical manifestations, and prevention strategies. In addition, early medical consultation should be encouraged for individuals who develop symptoms, particularly when there is a history of potential exposure, to facilitate timely diagnosis and management.

Prevention of Mpox in children and neonates extends beyond infection control measures, and awareness of preventive strategies is essential. The general principles of prevention do not differ substantially between children and adult populations. However, particular emphasis should be placed on vaccination for high-risk groups. In children, Mpox vaccination is generally recommended only as PEP. Hand hygiene and general hygiene should be strongly encouraged. Age-appropriate education regarding safe behaviors, including sexual health in adolescents, is also important as part of broader preventive strategies. In newborns born to mothers with Mpox infection, additional precautions are recommended. These include early bathing after birth to reduce potential viral exposure and temporary avoidance of breastfeeding, particularly if the mother has active disease or lesions involving the breast.

CONCLUSION

Mpox poses a significant risk to neonates and children, with more severe outcomes compared to adults. Early diagnosis, appropriate isolation and treatment and ongoing community education are crucial. Preventive measures like vaccination and safe sexual practices are essential to controlling transmission, especially in high-risk groups. Future directions should focus on improving surveillance, understanding the long-term effects of the disease, enhancing treatment options, and refining vaccination strategies to ensure effective prevention. Ongoing research and targeted interventions will be key to reducing the global impact of Mpox.

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Conflict of Interest

All authors declare no conflict of interest.

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Formal analysis: -
Funding acquisition: -
Investigation: -
Methodology: -
Project administration: T.K.
Resources: -
Software: -
Supervision: M.G.
Validation: -
Visualization: T.K.
Writing – original draft preparation: T.K.
Writing – review & editing: T.K., M.G.

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