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Monkeypox and Hand-Foot-Mouth Disease Outbreak in India: A Double Trouble?

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Abstract

Amidst the coronavirus disease pandemic, the recent concurrent Hand-Foot-Mouth Disease and monkeypox outbreak in India has been a major cause of public health concern. Currently, more than eighty-two children below the age of 5 years have been infected with Hand-Foot-Mouth Disease and ten confirmed cases and eight suspected cases of monkeypox have been identified in India. Hand-Foot-Mouth Disease or tomato fever is a viral infection commonly caused by coxsackievirus A16 and enterovirus A71. Monkeypox virus, belonging to the *Poxviridae* family, is the causative agent for monkeypox. Since both Hand-Foot-Mouth Disease and monkeypox are viral diseases having similar signs and symptoms, it is difficult to distinguish between the two clinically. Improper diagnosis will lead to incorrect treatment of the disease, thus adding the burden of the disease on society. It is, therefore, imperative to distinguish the two disease entities, to ensure that an accurate diagnosis is made and prompt management is initiated. The Government needs to standardize the treatment protocol and issue appropriate guidelines to curb the further outbreak of these infections in the country.

Keywords: Hand-Foot-Mouth Disease, Monkeypox, Outbreak

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INTRODUCTION

Amidst the COVID-19 pandemic, the recent concurrent surge in cases of Hand-Foot-Mouth Disease (HFMD) and monkeypox in India has been a major cause of public health concern.[1] Since both HFMD and monkeypox are viral diseases having similar signs and symptoms, it is difficult to distinguish between the two clinically.[2] Improper diagnosis will lead to incorrect treatment of the disease, thus adding the burden of the disease on society.[3] Therefore, it is the need of the hour to sensitize the medical fraternity towards the differences between the two viral diseases based on the etiology, epidemiology, transmission, and signs and symptoms so that the diagnosis and management can be done effectively.

Etiology and epidemiology

HFMD

HFMD or tomato fever is a viral infection commonly caused by coxsackievirus A16 and enterovirus A71.[4] HFMD is found to affect both genders equally. However, according to the available epidemiological data, the occurrence is slightly higher in males. It has also been noted that HFMD affects children (mostly below 10yrs of age) more as compared to adults.[4] Studies have reported that the outbreak is common in summer and early autumn. In a few studies, it has been reported that close contacts are at risk of developing the disease since the virus is shed from the stools of the infected person for many weeks.[5]

Monkeypox

Monkeypox virus, belonging to the Poxviridae family, is the causative agent for monkeypox.[6] Monkeypox is endemic to Central and Western Africa. Recent studies suggest that the virus is commonly found in African rodents. Two genetically distinct clades (Central and West African clade) exist currently.[7] The Central African clade (Congo Basin) shows propensity for human transmission.[7] The possible risk factors include inhabiting rural and forested areas of Africa, preparing bushmeat, looking after monkeypox-infected people, and lack of smallpox vaccination. The infection has been reported to showcase a male predilection, possibly due to constant contact with wild animals during frequent hunting.[8,9]

Current status of the outbreaks in India

HFMD

The first case of HFMD in 2022 was first reported in Kerala on 6th August 2022 and as of 22nd August 2022, more than eighty-two children below the age of 5 years have been infected.[10] Tamil Nadu and Odisha have also reported an outbreak of some cases.[10] As of now, no mortality has been reported in India due to HFMD.

Monkeypox

In India, the first case of monkeypox was reported on 15th July 2022 in a 35-year-old man who had returned from the Middle East.[11] As of 15th August 2022, India has reported ten confirmed cases and 8 suspected cases of monkeypox. The confirmed cases are from Kerala[12] and Delhi[13] and the suspected cases are from Telangana,[14] Uttar Pradesh,[15] Bihar,[16] and Delhi. The first monkeypox-related death in India was reported on 1st August 2022 in Kerala.[17]

The Indian government health officials have declared both these diseases as highly infectious, and have issued a warning regarding their spread to other states as well.

Mode of Transmission

HFMD

HFMD spreads by direct contact through saliva, nasal, and throat secretions, blister fluid, and stool of infected persons.[18] The virus may spread by unwashed or virally-contaminated hands, and by contact with contaminated surfaces. People infected with the virus are highly contagious during the first week of illness. However, the infection can still be transmitted to other people even if the infected person becomes asymptomatic.[18] Some people may also act as carriers (people infected and excreting the virus but not showing any symptoms). The disease is not transmitted through animals or pets.[18]

Monkeypox

According to the CDC, monkeypox spreads through direct contact with respiratory

Table 1. Signs and symptoms of monkeypox and HFMD

Category	Monkeypox	HFMD
Incubation period	5-21 days	3-7 days
Pyrexia	1-3 days before rash onset	1-2 days before appearance of oral vesicles
Lymphadenopathy	Common	Occasional
Rash	Site: oral mucosa, conjunctiva, genitals, palms, and soles Progression: macules, papules, vesicles, pustules, and scab. Duration: 14-28 days	Site: oral cavity, palms, soles knees, elbows, buttocks, and genitals Progression: Macules, may be with vesicles that may progress to scab Duration: 7-10 days

Table 2. Supportive management of HFMD

Symptoms	Management
Pain and fever	NSAIDs and acetaminophen
Oral ulcers	Gargle using a mixture of liquid ibuprofen and liquid diphenhydramine. This mixture coats the ulcers and helps in reducing the pain
Severe cases of enterovirus-induced HFMD	Ribavirin, amantadine, and quinacrine

secretions, rash, scabs, body fluids, or touching fomites that have been used by the infected individual.[19] Direct contact involves physical or intimate contact, or prolonged face-to-face contact with an infected person.[19] According to the WHO, some of the cases of the current outbreak have been reported in homosexual and bisexual communities. Transgender people may also be vulnerable to the disease.[20]

Signs and symptoms

HFMD and monkeypox can be differentiated based on the following signs and symptoms[21] (Table 1).

Diagnosis

HFMD

The diagnosis of HFMD is usually made clinically. Shedding of the virus from the oropharynx starts within 4 weeks of infection; however, the virus is detectable in the stool for about 6 weeks post-infection.[22] Microscopic examination of biopsies and swabs from vesicles can help differentiate HFMD from Varicella Zoster virus and Herpes Simplex Virus infections.[22] Serum IgG levels can be used to monitor the recovery from HFMD, but they are not very specific.[23] In certain cases, serological tests have been useful in differentiating HFMD from Enterovirus infection. However, RT-PCR has been a gold standard diagnostic tool for the final confirmatory diagnosis of HFMD.[23]

Monkeypox

Visual diagnostic methods like electron microscopy, immunohistochemistry and serum studies using IgG and IgM are sufficient for the diagnosis of Monkeypox infection.[24] However, the use of patient specimens for isolation of the virus in a culture medium, or amplification of the viral DNA using RT-PCR can be confirmatory.[24]

Management

HFMD

HFMD is a self-limiting disease that resolves on its own within 7-10 days.[25] Management should aim at lowering fever, pain relief, and adequate oral hydration. Enterovirus 71-induced HFMD has shown severe neurological complications. No drug has been approved for treating the same; however, novel agents such as translation inhibitors, molecular decoys, replication inhibitors, and receptor antagonists have shown promising results.[25] Pleconaril, a novel

Table 3. Adjunctive therapy for monkeypox

Clinical features	Therapy
Skin rash	The rash should be cleaned with simple antiseptic Mupironic Acid/Fucidin to be appliedon the rash **Extensive lesion** The lesion should be covered with a light dressing The lesions should not be touched or scratched **Secondary infection** Antibiotic coverage
Genital rash	Sitz bath
Oral ulcers	Warm saline gargles Oral topical anti-inflammatory gel
Conjunctivitis	Self-limiting An ophthalmologist consultation when required
Dehydration	Oral fluids Intravenous fluids Nutritious diet intake
Pyrexia	Tepid sponging Paracetamol (if required)
Pruritis	Calamine lotion (Topical) Anti-histaminics
Vomiting	Anti-emetics
Headache or Malaise	Paracetamol Adequate hydration

antiviral agent has been effective in the treatment of enterovirus-induced HFMD.[25] The supportive management of HFMD[26,27] has been discussed in Table 2.

Monkeypox

At present, there is no clinically proven management existing for monkeypox. However, certain preventive measures like isolation of infected patients, wearing surgical masks, and covering the lesions until their crusts naturally fall off, may prevent the further spread of the disease.[28]

Prior vaccination against smallpox was reported to be 85% effective in preventing monkeypox infection.[29]

In certain cases, post-exposure vaccination with a modified vaccine has been recommended. The Ankara vaccine is a live, modified vaccine. It is a two-dose vaccine, administered at an interval of four weeks. It has a greater safety profile, and stimulates antibody production in immunocompromised patients. It also does not invoke skin lesions or any local or distant spread of infection.[28]

Post-exposure vaccination is recommended in high-risk exposure patients with contact between broken skin or mucous membrane and body fluids. According to the CDC, initiating vaccination within 4 days of infection may prevent disease onset, while severity of the disease can be decreased by vaccinating within 14 days of infection.[28]

Adjunctive management of monkeypox,[30] has been discussed in Table 3.

CONCLUSION

While the country is still combating the COVID-19 pandemic, the outbreak of these two viral diseases simultaneously is a significant public health threat. Moreover, the sparsity of available data on the two diseases may underestimate the severity of the infections. It is, therefore, imperative to distinguish the two disease entities to ensure that an accurate diagnosis is made and prompt management is initiated. The Government needs to standardize the treatment protocol and issue appropriate guidelines to curb the further outbreak of these infections in the country.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

SM conceptualized, designed the study, performed acquisition, analysis, interpretation of data and wrote the manuscript. SM and RM revised the manuscript. Both authors read and approved the final manuscript for publication.

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DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

Not applicable.

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