Public Health Bulletin
South Africa

Hand, foot, and mouth disease (HFMD): Global overview and South African context, 2025

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PHBSA.2026;4(2): 83-91

Summary

Hand, foot, and mouth disease (HFMD) is a common childhood viral illness primarily caused by enteroviruses, including Coxsackievirus A6, Coxsackievirus A10, and Enterovirus A71 (EV-A71). Although traditionally viewed as a mild, self-limiting condition, the increasing global frequency of severe neurological and cardiopulmonary complications, especially from EV-A71, has increased its public health importance. Over the past three decades, the Asia-Pacific region has experienced repeated large-scale outbreaks, while smaller outbreaks and clusters have been documented in Africa, Europe, and the Americas. In South Africa, HFMD is not currently a notifiable medical condition, resulting in substantial gaps in national surveillance, clinical recognition, laboratory diagnosis, and public risk communication. The 2025 KwaZulu-Natal province outbreak highlighted these systemic gaps and underscored the need for a more structured national approach to HFMD detection and response. This opinion piece summarises global epidemiology, outlines the South African context, assesses risks related to delayed detection, and provides recommendations for strengthening surveillance and preparedness while maintaining the perspective that HFMD remains largely self-limiting for the majority of affected individuals.

Background

Hand, foot, and mouth disease (HFMD) was first formally described in 1957 in Toronto, Canada[1], and was shortly thereafter recognised as a distinct clinical syndrome characterised by vesicular eruptions on the hands, feet, and oral mucosa.[2] Enteroviruses, members of the Picornaviridae family, were identified as the primary causative pathogens.[3] Coxsackievirus A6 (CV-A6) and Coxsackievirus A10 (CV-A10), Coxsackie A16 (CV-A16), and Enterovirus A71 (EV-A71) have demonstrated consistent global involvement in outbreaks, with EV-A71 associated with more severe disease manifestations.[3,4,5] While HFMD is most common in children under ten years old, the infection does not spare older age groups; adults, including healthcare workers and caregivers, may develop symptomatic disease.[6,7] Transmission dynamics are complex and differ by setting, although temperate countries are typically described to experience peaks in spring, summer, and autumn, while tropical regions demonstrate continuous year-round circulation, with periodic winter outbreaks linked to CV-A6.[6,7] Seasonal patterns of HFMD across China appear to have shifted post–introduction of the EV-A71 vaccine.[8]

Although the majority of HFMD cases are mild, the expanding footprint of severe HFMD outbreaks, the emergence of atypical clinical presentations globally[3,8], and the recent outbreak in South Africa[9] justify improving national situational awareness and readiness.

Global epidemiology

The Asia-Pacific region remains the most affected globally. Malaysia experienced a landmark EV-A71 outbreak in 1997 with an unprecedented number of neurological complications.[3,10] China reported over

400 000 cases and 126 deaths in 2008[11], triggering substantial investment into multivalent enterovirus vaccine development.[12] China still records annual HFMD epidemics, often with alternating predominance of CV-A6, CV-A10, CV-A16, and EV-A71, demonstrating the shifting virological landscape.[8] Beyond HFMD-associated enteroviruses, other non-polio enteroviruses, including EV-D68, have caused severe neurological syndromes resembling poliomyelitis[3], illustrating the broader significance of enterovirus surveillance.

In Africa, documented HFMD outbreaks remain uncommon, reflecting under-recognition, under-reporting, and limited enterovirus diagnostic capacity. Published reports are largely restricted to sporadic cases and localised outbreaks, with the best-characterised event being the 2023 CV-A6-associated atypical HFMD outbreak in Cabo Verde[13], highlighting the likelihood that the burden of HFMD across Africa is underestimated. Importantly, non-polio enteroviruses circulate widely across the continent, as evidenced by acute flaccid paralysis (AFP) surveillance and environmental surveillance programmes.[14–16] The paucity of routine HFMD surveillance likely masks the true burden, which is expected to be substantially higher than reported.

Virus taxonomy and clinical relevance

Enteroviruses implicated in HFMD belong to Enterovirus species A. EV-A71 is uniquely associated with severe neurological disease, including brainstem encephalitis, aseptic meningitis, and neurogenic pulmonary oedema.[5] CV-A6, now dominant in many global settings, is linked to more severe mucocutaneous disease, widespread vesiculobullous rashes, and onychomadesis.[8] While traditionally overshadowed in incidence by EV-A71 and CV-A6, CV-A10 is increasingly recognised as an important cause of global HFMD outbreaks, with most infections being mild and self-limiting but some strains associated with greater genomic variability, more severe disease, and systemic complications.[8]

Although polioviruses and EV-D68 belong to the enterovirus genus, they do not cause HFMD and are excluded from HFMD case definitions to avoid diagnostic ambiguity.[3,17]

Transmission and risk factors

HFMD is primarily spread through the faecal-oral route, respiratory droplets, and contaminated surfaces.[18] Children in crèches, preschools, and early-grade classrooms represent the highest risk group due to intense close contact, high viral shedding, and immature hygiene behaviours.[19] Environmental determinants such as overcrowding, intermittent water supply, and poor sanitation are strongly associated with increased transmission.[3,4] Analyses from large Chinese outbreaks highlight the role of water, sanitation, and hygiene (WASH) vulnerabilities in amplifying transmission.[20] Comparable WASH challenges exist in many South African communities and educational institutions, suggesting similar susceptibility. Importantly, asymptomatic enterovirus infection is common and contributes significantly to community circulation, complicating intervention efforts.[4,21]

Diagnostic capacity and case management

HFMD is typically diagnosed clinically based on characteristic mucocutaneous manifestations. Laboratory confirmation is reserved for severe cases, atypical rashes, outbreak investigations, or surveillance purposes. Reverse-transcription polymerase chain reaction (RT-PCR) testing of throat swabs, vesicle fluid, or stool remains the diagnostic standard.[22,23] In South Africa, the National Institute for Communicable Diseases (NICD) poliovirus laboratory conducts non-polio enterovirus testing primarily for AFP and environmental surveillance, but HFMD-specific diagnostic capacity is not widely available across public-sector laboratories. Sporadic private-sector PCR testing occurs but is not integrated into national surveillance systems.

Management is largely supportive, consisting of hydration, analgesics, and antipyretics.[6] No specific antivirals are available for HFMD, although agents such as interferon-alpha, ribavirin, and intravenous immunoglobulin have been trialled in the Asia-Pacific region with inconclusive results.[4,22] Severe cases, particularly those suspected of EV-A71, require careful monitoring for neurological deterioration, cardiorespiratory compromise, and rapid progression.[3,22] China's 2015 approval of a monovalent EV-A71 vaccine significantly reduced EV-A71-associated severe disease but did not provide cross-protection against CV-A6 or CV-A10.[12] Global work on multivalent vaccines is ongoing but not yet near implementation.[4,12]

HFMD in South Africa: the 2025 outbreak

South Africa's 2025 KwaZulu-Natal province outbreak represented the first large-scale HFMD event to be recognised nationally. Rapid geographic spread, high levels of public anxiety, and unfamiliarity among clinicians contributed to operational challenges. Because HFMD is currently not a notifiable medical condition, no formal baseline data, thresholds, or seasonality profiles exist for South Africa. The absence of formal surveillance meant clinicians relied largely on anecdotal observations, leading to inconsistent case recognition. Social media intensified public concern, with several misleading claims regarding the severity of the outbreak circulating widely. WASH-related vulnerabilities, including classroom overcrowding, intermittent water supply, and inadequate sanitation infrastructure in schools, likely facilitated transmission across multiple districts.

Discussion

Public health significance and improved HFMD surveillance

The absence of routine HFMD surveillance in South Africa poses several risks. Firstly, the country lacks essential epidemiological metrics such as burden, incidence, seasonality, and age-specific patterns. Secondly, without strain characterisation, shifts towards more virulent or atypical strains could go undetected. Thirdly, delayed recognition of outbreaks impedes timely communication to caregivers and schools, contributing to unnecessary anxiety or delayed care-seeking. Furthermore, the absence of structured reporting limits opportunities for research, preparedness planning, and resource mobilisation. In the context of an already overburdened health system – i.e., managing HIV, tuberculosis, vaccine-preventable diseases, and periodic

zoonotic threats – unexpected viral outbreaks can strain clinical and laboratory capacity. Strengthening HFMD surveillance would improve situational awareness, guide risk communication, and provide evidence for potential future decisions on vaccination.

Surveillance approaches for South Africa

A pragmatic and scalable HFMD surveillance framework for South Africa would combine several complementary approaches to strengthen early detection and outbreak response. Surveillance networks such as the European non-polio enterovirus network, supported by the World Health Organization (WHO), can improve detection and diagnostics, and track circulation of associated diseases. Clinical surveillance, implemented through the District Health Information System (DHIS) or the Notifiable Medical Conditions Surveillance System (NMCSS) using standardised clinical case definitions, would allow routine monitoring of HFMD-like presentations. This could be reinforced by sentinel surveillance in paediatric outpatient departments, emergency units, and districts with historically high burdens of enterovirus-associated illness, enabling more detailed trend analysis and rapid identification of severe or atypical cases. Laboratory-supported surveillance would play a targeted but critical role, particularly for outbreak-associated or clinically severe cases, through integration of RT-PCR testing and sequencing in NICD partner laboratories to characterise circulating strains. Environmental monitoring could further enhance situational awareness by leveraging existing poliovirus wastewater surveillance networks to detect shifts in enterovirus circulation before clinical cases escalate. Community-level event-based surveillance, particularly through schools, crèches, and early-childhood centres, would facilitate the rapid reporting of unusual clusters and support timely public health action. Finally, integrating HFMD surveillance into the National Integrated Disease Surveillance and Response (IDSR) platform would ensure alignment with broader communicable disease preparedness structures, enabling co-ordinated reporting, analysis, and response across sectors.

Limitations and operational challenges

Implementing HFMD surveillance will face several obstacles. Awareness among clinicians remains low, leading to misdiagnosis or under-recognition. Laboratory system demands pose another challenge, particularly given existing pressures on molecular testing capacity. Competing public health priorities may limit available resources. Public communication must balance transparency with reassurance to avoid unnecessary concern over a disease that remains largely mild in presentation and nature. Effective surveillance will therefore, require co-ordinated clinician training, targeted community messaging, and clear escalation pathways for reporting suspected outbreaks.

Recommendations

Strengthening South Africa's preparedness for HFMD requires a co-ordinated set of practical and scalable recommendations:

- HFMD should be integrated into DHIS and the NMCSS as a clinical condition, under IDSR, to enable consistent routine reporting and trend monitoring, supported by sentinel surveillance in high-risk

provinces such as KwaZulu-Natal, Gauteng, and the Western Cape, where paediatric and emergency-care platforms can provide early insights into severe or atypical presentations. Incorporating HFMD into the IDSR platform will streamline reporting pathways, ensure alignment with broader early warning systems, and enhance intersectoral co-ordination.

- Wastewater surveillance capacity should be expanded to include enterovirus monitoring in outbreak-prone districts, complementing clinical surveillance by offering an early indication of shifts in viral circulation.
- Clinician training remains essential to improve early recognition, case management, and timely reporting, while clear and accessible public messaging delivered through schools, childcare centres, and primary-care networks can reduce misinformation and support appropriate care-seeking.
- Continued monitoring of global HFMD vaccine developments will be important for future preparedness, particularly if multivalent formulations become viable options for public health implementation.
- Finally, targeted clinician alerts should be issued whenever wastewater or sentinel surveillance systems detect increases in enterovirus activity, enabling rapid clinical vigilance and early intervention in affected catchment areas.

Acknowledgements

We acknowledge the KwaZulu-Natal Department of Health, the Centre for Vaccines and Immunology at the NICD, and the NICD Outbreak Response Unit.

Conflict of interest

The authors declare no conflicts of interest.

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