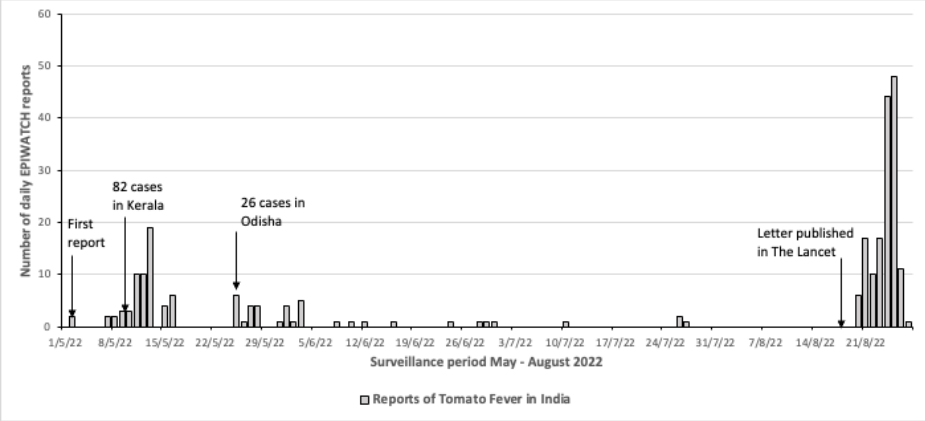


Feedback from operational stakeholders who manage or respond to outbreaks is that they are often too busy to review literature or obtain relevant background information to assist them with acute response. Unlike a traditional analytical outbreak investigation report, **Watching Briefs** are intended as a rapid resource for public health or other first responders in the field on topical, serious or current outbreaks, and provide a digest of relevant information including key features of an outbreak, comparison with past outbreaks and a literature review. They can be completed by responders to an outbreak, or by anyone interested in or following an outbreak using public or open-source data, including news reports.

Watching brief	
Title	Tomato Flu/Fever - An analysis of the Hand Foot and Mouth Disease outbreak reported in India.
Authors	Ashley Quigley, Mohana Kunasekaran, Danielle Hutchinson, Evangeline Gardiner, Anjali Kannan, Susan Abraham.
Date of first report of the outbreak	The outbreak was first reported on 6 th May 2022 (1).
Disease or outbreak	Tomato Flu/Fever
Origin (country, city, region)	First cases of the current outbreak were identified in the Kollam district of Kerala, India (1).
Suspected Source (specify food source, zoonotic or human origin or other)	India's Ministry of Health and Family Welfare recently suggested that Tomato Flu/Fever may be caused by Coxsackieviruses (a group of Enteroviruses), which also cause hand, foot and mouth disease (HFMD) (2, 3). Doctors in Kerala support this, stating that Tomato Flu/Fever is a variant of HFMD and has been observed in children in India as far back as 2001 (4). Historically, 'Tomato Flu' or 'Tomato Fever' are the colloquial terms provided to the unusual blisters observed in some HFMD cases.
Date of outbreak beginning	Reported cases in the current outbreak have been documented since May 6 th , 2022 (1).
Date outbreak declared over	Ongoing as of 1 st September 2022.
Affected countries & regions	India is so far the only country in the world with reported cases of this disease. The regions in India that have been affected include Haryana, Odisha, Kerala and Tamil Nadu (5, 6). Two cases of possible Tomato Flu/Fever were reported in the United Kingdom, where a 13-month-old girl and her 5-year-old brother returned from a family holiday in Kerala and presented with rashes on their hands and legs (7). Both children tested positive for Enterovirus (EV) and sequencing confirmed it was caused by Coxsackie A16, one of the most common EV causes of HFMD in India (7).

Number of cases (specify at what date if ongoing)	In the current outbreak, more than 100 cases have been reported as of 26 th July 2022 (1, 8, 9).
Clinical features	<p>Clinical signs typically appear in children. These include (1) :</p> <ul style="list-style-type: none"> • Red, painful enlarged blisters (tomato like) • Rashes • High fever • Swelling of joints • Body aches • Fatigue • Nausea • Vomiting • Diarrhoea • Fever • Dehydration
Mode of transmission (dominant mode and other documented modes)	The primary mode of transmission for HFMD virus (HFMDv) is via faeces, respiratory droplets, or through fluid from blisters or scabs (2, 10). Transmission can occur through direct contact, such as touching an infected person, or indirect contact, such as touching surfaces (2). HFMD is highly contagious (11).
Demographics of cases	Tomato Flu/Fever presents in children younger than 5 years of age (4), which is typical of HFMD (1). Some cases have been reported in children aged up to 9 years old for Tomato Flu (12).
Case fatality rate	India has not recorded a death attributable to Tomato Flu (CFR: 0%) (4).
Complications	No complications of HFMD or Tomato Flu have been reported in India to date. One of the largest outbreaks of HFMD in Singapore (30,000 cases) reported major complications of infection such as paralysis, pulmonary oedema and neurological disorders (4). Additionally, if the virus spreads to vulnerable populations such as the elderly and immunocompromised persons, this could result in significant complications. The unusual presence of the tomato-like blisters, which are typically larger in size than the clinical manifestations of typical HFMD, is something to be considered.
Available prevention	No vaccine exists to prevent Tomato Flu/Fever. Recommended means of prevention involve practicing proper hygiene and sanitation (1, 2, 12).

<p>Available treatment</p>	<p>Currently, no antiviral drugs exist to treat Tomato Flu/Fever. Isolation is recommended for 5 to 7 days from when symptoms present themselves, in order to manage the disease (12). Children are mostly treated with anti-allergic medicines and ointments (13).</p>
<p>Comparison with past outbreaks</p>	<p>The current outbreak in India was first recorded in the EPIWATCH system on May 2nd, 2022, in an article reporting an outbreak of Tomato Flu/Fever, also referred to as HFMD, in the district of Wayanad in Kerala, India (14, 15). On 10th May, 82 cases were reported in the Kollam area (16), with cases also reported in the bordering area of Tamil Nadu, although no case numbers were reported in this outbreak (17). The outbreak spread to Odisha, where a further 26 cases (referred to as both Tomato Flu/Fever and HFMD) were reported on the 25th of May 2022 (18). There have been no further cases reported, however due to correspondence published online in The Lancet on 17th August 2022 (1), there has been an increased interest in “Tomato Flu/Fever” (Figure 1).</p> <p>Figure 1. The number of daily EPIWATCH reports for Tomato Flu during the surveillance period of May – August 2022.</p>  <p>The Health Ministry of India has responded with the issuing of an advisory on Tomato Flu/Fever – which they confirm is the colloquial term for HFMD – to note the symptoms and be aware that it is highly contagious among school aged children (19). The advisory states that the name “Tomato Flu/Fever” comes from the symptoms of small red round blisters that “resemble tomatoes when they enlarge” (19). Genotyping was performed in swabs of blisters in two children suffering tomato fever who recently returned to the United Kingdom from Kerala, India (7). The results showed evidence of infection with enterovirus (EV) by PCR assay, and genotyping showed a Coxsackie A16 infection, which is a known cause of HFMD (7).</p>

	<p>A previously documented outbreak of “Tomato Flu/Fever” in 2007 in the same state of India, Kerala, affected approximately 2,800 people (20). The symptoms included fluid-filled “tomato-like wounds”, especially on the hands and legs (20). At the time, this was assumed to be a complication of a recent infection with Chikungunya, due to a large epidemic the previous month in the same region (7, 20). However, this was not confirmed.</p> <p>In 2008, an epidemic of Chikungunya occurred in the coastal region of the state of Karnataka, just north of Kerala (21). A total of 39,042 suspected cases were recorded by the local health authorities, and a study was done on the mucocutaneous presentations of Chikungunya in a proportion of these cases (21). A generalized maculopapular rash was found to be the most common, and the authors found that due to the intense erythema, the local population called the rash “Tomato Fever” (21). Even though cutaneous presentations of Chikungunya have been reported, such as the maculopapular rash and apthae-like ulcers, the pathogenesis of these symptoms is unknown (21).</p>
<p>Unusual features</p>	<p>Symptoms of Tomato Flu/Fever include fever, fatigue and body ache together with a rash. The rash is unusual in that the HFMD virus causes red and painful blisters throughout the body that can gradually enlarge to the size of a tomato, which are red in colour (1).</p>
<p>Critical analysis</p>	<p>Some controversy exists on this ‘new’ illness. In a recent report published in August 2022, it was claimed to be a new viral “flu” that emerged in May 2022 over a period of 2 weeks in areas in the south of India: Kerala, Haryana, Karnataka, Tamil Nadu and Odisha (23). Interesting to note that HFMD is one of the diseases under surveillance by the Kerala State Health department (sporadic appearance in the period 2011- 2021 for which reporting is available) and on 8th May 2022, the Kollam district of India issued a health alert for HFMD (22).</p> <p>The term “Tomato Flu” or “Tomato Fever” is the colloquial term based on the characteristic red, “tomato”-shaped blister that appears on different parts of the body, which begin small and increase in size as disease progresses.</p> <p>HFMD is a common febrile rash illness in children, caused by enteroviruses Coxsackie A16 (CA16), EV A71, Coxsackie A6, Coxsackie B and Echo viruses (24). Recent media reports from the Indian state of Kerala have highlighted cases of “Tomato Flu” in young children described as a febrile rash illness with round, red skin lesions looking similar to tomatoes (25). In a case report, the CA16 sequence, one of the most common enteroviruses causes of HFMD in India was identified in 2 children from the same household that developed the rash after returning from travel to India to the UK (7). Currently, there has been</p>

	<p>a push from experts to move away from the misleading name attributed to the illness (26). Local healthcare workers have been encouraged to address the disease as a variant of HFMDv and not stir up unnecessary panic on the emergence of a “new outbreak” which could just be a result of inaccurate terminology, as these reports of Tomato Flu/Fever emerged in a published article at the same time as a HFMD alert was issued in Kollam in May 2022, for the same cases.</p> <p>In addition, the effects of the ongoing COVID-19 pandemic should not be overlooked. Besides the typical symptoms, there have been increasing reports of skin lesions being observed in those positive for COVID-19 or suspected cases globally (27-30). During the last two years, schools in India had been closed due to the COVID-19 pandemic and HFMD being a highly infectious disease, had less scope to spread among the larger paediatric population. The rise in cases this year could be attributed to re-opening of the schools and possibly a different, more infectious strain. With the circulation of other viruses, inadequate testing and poor-quality surveillance in a low resource setting, where healthcare systems are already burdened with ongoing monkeypox outbreak and COVID-19 pandemic, the use of colloquial terms may cause unnecessary panic in the current hypervigilant climate.</p>
<p>Key questions</p>	<ul style="list-style-type: none"> • Is the unusual presentation of the enlarged ‘tomato’ like blisters in this outbreak due to a new variant of HFMDv or is this presentation seen in immunocompromised children, or those who have recently been exposed to COVID-19? • Could the colloquial term ‘Tomato Flu’ or ‘Tomato Fever’ be misleading and confusing and therefore affect treatment if HFMDv cause is not suspected or clinically determined? • The term Tomato Flu/Fever is used to describe multiple diseases. Has there been diagnostic confirmation from India that this is not a mixed outbreak? • Can hypervigilance in the aftermath of the COVID-19 pandemic together with heightened media and journal interest can cause fear and panic in the population?

References

1. Chavda VP, Patel K, Apostolopoulos V. Tomato flu outbreak in India. *The Lancet Respiratory Medicine*. 2022.
2. Centers for Disease Control and Prevention (CDC). Hand, Foot, and Mouth Disease (HFMD) Causes & Transmission Atlant, United States2021 [updated 2 February 2021. Available from: <https://www.cdc.gov/hand-foot-mouth/about/transmission.html>.
3. Perappadan BS. Tomato flu a self-limiting illness: Centre: The Hindu; 2022 [updated 23 August 2022. Available from: <https://www.thehindu.com/news/national/tomato-flu-a-self-limiting-illness-centre/article65801915.ece>.
4. Thiagarajan K. Reports of “tomato flu” outbreak in India are not due to new virus, say doctors. *British Medical Journal Publishing Group*; 2022.
5. Business Standard. What is Tomato Flu? Causes, symptoms, prevention, and treatment 2022 [updated 29 August 2022. Available from: https://www.business-standard.com/article/current-affairs/what-is-tomato-flu-causes-symptoms-and-treatment-122082201034_1.html.
6. Singh H. Researchers race to identify and understand the new virus behind blistering ‘tomato flu’: *The New Daily*. ; 2022 [updated 25 August 2022. Available from: <https://thenewdaily.com.au/news/2022/08/25/tomato-flu-india/>.
7. Tang JW, Iqbal A, Hamal S, Mohamedanif T, Tipping LF, Toovey OT, et al. Kerala Tomato Flu—A Manifestation of Hand Foot and Mouth Disease. *The Pediatric Infectious Disease Journal*. 2022;10.1097.
8. India Today. 82 children aged below 5 years infected with tomato flu in India: Lancet report New Delhi, India2022 [updated 20 August 2022. Available from: <https://www.indiatoday.in/india/story/tomato-flu-india-kerala-82-tomato-fever-cases-lancet-1990499-2022-08-20>.
9. Rana RC. Monkeypox vs tomato flu: Know difference in symptoms from exper New Delhi, India: *XPERT TIMES News of World*; 2022 [updated 26 August 2022. Available from: <https://xperttimes.com/monkeypox-vs-tomato-flu-know-difference-in-symptoms-from-expert/>.
10. Wang J-f, Guo Y-S, Christakos G, Yang W-Z, Liao Y-L, Li Z-J, et al. Hand, foot and mouth disease: spatiotemporal transmission and climate. *International journal of health geographics*. 2011;10(1):1-10.
11. Sarma N. Hand, foot, and mouth disease: current scenario and Indian perspective. *Indian J Dermatol Venereol Leprol*. 2013;79(2):165-75.
12. ABC News. 'Tomato flu' cases have been reported in children in India. This is what experts know 2022 [updated 24 August 2022. Available from: https://www.abc.net.au/news/2022-08-24/tomato-flu-india-after-reports-of-82-cases-in-children/101367878?utm_campaign=abc_news_web&utm_content=link&utm_medium=content_shared&utm_source=abc_news_web.
13. Chakraborty R. Hand, Foot, and Mouth Disease: symptoms, treatment and prevention, explained Mumbai, India: *The Indian Express*. ; 2022 [updated 30 August 2022. Available from: <https://indianexpress.com/article/explained/explained-health/hand-foot-and-mouth-disease-tomato-flu-symptoms-treatment-prevention-explained-8120387/>.
14. The East Coast Daily. Tomato fever spreads panic among children 2022 [updated 2 May 2022. Available from: <https://www.eastcoastdaily.com/2022/05/02/tomato-fever-hand-foot-and-mouth-disease-symptoms.html>.
15. mathrubhumi. Tomato fever in children, more common symptoms; Health department to be careful..... 2022 [updated 7 May 2022. Available

from: <https://www.mathrubhumi.com/health/news/tomato-fever-hand-foot-mouth-disease-causes-treatment-1.7494445>.

16. Bhasbar. Risk of Tomato fever in children: Severe symptoms showing fever in children below 5 years, maximum 82 cases were found in Kerala Kollam, Kerala 2022 [updated May 2022]. Available from: <https://www.bhaskar.com/national/news/kerala-tomato-fever-cases-updates-children-kollam-129787840.html>.

17. Pandey K. Tomato flu outbreak in Kerala, Tamil Nadu, children under 5 affected: Check symptoms, causes and treatment details: Times Now; 2022 [updated 11 May 2022]. Available from: <https://www.timesnownews.com/health/tomato-flu-outbreak-in-kerala-tamil-nadu-check-symptoms-causes-and-treatment-details-article-91492554>.

18. Veni A. 26 children get tomato fever in Odisha: The Times of India; 2022 [updated 24 May 2022]. Available from: <https://telugu.samayam.com/latest-news/india-news/twenty-six-cases-of-tomato-flu-detected-in-odisha/articleshow/91772116.cms>.

19. Sisodia SS. Indian government issues advisory for tomato flu: All you need to know about symptoms and treatment New Delhi, India: WION; 2022 [updated 23 August 2022]. Available from: <https://www.wionews.com/india-news/indian-government-issues-advisory-for-tomato-flu-all-you-need-to-know-about-symptoms-and-treatment-509575>.

20. VR. S. 'Tomato Fever' Replaces Chikungunya in Kerala India: Med India; 2007 [updated 16 July 2007]. Available from: <https://www.medindia.net/news/tomato-fever-replaces-chikungunya-in-kerala-23631-1.htm>.

21. Bhat RM, Rai Y, Ramesh A, Nandakishore B, Sukumar D, Martis J, et al. Mucocutaneous manifestations of chikungunya fever: A study from an epidemic in coastal Karnataka. Indian journal of dermatology. 2011;56(3):290.

22. The Times of India. HFMD alert issues in Kollam. 2022 [updated 8 May 2022]. Available from: <https://www.thetimesoftruth.com/hfmd-alert-issued-in-kollam/>.

23. Zee Media Bureau. Tomato fever grips Kerala, Tamil Nadu steps up vigil on border New Delhi, India: ZEE News; 2022 [updated 14 May 2022]. Available from: <https://zeenews.india.com/india/tomato-fever-grips-kerala-tamil-nadu-steps-up-vigil-on-border-2463348.html#:~:text=The%20main%20symptom%20of%20tomato,diarrhea%20and%20nausea,%20and%20vomiting>.

24. Mukherjee D, Ruchika F, Pokhrel NB, Jaiswal V. Tomato fever and COVID 19, a double hit in the Indian health system. Immunity, Inflammation and Disease. 2022;10(8).

25. Karmakar S. Tomato Flu Confirmed In Kerala, 82 Kids Infected By The Virus: Symptoms, Causes And Other Details: TheHealthSite.com; 2022 [updated 11 May 2022]. Available from: <https://www.thehealthsite.com/news/tomato-flu-confirmed-in-kerala-82-kids-infected-by-the-virus-symptoms-causes-and-other-details-879706/>.

26. Sharma M. Tomato fever is misleading name for Hand, Foot and Mouth Disease, say doctors: India Today; 2022 [updated 22 August 2022]. Available from: <https://www.indiatoday.in/health/story/tomato-fever-misleading-name-hand-foot-mouth-disease-doctors-1991088-2022-08-22>.

27. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective [published online March 26, 2020]. J Eur Acad Dermatol Venereol doi.10.

	<p>28. Wollina U, Abdel NM, Kruglikov I. Dermal adipose tissue in hair follicle cycling: possible applications in alopecia? <i>Georgian Medical News</i>. 2017(265):41-5.</p> <p>29. Matar S, Oulès B, Sohier P, Chosidow O, Beylot-Barry M, Dupin N, et al. Cutaneous manifestations in SARS-CoV-2 infection (COVID-19): a French experience and a systematic review of the literature. <i>Journal of the European Academy of Dermatology and Venereology</i>. 2020;34(11):e686.</p> <p>30. Gisondi P, Plasero S, Bordin C, Alaibac M, Girolomoni G, Naldi L. Cutaneous manifestations of SARS-CoV-2 infection: a clinical update. <i>Journal of the European Academy of Dermatology and Venereology</i>. 2020;34(11):2499-504.</p>
--	--