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REVIEW ARTICLE

An update on Tomato Flu Virus: A Mini-review

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Abstract:

This article aims to highlight the most recent information on the “tomato flu” epidemic in India. A new disease has sprung out in several areas of India. The illness had a rash that was predominantly seen in children under the age of five and was highly infectious. It was known as “tomato flu” because the rash was excruciatingly painful, and the blisters were the size of tiny tomatoes. None of the afflicted children experienced problems that would have resulted in death. The focus of the therapy was primarily symptomatic, supportive care along with isolation and sustaining hygiene standards. The RNA virus Cocksackievirus A16, a member of the Picornaviridae family, was shown to be the cause of this disease. A detailed literature review was performed on the epidemiology, aetiology, evolution, transmission, outbreak, preventive measures and management and treatment of tomato flu. The leading prevention is preventing infected children and infants from sharing clothes, food, and toys. Few drugs are used to prevent fever, but no antiviral drugs or vaccines are available to prevent tomato fever. We came to the conclusion that a novel form of Cocksackievirus A16 may be responsible for the current pandemic of this disease in India.

Keywords: Tomato flu, Hand, Foot and mouth disease (HFMD), Tomato-like blisters, Infectious disease, Cocksackie virus A16.

Article History

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1. INTRODUCTION

In India's state of Kerala, children under the age of five have been diagnosed with tomato flu, also known as tomato fever, because of the reddish tomato-shaped pustular blisters that develop on afflicted people's bodies [1 - 3]. The medical term for tomato flu is Hand, Foot, and Mouth Disease (HFMD), according to Dr Archana M, a consultant in paediatric infectious [4]. The enteroviruses (EV) Cocksackie A16 (CA16), EV A71, Cocksackie A6, Cocksackie B, and Echo viruses are responsible for the common febrile rash condition known as hand, foot, and mouth disease (HFMD) [5]. Fever, exhaustion, red skin blisters, rashes, irritability, and dehydration are some of the flu symptoms. The possibility of HFMD being the disease's aetiology has been raised in certain research and publications [6]. According to some accounts, there is no relationship between this illness and coronavirus, monkeypox, or chikungunya. Children between the ages of 1 and 9 are susceptible, as are adults with weakened immune systems. Cocksackie virus A16, which causes HFMD, usually affects children and newborns. The Picornaviridae family, comprising non-enveloped single-stranded RNA viruses, contains the coxsackievirus [7]. Children under the age of five are the main victims. The low frequency of tomato flu in adults may be due to strong protection against the virus. However,

people who interact with children may function as viral carriers and spread the disease. Tomato flu virus is considered as the new variant of Hand Foot and Mouth Disease [1, 2, 7 - 12]. HFMD, also known as tomato flu, has become a significant health concern to the experts [13].

2. METHODS

The search parameters tomato flu, HFMD, epidemiology, aetiology, evolving, outbreak, Cocksackievirus A 16, blisters, rash, transmission, and prophylaxis were thoroughly reviewed in the literature. The data source was obtained from PubMed, Google Scholar, Embase and other websites. The inclusion criteria for this study were review articles, original articles, case reports and articles written in English published between the period May 2022 to January 2023. The exclusion criteria for the articles were applied based on studies prior to May 2022 and articles with insufficient data.

2.1. Epidemiology

The article reporting an epidemic of Tomato Flu/Fever, commonly known as HFMD, in the district of Wayanad in Kerala, India, on May 2, 2022, is where the current outbreak in India was first noted in the EPIWATCH system [14]. The first outbreak was found in the Kollam district of Kerala, in which the total number of cases was 82 on May 13, 2022, and is believed to increase further. The first case of tomato flu was found in Aryankavu, a village near the Kerala- Tamil Nadu

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border. In Odisha, 26 (1-9 years) cases were found to be positive for Hand, Foot and Mouth Disease (HFMD), which is assumed to be tomato flu [8, 15, 16]. Mudakayam, Varzur, and Kanirapally in the Kottayam and Pathanamthitta districts, which had previously been hit by Chikungunya, were among the hotspots at the time of infection [6]. HFMD disease occurs at an equal frequency in both genders, but older epidemiological data suggest that the infection frequency is slightly higher in males [17]. According to the Integrated Disease Surveillance Program (IDSP), 13 cases of Hand Foot and Mouth Disease or tomato flu have been reported in Srinagar, Jammu and Kashmir, ages 4 to 5 years old [18]. According to the National Health Mission (NHM), Assam state has reported 24 and 22 cases of tomato flu from two schools clinically based on symptoms, most of which were reported from Dibrugarh district [19].

2.2. Aetiology

Some reports say that the cause of tomato flu or fever might be HFMD, caused by the family of enteroviruses that are known to commonly affect children and adults with weaker immunity [7, 11]. An RNA virus from the Picornaviridae family known as Cocksackie virus A16 was shown to be the cause of tomato flu [1, 6, 12, 20 - 26]. According to British Medical Journal report it was found that it is not a distinct virus but coxsackie virus A16. Samples of two children were collected by swabs who returned from India with tomato flu were found positive of coxsackie virus A16 [8]. To try to determine the source of the illness, scientists have been investigating swabs from children suffering from tomato flu. The findings of the lab tests showed that the children had the enterovirus coxsackie A16 [27 - 30]. Therefore, it appears that Disease has been indeed tomato flu. It is not a sort of influenza, has nothing to do with tomatoes, and is not even remotely a novel illness [23].

2.3. Evolving

A 13-month-old baby and her 5-year-old sibling may have had two incidents in May 2022, when they were returning from a trip to Kerala and were experiencing rashes on either leg or their hands. It was discovered by PCR testing that the coxsackie virus A16, a prevalent cause of HFMD, was present. According to the professor at MES Medical College in Malappuram, specifically Purushothaman, Kerala, it predominantly affected young children under the age of five in the formative days after 2001. Children between the ages of 5 and 10 were more frequently seen later. According to certain statistics, incidences among adults and teenagers have increased in recent years. Earlier, it was seen that children younger than 6 months and older than 5 years were not affected, but these two age groups are also now affected. Some practitioners said that earlier the effect was seen on palms and soles but now it is seen on the pelvis, abdomen, chest, and back. Some medical professionals are perplexed by the symptoms of the varicella virus, which causes chickenpox. [7, 5, 14, 22 - 25].

2.4. Transmission

The HFMD virus is primarily spread by faeces, respiratory

droplets, or fluid from blisters or scabs. Transmission can occur directly by touching an infected individual or indirectly by touching surfaces. The HFMD virus is very infectious. Children are more susceptible to viral infections and tomato flu due to this higher risk. Close contact is most likely to spread the illness. The Lancet paper claims that using diapers, touching filthy surfaces, and placing objects directly in their mouths increase the risk of young infants becoming infected with the tomato flu virus. If the disease's epidemic in infants is not contained and halted, tomato flu can potentially spread to adults and have terrible ramifications. Like other viruses, tomato flu is very infectious [14, 26].

2.5. Clinical Features

Symptoms include nausea, fatigue, dehydration, swelling of joints, fever, rashes with blisters on hands, feet and buttocks, body aches, and skin irritation [9, 27]. Small red spots emerge on the body one to two days after the fever starts, and they gradually develop into blisters and ulcers. The lesions are typically found on the tongue, inside of the cheeks, gums, palms, and soles. However, they can occur elsewhere in the body. Flu-like symptoms, including coughing, sneezing, rhinorrhoea (runny nose), and discolouration of the hands, knees, and buttocks, are other indications that you have the tomato flu [23].

According to the study, the various population groups which are vulnerable to tomato fever are older persons, consisting of 11.8% (> 45 years); adult persons, consisting of 28.2% (> 18 years to 45 years), and children consisting of 60% (< 15 years) as given in Table 1 [21].

Table 1. Population at risk for this disease.

Population	Age	Percentage
Older persons	>45 years	11.8%
Adult persons	>18 to 45 years	28.2%
Children's	<15 years	60%

In a study, various complications were found due to tomato fever, with which 52.7% as skin discolourations, 20.9% as sore formation, 10.9% as type-1 diabetes mellitus and 15.5% as neuropathic complications, as given in Table 2 [21].

Table 2. Complications of tomato fever.

Complications	Percentage
Skin discolouration	52.7%
Sore formation	20.9%
Type-1 diabetes mellitus	10.9%
Neuropathic complications	15.5%

2.6. Outbreak of Tomato Flu

The virus could also be a new variant of the viral hand, foot, and mouth disease, a common infectious disease targeting mostly children aged 1-5 years and adults with weaker immunity. There are no specific drugs to treat this infection, but isolation, relaxation, drinking a lot of water, and steam sponging are recommended to relieve itch and rashes. Supportive therapy of paracetamol is given for the symptomatic treatment of body aches and fever. It is a self-

limiting disease and is very contagious with other similar types of influenza. So, it is mandatory to isolate suspected cases strictly, and other preventive measures should be taken to prevent this disease in India [11]. Children need to be looked after since they are more susceptible to certain illnesses. It is advisable to avoid contacting filthy surfaces with unwashed hands since it is infectious. It is recommended to stay away from the infected individual immediately, teach your child the symptoms and side effects of diseases, and urge them to use handkerchiefs when they have a runny nose. Try to stay hydrated and separate all your clothing, towels, and other utility things. Obtain adequate rest and sleep and practise frequent hand washing to aid in recovery [21]. Parents are encouraged that if they find any HFMD symptoms, then they should consult a doctor as soon as possible. However, if children show unusual behaviour such as refusal of eating and drinking or persistent drowsiness and vomiting, they should be aware. They should wash their hands thoroughly especially when changing children's diapers or using toilet. Consultation rooms should be set up for febrile rash cases in outpatient clinics or paediatric wards, and the equipment used should be sterilised [15]. Tomato flu is considered the subtype of hand foot and mouth disease. According to studies, HFMD may potentially affect incompetent patients [1].

2.7. The Innate Immune System's Role in the Detection of Pathogens

Pattern recognition, another name for innate immune identification, is based on detecting molecules specific to bacteria. Each host receptor (PRR) in pattern recognition has broad specificity and may be able to bind to a large number of compounds that share a certain structural motif or pattern. This makes pattern recognition uncommon. The targets of PRRs are known as pathogen-associated molecular patterns (PAMPs) despite the fact that they may be found on both pathogenic and non-pathogenic microbes. PAMPs are ideal for innate immune system detection for three key reasons. They are foremost among microorganisms of a certain class invariant. Second, they are the end result of pathways that are specific to bacteria and enable the differentiation between self- and non-self-molecules. Thirdly, they play crucial roles in microbial physiology, which limits the capacity of the microbes to avoid innate immune detection through adaptive evolution of these molecules. Bacterial PAMPs, such as lipopolysaccharides, peptidoglycan, lipoteichoic acids, and cell wall lipoproteins, are frequently found in the cell wall. -glucan, an ingredient of fungal cell walls, is a significant fungus PAMP. The innate immune system's perception of these structures can indicate the presence of microbes. A significant component of pattern recognition is that PRRs do not differentiate between pathogenic and symbiotic (non-pathogenic) bacteria since their ligands are not specific to pathogens. Furthermore, the detection of symbiotic microbes by the innate immune system is crucial for maintaining intestinal homeostasis [28 - 30].

2.8. Diagnosis

In children's who shows symptoms are being diagnosed by two tests such as serological and molecular tests and shows some similar clinical presentations of dengue, zika virus, chikungunya *etc.* in these tests if the patient shows negative test, then the contraction of tomato virus is confirmed [11, 21,

26]. Polymerase chain reaction was used to test for enteroviruses and monkeypox at Porton Down, Salisbury, a national reference laboratory in the United Kingdom. Additional sequencing at UKHSA-Colindale, another national reference laboratory, allowed for the identification of CV-A16 serotype as the primary disease-causing agent [5, 23].

2.9. Preventive Techniques

The disease can be prevented by applying precautionary measures. Prevention is the better cure to keep children safe and away from disease. There are some following measures such as [4].

- Education should be provided to make them aware of the signs and symptoms of the disease.
- Close contact should be avoided from infected persons.
- Children should be taught about the symptoms of the disease.
- Toys, clothes, food, and other things should be prevented from sharing with infected persons.
- A handkerchief should be used while coughing and sneezing to avoid the spread of disease.
- Children should be hydrated by drinking plenty of water, juice, milk *etc.*
- The food that is rich in vitamins and nutrient-rich foods should be included.
- Toys, utensils, and clothes of the children should be cleaned and sanitised properly to avoid disease.
- If the child shows any disease-related symptoms, they should be isolated.

2.10. Management and Treatment of Tomato Flu

The viral fever known as "tomato flu" is self-remitting. Because of this, it often resolves itself in 7-10 days. Particularly in areas where outbreaks are present, the illness is diagnosed clinically by a history and a physical examination [1, 15, 23].

2.10.1. Non-pharmacological Treatment

According to healthcare professionals, the mortality of this disease is not too high, and it can be treated. So, there are some ways to prevent this disease non-pharmacologically, such as maintaining good personal hygiene, maintaining physical distance from suspected cases, and drinking more water, juices, and liquid content. It is better not to touch the blisters, try to drink more boiled water and rest sufficiently to avoid the long-lasting effects of Tomato Flu [29].

2.10.2. Pharmacological Treatment

No specific drug exists to treat this disease yet as it is a self-limiting infection, and for prevention, no antiviral drugs or vaccination is available; according to the Lancet report, Ibuprofen and paracetamol are the drugs used to treat fever for body aches and other symptomatic treatments [4]. Although HFMD has no known antiviral treatments, oseltamivir and acyclovir have demonstrated efficacy by reducing symptom severity. Immunoglobulin usage in HFMD has also been demonstrated to speed up clinical recovery and reduce fatalities [23].

CONCLUSION

It was eventually shown that a Coxsackie virus A-16 variety was responsible for India's recent "tomato flu" pandemic, which was characterised by huge red blisters on the hands, feet, and cheeks. As a result, the name "tomato flu" is no longer in use, and HFMD is now recognised as the cause of the pandemic. In order to control the disease and prevent new outbreaks, prompt preventative measures, such as maintaining good hygiene and sanitation and five to seven days of isolation following disease contractility, are crucial. Preventing infected children and infants from sharing clothes, food, toys are the leading prevention. Although HFMD has no known antiviral treatments, oseltamivir and acyclovir have demonstrated efficacy by symptom severity is being reduced. Monitoring and follow up is needed for better understanding the potential treatment. Union home ministry and some state government has already issued advisory regarding tomato fever.

LIST OF ABBREVIATIONS

EV	=	Enteroviruses
HFMD	=	Hand Foot and Mouth Disease

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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