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## HAND, FOOT AND MOUTH DISEASE : A REVIEW

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### ABSTRACT

**Background:** Hand, foot and mouth disease or HFMD is a common childhood infectious disease mainly caused by coxsackievirus A16 (CVA 16) and enterovirus 71 (EV71). This HFMD disease can spread throughout the world and also cause outbreaks. Occurrence of this disease is mostly reported in the summer and fall. However, in Indonesia itself, HFMD is still not getting enough attention due to its self-limiting nature, so there is not enough epidemiological data.

**Objective:** This research was conducted to find out the description of hand, foot, and mouth disease or HFMD.

**Methods:** Conducting a literature review of previous journal articles related to hand, foot, and mouth disease or HFMD.

**Results:** HFMD caused by coxsackievirus A16 or CVA16 and enterovirus 71 or EV71 which are self-limiting. Contact with saliva, fluids, and feces of HFMD patients can trigger transmission. Meanwhile, vaccines and antivirals have not been found that can be a way to treat and prevent EV71. **Conclusion:** One solution that is considered effective for preventing HFMD is to always practice clean living.

**Keywords:** *Hand, foot and mouth disease; HFMD; eEV71; CVA16; A16*

### INTRODUCTION

In this world there are many kinds of diseases. From the easiest to understand to the ones that are not easy to understand. There are diseases that are caused by viruses. A large number of viruses from various families cause rampant disease in humans, ranging from mild and self-limited illnesses to acute fatal diseases<sup>1</sup>. One of them is hand, foot and mouth disease or hand-foot-and-mouth disease, which is abbreviated as HFMD. It is a common childhood infectious disease mainly caused by various human enteroviruses<sup>2</sup> which are among the most widespread pediatric diseases in Asia<sup>3</sup>. The cause of this disease is a virus. Thus, hand, foot and mouth disease is one of the most common acute viral infections caused by coxsackievirus A16 (CVA 16) and enterovirus 71 (EV71). The nature of this disease is self-limiting<sup>4</sup>.

Meanwhile, signs of HFMD include vesicles on the palms, soles, and oral mucosa, which can produce discomfort and difficulty swallowing food. Another name for this disease is Singapore flu. In 1970 HFMD was first detected in Singapore. However, back in 2000, it was suspected that this disease had become an epidemic in Singapore by causing several children with sufferers to die. Due to the flu epidemic that year, the Singaporean government recommended that fast food restaurants be closed, as well as shared public facilities such as swimming pools and playgrounds for children. This

was an effort by the Singapore government at that time to reduce and prevent the transmission of the flu epidemic<sup>4</sup>.

This HFMD disease can spread throughout the world and also cause outbreaks. Plague itself is not something new for humans because it has happened frequently for thousands of years. Meanwhile, those who are most often affected by HFMD are children aged around under ten years. The reason is, it was found that this disease rarely affects adults. Occurrence of this disease is mostly reported in the summer and fall. Meanwhile, for tropical areas, this disease can live a long time, namely throughout the year. This disease is of concern to many countries. However, in Indonesia itself, due to its self-limiting nature, HFMD still receives insufficient attention, resulting in insufficient epidemiological data<sup>5</sup>.

There are other self-limiting infectious diseases such as influenza, chickenpox, hepatitis A, acute hepatitis B, Ebola virus, and Norovirus which become self-limiting epidemics<sup>6</sup>. Even though HFMD is mild and self-limiting, this disease can cause serious complications in children who suffer from it. For HFMD, for example, children can suffer from meningitis, encephalitis, and pulmonary oedema which can end in death. This is caused by an enterovirus (EV 71) as one of the viruses that cause HFMD. In addition, this hand, foot and mouth disease is highly contagious and a vaccine has not yet been found. Likewise, antiviral treatment that is



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considered effective has not yet been found. Even so, it is important for the general public and the medical community to know what HFMD actually is. Therefore, in this article, the clinical findings of this disease is described to help provide an understanding of what to do when infected and how to prevent it.

### ETIOLOGY OF HFMD

As previously explained, the cause of hand, foot and mouth disease or HFMD is a non-polio enterovirus that causes various infections in humans<sup>7</sup>. For example, such as coxsackievirus A5, A7, A9, A10, A16, B1, B2, B3, B5, then echovirus, and other types of enteroviruses. However, it is known that the most common causes of this disease are coxsackievirus A16 or CVA 16 and enterovirus 71 or EV 71. Actually, this enterovirus belongs to the Picornaviridae family which is a single-stranded RNA virus. For hand, foot and mouth disease viruses, this will usually result in mild illness in children. Meanwhile, EV71 is more associated with neurological complications and death<sup>8</sup>.

If one looks at this enterovirus is actually a small virus where the virion is about 30 nm in diameter and also consists of the proteins VP1, VP2, VP3, and VP4. Meanwhile, the incubation period for enterovirus and coxsackievirus itself takes approximately three to six days. Meanwhile, transmission can occur through the respiratory route, direct contact with saliva, body fluids, or faeces. It is known that this virus can survive in the stool of sufferers for up to five weeks. In general, transmission can occur if the level of population density increases and bad sanitation increases. In past outbreaks, it was mostly household, family, and childcare-acquired infections<sup>8</sup>.

However, the pathogenesis of hand, foot and mouth disease is not fully understood. Moreover, changes in the spectrum of pathogens raise new challenges in the prevention and control of HFMD<sup>9</sup>. This makes it difficult to explain in general the pathogenesis of HFMD. What is known is that enteroviruses infect humans by passing through cells of the gastrointestinal and respiratory tract. This virus then replicates in the pharynx and intestine, followed by multiplication in lymphoid tissue and regional lymph nodes. Meanwhile, scattered regional lymph nodes persist for twenty-four hours,

followed by primary viremia. In primary viremia, the virus spreads to the reticuloendothelial system, which is more distant, including the spleen, liver, bone marrow, and more lymph nodes. Subclinical infection occurs when the immune response can limit replication and outgrowth of the reticuloendothelial system<sup>10</sup>.

Replication that continues in the reticuloendothelial system will cause clinical infection. Moreover, children aged 2 years or younger tend to have more atypical clinical symptoms than older children<sup>10</sup>. The causes of patients developing viral diseases with skin manifestations are coxsackievirus, echovirus, and EV71. Meanwhile, for hand, foot and mouth disease, the cause is CVA16 which is generally a mild mucocutaneous lesion that can improve in seven to ten days and also rarely has complications. Meanwhile, the neurovirulence of EV71 is still unclear. Pathological features of the central nervous system resulting from EV71 infection include neuronophagia, perivascular cuffing, focal oedema, and inflammatory cell infiltration. It is suspected that viral cytolysis is the causative mechanism of nerve damage<sup>10,11</sup>.

### CHARACTERISTICS OF HFMD

The nature of hand, foot, and mouth disease or HFMD is self-limiting. What is meant by self-limiting is that the recovery period occurs within seven to ten days. The nature of the treatment is symptomatic and observation is made for signs of CNS involvement. Meanwhile, the cure for this disease is based on the patient's immune system because a more specific and clearer antiviral has not yet been found. Therefore, appropriate fluid intake is required to prevent dehydration as a result of painful oral lesions, which is likely to be required in patients with intravenous dehydration for moderate to severe dehydration. However, it could also if oral intake is limited. Meanwhile, fever itself can be treated with antipyretics. On the other hand, paracetamol and ibuprofen can be used to treat fever. Meanwhile, if there is a secondary infection, what is given is topical or oral antibiotics.

For children whose infection is related to mucocutaneous only, it can be treated at home by being given education on how to care for patients. So, it is important to provide education on how to



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care for patients and clear instructions so that they can return to the main health service if warning signs are found. Meanwhile, in many countries that have had outbreaks of hand, foot and mouth disease, intravenous immunoglobulin or IVIG is used. The assumption is that neutralizing antibodies in IVIG can help neutralize enteroviruses. This is because IVIG has been used for other severe enterovirus infections, such as neonatal enterovirus sepsis or enterovirus meningoencephalitis persistent in children with primary immunodeficiency<sup>10</sup>.

### PREVENTION OF HFMD

Vaccines or antivirals that are considered effective for treating or preventing EV71 infection have not yet been found. In fact, vaccines are very helpful in reducing outbreaks of infectious diseases<sup>11</sup>. Prior to clinical trials, the EV71 vaccine ingredients, including formalin-inactivated whole virus vaccine, DNA vaccine and recombinant protein vaccine, still need improvement. Meanwhile, the unexpected thing that is important to do and get used to is living clean. This is the best way to try to stop the spread of the virus. Clean living is like an example by washing hands with water and soap. Mainly, for children and those who care for toddlers such as in the process of changing diapers and also from the toilet. In addition, it is also important to always cover your nose and mouth when you sneeze and cough. Contacts such as kissing, hugging and sharing eating utensils should be stopped for people with hand, foot and mouth disease<sup>10,11</sup>.

During the acute stage, hand, foot, and mouth disease or HFMD is highly contagious and may last longer. This is because the virus is able to survive for several weeks in the stool even after recovery. The most visible is the appearance of vesicles. However, the vesicles should still be allowed to dry naturally. In particular, these vesicles should not be pierced because there is fluid inside which can be a source of transmission. Therefore, it is important for children or patients with HFMD not to attend school and be incubated according to the time frame required for recovery<sup>12</sup>.

### CONCLUSION

Based on the description above, it can be concluded that hand-foot-and-mouth disease (HFMD) is an acute viral infectious disease caused

by coxsackievirus A16 or CVA16 and enterovirus 71 or EV71 which are self-limiting. limiting. Meanwhile, transmission is through direct contact such as saliva, nasal and throat droplets, fluids, and patient feces. There is no vaccine that is precise and efficient in treating and preventing EV71. Treatment is carried out symptomatic and with observation of the involvement of the central nervous system. Meanwhile, the best solution to prevent the spread of this disease is to strive for clean living habits.

### ETHICAL APPROVAL

No ethical approval.

### CONFLICTS OF INTEREST

The author declares no conflict of interest.

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### AUTHOR CONTRIBUTIONS

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