

## Foot and Mouth Disease (FMD): Etiology, Pathogenesis, Prevention and Control in Even or Split Hoofed Livestock

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Revised: 2023-12-21, Accepted: 2023-12-23, Publish: 2023-12-30

### ABSTRACT

Foot and Mouth Disease (FMD) was first reported in 1987 in Malang, East Java, caused by imported dairy cattle from the Netherlands. After 36 years of FMD freedom, the disease was re-introduced on 5 May 2022 in East Java. The disease is caused by a virus of the genus Aphthovirus of the Picornaviridae family, which affects even-toed or split-hoofed livestock, both wild and domesticated. Transmission of FMD virus from sick animals to other susceptible animals can occur directly and indirectly. FMD virus can be transmitted rapidly, entering the animal's body directly through the mouth or nose and replicating in epithelial cells in the nasopharyngeal area, then entering the blood (viremia), then multiplying in lymphoglandular glands and epithelial cells in the mouth and footpads resulting in vesicle lesions and blisters. Animals or livestock infected with FMD will show clinical symptoms such as fever up to 41°C, the formation of vesicles or blisters on the mouth, gums, tongue, nipples, and skin around the hooves, hypersalivation, weight loss, and livestock production. Handling and controlling FMD in livestock or animals can be done by isolating and quarantining sick animals, vaccination programs, biosecurity measures in animal husbandry, monitoring livestock traffic, and conducting surveillance.

**Keywords:** Etiology, Pathogenesis, Prevention and Control, FMD

### INTRODUCTION

Foot and Mouth Disease (FMD) is an infectious and acute disease that affects even-toed or cloven-hoofed livestock such as cattle, goats, sheep, buffalo, and pigs. In addition to these animals, FMD can also attack wild animals with even or split hooves, such as elephants, deer, camels, African buffaloes, and others (Rohma et al., 2022). FMD is still endemic in parts of Africa, Asia, and Latin America (Livestock and Animal Health Service Office, West Nusa Tenggara Province, 2020) and sporadically causes outbreaks in previously disease-free countries (Brown et al., 2022). In fact, according to the results of research conducted by Mesfine et al. (2019) on the seroepidemiology of FMD in the Amhara region of Ethiopia, the disease affects ruminants with an overall seroprevalence of 11.48%, where cattle (14.48%) were more affected by FMD than other livestock, namely goats (7.10%) and sheep (7.07%).

In Indonesia, the disease was first reported in 1987 in Malang, East Java, due to the importation of dairy cattle from the Netherlands.

In 1983, the disease was last in Java and eradicated by mass vaccination, so in 1986, Indonesia was declared free from FMD (Budiono et al., 2023). However, Indonesia was officially proclaimed FMD-free by the OIE in 1990 and is obliged to maintain this free status without vaccination (Dharmawibawa et al., 2022). After 36 years of FMD freedom, the disease re-entered on 5 May 2022 in East Java (CNBC Indonesia, 2023) and has even spread to various regions in Indonesia. In fact, according to data from the Ministry of Agriculture of the Republic of Indonesia as of 7 November 2023, active FMD cases were detected in 19 provinces in Indonesia such as North Sumatra, West Sumatra, Southeast Sulawesi, Central Sulawesi, South Sulawesi, West Sulawesi, Riau, West Nusa Tenggara, Riau Islands, West Kalimantan, East Java, Central Java, West Java, Jambi, Yogyakarta, Bengkulu, Banten, Bangka Belitung, and Aceh. The disease affected 615,576 animals and caused the death of 11,839 animals, most of which were beef cattle (82.2%), followed by dairy cattle (11.9%) and water buffalo (4.5%), with the rest being goats, sheep and pigs (Ministry of Agriculture of the

Republic of Indonesia, 2023). It indicates that FMD has become an extraordinary event (KLB) and needs to be handled quickly (Pamungkas et al., 2023).

The disease is caused by a virus of the genus Aphthovirus of the Picornaviridae family (Budiono et al., 2023). The virus can spread by directly contacting infected livestock, semen, aerosols, fomites, and food products (Silitonga et al., 2016). Infected livestock or animals will show clinical symptoms such as excessive salivation, fever over 40°C, anorexia, cheeks, nostrils, muzzle, gums, inner lips, and nail lesions (Wulandani, 2022). The disease has a morbidity rate of 100% and a low mortality of about 1.53%. The condition is rarely fatal except in young livestock and animals (Al-Salihi, 2019).

FMD is not a zoonotic disease, but even so, it can cause significant economic losses (Budiono et al., 2023; Awel et al., 2021). Firman et al. (2022) stated that the financial losses caused by FMD are a decrease in milk production by 25% per year, decreased fertility, decreased growth rates in beef cattle, culling of chronically infected livestock, loss of labour, disruption of domestic trade, loss of livestock export opportunities eradication costs and mortality. Due to these losses, it is necessary to control and prevent FMD. This paper discusses Foot and Mouth disease (FMD), especially the causes (etiology), pathogenesis, and prevention and control of the disease. It will also discuss clinical symptoms, susceptible animals, and virus transmission to animals.

## ETIOLOGY

FMD disease is caused by foot mouth disease virus (FMDV) (Aslam and Alkheraije, 2023), which belongs to the genus Aphthovirus and the Picornaviridae family. The virus is a small, 26 nm diameter, non-enveloped, positive sense, single-stranded RNA virus with a genome of about 8500 bases surrounded by four structural proteins that form an icosahedral capsid (Al-Salihi, 2019). In addition, this virus also has a strong capsid, so it is resistant to disinfectants that work by dissolving fat (Andrian, 2020). However, several studies have shown that sodium hypochlorite solution is widely used to inactivate viruses, including FMDV. However, this solution must be stored in cool and dark conditions to maintain its viral effect (Onodera et al., 2023). The virus can infect even- or split-clawed ruminant animals, both domesticated and wild,

such as cattle, goats, sheep, buffalo, pigs, elephants, deer, camels, and African buffalo (Rohma et al., 2022).

Aphthovirus is an RNA virus that has seven different serotypes, such as German Strain (C), Oise (O), Allemagne (A), South African Territories (SAT)1, SAT2, SAT3, and Asia1, and more than 60 subtypes. There are 60 structural copies of proteins present in the FMDV capsid. These proteins are VP2, VP3, VP1 and there are 8 nonstructural proteins (3A, 3B, 3C, L, 2A, 2B, 2C and 3D) (Azeem et al., 2020). Serotypes O and A have the widest distribution as they have infected livestock in Africa, Asia, and South America. Types SAT-1, 2, and 3 are currently found only in Africa, and serotype Asia-1 for Asia. All FMD virus serotypes can invade free areas, and periodically, SAT spreads to the Middle East and Asia-1 to Western and Eastern Eurasia. In India, most FMD outbreaks are caused by serotype O, followed by serotype A and Asia-1 (Pamungkas et al., 2023). All FMDV serotypes cause similar clinical symptoms 2-14 days post-infection (Onodera et al., 2023). The large diversity is thought to result from high mutation rates, quasi-species dynamics, and recombination. Genetic variation can occur through mutation or homologous recombination between two different FMD virus strains, resulting in new FMDV variants. These new variants significantly affect vaccine strain selection (Al-Salihi, 2019).

## MODE OF TRANSMISSION

FMD is a disease that is highly contagious from one animal to another. The virus that causes FMD enters the body of livestock or animals through inhalation, ingestion, and contact wounds on the skin and mucous membranes. Vertical transmission to the fetus has also been reported (Ismail et al., 2023). Transmission of the disease occurs through direct and indirect contact (Paton et al., 2018). Direct transmission occurs through inhalation of virus particles from the respiratory tract of infected animals. Even the spread of the virus through the air can cause the virus to move from one place to another over a considerable distance, even up to 2-3 miles, and if the wind conditions are strong, the virus can be transmitted as far as 10 miles and infection can still occur after the virus is 14 days in the air (Firman et al., 2022). The virus can survive in the air in temperate or sub-tropical regions, but in hot and dry climates, the virus cannot stay for long

(Azeem et al., 2020). Transmission of the virus through the air or respiratory system is frequent and causes rapid spread. Indirect transmission occurs due to the environment being contaminated by FMDV. In addition, transmission can also occur through contact with contaminated farm materials or tools such as officers, vehicles, feed, drinking places, and farm products such as meat and milk (Pramitasari and Khofifah, 2022). The virus can survive in glandular organs, bones, and milk (Maulana et al., 2023). The virus can also stay for a long time when in favourable environmental conditions. The ideal conditions for FMDV survival are temperatures below 50°C, humidity above 55%, and neutral pH (Brown et al., 2022).

Foot mouth disease virus is found in the secretions and excretions of acutely infected animals, such as air, milk, saliva, urine, feces, semen, fluid in vesicle lesions, amniotic fluid, and fetuses resulting from abortion. The amount of virus secreted is highly variable and depends on the host species and virus strain. Animals with FMD can shed new viruses for 50 hours and transmit them to other livestock. In pigs, the virus is released through aerosols, and the animal can even remove 100 to 1000 times more virus than infected sheep or cattle (Brown et al., 2022). Therefore, the presence of these animals is essential in FMD transmission, as it increases the risk of airborne disease spread. Cattle are more susceptible to aerosolized viruses than other livestock or animals.

Meanwhile, pigs are more resistant to airborne FMD infection. Affected animals can act as carriers and survive for 8-24 months. In addition to the transmission described above, FMD can be transmitted through sexual, mechanical (vomites), and live vectors such as goats, cattle, and sheep (Pamungkas et al., 2023). High traffic of infected livestock or animals and lack of strict biosecurity practices are factors in transferring the virus from one animal to another. In addition, the purchase of breeders and cattle from outside the region, owner anxiety in selling sick cattle, and officers serving in several areas are potential factors in the spread and transmission of FMD (Wulandani, 2022). The high rate of disease spread from one region to another is generally through the movement of infected livestock, carrier animals, exposed animal products, and air (Sarsana and Merdana, 2022).

## **PATHOGENESIS AND CLINICAL SYMPTOMS**

Scientists initially considered the route of entry of FMD viruses to be through the upper gastrointestinal tract. However, as early as 1952, the susceptibility of cattle to respiratory tract inoculation was experimentally demonstrated (Arzt et al., 2011). The respiratory system is the main route of FMD virus infection. After that, the virus will multiply in the pharyngeal membrane, enter the blood (viremia) and lymphatics, and then spread and develop to organs such as around the mouth, mammary glands, and feet, causing wounds or blisters (Sarsana and Merdana, 2022). The virus can be found up to 2 years after infection in cattle and sheep. The virus can also be found in many body fluids, such as urine, semen, respiratory secretions, and milk. In the oral cavity of infected animals, the virus can survive for long periods (Azeem et al., 2020). In addition to inhalation, FMD viruses can also enter the body of susceptible animals by ingestion, skin abrasions, and mucous membranes of infected animals. After entering through the mouth, the virus will multiply and reproduce in the epithelial cells of the mouth, causing inflammation around the mouth (Wulandani, 2022).

Animals or livestock infected with FMD will show clinical symptoms such as the formation of vesicles or blisters on the mouth, gums, tongue, nipples, and skin around the hooves, hypersalivation, weight loss, and livestock production (Okti et al., 2023). Ismail et al. (2023) conducted research for the clinical examination of foot and mouth disease in dairy cows in Sukarmurni, Cilawu, Garut, West Java. The results showed that the clinical symptoms found in dairy cows that were positively infected with FMD were lameness (lesions on the feet) and hypersalivation. FMD also causes abortus in pregnant cows and myocarditis in lactating cows. In addition to these symptoms, the disease causes other clinical signs such as fever reaching 41°C, anorexia, and blisters in the mouth and feet; after 24 hours, the blisters will burst and cause erosion. This follows the results of research conducted by Wulandani (2022), which stated that symptoms appearing in FMD-infected beef cattle in Central Bangka Regency, Bangka Belitung Islands Province, such as anorexia, blister lesions on the tongue, lips, gums, and between the scrambled, and hypersalivation. The lesions are less evident in sheep and goats, but

lesions around sheep's teeth and death in young animals. In pigs, the clinical symptoms appear as blisters on the gums, tongue, cheeks, between the teeth, palate, snout, lips, coronary ring, udder nipples, nail tips and between the nails. Lesions in animals after death will be found in the rumen and myocardium, and some young animals are called tiger livers (Amiruddin et al., 2022).

## DIAGNOSIS

Accurate diagnosis of FMD is essential because it is related to efforts to control and eradicate the disease in endemic areas and as a supporting step in eradicating FMD in an area. Diagnosis of FMD is based on clinical symptoms such as high temperature, excessive salivation, and vesicle formation on the oral mucosa, nose, and feet (Wulandani, 2022). However, these clinical symptoms can be confused with other diseases, such as vascular stomatitis; therefore, laboratory diagnosis is necessary. In addition, there is no cross-protection between serotypes, and the serotype of the virus involved in the outbreak cannot be ascertained based on clinical signs. Therefore, the serotype involved in a field outbreak must be determined in the laboratory to ensure a proper control program. Various techniques have been used to diagnose the disease and confirm the serotype of the virus, such as the Virus Neutralization Test (VNT), which is the gold standard for detecting antibodies against FMDV structural proteins and is the prescribed test for import/export certification of animals/animal products. Enzyme-linked immunosorbent assay (ELISA), Virus isolation, Reverse transcription-polymerase chain reaction (RT-PCR), Reverse transcription loop-mediated isothermal amplification (RT-LAMP), Chromatographic strip test, Differentiation between infected and vaccinated animals (DIVA) (Jamal and Belsham, 2013). Longjam (2011) stated that PCR makes diagnosis faster and more precise. Multiplex PCR can detect FMDV in the highest number of samples at 65.47%, followed by sandwich ELISA (53.57%) and virus isolation (42.85%). Specimens needed to detect the virus are fluid from blisters, epithelial cells in blisters, or liquid from the oropharynx and blood. If the animal dies, lymphoglandula, thyroid, kidney, spleen, and liver tissue can be taken. Specimens to be tested are expected to be stored properly so that laboratory tests follow the condition of the animal being tested (Rohma et al., 2023).

## PREVENTION AND CONTROL

FMD is not a zoonotic disease, but even so, it can cause significant economic losses, so efforts need to be made to prevent and control the disease. Some of the measures that can be made to prevent and control FMD are implementing strict biosecurity such as protection of free zones by restricting the movement of livestock or animals, traffic control and surveillance, banning the entry of livestock from infected areas, slaughtering infected animals or those that act as carriers, disinfecting all exposed cage equipment (vehicles, clothes, cage equipment, etc.), destruction of carcasses and animal products in infected areas, isolation and quarantine of livestock (Dinas Ketahanan Pertanian dan Ketahanan Pangan Provinsi Bali, 2023; Rohma et al., 2022). In addition, prevention and control can also be done by vaccination. However, it is difficult to do because several serotypes of viruses cause FMD, many host species, and extreme transmission rates (Paton et al., 2009). Meanwhile, according to Rohma et al. (2022), vaccination effectively eradicates FMD in cattle. FMD vaccination can only be carried out on healthy cattle and cattle from 2 weeks old, which aims to induce immunity to FMD disease (Yuliana et al., 2023).

## CONCLUSION

Foot and Mouth Disease (FMD) is caused by the foot-mouth disease virus (FMDV), which belongs to the genus Aphthovirus and family Picornaviridae. The disease affects even-toed or cloven-hoofed farm animals, both wild and domesticated. FMD viruses are highly contagious, entering the animal directly through the mouth or nose and replicating on epithelial cells in the nasopharyngeal area, then entering the blood (viremia), then multiplying on lymphoglandular glands and epithelial cells in the mouth and paw prints, resulting in vesicle lesions and blistering. Animals or livestock infected with FMD will show clinical symptoms such as fever up to 41°C, the formation of vesicles or blisters on the mouth, gums, tongue, nipples, and skin around the hooves, hypersalivation, weight loss, and livestock production. Handling and controlling FMD in livestock or animals can be done by isolating and quarantining sick animals, vaccination programs, biosecurity measures in animal husbandry, monitoring livestock traffic, and conducting surveillance.

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