



# Epidemiology and Diagnostic Methods of Foot-and-Mouth Disease: A Review

Betelihem Yirdaw<sup>1</sup>, Dessie Abera<sup>2, \*</sup>

<sup>1</sup>Assosa Agricultural Research Center, Ethiopian Institute of Agricultural Research, Assosa, Ethiopia

<sup>2</sup>Debre Markos Agricultural Research Center, Ethiopian Institute of Agricultural Research, Debre Markos, Ethiopia

## Email address:

vet07@yahoo.com (Dessie Abera)

\*Corresponding author

## To cite this article:

Betelihem Yirdaw, Dessie Abera. Epidemiology and Diagnostic Methods of Foot-and-Mouth Disease: A Review. *International Journal of Biomedical Engineering and Clinical Science*. Vol. 9, No. 3, 2023, pp. 38-46. doi: 10.11648/j.ijbecs.20230903.12

**Received:** April 24, 2023; **Accepted:** July 5, 2023; **Published:** July 13, 2023

**Abstract:** Foot-and-mouth disease (FMD) is a viral disease that primarily affects animals with cloven hooves. It is a highly contagious disease and difficult to control due to its complex epidemiological nature and poor diagnostic facilities. Thus, this paper aimed to review the epidemiology of FMD, and its economic impact on farmers, discuss the available diagnostic, and prevention and control methods that can be practiced. Foot-and-mouth disease virus (FMDV) is the causative agent of FMD, and it is a single-stranded RNA virus with a positive sense that belongs to the genus Aphthovirus and the family Picornaviridae. The virus has seven serologically and genetically distinct serotypes, namely O, A, C, Asia1, SAT1, SAT2, and SAT3, as well as over 60 subtypes. The virus is inactivated by heat, UV radiation, pH levels below 6.5 or above 9, gamma irradiation, chemicals, and disinfectants, but it is almost indefinitely stable at temperatures below freezing point. The tongue, dental pad, gums, cheek, hard and soft palates, lips, nostrils, muzzle, interdigital space (between the hooves), and a coronary band of affected animals develop vesicular lesions. Viruses can be spread orally or via the respiratory tract. FMD is diagnosed based on clinical signs, and using epidemiological methods and laboratory techniques. FMD causes severe economic losses as a result of high morbidity associated with outbreak occurrences, limiting the introduction of improved production technologies in the area, restrictions on international trade, and costs associated with the application of control measures. Some of the control and prevention methods for FMD are vaccination, animal movement control, physical separation from wildlife, and symptomatic treatment. But due to its complex epidemiological nature, limited diagnostic capabilities, and no cross-immunity between strains, FMD was difficult to control. Therefore, awareness creation among animal owners about the disease, and possible prevention and control methods that can be practiced is required. And also, research in the development of a multivalent and protective vaccine is recommended.

**Keywords:** Diagnosis, Epidemiology, Foot-and-Mouth Disease

## 1. Introduction

Foot-and-mouth disease (FMD) is a transboundary disease of animals. It is a highly contagious viral infectious disease that affects both wild and domestic cloven-hoofed animal species. It causes weight loss, decreased milk production, and growth delays in susceptible animals [1, 2]. FMDV is the causative agent of FMD disease. It is a positive-sense single-stranded RNA virus of the genus Aphthovirus in the Picornaviridae family [3]. FMDV virus (FMDV) is classified into seven serotypes: O, A, C, SAT 1, SAT 2, SAT 3, and

Asia 1, as well as numerous subtypes based on the antigenicity of the capsid coating proteins [4, 5]. FMD is found all over the world and is classified by the World Health Organization as a notifiable disease. FMDV serotypes are not evenly distributed throughout the world. In most parts of the world, serotype O is the most common [6].

Affected animals develop vesicular lesions of the tongue, dental pad, gums, cheek, hard and soft palates, lips, nostrils, muzzle, interdigital space (between the hooves), and the coronary band. In ruminants, vesicular lesions were also observed on the udder and teats. Vesicular formation of the tongue epithelium causes the animals to salivate excessively,

and erosion between the hooves causes them to become lame [7]. The virus can be transmitted directly by coming into contact with an infected host or indirectly by coming into contact with a contaminated environment. In addition, it can also be transmitted orally or through the respiratory tract to a new susceptible animal. The most common method of spreading within a herd is aerosol transmission [8].

Samples of affected tissues or esophageal-pharyngeal fluid are used to diagnose the disease. The enzyme-linked immunosorbent assay (ELISA), complement fixation, virus neutralization, and polymerase chain reaction are some of the laboratory methods that can be used to confirm the disease [7]. A definitive diagnosis is a prerequisite for the control and prevention of FMD. Diseases with similar clinical signs and species with mild or indistinct disease presentations can make FMD diagnosis difficult [9].

Control and prevention methods for FMD in endemic countries are symptomatic treatment and vaccination [10]. However, it is difficult to control the disease due to its highly contagious nature, multiple hosts, and multiple antigenic types, or subtypes with no cross-protection between strains. So, due to antigenic differences between the strains, there are no effective vaccination control methods available. And also, the presence of free animal movement, a high rate of contact among animals at the markets, communal grazing areas and watering points, poor diagnostic facilities, poor surveillance, and limited government prevention and control strategies have all been linked to the high incidence of FMD [11, 12]. And also, the distribution and severity of the disease are complicated due to a variety of factors, such as virus properties, a large number of susceptible hosts, ecology, and environment. FMDV multiplication and spread are also affected by host species, nutritional and immunological status, population density, and interactions between domestic and wild host species [13].

The variety of species involved, the disease's rapid spread, and the difficulty in controlling outbreaks caused FMD to be the most economically devastating livestock disease [7]. It causes enormous losses in the animal industry due to the costs of control or eradication measures such as mass vaccination or herd destruction, as well as reductions in milk and beef production due to clinical disease [10]. Understanding FMD epidemiology is useful in defining strains, identifying transmission events, and characterizing biodiversity for performing effective quarantine measures against reintroduction, developing specific diagnostic tests, and producing effective protective vaccines [14]. Therefore, the objectives of this review were to develop a common understanding of the epidemiology of Foot-and-mouth disease and its economic impact on livestock farmers, to discuss the available diagnosis techniques, and prevention and control methods of the disease.

## 2. Etiology and Taxonomy of the FMD Virus

Foot-and-mouth disease is also known as aphthous fever,

epizootic aphthae, Infectious aphthous stomatitis, and Aftosa in Italian and Spanish, fever aphtheuse in French, and Maul and Klavenseuch in German [1, 12]. It was first identified in 1546 during an outbreak near Verona, Italy, and in 1780 in South Africa. The disease posed a significant threat to the cattle industry in previous centuries, but it was not widely known until the end of the 19<sup>th</sup> century. Detailed information about FMDV was gained in the twentieth century, including its genetic and physical structure, which has a three-dimensional structure when observed by X-ray crystallography [15]. In 1897, two scientists, Löffler and Frosch, identified FMDV as a filterable viral causative agent of animal disease [16]. Then it was first identified in 1963 by the International Committee on Virus Taxonomy. It belongs to the Aphthovirus genus in the Picornaviridae family. Picornaviridae is derived from the Latin words 'Pico' meaning small, and 'rna' meaning RNA (ribonucleic acid), which refers to the virus's size and genome type. The genus name 'Aphthovirus' refers to the vesicular lesions produced in the animals' feet and mouths [17].

The FMD viral particle or virion is made up of a non-enveloped icosahedral protein coat (capsid) and genetic material [12, 17, 18]. The external part of the virus (capsid) consists of 60 capsomers, each consisting of four structural polypeptides [19]. The FMDV genome has a very low molecular weight ranging from 7.2 to 8.4 kb of single-stranded positive-sense RNA, and whole virus particles have a sedimentation coefficient of 146S [13].

The virus can be inactivated when exposed to pH levels below 6.5 or above 9. However, it can survive in milk and milk products with a pH of 4.6. Its capsid is composed of polypeptides but lacks lipoprotein, making it resistant to lipid solvents [19]. The virus could be easily inactivated by heat, UV and gamma irradiation, chemicals, and disinfectants, but it is stable almost indefinitely at a temperature below the freezing point. The virus may persist for days or weeks in organic matter under moist and cold conditions. It can survive in frozen bone marrow, lymph nodes, and even in cheese during its processing. The virus in milk and meat can be inactivated by heating at 70°C for at least 30 min [20].

Molecular epidemiology is a relatively new science that aids in the taxonomic classification of FMDV. It is also an important tool for understanding FMDV dynamics and for determining the new topotype and origin of new FMDV lineages [21]. So, there are seven serologically and genetically distinct types of the virus, namely O, A, C, Asia1, SAT1, SAT2, and SAT3, with over 60 subtypes. Because the viral RNA-dependent RNA polymerase is incapable of proofreading, FMDV has a high mutation rate. There is no cross-immunity between strains [13, 22]. Although clinical signs are indistinguishable between serotypes, the immunological response is distinct due to differences in antigenic structure between serotypes [23]. The serotype is further classified as a topotype, which expresses the geographic, antigenic, and genetic relationships between the serotypes [24]. It is more concerned with comparing genetic and phenotypic differences in the capsid protein part. The

virus's capsid protein, particularly the VP1 region, is the most important part of the virus for studying its molecular epidemiology [25].

### 3. Epidemiology and Risk Factors for the Occurrence of FMD

#### 3.1. Epidemiology of the Disease

The virus is prevalent all over the world, with the seven heterogeneous serotypes A, O, C, SAT1, SAT2, SAT3, and Asia1, particularly in Asia, Africa, and the Middle East. However, Japan, New Zealand, Australia, and some other countries are FMD-free countries. Among the seven serotypes of FMDV, serotype O is broadly distributed in the world, while serotype C has low reports, with the last report in 2005 in Kenya [19, 26]. Generally, more than 100 countries are still affected by FMD globally, and it is believed that the disease is still found in about two-thirds of the world [16, 27].

#### 3.2. Risk Factors for the Occurrence of FMD

The most common causes for the occurrence of FMDV are host, pathogen, and environment-related factors. The common factors identified in Ethiopia for FMDV spread are the production system, geographic location, age of animals, contact with wildlife, and season of the year [28]. Some of the host-related risk factors are breed, age, immunity status, nutritional status, population density, animal species, animal movements, and contacts between different domestic and wild host species [29].

FMDV affects animals classified as the suborder ruminant and the family Suidae of the order Artiodactyla [6]. FMD is an infectious epitheliotropic disease that affects up to 70 species of cloven-hoofed mammals, including cattle, sheep, goats, pigs, and artiodactyl wild ruminants [30]. But it does not affect humans, horses, pets, or birds. FMD may be able to survive in the human respiratory tract for 24 hours, allowing people who have had very close contact with infected animals to potentially serve as a source of virus exposure for susceptible animals, implying that humans may mechanically transfer the disease to other animals. Bactrian camels can be infected experimentally, but dromedary camels can be infected both naturally and experimentally [16]. Small ruminants may be naturally infected but do not show clinical signs, whereas cattle do show clinical signs and are considered indicator hosts. It occurs less frequently and for a shorter period in small ruminants than in cattle and is regarded as a maintenance host. Pigs are highly susceptible to FMDV and are regarded as disease amplifier hosts because they emit high levels of the air-borne virus but are relatively resistant to infection via the air-borne route [31]. Sheep excrete air-borne viruses at comparable levels to cattle but are thought to be less susceptible to air-borne infection due to their smaller respiration volumes. Deer and buffaloes can also be infected in sufficient numbers [23].

The FMD virus has also been shown to persist in lymph nodes and oropharyngeal fluid in a non-replicative form. In carrier animals, the virus remains in the oropharynx for more than 28 days after infection. Pigs do not become carriers but in cattle, the carrier state usually lasts for about 6 months. Individual African buffalo have been shown to harbor the virus for at least 5 years, but within a herd, it can survive for 24 years or longer. Sheep and goats typically do not carry FMD viruses for more than a few months. The age of the animal is also a factor in the occurrence of death in animals. FMDV rarely causes death in adult animals, but the virus can cause severe myocardial damage in calves and piglets, resulting in high mortality rates for young animals [13]. Physical characteristics of the virus, such as variations in its virulence factor, virus infection dose, antigenic variability, particle stability in different microenvironments, chances of long-term persistence, and host-specific properties of the virus, are examples of pathogenic factors. FMDV is classified as seven immunologically distinct diseases, owing to the seven recognized serotypes that are currently circulating globally; immunity developed by animals to one FMDV serotype does not protect them from other serotypes [18].

Seasonal and environmental factors act as geographical barriers to virus spread and promote spread when suitable atmospheric conditions exist. The agent is also widely distributed across different agro-climatic and socioeconomic factors. Mixed animal husbandry practices, unrestricted animal movement and trade, and porous international borders provide a conducive epidemiology niche for the FMDV to flourish, mutate, and persist over time, affecting the susceptible animal population [13]. The number of outbreaks increased after the monsoons and remained high throughout the winter. FMD was found to be more prevalent during the dry season than during the cold, dry season. During the rainy season, the incidence was the lowest. Furthermore, herd contact with wild animals was greater during the dry season than during the rainy season [32]. Heavy rain, high relative humidity (60%), extremely hot weather, and moist winds during the rainy season may inhibit the aerosol transmission of Foot-and-mouth disease [33]. FMD diseases are more prevalent in the winter because of favourable climatic conditions such as dry weather and dry winds, low temperatures (weak sunlight), movement of animals, and moderate humidity [31].

### 4. Sources of Infection and Transmission

Before clinical manifestations of the diseases, affected animals shed the virus in all body secretions and excretions, including air, saliva, nasal and lachrymal fluid, milk, urine, faeces, semen, and blood. The availability of the virus before the onset of clinical signs of the disease increases the possibility of virus transmission within the farm and from farm to farm. Infected animals can transmit the virus for days before symptoms appear, and some animals can excrete the virus for years after re-infection [16]. A small number of infective particles can infect a susceptible animal. The main

route of ruminant infection is the inhalation of the airborne virus, which can be spread over long distances depending on wind speed and direction. The virus's structure is so simple that facilitated its transmission through the air. Ingestion of contaminated food, direct inoculation of susceptible animals, and infection of skin lesions are other possible modes of infection. Virus transmission is generally accomplished through direct contact, airborne and via fomites, or mechanically (contaminated animal products, non-susceptible animals, agricultural tools, people, and vehicles) or indirectly through contaminated organic debris, fomites, personnel, and materials [29].

## 5. Pathogenesis

The virus enters the body via inhalation, skin abrasion, or mucous membrane abrasion. The respiratory tract is the virus's primary replication site. The virus prefers epithelial tissue in adults and heart muscle in young. Following primary multiplicity in the host's pharynx and mucous membrane, the virus affects lymphatic glands, epithelial tissues around the mouth or feet, and mammary glands via the lymphatic system and bloodstream. The virus spreads throughout the body after a 3 to 5-day period of febrile viremia, resulting in a secondary infection [20]. FMDV RNA replicates within the cytoplasm of infected cells and requires the virus-encoded RNA-dependent RNA polymerase to do so. This enzyme catalyzes the synthesis of a negative-strand copy of the viral genome, which is then used as a template for the production of new positive-strand RNA molecules [12].

The virus attacks the pituitary gland, which regulates the body's metabolic functions. Panting, restlessness, reduced breeding capacity, and weakness are all symptoms of gland failure in draught animals. FMDV infection of the udders and teats can cause mastitis, which results in permanent teat loss and reduced milk yield [31]. The viral structural and nonstructural protein elements of the viral RNA, as well as host proteins or membranes that participate in the viral replication cycle, can be considered virulence factors that aid in FMD transmission [34]. Poly "C" tracts comprising over 90% "C" residues cause virulence. The length of this tract is extremely variable. There are some pieces of evidence that the length of this tract is associated with virulence and hence persistence [13].

## 6. Clinical Signs and Differential Diagnosis of FMD

The clinical signs of diseases are used to determine a tentative diagnosis of diseases. Studying differential diagnosis is important to differentiate diseases with similar clinical observations. Clinical signs of FMD can vary from mild to severe, and there is species variation [23]. In natural conditions, the incubation period varies depending on the virus strain, the susceptibility of the individual host, the exposure dose, and the route of entry. It can last anywhere

from 2 days to 14 days in most cases. Signs are mostly seen in cattle because the bovine species is an indicator host. Vesicular lesions on the teats or mammary glands in females, interdigital space of feet, and other hairless parts of the skin, pyrexia, shivering, and drooling are the main signs of FMDV [16]. Even if the animal shows no clinical signs, the virus remains in the esophageal-pharyngeal region for more than 28 days after infection [22].

Differential diagnosis is required to distinguish diseases with similar clinical signs. Diseases such as bovine mucosal disease, rinderpest, peste des petits ruminants, malignant catarrhal fever, blue tongue, epizootic hemorrhagic disease, vesicular stomatitis, and swine vesicular disease have clinical signs that are similar to FMD. Laboratory diagnosis is critical for distinguishing between these diseases [16, 23].

## 7. Diagnosis Techniques of Foot-and-Mouth Disease

A timely and accurate diagnosis of FMD is critical for controlling the disease by treating patients and preventing it from spreading further. In susceptible animals, it is diagnosed using clinical signs, epidemiological methods, and laboratory techniques. A physical examination cannot determine whether a disease is 100% FMD-positive or not due to the presence of diseases with similar clinical signs [35].

### 7.1. Clinical Diagnosis

Clinical examination is an important type of diagnosis that can either provide a preliminary diagnosis or lead to a laboratory diagnosis. The disease is diagnosed based on its clinical manifestations. The FMD examination includes measuring body temperature, auscultation, vision, palpation to determine whether there are vesicles on the oral mucosa and non-haired parts of the body, looking at inter-digital spaces (laminae), and determining whether or not salivation is present. Other methods of diagnosis include postmortem findings such as rumen mucous membrane erosions and oropharyngeal lesions from deceased animals [36].

### 7.2. Epidemiological Diagnosis

Epidemiological type of diagnosis is expressed by the risks of introducing live animals and animal products from infected areas, the history of animals, the farming system, the cross-border movement of animals, the geographical area, the season of the year, and herd size. However, clinical signs can be confused with those of other diseases with similar clinical findings, and epidemiological observation may not always provide an accurate perception, so other methods of diagnosis are necessary for disease screening [37].

### 7.3. Laboratory Diagnosis

The majority of FMD diagnoses are made in the clinic based on clinical signs, but laboratory testing is also very important, especially to distinguish FMDV from other

vesicular diseases due to having similar clinical signs. Samples like vesicular fluids, epithelial samples, oropharyngeal fluid, throat swabs, blood, sperm, serum, milk, and environmental samples (air samples) can all be used for laboratory diagnosis. The most preferred sample type is epithelial tissue samples [23]. The virus can be detected using a variety of methods, including the complement fixation test (CFT), virus isolation (primary cell culture), enzyme-linked immunosorbent assay (ELISA), reverse transcription-polymerase chain reaction (RT-PCR), real-time polymerase chain reaction, and multiplex polymerase chain reaction (mPCR) [13].

Virus isolation (culture), immunological (serological), and antigen detection methods are the three broad categories of diagnostic methods [10]. Virus isolation and characterization are the "gold standard" for diagnosing viral diseases. Virus isolation is the only sure way to diagnose FMD. The presence of infectious viruses is required for virus isolation, but sample quality determines the reliability of the results [12]. The cultures were examined for viral cytopathic effects (CPE) [10]. The cell culture method is extremely sensitive, but it is time-consuming, taking between 1 and 4 days and necessitating extraordinary laboratory facilities. FMDV is cultured in bovine thyroid cells, primary lamb kidney (LK) cells, and baby hamster kidney (BHK-21). Bovine thyroid cells are extremely sensitive to FMDV, but BHK-21 is preferable for refrigerator preservation. CPE cultures were stored at  $-70^{\circ}\text{C}$  until the next procedure [36].

PCR is one of the most recent and widely used nucleic-acid-based diagnostic techniques for amplifying and detecting FMDV genome fragments in genome-based methods. Specific primers are used in diagnostic tools to detect serotypes. For FMD diagnosis, amplification of RT-PCR followed by nucleotide sequencing is a more reliable method [25, 38]. Depending on the magnification of the VP1

gene 43, conventional RT-PCR techniques can identify serotypes. Because of its improved speed and sensitivity, real-time PCR has gained widespread acceptance [13].

The most common immunological diagnostic methods include ELISA, complete fixation tests, and viral neutralization tests. ELISA has been used as a diagnostic method for many infectious diseases, including FMD, since 1975 [39]. ELISA and its various modifications were used with high specificity and sensitivity for FMDV detection, typing, quantification, and strain differentiation. It is the preferred method for detecting FMD viral antigen and identifying viral serotypes within 3-4 hours of receiving the sample at the laboratory. ELISA is a more sensitive serological test than CFT, but it has been criticized for its specificity [13]. Different types of ELISA (direct, indirect, competitive, sandwich, and liquid phase blocking ELISA) and DIVA (discrimination vaccination and animal infection assay) tests are used for serological diagnosis. DIVA is a test for antibodies to FMDV non-structural proteins (NSPs), which detects antibodies to FMDV NSPs. Antibodies against the 3ABC non-structural polypeptides of the FMD virus in the serum are important for distinguishing sera positive for the vaccine or infection. This assay can detect antibodies 3ABC from 10-900 days after infection in experimentally infected cattle [40]. Virus neutralization tests are the gold standard for detecting antibodies. It was once one of the most widely used serological techniques. It takes time and has varying sensitivity when used in the certification trade of animals and animal products [36]. Serological tests (virus neutralization and liquid-phase enzyme-linked immunosorbent assay) are not time-consuming, but they are indirect tests that do not always distinguish between infected and vaccinated animals. So they are not the first choice for detecting acute infections [10]. Table 1 shows the details of the major FMD diagnostic methods used.

**Table 1.** Diagnostic test values, advantages, and disadvantages of common laboratory diagnostic methods.

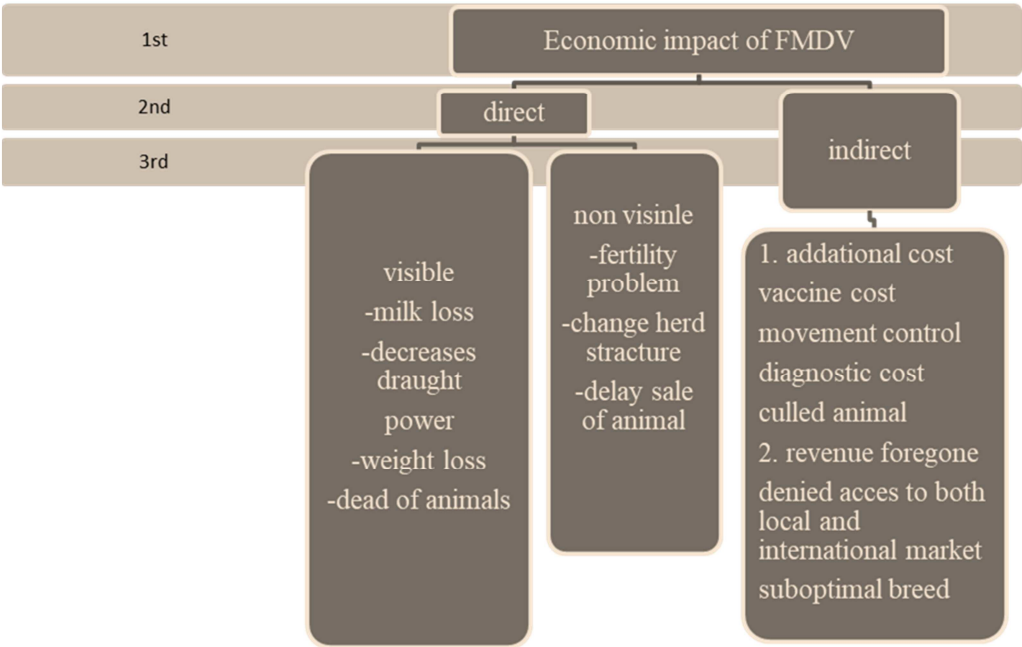
FMD diagnostic assay	Sensitivity	Specificity	Advantage	Disadvantage
Sandwiched ELISA (Enzyme-Linked Immuno servant Assay)	80%	100%	Easy to perform, suitable for handling a large number of samples	Less sensitive and not suitable for certain clinical samples
Multiplex PCR (Polymerase Chain Reaction)	Minimum detection limit of $1 \times 10^{-1}$ TCID <sub>50</sub> mL <sup>-1</sup>	100% specific for cross-serotype detection	Rapid and sensitive, suitable for samples like semen and milk	High risk of generating false positives
TaqMan RT PCR (Real-Time Polymerase Chain Reaction)	Minimum detection limit of $10^{-1}$ TCID <sub>50</sub> mL <sup>-1</sup>	100% specific for cross-serotype detection	More sensitive and specific than gel-based assay	High risk of generating false positives
Virus isolation and neutralization			Gold standard assay for FMD for Diagnosis	Slow takes 1-4 days for confirmatory results Require
3AB3 I ELISA (Indirect Enzyme Linked Immuno servant Assay)	95.8%	97.45%	Sensitive and specific respectively	Only for Bovine specious
3AB-C ELISA(Competitive Enzyme Linked Immuno servant Assay)	91.7%	(96-98)%	Specific assay Universal for all species	Less sensitive than I ELISA

Source: [36, 41, 42].

## 8. Economic Impact of Foot-and-Mouth Disease

FMD is regarded as the most important livestock disease in the world in terms of its economic impact. The majority of the world's countries are currently affected, including Africa, Asia, South America, and parts of Europe, but the consequences are not uniform. The effects differ between endemic and non-endemic countries, developed and developing countries, and even within developing countries [29]. Even though FMD has a low mortality rate of less than 5%, it is considered one of the most economically important livestock diseases in the world because it reduces livestock productivity. Severe economic losses occurred as a result of high morbidity associated with outbreak frequency, large numbers of animals affected in each outbreak, and export

trade restrictions imposed on affected countries [43]. The disease has both direct and indirect economic consequences; primarily, it limits the trade of animals and animal products internationally, as well as the costs related to disease outbreak control. Indirect losses are those related to the significant costs of FMD control methods, the limited use of improved production technologies, and poor access to international markets, which are often less visible than the obvious effects of clinical disease but may be equal to or more important in their overall economic impact [5, 29, 44]. Additional costs include the application of control measures such as quarantines, slaughter, compensation, and vaccination, as well as conducting scientific surveillance after an outbreak to confirm the disease [14]. FMD has the following general consequences, as shown in Figure 1 below, which depicts the impact of the disease on production and productivity in both developed and developing countries.



Source: [20].

**Figure 1.** Generalized economic consequences of FMD.

## 9. Control and Prevention Methods

Disease control and prevention methods are used to reduce the further spread of disease in animals [23]. Those practices should always be rational and logical in veterinary science. Controlling strategies may differ between countries depending on the disease's status as well as each country's financial and technical capabilities [45]. Controlling virus transmission entails reducing an animal's risk of virus exposure as well as its susceptibility, either through vaccination or by limiting animal movement. Because of socioeconomic factors, cost-effective management is always considered in veterinary science [43, 46].

FMD is difficult to control due to its highly contagious

nature, multiple hosts, viral stability, multiple antigenic types or subtypes, and short-term immunity, as well as the FMD virus's exceptional genetic and antigenic complexity. Because one serotype of FMDV does not cross-protect against other serotypes, even within a single serotype, vaccination against one strain may not cross-protect against other strains, and due to antigenic differences between the strains, there are no effective vaccination control methods available. In general, there has never been an official FMD control plan in Ethiopia, except for vaccination in some market-oriented dairy farms and ring vaccination in urban and peri-urban areas during disease outbreaks [11].

In both epidemically affected countries and disease-free zones, disease control is commonly accomplished through the use of an equipped laboratory, rapid and accurate diagnostics,

rapid response measures, continuous monitoring or surveillance, vaccination (mass and compulsory vaccination), quarantine, restriction of animal movement, isolation of infected animals, and implementing a stamping out policy. However, due to economic, social, and regional barriers, the test and slaughter policy should not be implemented in Ethiopia but rather in developed countries (Leon, 2012). Furthermore, for effective control of the disease, good infrastructure, trained veterinary staff, and good governance are required [11]. However, in endemic countries, FMD control and prevention rely primarily on repeated vaccination, good infrastructure, trained veterinary staff, and good governance, as well as animal movement control and physical separation of wildlife and livestock [23]. Vaccination is the most widely used disease prevention method in both endemic and disease-free regions of the world. Vaccination can be classified into many types based on preparation: conventional vaccine; protein vaccine, protein fragments, and viral subunits vaccine; peptide vaccine; genetically engineered attenuated strain vaccine; and DNA vaccine [47]. There are two types of vaccinations based on their application: emergency FMD vaccine and protective vaccination. Emergency FMD vaccines are used to provide protective immunity to susceptible stocks as soon as possible and to reduce virus release or limit disease spread. The protective vaccination is effective in animals that have not previously been exposed to the FMD virus. It would thus be used outside the 3 km protection zone, and a form of ring vaccination would be used [15].

The majority of viral diseases, including FMD, have no cure. Depending on the clinical presentation of the disease, symptomatic treatment rather than specific treatment may be used. Treatments include potassium permanganate-mixed antiseptic mouthwash, sodium carbonate, boric acid, and glycerin, which can be applied over the lesions. Foot lesions are treated by washing the affected animals' feet with a solution of washing soda and 2% copper sulfate, and a topical application of honey or finger millet has traditionally been found to be effective. Proper animal husbandry practices, secondary bacterial infection treatment, and dressing of inflamed areas to prevent secondary infection are all recommended, especially in endemic countries where the slaughter policy is not followed [48].

## 10. Conclusion and Recommendations

Foot-and-mouth disease is still a significant disease that is highly contagious, genetically and antigenically diverse, and it is infectious in a wide range of livestock species. The diseases are capable of establishing subclinically infected carriers in some species and are widely distributed geographically. FMDV is classified into seven serotypes: O, A, C, SAT 1, SAT 2, SAT 3, and Asia 1, as well as numerous subtypes based on the antigenicity of the capsid-coating proteins. Due to its complex epidemiological nature and limited diagnostic capabilities, FMD was difficult to control in the country. The epidemiology of FMD is complicated by several factors, including virus properties, a large number of

susceptible hosts, ecology, and the environment. FMDV diagnosis and surveillance have been carried out through different antigen and antibody detection methods. But it is inconvenient and costly for disease surveillance in disease-endemic and emerging nations. Because of the high morbidity effect of a disease, restrictions on international trade in animals and animal products, and the costs associated with disease outbreak control, the disease causes a severe economic loss. Therefore, research in the development of a multivalent and protective vaccine trial and epidemiological distribution of FMD should be conducted, awareness-building among animal owners about the disease, and available prevention and control methods are required.

## References

- [1] Admassu, B., Getnet, K., Shite, A. and Mohammed, S., 2015. Review on foot and mouth disease: distribution and economic significance. *Academic Journal of Animal Diseases*. 4 (3): 160-169. DOI: 10.5829/idosi.ajad.2015.4.3.95165.
- [2] Park, M. E., Lee, S. Y., Kim, R. H., Ko, M. K., Park, J. N., Lee, K. N., Kim, S. M., Choi, J. H., You, S. H., Kim, B. and Lee, J. S., 2016. Altered adjuvant of foot-and-mouth disease vaccine improves immune response and protection from virus challenge. *Trials in Vaccinology*, 5 (1): 97-104. <http://dx.doi.org/10.1016/j.trivac.2016.04.006>.
- [3] Woldemariam, F. T., De Vleeschauwer, A., Hundessa, N., Muluneh, A., Gizaw, D., Tinel, S., De Clercq, K., Lefebvre, D. and Paeshuyse, J., 2021. Risk Factor Assessment, Sero-Prevalence, and Genotyping of the Virus That Causes Foot-and-Mouth Disease on Commercial Farms in Ethiopia from October 2018 to February 2020. *Agriculture*, 12 (1): 1-49. DOI: 10.3390/agriculture12010049.
- [4] OIE, P. B., 2009. NB: Version adapted by the World Assembly of Delegates of the Office International des epizooties. Paris, France.
- [5] Tadesse, B., Tesfahun, A., Molla, W., Demisse, E. and Jemberu, W. T. (2020): Foot and mouth disease outbreak investigation and estimation of its economic impact in selected districts in northwest Ethiopia. *Veterinary Medicine and Science*, 6 (1): 122-132. DOI: 10.1002/vms3.208.
- [6] Aman, E., Molla, W., Gebregeezabher, Z. and Jemberu, W. T. (2020): Spatial and temporal distribution of foot and mouth disease outbreaks in Amhara region of Ethiopia in the period 1999 to 2016. *BMC Veterinary Research*, 16 (1): 1-8. <https://doi.org/10.1186/s12917-020-02411-6>.
- [7] Greger, M. 2007. The long haul: risks associated with livestock transport. *Biosecurity and bioterrorism: biodefense strategy, practice, and science*, 5 (4): 301-312.
- [8] Tadesse, B., Molla, W., Mengistu, A. and Jemberu, W. T. (2019): Transmission dynamics of foot and mouth disease in selected outbreak areas of northwest Ethiopia. *Epidemiology & Infection*, 147: e189. DOI: 10.1017/S0950268819000803.
- [9] Hindson, B. J., Reid, S. M., Baker, B. R., Ebert, K., Ferris, N. P., Tammero, L. F. B., Lenhoff, R. J., Naraghi-Arani, P., Vitalis, E. A., Slezak, T. R. and Hullinger, P. J., 2008: Diagnostic evaluation of multiplexed reverse transcription-PCR microsphere array assay for detection of foot-and-mouth and look-alike disease viruses. *Journal of Clinical Microbiology*, 46 (3), pp. 1081-1089.



- [10] Paixão, T. A., Neta, A. V. C., Paiva, N., Reis, J. R., Barbosa, M. S., Serra, C. V., Silva, R. R., Beckham, T. R., Martin, B. M., Clarke, N. P. and Adams, L. G. (2008): Diagnosis of foot-and-mouth disease by real-time reverse transcription polymerase chain reaction under field conditions in Brazil. *BMC Veterinary Research*, 4 (53): 1-6. DOI: 10.1186/1746-6148-4-53.
- [11] Jemberu, W. T. (2016): Bioeconomic modeling of foot and mouth disease and its control in Ethiopia. PhD thesis, Wageningen University, Wageningen.
- [12] Shimels, T. Y. (2019): Antigen detection and molecular characterization of foot and mouth disease virus from outbreak cases in Ethiopia. MVSc thesis, College of Veterinary Medicine and Agriculture, Addis Ababa University, Ethiopia.
- [13] Longjam, N., Deb, R., Sarmah, A. K., Tayo, T., Awachat, V. B. and Saxena, V. K. (2011): A brief review on diagnosis of foot-and-mouth disease of livestock: conventional to molecular tools. *Veterinary Medicine International*, 2011: 232, 1-17. DOI: 10.4061/2011/905768.
- [14] Menda, S., Jenberie, S., Negussie, H., Ayelet, G. and Amasalu, K. (2014): Molecular epidemiology of foot and mouth disease Virus Outbreaks in Ethiopia in 2011/2012. *Academic Journal of Animal Diseases*, 3 (2): 8-16. DOI: 10.5829/idosi.ajad.2014.3.2.85169.
- [15] Mahy, B. W. (2005): Introduction and history of foot-and-mouth disease virus. *Curr. Top. Microbiol. Immunol.*, 288: 1-8. DOI: 10.1007/3-540-27109-0\_1.
- [16] Chakraborty, S., Kumar, N., Dhama, K., Verma, A. K., Tiwari, R., Kumar, A., Kapoor, S. and Singh, S. V. (2014): Foot-and-mouth disease, an economically important disease of animals. *Adv. Anim. Vet. Sci*, 2 (2): 1-18.
- [17] Mishamo, S. I. (2016): Isolation, Molecular Characterization and Sero-prevalence study of foot-and-mouth disease virus circulating in central Ethiopia. MVSc thesis, College of Veterinary Medicine and Agriculture, Addis Ababa University, Ethiopia.
- [18] Wubshet, A. K., Dai, J., Li, Q. and Zhang, J. (2019): Review on outbreak dynamics, the endemic serotypes, and diversified topotypic profiles of foot and mouth disease virus isolates in Ethiopia from 2008 to 2018. *Viruses*, 11 (11): 1-17. <https://doi.org/10.3390/v11111076>.
- [19] Wondwossen T. (2017): Isolation, molecular characterization and vaccine matching of foot-and-mouth disease virus circulating in central Ethiopia. MVSc thesis, College of Veterinary Medicine and Agriculture, Addis Ababa University, Ethiopia.
- [20] Tesfaye, J. (2019): Review on the Epidemiology and Economic Impact of Foot and Mouth Disease in Ethiopia. *Agricultural Journal*, 14 (5): 79-93. DOI: 10.36478/aj.2019.79.93.
- [21] Klein, J. (2009): Understanding the molecular epidemiology of foot-and-mouth-disease virus. *Infection, Genetics and Evolution*, 9 (2): 153-161. DOI: 10.1016/j.meegid.2008.11.005.
- [22] Wernery, U. and Kinne, J. (2012): Foot and mouth disease and similar virus infections in camelids: a review. *Rev. Sci. Tech.*, 31 (3): 907-918. DOI: 10.20506/rst.31.3.2160.
- [23] Leon, E. A. (2012): Foot-and-Mouth Disease in pigs: current epidemiological situation and control methods. *Transboundary and emerging diseases*, 59: 36-49. DOI: 10.1111/j.1865-1682.2011.01290.x.
- [24] Tesfaye, Y., Khan F. and Gelaye E. (2020): Molecular characterization of foot-and-mouth disease viruses collected from Northern and Central Ethiopia during the 2018 outbreak. *Vet. World*, 13 (3): 542-548. DOI: 10.14202/vetworld.2020.542-548.
- [25] Bayush, W. (2020): Isolation and molecular characterization of foot and mouth disease viruses in cattle from outbreaks occurred in different parts of Ethiopia. MVSc thesis, College of Veterinary Medicine and Agriculture, Addis Ababa University, Ethiopia.
- [26] Yan, H., Wang, J., Zhu, M., Miao, H., Peng, Z., Li, H. and Xin, A. (2017): Complete Genome Sequence of Foot-and-Mouth Disease Virus Serotype O Strain YNTBa from Yunnan Province of China. *Genome announcements*, 5 (22): e00393-17. DOI: 10.1128/genomeA.00393-17.
- [27] USDA (2020): The Foreign Animal Disease Preparedness and Response Plan, in: 4700, U. S. D. of A. (Ed.), Foot-and-Mouth Disease (FMD) Response Plan. Animal and Plant Health Inspection Service, United States, p3-46.
- [28] Bayissa, B., Ayelet, G., Kyule, M., Jibril, Y. and Gelaye, E. (2011): Study on seroprevalence, risk factors, and economic impact of foot-and-mouth disease in Borena pastoral and agro-pastoral system, southern Ethiopia. *Tropical Animal Health and Production*, 43 (4): 759-766. DOI: 10.1007/s11250-010-9728-6.
- [29] Souley Kouato, B., De Clercq, K., Abatih, E., Dal Pozzo, F., King, D. P., Thys, E., Marichatou, H. and Saegerman, C. (2018): Review of epidemiological risk models for foot-and-mouth disease: implications for prevention strategies with a focus on Africa. *PLoS ONE*, 13 (12): e0208296. <https://doi.org/10.1371/journal.pone.0208296>.
- [30] Al-Salihi, K. A. (2019): The epidemiology of foot-and-mouth disease outbreaks and its history in Iraq. *Veterinary World*, 12 (5): 706-712.
- [31] Verma A. K., Kumar A., Mahima and Sahzad (2012): Epidemiology and diagnosis of foot-and-mouth disease: A review. *Indian Journal of Animal Sciences*, 82 (6): 543-551.
- [32] Molla, B., Ayelet, G., Asfaw, Y., Jibril, Y. and Gelaye, E. (2013): Participatory epidemiology and associated risk factors of foot-and-mouth disease in cattle in South Omo zone, South-Western Ethiopia. *Journal of Veterinary Medicine and Animal Health*, 5 (11): 322-328.
- [33] Jamal, S. M. and Belsham, G. J. (2013): Foot-and-mouth disease: past, present and future. *Veterinary Research*, 44 (1): 1-14. <http://www.veterinaryresearch.org/content/44/1/116>
- [34] Grubman, M. J. and Baxt, B. (2004): Foot-and-mouth disease. *Clinical Microbiology Reviews*, 17 (2): 465-493. DOI: 10.1128/CMR.17.2.465-493.2004.
- [35] Sharma, G. K., Mahajan, S., Matura, R., Subramaniam, S., Ranjan, R., Biswal, J., Rout, M., Mohapatra, J. K., Dash, B. B., Sanyal, A. and Pattnaik, B. (2015): Diagnostic assays developed for the control of foot-and-mouth disease in India. *World Journal of Virology*, 4 (3): 295-302. DOI: 10.5501/wjv.v4.i3.295.



- [36] Mahmoud, M. A. E., Ghazy, A. A., Shaapan, R. M. (2019): Diagnosis and Control of Foot and Mouth Disease (FMD) in Dairy Small Ruminants; Sheep and Goats. *International Journal of Dairy Science*, 14 (1): 45–52. DOI: 10.3923/ijds.2019.45.52.
- [37] EL-Shehawy, L., Abu-Elnaga, H., Abdel Atty, Ma, Fawzy, H., A.-W. (2011): Laboratory diagnosis of FMD using real-time RT-PCR in Egypt. *Life Sci. J.*, 8: 384–387.
- [38] Tesfaye, Y. (2014): Isolation, Molecular characterization and vaccine matching of foot and mouth disease virus circulating in Ethiopia. MVS thesis, College of Veterinary Medicine and Agriculture, Addis Ababa University, Ethiopia.
- [39] Fosgate, G. T. (2009): Practical sample size calculations for surveillance and diagnostic investigations. *Journal of Veterinary Diagnostic Investigation*, 21 (1): 3-14. DOI: 10.1177/104063870902100102.
- [40] Adege, H. and Masebo M. (2017): Assessment of the Major Animal Health Problems and its Economic Impact on Beef Cattle Export Industry at Adama Quarantine Station, Central Ethiopia. *Int. J. Vet. Heal. Sci. Res.* 5: 165–170. DOI: <http://dx.doi.org/10.19070/2332-2748-1700034>.
- [41] Hosamani, M., Basagoudanavar, S. H., Selvan, R. T., Das, V., Ngangom, P., Sreenivasa, B. P., Hegde, R. and Venkataramanan, R. (2015): A multi-species indirect ELISA for detection of non-structural protein 3ABC specific antibodies to foot-and-mouth disease virus. *Archives of Virology*, 160 (4): 937-944. DOI: 10.1007/s00705-015-2339-9.
- [42] Roche, S. E., Garner, M. G., Sanson, R. L., Cook, C., Birch, C., Backer, J. A., Dube, C., Patyk, K. A., Stevenson, M. A., Yu, Z. D., and Rawdon, T. G. (2015): Evaluating vaccination strategies to control the foot-and-mouth disease: a model comparison study. *Epidemiology & Infection*, 143 (6): 1256-1275. DOI: 10.1017/S0950268814001927.
- [43] Knight, T. J. D. and Rushton, J. (2013): The economic impacts of foot and mouth disease—What are they, how big are they and where do they occur? *Preventive Veterinary Medicine*, 112 (3-4): 161-173. DOI: 10.1016/j.prevetmed.2013.07.013.
- [44] Alemayehu, G., Zewde, G. and Admassu, B. (2014): Seroprevalence of foot and mouth disease (FMD) and associated economic impact on Central Ethiopian cattle feedlots. *Journal of Veterinary Medicine and Animal Health*, 6 (5): 154-158. DOI: 10.5897/JVMAH2013.0247.
- [45] Tadesse, B., Alamir, K. and Demssie, E. (2017): Review on the Control of Foot and Mouth Disease by Vaccination. *International Journal of Basic and Applied Virology*, 6 (2): 09-18. DOI: 10.5829/idosi.ijbav.2017.09.18.
- [46] Akalu, B., (2017): Review on Common Impact and Management of Transboundary Animal Diseases. *Juniper Online J. ImmunoVirology*, 2: 1–7. DOI: 10.19080/JOJIV.2017.02.555583.
- [47] Sobrino, F., Sáiz, M., Jiménez-Clavero, M. A., Núñez, J. I., Rosas, M. F., Baranowski, E. and Ley, V. (2001): Foot-and-mouth disease virus: a long known virus, but a current threat. *Veterinary Research*, 32 (1): 1-30. DOI: 10.1051/vetres:2001106.
- [48] Yirgalem, M., Dawo, F., Gizaw, D., Mamo, B., Bilata, T. and Shegu, D. (2020): Phylogenetic and Sequence Variability Analyses of Vp1 Protein of Foot and Mouth Disease Viruses in Cattle in Amhara Region of Ethiopia. Researchsquare. 1-26. DOI: 10.21203/rs.2.20380/v1.