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A review on foot and mouth disease and its economic significance in Ethiopia

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Abstract

Foot and Mouth Disease (FMD) is extremely contagious, acute viral disease of cloven-hoofed animals. The disease is caused by genus *Aphtovirus* of the family *Picornaviridae* which occurs as seven serotypes O, A, C, SAT1, SAT2, SAT3 and Asia1.It has worldwide distribution and one of the most infectious diseases found in nature.The disease has a wide host range and easily transmitted by ingestion, direct and indirect contact, as well as by aerosols.It can cause a high number of deaths among young animals and losses in adult livestock. Losses occur in many ways in which loss of production, prevention, treatment and control.Globally, control of the virus can be made by slaughter of affected and in contact animals together with strict regulation of trade in animal and animal products, or by regular vaccination using appropriate vaccine. In Ethiopia, the disease is endemic and the country is economically less developed, the recommended option for control is vaccination against the circulating serotypes based on the continuous surveillance of the disease.

Keywords: Foot and mouth disease, economic significance, Ethiopia

Introduction

Foot and Mouth Disease (FMD) is one of the most devastating, severe, and highly contagious viral disease of cloven-footed animals caused by a group of seven antigenically different serotypes of extremely contagious and has a great potential for causing severe economic loss to both livestock and agricultural production. FMD is endemic in majority of developing countries (Cottral*et al.*, 1970). It is not only results in severe In Ethiopia, FMD is a notifiable disease and the Federal Veterinary Service sends official reports to Office of International Epizootics (OIE) monthly and annually (CSA, 2006).FMD is characterized by expanding boundaries and increasing total incidences (Asfaw and Sintaro, 2000). For example, during the periods from 1988 to 1991 sixteen FMD outbreaks were recorded. The records from Food and Agriculture (FAO) World production losses of infected animals, but also loss of export potential of livestock and livestock products which could be instrumental in the development of livestock sector in developing countries (Aftosa 2007). This disease causes significant financial losses (Perry *et al*., 1999).

The cost incurred for control or eradication is quite high. Besides, there are major indirect losses due to the imposition of trade restrictions (Mazengia *et al*., 2010).

Foot and mouth disease (FMD) is caused by an *Aphthovirus* of the family *Picornaviridae.* FMD virus has seven serotypes: A, O, C, Asia 1, SAT (Southern African Territories) 1, 2, and 3 (OIE, 2019). Serotypes reported in Ethiopia are O, A, C, SAT 1, and SAT 2 (Martel, 1974). There is also diversity of strains within each serotype (Jamal *et al.*, 2011). The disease is characterized by fever, loss of appetite, salivation, and vesicular eruptions in the mouth, on the feet, and teats (OIE, 2019).Foot and mouth disease is endemic and economically highly important disease in Ethiopia. Outbreaks were geographically widespread affecting all major regional states in the country and were more frequent in the central, Southern and Southeastern parts of the country (Ayelet*et al*., 2009).The high incidence in central Ethiopia could be associated with trade related animal movements. In Ethiopia, prices are higher in urban centers, the largest of which is Addis Ababa that is found in the center of the country and livestock usually move toward the center from other parts of the country. The Southern and Southeastern parts of the country are the main areas for cattle pastoralism and are also the main source of export animals. The higher incidence in these areas could be due to intensive animal movement both as a normal routine of the pastoral husbandry system and for the purpose of trade (Jemberu*et al*., 2016).

World Reference Laboratory (WRL) indicates that FMD serotypes O, A, C were responsible for FMD outbreaks during the period1957 to 1979(Roeder *et al.*, 1994). Recently, it had become the major constraint hampering export of livestock and livestock products to the Middle East and African countries. For instance, the Egyptian trade bans export of live animal livestock products, in which Ethiopia can lose 14 million $US annually (Leforban, 2005). Such losses and the strict requirements of international trade warn Ethiopia to control the disease.

The predominant entrance of virus is most commonly through the upper respiratory tract by inspiration of infected aerosols but infection may also occur through a skin injury (Lyytikainen*et al*., 2011). After inhalation, the virus can affect the pharynx and primary multiplication of the virus in the mucous membrane is transported by lymphatic and blood circulation to the sites of secondary multiplication (Lefebvre *et al*., 2014). The severity of clinical signs of the disease varies with the strain of the virus, the exposure dose, the age and breed of the animal, the host species and its, degree of immunity. The signs can range from a mild or in apparent in sheep and goats to a severe disease occurring in cattle and pigs (DACA, 2004).Foot and mouth disease preventive measures include: control of national borders, prohibition of import of animals and livestock products from endemic countries in accordance with the OIE standards, emergency measures in the event of outbreaksthrough: stamping-out, followed by cleaning and disinfection to reduce the risk of re-infection, strict movement controls, extending to movement on and off farms of livestock products. And also possible emergency vaccination is important (Ding *et al*., 2013).

Literature review

Etiology of the Disease

Foot and mouth disease is associated with foot and mouth disease virus (FMDV), is classified within the *Aphthovirus* genus as a member of the *Picornaviridae* family, being small, a non-enveloped, single stranded RNA virus, icosahedral and is 26nm in diameter which occurs as seven major serotypes, over 60 subtypes have been described (Arzt*et al.*,2010).

Genomic Structure of FMDV

The FMDV genome is an 8.3kb single stranded positive sense RNA. It is divided into three sections; 5'Untranslated Region (UTR), a single Open Reading Frame (ORF) and 3'UTR (Yang *et al*., 2014). The organization of the FMDV genome is shown in Figure 1. Following this protein is the 5'UTR which consists of an S

fragment, poly C tract, pseudoknot structures, a cis-acting replication element (cre) and the internal ribosome entry site (IRES) (Naveed*et al*., 2018).

The viral genome is enclosed in a protein capsid (Bari *et al*., 2015). The viral genome encodes the four structural proteins which form the capsid (VP1-VP4); the VP1-3 proteins are located on the surface, while VP4 is internal (Ashfaq*et al*., 2015) and ten non-structural proteins (L, 2A, 2B, 2C, 3A, 3B1-3, 3C and 3D) (Jamal and Belsham, 2013). These four proteins form the capsid of the virus and are coded for by 1D, 1B, 1C and 1A coding sequences respectively. The genome is subject to a high rate of mutation because the FMDV RNA-dependent RNA polymerase lacks proof reading ability (Lordwin, 2011). Lastly, the 3'UTR follows the ORF termination codon. It is involved in the replication of the RNA and consists of a stem-loop structure and a poly A tract which plays a role in the translation process (Grubman, 2004).

Host Range

All domestic and wild ungulate species can be infected by the FMD virus but the development of the disease is variable depending on the species and virus strain (Lefevre*et al.,* 2010). Among the domestic species; bovines, water buffalo, pigs. Sheep and goats are the most sensitive with more severe disease in bovine and porcine species (Admasu*et al.,* 2015). In addition, many species of cloven-hoofed wild life, such as deer, antelope and wild pigs, may become infected and several species of such as African buffalo (*Synceruscaffer*), Impala (*Aepycerosmelampus*), Kudu (*Tragelaphusstrepsiceros*) species, Warthog (*Phacochoerusaethiopicus*) and elephants that has a role in epidemiology of the disease (Rufael*et al.,*2006).

Transmission of the Disease

Susceptible animals are infected through direct or indirect contact with infected animals or other objects exposed to live virus. The most common route of infection of susceptible animals is by direct contact, either by mechanical transfer or by aerosol infection. Oral transmission is also possible especially when the animal has damaged skin in and around the mouth as well as on pre-existing abrasions on animals (Alexandersen*et al.,* 2003). Some cases of airborne transmission as far as 300km from source of infection have been described (Sørensen *et al.,* 2001).Inhalation of aerosolized virus is also common mode of transmission for cattle (Alexandersen*et al.,* 2003). Pigs are more likely to get infected by eating contaminated food (Alexandersen& Donaldson, 2002). Pigs can be infected by FMDV if placed in premises previously housing infected animals and like cattle; they are at risk of infection due to direct contact with infected animals (Grubman&Baxt, 2004).

Pathogenesis of the Disease

The predominant entrance of virus is most commonly through the upper respiratory tract by inspiration of infected aerosols, but infection may also occur through a skin injury (Lyytikäinen*et al.,* 2011). After inhalation, the virus can affect the pharynx and primary multiplication of the virus in the mucous membrane is transported by lymphatic and blood circulation to the sites of secondary multiplication in the lymphatic glands, epithelial tissues in and around the mouth, feet and in the mammary glands. Secondary replication in other glandular tissues, the virus appears in different body fluids such as milk, urine, respiratory secretions and semen before the appearance of clinical signs of FMD. The virus can also persist in oral cavity of infected animals for long periods after the acute infection (Alexandersen*et al.,* 2003).

Clinical Signs of the Disease

In cattle, the incubation period varies from two to 14 days, depending on the dose of the virus and route of infection. In pigs, the incubation period is usually two days or more, but can be as short as 18-24 hours. The incubation period in sheep is usually 3 to 8 days. Incubation periods have been reported in these species as short as 24 hours and

as long as 12 days after experimental infections (Knowles *et al*., 2016).

The common characteristics of the disease are fever, loss of appetite, salivation, and sudden death of young stock (Knight-Jones and Rushton, 2013), death in young calves may occur due to myocarditis and mortality may reach up to 20% in young calves (Pal, 2018). Clinical signs of FMD usually develop in 3–5 days although, in natural infection, the incubation period ranges from 2 to 14 days (Balemual, 2018). FMD is typically an acute febrile disease with vesicles (blisters) localized on the dental pad, tongue, muzzle or snout, hooves, teat, and another site of the skin that ruptures within 3 days to leave shallow erosions that ill rapidly (Pal, 2018).Lameness is usually the primary ascertained clinical sign in sheep and goats. Affected animals develop fever, show reluctance to walk, and might separate themselves from the rest of the flock. The vesicles square measure shaped in the mouth that ruptures simply feat shallow erosions, however, usually seen in the dental pad, adjacent to the incisors, additionally on the tongue, surface lips, and gums (Rout *et al.,* 2012).

Postmortem Lesions of the Disease

The characteristic lesions of foot-and-mouth disease are single or multiple, fluid-filled vesicles or bullae from 2 mm to 10 cm in diameter. The earliest lesions can appear as small pale areas or vesicles. Some vesicles may coalesce to form bullae. Vesicles are generally present for only a short period. Once they rupture, red, eroded areas or ulcers will be seen. These erosions may be covered with a gray fibrinous coating, and a demarcation line of newly developing epithelium may be noted. Loss of vesicular fluid through the epidermis can lead to the development of “dry” lesions, which appear necrotic rather than vesicular. Dry lesions are particularly common in the oral cavity of pigs (Radostits*et al.,* 2007).

The location and prominence of FMD lesions varies with the species. In cattle, numerous erosions, ulcers or vesicles may be found in the oral cavity. In pigs, sheep and goats, these lesions may be more common on the heel, coronary band and interdigital cleft of the feet. Some lesions may extend to the skin. Coronitis may be seen on the hooves, and animals with severe disease may slough their hooves or claws. In addition, vesicles may be found in other locations including the teats or udder; pressure points of the legs, ruminal pillars, prepuce or vulva. In young animals, cardiac degeneration and necrosis can cause gray or yellow streaking in the myocardium; these lesions are sometimes called “tiger heart” lesions (Balemual, 2018).

Epidemiology of the Disease

Geographic Distribution

FMD is endemic in most sub-Saharan African countries. It has been effectively controlled in South Africa, Botswana, Namibia, Swaziland and Lesotho which manage to maintain FMD freedom without vaccination in large zones of their territories through control zones in which vaccination is routinely practiced and cordon fences prevent entry into free zones from the wildlife reservoir (Sumption*et al*., 2007). Studies indicated that the occurrence of foot and mouth disease outbreak has been serious challenge every year in Ethiopia (Ayelet*et al*., 2009). The national incidence of FMD outbreaks during 2007-2012 was 1.45 outbreaks per 5 district years. Outbreaks were geographically widespread affecting all major regional states in the country and were more frequent in the central, Southern and Southeastern parts of the country (Jemberu*et al*., 2016).

Morbidity and Mortality

Foot and mouth disease has high morbidity rate and low mortality rate. The type of breed, the production system, age group, absence of restriction of animal movement, animal density, use of communal pasture and watering points and season are among the major factors associated with the morbidity and mortality rate of the disease (Jemberu*et al*., 2016). Exotic breeds appeared more susceptible to the FMD viruses endemic to Ethiopia. The morbidity rate of the

disease was relatively lower in indigenous breed of cattle (8.5%) than the other breeds (Negusssie*et al*., 2011). The putative risk factors such as age, agro ecology and production systems were statistically significantly associated with FMD seropositivity in cattle (Mesfine*et al*., 2019).

Risk Factors

The species of animals is important factor for the spread of disease as well as susceptible of animals. Cattle and pigs are more susceptible, but goats, sheep, buffalo and other wildlife such as antelope, deer, hedgehogs, elephants, llama and alpaca are also develop a mild symptomatic disease. Although, cattle, sheep and goats can be carriers, they are not regularly source of infection (Kitching and Alexandersen, 2002). Immature animals are relatively more susceptible. The wildlife species also play a great role as reservoirs of infection for domestic animals which is difficult to eradicate the disease as well as important for disease control when an outbreak is occurred (Radostits *et al.,* 2007).

The virus is resistant to external influences including common disinfectants and the usual storage practices of meat trade. It may persist over one year in infected premises, for 10-12 weeks on clothes and feeds (Hirsh *et al*., 2004). Foot and mouth disease virus can survive in dry fecal material for 14 days in summer, up to 6 months in slurry in winter, for 30 days in urine and 3 days in summer and 28 days in winter (Radostits*et al.*, 2007).

Under favorable condition of low temperature, high humidity, moderate wind and comfortable topography, the virus in aerosols may spread to for long distance. Generally, the integrations of these three factors are important for the disease occurrence, of which if one is not available, the disease does not occur (Mekonen*et al*., 2011).

Diagnosis of the Disease

An essential component of the FMD control strategy includes diagnostic assays to rapidly confirm the initial clinical determination of infection. The diagnosis is mainly relying on the clinical signs, in combination with laboratory examination to establish the serotypes of the causal virus (Admassu*et al.,* 2015).Diagnosis by clinical signs alone is complicated by other viral diseases of livestock, vesicular stomatitis and swine vesicular disease produce lesions that are identical to those of FMD. Lesions induced by bovine popular stomatitis, bovine herpes mammillitis, infections of bovine rhinotracheitis, bovine mucosal disease, malignant catarrhal fever, rinderpest in cattle, bluetongue, Parapoxvirus, peste des petits ruminants, and foot root in sheep might also be mistaken for FMD and all these listed diseases should be considered during the diagnosis (Balemual, 2018).

Serological Tests

Serological tests are necessary for an additional diagnosis of FMD, for certification of animals for import/export, in determining the freedom from infection, and for demonstrating vaccine efficacy. Virus infections are often diagnosed by the detection of a particular protein response. Enzyme-linked immunosorbent assay (ELISA), agar gel immune diffusion test and virus neutralization test, and complement fixation test are used for serological diagnosis of FMDV. Previous or current infections can be diagnosed using antibodies to FMDV structural proteins and include ELISA (solid-phase competition ELISA and liquid-phase blocking ELISA) and virus neutralization tests which are serotype specific.The virus neutralization test could be a gold standard test for the detection of antibodies to structural proteins of FMDV (Deb *et al.*,2013). The presence of FMDV viral antigens in high concentrations and types of the virus can be detected using an antigen ELISA (Sandwich ELISA) from active outbreak samples (Foot, OIE, 2012).

Nucleic Acid Recognition Method

Polymerase chain reaction (PCR) techniques are the most broadly used nucleic acid-based diagnostic technique for rapid detection of FMDV

and sequence analysis of any PCR positive result (Xu*et al.*, 2013).

Treatment of the Disease

Antiviral approaches including 2-C-methylcytidine (Lefebvre *et al*., 2014) and ribavirin (Yoon *et al*., 2012) are useful for prophylaxis in susceptible animals. Treatment of secondary bacterial infection and dressing of lesions with proper animal husbandry practices is recommended in FMD endemic countries in which slaughter policy is hard to apply. Furthermore, sick animals could be treated by applying broad-spectrum antibiotics, such as tetracycline by parenteral route in particular, to control secondary bacterial infections (Radostits*et al*., 2007).

Control and Prevention of the Disease

Being a viral disease FMD has no treatment, so, preventive measures in the absence of disease should be implemented as follows: control of national borders to prevent significant movement of animals and livestock products, prohibition of imports of animals and livestock products from endemic countries, emergency measures in the event of outbreaks through: rapid slaughter of infected animals and in contact animals followed by cleaning and disinfection to reduce the risk of re-infection, strict movement controls, extending to movement on and off farms of livestock products. And also possible emergency vaccination is important (Ding *et al*., 2013). In Ethiopia context the control of FMD is practiced by involvement of quarantine, isolation of infected animals, vaccination programs, proper disposal of infected carcass and other methods which are feasible to Ethiopian economy (Admassu*et al*., 2015).

Two factors could explain the upsurge of outbreaks of FMD in some endemic areas like Ethiopia. One factor is the low level of immunity caused by inadequate vaccination strategies (quality, coverage and timing). The other is uncontrolled animal movement and products. Animal diseases such as FMD can only be successfully controlled if there is astrong regional focus and integrated regional strategies to improve biosecurity and regulatory oversight of the movement of animals between and within countries (Ayelet*et al*., 2012).

Occurrence in Ethiopia

FMD virus is endemic in Ethiopia causing several outbreaks every year. Sero surveys in different parts of the country reported seroprevalence of 9%-26% at the animal level and up to 48% at the herd level in cattle. Another research that covered broader areas of the country showed Sero-positivity of 44.2% with 1.6% and 8.9% mortality and case fatality rates. Serotypes A, O, C, SAT2, have been identified and characterized by the National Animal health research center at Sebeta and the world reference laboratoryfor FMD at UK in the years 1969-1994 on samples submitted by Sholla disease investigation laboratory, but from the record of outbreak investigation in cattle by NVI between 1982-2000, three serotype O, A and SAT2 FMD were identified. Serotype O, A, C, SAT1 and SAT2 were identified in Ethiopia. Serotypes O and A are more prevalent and are the major causes of economic losses. The last reported outbreak due to serotype C FMDV in Ethiopia was during 2005 and so serotype C viruses may no longer exist outside of laboratories (Dabasa and Abunna, 2021).

FMD impedes export of livestock and livestock products and causes production losses and the number of outbreaks reported annually varies between 12 in 1997 and 198 in 1999. The predominant serotypes recently reported were FMDV serotype O (34.2%), followed by serotype A (17.1%), serotype SAT1 (4.9%) and serotype SAT 2 (2.4%). On average 93 numbers of FMD outbreaks were reported to MoLF annually. The outbreaks occurred every year, but most were reported in 2011 and 2012 each 124 and 205 outbreaks, respectively. However, considering the figures provided are definitely underestimated and do not reflect the reality of the epidemiological situation in the country due to endemic nature of the disease and the unreported cases by farmers (Dabasa and Abunna, 2021).

Economic Significance of the Disease in Ethiopia

FMD is a potential threat to Ethiopia's live animal export trade to Middle East and North Africa (MENA) which accounts for about 140 thousand heads, 23.9 million USD. The Egyptian ban 2005/2006 on cattle alone cost Ethiopia a market lose ranging 12.36 million USD (36%) of the total market to MENA. Hence, FMD is the number one TAD which is impeding export of live cattle (SPS/ LMM, 2008). The total annual (2011) economic loss due to bulls rejection from international market was estimated to be 3,322,269 USD which is equivalent to 56,345,682.24 ETB (1 USD=16.96 ETB) (Seyoum and Teshome, 2017).Currently, the single largest impact of FMD is undoubtedly its critical role as a restriction to international trade. The highest value markets for livestock products are in FMD free countries, and these countries are allowed to restrict or ban imports of livestock products and sometimes other products as well as a potential risk of introducing FMD. Pastoralists are severely affected by the direct impact of the disease since their livelihood is directly linked to livestock production. Owing to the low productivity of pastoral herds as compared with commercial or semi-commercial diary units, FMD infection in pastoral areas is considered relatively as minor disease. However, pastoralists severely suffered by impact of the disease on milk yield since they rely more on milk as a subsistence food than any other population in the country (Dabasa and abunna, 2021).

Milk losses due to the disease are not clearly stated. The disease is also associated with abortion and mortality in calves in acute cases and "chronic FMD" cases showing heat intolerance, reduced fertility. FMD has a high economic impact in Ethiopia. Its control is predicted to be economically profitable even without a full consideration of gains from export. The targeted vaccination strategy is shown to provide the largest economic return with a relatively low risk of losses. The annual costs of FMD were assessed based on production losses, export loss and control costs. The total annual costs of FMD under the current status quo of no official control were estimated at 1,354 (90% CR: 864-2,042) million birr. The major cost (94%) was due to production losses (Dabasa and abunna, 2021).

Conclusion

Foot and mouth disease is a highly contagious and economically important trans-boundary animal disease which affects cloven hoofed animals and is distributed worldwide. Serotypes A and O have the highest worldwide distribution. Serotypes SAT 1, 2 and 3 are currently restricted to Africa only and Asian 1 to Asia. Serotype O, A, SAT1 and SAT2 are currently circulating in Ethiopia with serotype O being the predominantly distributed serotype in the country. Serotype C is extinct from the country, since, 1984, when it is reported from Ethiopia. Foot and mouth disease outbreaks are reported every year and in all regions with the most frequent outbreak occurrence being in the central, Southern and Southeastern Ethiopia and in dry seasons. FMD is the most economically important disease in Ethiopia and can cause both direct and indirect impacts on the economy. These economic losses are due to production losses (i.e., reduction of milk production, loss of draft power, mortality), restriction of export, control costs and prevention costs. Therefore, based on the above information the following points are recommended:

- The epidemiology of FMD in Ethiopia along with the associated risk factors should be studied further in different areas nationally.
- Control of animal's movement should be strengthened to limit spreading of serotypes. Molecular characterization of the serotypes present, especially in pastoral areas should be thoroughly conducted.
- The vaccine present in Ethiopia is not effective for all the serotypes present in the country, so, vaccines should be developed according to the strains prevalent.

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