

Review on Epidemiology, Prevention and Control of FMD

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Foot-and-mouth disease (FMD) is a highly devastating and debilitating viral disease of the cloven-hoofed animals and considered as a serious threat to the livestock industry worldwide. Worldwide 70 countries are officially recognized by the OIE as FMD free irrespective of vaccination, while India along with around 100 other countries are still considered as endemic or sporadic zones. The disease is most important in cattle and pigs but goats, sheep, buffaloes in India and llama in South America are also affected. The virus is resistant to external influences including common disinfectants and the usual storage practices of the meat trade. Following an acute disease, affected animals shed the virus in all the body secretions and excretions (including exhaled air) like saliva, nasal and lachrymal fluid, milk, urine, feces and semen. Preventive measures in the absence of disease should be implemented as Control of national borders to prevent significant movement of animals and livestock products from non-free neighbors or trade partners. Currently FMD is widely prevalent and distributed in all areas of Ethiopia, although the level of the disease prevalence may show significant variations across the different farming systems and agro-ecological zones of the country. Endemic distributions of five of seven serotypes of FMDV are maintained in the country and Serotypes O, A, C, SAT1 and SAT2 were responsible for FMD outbreaks during 1974–2007). The most dominant serotype is O, accounting for 72% of the investigated outbreaks occurring in the country. Global eradication of FMD in the world include control by eradication, strengthens veterinary services, and control and prevention of other diseases. The main challenges faced during the FMD eradication are the virus related challenges, economic considerations of FMD enzootic considerations, and social and political challenges.

Keywords: Eradication; FMD; Ethiopia**Abbreviations**

CBPP: Contagious Bovine Pleuro Pneumonia; ELISA: Enzyme Linked Immunosorbent Assay; FMD: Food and Mouth Disease; FM-DCP: Foot and Mouth Disease Control Programme; GF-TADs: Global Framework for control for Transboundary Animal Diseases; MoLF: Ministry of Livestock and Fishery; OIE: Office International des Epizooties; PCP: Progressive Control Pathway

Introduction

Foot-and-mouth disease (FMD) is a highly devastating and debilitating viral disease of the cloven-hoofed animals and considered as a serious threat to the livestock industry worldwide. Foot-and-mouth disease (FMD), a clinically acute, contagious viral disease of domesticated ruminants, pigs, camel lids and more than 70 wild-life species including elephant, is of transboundary nature posing threat to global food security, and causes severe economic loss to

livestock farmers and industry. The causative agent, FMD virus (FMDV) is a member of the genus Aphthovirus, in the family Picornaviridae [11].

The virus exists in 7 immunologically distinct serotypes: A, O, C, Southern African territories (SAT)-1, 2, 3 and Asia-1, and within each serotype there are a substantial number of strains showing variable degree of genetic and antigenic diversities. Clinically, the disease is characterised by fever, lameness and vesicular lesions on the mouth, tongue, feet, snout and teats of infected animals [2].

A property of this virus is that it is difficult to stop its transmission which makes it difficult to control and eradicate the disease worldwide. Although the virus can be rapidly inactivated at pH values of less than 7.0 (below neutral pH), it can withstand high temperatures when protected by proteins e.g. from milk limiting virus inactivation and therefore enhancing virus persistence in the environment [41].

In Ethiopia, many of the known infectious diseases of animals occur commonly and are poorly controlled. Foot and mouth disease (FMD) has a great impact on economic development, causing both direct and indirect losses. In terms of potential livestock exports from Ethiopia, FMD is seen as a major hindrance to international trade. In part, this perception is based on the assumption that national freedom from FMD is required before exports are possible. At present, the Ethiopian government is hoping to establish a disease-free zone for export purposes – an approach that is supported by the World Organization for Animal Health (OIE) [30].

FMDV is endemic in Ethiopia causing several outbreaks every year. Previous studies have provided evidence for the presence of five FMDV serotypes from the seven serotypes (O, A, C, SAT1, SAT2) were reported in Ethiopia samples collected from different outbreaks. Currently the occurrence of FMD outbreaks in Ethiopia is increasing from time to time and cattle were under risk of infection, however, there is no government strategy in FMD control. Lack of vaccination strategies, presence of free animal movement, high rate of contact among animals at commercial markets, in communal grazing areas and watering points, poor surveillance and diagnostic facilities were among the reasons forwarded for increasing incidence of the disease [5].

Therefore the objective of this paper is to review the epidemiology and prevention and control of food and mouth disease.

Epidemiology

Geographic distribution

The FMD was once prevalent all over the world but strict control and eradication measures adopted by developing countries have resulted in its lower prevalence. Worldwide 70 countries are officially recognized by the OIE as FMD free irrespective of vaccination, while India along with around 100 other countries are still considered as endemic or sporadic zones [36]. Except New Zealand, outbreaks have occurred wherever livestock are present. However, the disease is present in enzootic form in all continents (except Australia and North America). In the eastern parts of Africa however serotypes: O and A; along with South African Territory (SAT-1 and 2) are still circulating [19].

Endemicity of FMD is observed in large areas of Asia (including Middle East), Africa, and South America. Occasional outbreaks of FMD have been reported from Europe, while Canada and United States are FMD free. Eradication is unfeasible due to persistence of the virus in wild African buffalo. Among the seven Serotypes of FMDV, the most common serotype that is prevalent all over world is type "O". It was also reported from pan-Asian epidemic that (1990) that resulted in severe economic losses in many countries throughout the world. There is also a few report of seasonal occurrence of FMD at low level sporadically in certain parts of Pakistan and northern states of India [36].

Many countries have eradicated the FMD and are supposed to be free from this disease e. g. South Africa, Botswana, Namibia, Zimbabwe, Tunisia and Morocco in Africa and Chile, southern Argentina; Uruguay and Guyana; Surinam and French Guiana in South America. Countries like Iran, the southern countries of the former Soviet Union and South-East Asia including India and Pakistan, Philippines, Malaysia, Sub-Saharan Africa, Tanzania, Egypt, Ethiopia, and Eritrea [1,44]. Many European countries claim to be free from FMD but sporadic outbreaks as in Greece in year 2000 and from UK, Republic of Ireland, Netherlands, and France in the year 2001 have been reported. The same strain caused outbreak throughout Asia. Eventually this outbreak was controlled in UK after slaughter of more than 4 million animals and no vaccination policy was adopted [44].

Serotype prevalent: Continent

O, A, C: South America, Europe

O, A, C, Sat 1,2,3: Africa

O, A, C, Asia 1: Asia

Virus free: North and Central America, Newziland, Australia [27].

Risk factors

Host factors

The disease is most important in cattle and pigs but goats, sheep, buffaloes in India and llama in South America are also affected. Some strains of the virus are limited in their infectivity to particular species. Although cattle, sheep and goats can be carriers, they are not regular sources of infection, and early studies in Kenya showed that goats were infrequent carriers, and sheep not at all. Immature animals and those in good condition are relatively more susceptible and hereditary differences in susceptibility have also been observed. Horses are not susceptible to the disease [20].

A variety of wildlife species such as the deer in England, the water buffalo (*Bubalus bubalis*) in Brazil and wild ungulates in Africa become infected periodically but are believed to play little or no role as reservoirs of infection for domestic animals. A notable exception is the African buffalo (*Syncerus caffer*), probably the natural host of the SAT types of the virus and the major source of infection for cattle in southern Africa. The disease in buffalo populations is mild but the infection rate is often high and can be persistent. On the other hand, the domesticated Asian buffalo shows typical clinical disease and spread from buffalo to other species. Small rodents and hedgehogs in Europe and capybaras in South America may also act as reservoirs [11].

Environmental and Pathogen factors

The virus is resistant to external influences including common disinfectants and the usual storage practices of the meat trade. It may persist for over 1 year in infected premises, for 10-12 weeks on clothing and feed, and up to a month on hair. It is particularly susceptible to changes in pH away from neutral. Sunlight destroys the virus quickly but it may persist on pasture for long periods at low temperatures. Boiling effectively destroys the virus if it is free of tissue but autoclaving under pressure is the safest procedure when heat disinfection is used. The virus can survive for more than 60 days in bull semen frozen to -79°C. In general, the virus is relatively susceptible to heat and insensitive to cold. Most common disinfectants exert practically no effect, but sodium hydroxide or formalin (1-2%) or sodium carbonate (4%) will destroy the virus within a few minutes [4].

All uncooked meat tissues, including bone, are likely to remain infective for long periods, especially if quick-frozen, and to a lesser extent meat chilled or frozen by a slow process. The survival of the virus is closely associated with the pH of the medium. The development of acidity in rigor mortis inactivates the virus but quick freezing suspends acid formation and the virus is likely to survive. However, on thawing, the suspended acid formation recommences and the virus may be destroyed. Prolonged survival is more likely in viscera, bone marrow and in blood vessels and lymph nodes, where acid production is not so great. Meat pickled in brine, or salted by dry methods may also remain infective. Fomites, including bedding, mangers, clothing, motor tires, harness, feedstuffs and hides, may also remain a source of infection for long periods. There are claims that the virus can pass unchanged through the alimentary tracts of birds which may thus act as carriers and transport infection for long distances and over natural topographical barriers such as mountain ranges and sea [7].

Mode of transmission

Following an acute disease, affected animals shed the virus in all the body secretions and excretions (including exhaled air) like saliva, nasal and lachrymal fluid, milk, urine, feces and semen. Mucosa of the pharynx is the primary predilection as well as replication site in spite of the viral entry via skin wounds or the gastrointestinal tract. Large quantities of viruses in aerosolized form are shed by pigs in particular. Four days prior to onset of symptoms, the infected animals usually start shedding the virus. Some animals can continue to excrete the virus for long periods (up to years) after recovery. The vesicles in buccal mucosa (especially tongue and dental pad), bulbs of heels and in the inter-digital space, normally rupture within 24 hrs, releasing vesicular fluid containing up to 108 infectious virus units per ml [40].

Contact with infected animals and contaminated fomites and fodder directly or indirectly can transmit the disease but majority of the transmission events occur by the movement of the infected animals. Many other sources of infections viz., wool as well as hair of infected animals, contaminated grass or straw, footwear and clothing of animal handlers stuck with mud or manure, livestock equipment or vehicle tires or wind can play important role for spread of the disease [36].

Infected milk may be the source of infection to young calves and between the farms. Milk tankers have also been found to spread

the virus [45]. Inhaled aerosolized virus may also serve as cause infection, ingestion of contaminated feed, fodder and the exposure of contaminated utensils which can lead to virus entry through skin wounds and mucosal barrier and hence spread the disease. However, the role of sources and chances of exposure through different routes show species variation as aerosolized virus more severely affect cattle or sheep in comparison to pigs [3].

The virus survives well below 40 °C temperatures, but it can be easily inactivated with the rise of temperature and reduction in relative humidity less than 60%. Under favorable climatic conditions (high humidity), aerosol transmission of virus up to 250 km has been reported. The virus may survive at 4°C for up to a year. The virus loses its infectivity by rapidly heating at 56°C. A proportion of FMDV in infected milk will survive pasteurization as they are associated with animal proteins. The virus may survive for 14 days in dry faeces, more than 6 months in slurry and for 39 days in winter. Virus survivability in animal products including meat depend upon the pH; the virus survive best at pH>6.0 but is inactivated when there is rigor mortis that resulting in acidification of muscles. Frozen or chilled lymph nodes or bone marrow can also maintain the virus for long periods. Carriers (especially cattle and water buffalo) convalescent animals and exposed vaccinates can also transmit the disease [25].

Different prevention and control options

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 from non-free neighbors or trade partners. For officially free countries, prohibition of imports of animals and livestock products from endemic countries in accordance with the OIE standards. Emergency measures in the event of outbreaks through: Rapid slaughter of infected animals, in contact animals and herds considered to have received infection by contact, to reduce the quantity of virus released policy of “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 [14].

To control FMD effectively, there is need of good infrastructure, trained veterinary staff, well equipped laboratories, good governance, rapid and accurate diagnostics, rapid response measures, continuous monitoring and surveillance, and compulsory vaccina-

tion. Timely determination of exact status of disease in ruminants, particularly in small ruminants, is considered as gauge to monitor the virus activity in an area. In order to protect FMD free countries stringent import and cross-border animal movement, controls and surveillance are required in specific areas or zones. If FMD is suspected, notification of regulatory veterinary authorities immediately to obtain a rapid diagnosis is essential. For containment of an FMD outbreak a quick response is vital. If there is any suspicion regarding vesicular disease, immediate information must be provided to the state and central veterinary authority [34].

Due to the detrimental economic consequences resulting from the presence of FMD, there have been introduction of certain measures to retain a country's disease free status. There is requirement of initial implementation of test and slaughter policy of all infected as well as susceptible animals (at close proximity) for controlling FMD in a disease free country with movement restriction of susceptible animals, disinfecting infective premises and intensified surveillance to prevent further spread. Restriction over the import of suspected livestock or animal products including fresh meat from countries where FMD prevails is essential. FMD endemic countries like India are facing problems such as economic barriers and social or religious taboos in implementing test and slaughter policy. Vaccination followed by sero-monitoring is best alternative for effective control in endemic countries. In fact, in past many European countries like France have adopted vaccination and after control seized the vaccination [13].

For the development of an efficacious strategy of vaccination it is important to understand the disease dynamics. It indicates the suitable time points to administer vaccine. It is thereby easy to perform individual vaccination in population of large ruminants. It must be kept in mind that majority of the infections due to this virus is sub clinical in nature and thereby becomes unrecognizable for which vaccines having varying quality as well as efficiency must be used with caution [25].

Some developed countries do not allow emergency vaccination as the vaccine interferes in effective diagnosis. There has been assumption regarding carrier animals and their role in the epidemiology of FMD; any animal with FMD virus antibody is considered a potential carrier thereby must not be considered for international trade. If there is recurrence of any epidemic similar to the one in UK (in 2001), safe and effective vaccination is mandatory [15]. Im-

plementation of a programme (location specific) called 'Foot and Mouth Disease Control Programme' (FMDCP) in India in more than 200 specified districts has been undertaken. This has prevented significant economic losses and facilitated the development of herd immunity in cloven footed animals. For this purpose funds are being provided by the central authority to purchase vaccine and to maintain cold chain and other logistic support along with support from the state authorities to provide manpower [12].

Vaccination

The most effective strategy of the prevention of the viral diseases is through vaccination including FMD. The veterinary vaccines account for 26% of global vaccine market [40]. However there is lack of vaccines which can prevent infection and its transmission. The currently available vaccine provides protection from the disease but not from infection/virus replication. Moreover the vaccinated animals may become asymptomatic carrier that shed the virus for months or even up to years. During outbreaks, besides providing protection, the vaccination decreases FMDV spread to the adjoining areas. Decision to vaccinate varies with the specific scientific and economic as well as political and social factors and is complex [13].

Killed trivalent (containing O, A, and C strains) vaccines are in general use, but because of the increasing occurrence of antigenically dissimilar sub strains, the production of vaccines from locally isolated virus is becoming a more common practice. The virus is obtained from infected tongue tissue, a cell culture of bovine tongue epithelium or other cell culture. Baby hamster kidney (BHK) is a favored viral cultural medium and BHK vaccine is now in general use. Its principal virtue is its adaptability to deep suspension culture in contrast with its growth on monolayer culture, enabling large-scale production of virus to be carried out within practicable space limits. Inactivation of the virus to produce a killed vaccine used to be done with formalin but there are disadvantages with its use and more sophisticated agents, especially binary ethylene immine (BEI) are now used. Serviceable immunity after a single vaccination can be relied on for only 6-8 months. Vaccines produced from 'natural' virus give longer immunity than those produced from 'culture' virus. Vaccines produced in oil-adjuvant offer promise of providing longer immunity, and require only annual revaccination in adult cattle and biannual revaccination for young stock or every 4-6 months in pigs (Liao, *et al.* 2003).

General vaccination as a means of control is recommended for countries where the disease is enzootic, or where the threat of introduction is very great, e.g. Israel. If an outbreak occurs, a booster vaccination with the relevant serotype will greatly increase the resistance of the population. However, the strategy of general vaccination has many difficulties. Inapparent infections may occur in animals whose susceptibility has been reduced by vaccination, permitting the existence of 'carrier' foci. It has become generally recognized that the number of carrier animals produced by vaccination is very much greater than was previously thought. Apart from the fact that these animals are a potent method of spreading the disease, they also provide an excellent medium for the mutation of existing virus strains, because the hosts are immune. The carrier state in vaccinated and unvaccinated cattle may persist for as long as 6 months and be capable of causing new outbreaks in all species [4].

Control by eradication

The success of an eradication program depends on the thoroughness with which it is applied. As soon as the diagnosis is established, all cloven-footed animals in the exposed groups should be immediately slaughtered and burned or buried on site. No reclamation of meat should be permitted and milk must be regarded as infected. Inert materials which may be contaminated must not leave infected premises without proper disinfection. This applies particularly to human clothing, motor vehicles and farm machinery. Bedding, feed, feeding utensils, animal products and other articles which cannot be adequately disinfected must be burned. Barns and small yards must be cleaned and disinfected with 1-2% sodium hydroxide or formalin or 4% sodium carbonate solution. Acids and alkalis are the best in activators of the virus and their activity is greatly enhanced by the presence of a detergent. The effective pH at a disinfection surface may be grossly altered by the presence of organic matter and needs to be adequately maintained. When all possible sources of infection are destroyed, the farm should be left unstocked for 6 months and restocking permitted only when 'sentinel' test animals are introduced and remain uninfected. There are strict international requirements for demonstrating freedom from infection. Recommendations for outdoor sites are difficult to make. Observations in Argentina suggest that contaminated pastures and unsheltered yards are clear of infection if left unstocked for 8-10 d. No animal movement can be permitted and human and motor traffic must be reduced to a minimum. Persons working on the farm

should wear waterproof clothing which can be easily disinfected by spraying and subsequently removed as the person leaves the farm [10].

Quarantine

Diagnosis of FMD is sufficient to initiate the immediate closing of the border of the neighboring disease-free countries and the placing of embargos by other countries. Local veterinary authorities prohibit movement of animals to or from the infected premise. Movement of animals, supplies, and vehicles in an area of no less than 10-km radius of the infected premise is permitted only under authorization of veterinary authorities. Decontamination of infected premises by cleaning and disinfecting with acid or alkali compounds of recommended concentrations is the method of choice. Premises should not be restocked until sentinel animals have remained free of the disease and the premises have been found acceptable by veterinary authorities [37].

Status of the disease in Ethiopia

In Ethiopia reports indicated that during the period of 1957–73, 62 outbreaks of serotype O, 24 of serotype C and 12 of serotype A were recorded. From record of outbreak investigation in cattle by National Veterinary Institute, between 1982 and 2000, three serotypes: O, A and SAT2 FMDV were identified [18]. Currently FMD is widely prevalent and distributed in all areas of Ethiopia, although the level of the disease prevalence may show significant variations across the different farming systems and agro-ecological zones of the country. Previously the disease occurs frequently in the pastoral herds of the marginal low-land areas of the country. However, this trend has been changed and currently the disease is frequently noted in the highlands of the country [43].

Endemic distributions of five of seven serotypes of FMDV are maintained in the country and Serotypes O, A, C, SAT1 and SAT2 were responsible for FMD outbreaks during 1974–2007). The most dominant serotype is O, accounting for 72% of the investigated outbreaks occurring in the country, followed by A (19.5%) and Serotype C has not been reported in Ethiopia since 1983 [6]. However, a serotype C specific antibody was detected in cattle indicating that circulation of serotype C viruses in the country may have gone unnoticed [42]. Recently Jemberu [21] identified as serotypes O, A, SAT2 and SAT 1 were the causal serotypes of the outbreaks during the year 2007-2012. In the past seven years (2009-2015) on aver-

age 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 [32].

The prevalence of the disease is varying from place to place, and the studies conducted so far did not cover all corners of the country. However, recent serological investigation conducted in southern part of Ethiopia [42], central part of Ethiopia, Northern, South-west Ethiopia [17], Northwest Ethiopia, Eastern Ethiopia [31] and different regions of the country [6] showed that FMD is posing a major threat in many parts of the country thereby causing considerable economic losses through morbidity, mortality and trade restriction.

Rufael [42] investigated seroprevalence of FMD in three districts of Borana pastoral area of Oromia regional State namely Yabello, Dire and Moyale. Out of 920 cattle investigated over all of 193 (21%) was found to be positive at individual animal level. On the other hand from 116 herds examined for the presence of antibodies to the 3ABC non-structural protein of FMD virus, 68(59%) contained, at least, one positive animal. Moreover, significantly higher herd seroprevalence was recorded in Yabello district (61%), followed by Dirre (59%) and Moyale (52) districts. Similarly on animal basis Yabello district recorded the highest FMD seroprevalence (26.1%) followed by Dire (18.8%) and Moyale (16.1%). At Pastoral Associations level the highest herd seroprevalence was found in Dida Tiyara (100%), Romso (100%), Dida Yabello (80%), and Garbi Minch (77%). On individual level, seropositivity was highest at Dida Tiyara (43.35%) Garbi Minch (33.3%), Magado (32.4%), and Medhecho (26.9%).

Gelaye, *et al.* [17] performed sero-epidemiological investigation in two districts (Surma and Semen Bench) of the Bench Maji Zone between November 2007 and February 2008 with the objective of determining the seroprevalence of Foot and Mouth Disease (FMD) in cattle and identifying the potential risk factors associated with the disease. They collected sera samples from a total of 273 cattle in 98 herds and reported an overall seroprevalence of 12.08% using the 3ABC-ELISA. Regarding the seroprevalence at district level

significantly higher seroprevalence (20%) they found was in the Surma district compared to the Semen Bench district (5.88%). The highest seroprevalence at peas-ant association level was observed in Kibish 25% (n = 40), followed by Tulgit 20% (n = 40), Koka 15% (n = 40), Aman 8.6% (n = 49), Mizan 5.66% (n = 53) and the lowest was in Temenga yasz 3.92% (n = 51). Furthermore, they evaluated herds for the presence or absence of other species with respect to FMD prevalence and found that herds with different species present had an FMD prevalence rate of 15.52% while those which did not have any other species had a prevalence rate of 6.06%.

In Southern Ethiopia Megersa, *et al.* [28] investigated FMD in endogenous cattle between October 2007 and March 2008 using 3ABC ELISA. They found seroprevalence of 9.5% and 48.1% at animal and herd levels, respectively. Moreover, they reported significantly higher Seroprevalence in South Omo than Sidama and Gamo Gofa areas.

Molla [33] Conducted sero-epidemiological study between October 2008 and May 2009 in seven districts of the South Omo zone, south-western Ethiopia. A total of 770 cattle sera were investigated using the 3ABC-ELISA and the overall seroprevalence of 8.18% was reported. The highest district-level prevalence was documented in Bennatsemay district (30.2%), and the lowest prevalence was in Malle and Debub Aari districts, each with prevalence of 6.3%. A total of eight FMD outbreaks three in Oromia, one in Addis Ababa and four outbreaks in Amhara national regional States were investigated. A total of 496 cattle were examined for the presence of antibodies to the 3ABC non-structural protein of FMD virus and 219 (44.2%) were found to be positive. The highest seropositivity was recorded in Haremaya University dairy farm (80.0%), and the lowest was documented in Akakikality sub-city (28.3%).

Jenberu [21] performed sero-prevalence investigation from October 2007 to April 2008 in Afar pastoral area of Ethiopia to determine seroprevalence and associated risk factors for seropositivity of cattle FMD using 3ABC ELISA. Four districts of Afar pastoral area from where the study animals were selected were Chifra from zone one, Amibara and Gewane from zone three and Ewa from zone four. At district level seroprevalence was significantly higher in Gewane (11.9%) as compared to Amibara (4.2%), Ewa (2.9%) and Chifra (5.2%). An overall seroprevalence at individual and herds level were found to be 5.6 and 48.4% respectively.

The study from Eastern Ethiopia by Mohamoud [31] also conducted seroprevalence investigation on indigenous cattle from October 2009 to March 2010 in Somalia Regional State in Awbere and Babille Districts of Jijiga zone, A total of 384 sera were tested for antibodies against non-structural protein of FMD virus by using the 3ABC-ELISA and the overall individual animal antibody seroprevalence documented was 14.05%. At district level the prevalence in Awbere District animal was determined as 14.2% (n = 225) while in Babille was 15.1% (n = 159).

Mekonen, *et al.* [29] performed Seroprevalence investigation from November 2007 to March 2008 on Borana plateau and Guji highlands of southern Ethiopia to determine the prevalence of Foot and Mouth Disease (FMD) in bovine They reported an over-all prevalence of 24.6% (113/460) by using 3ABC- ELISA technique. Moreover, they reported significantly higher prevalence in Borana 53.6% (82/153) compared to Guji 10.1% (31/307).

Bayissa, *et al.* [8] conducted Cross-sectional serological study in Borana pastoral and agro-pastoral area to determine seroprevalence and risk factors associated with foot and mouth disease infection and to assess community perceptions as to importance of the disease. Their investigation was in Borana zone of Oromiya Regional State, Southern Ethiopia in three districts namely, Arero, Teltele, and Yabello. A totally, 768 cattle sera were investigated from 111 herds using 3ABC ELISA test and they reported an overall individual level seroprevalence of 23.0%. From 111 herds examined, 65 (58.6%) found to have at least one positive cattle and The herd level seroprevalence reported was 67.6% in Arero district, 62.5% in Yabello district, and the lowest was found in Teltele district (45.9%).

Global eradication or control programmes

Control by eradication

Some areas of the world, such as Central and North America and Australia-Oceania, have succeeded in protecting their FMD-free status for decades. In others, most notably Europe, South America and some countries of South-East Asia, FMD prevalence has decreased markedly. However, FMD remains endemic in many countries of Africa, the Middle East and Asia. Furthermore, the risk of FMD for countries free from the disease has increased due to the increased global movement and trade of livestock and animal products.. In addition to the economic damage, FMD outbreaks and

the way they have been controlled in developed countries, with massive culling, have been a source of great concern, not just in the farming community, but in society at large. The questions raised include animal welfare, ethical issues and possible threats to domestic animal biodiversity [38].

Following the recommendations of the first international conference on FMD control, organised by the OIE and FAO and held in Asuncion, Paraguay, in 2009, the two Organisations have embarked, under the umbrella of the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs), on a Global Strategy and Global Action Plan for FMD control. A first outline was presented during the 79th General Session of the World Assembly of Delegates of the OIE in May 2011. The Global Strategy proposes a step-wise approach to improve the FMD control capacity of a country in a sustainable manner, the Progressive Control Pathway (PCP), which is also expected to have a positive effect on the performance of the VS and, in turn, improve animal health status in general. The Strategy focuses on regions of the world where the disease is endemic. A successful outcome will be of great benefit not only to countries where FMD is still present, the majority of which are developing countries, but also to countries that are currently FMD-free [38].

The national and regional levels will be the priority for intervention and where most activities will be carried out. The global level will focus on international coordination and the monitoring of overall progress. The programme will be long-term: an overall period of 15 years has been set, with 5-year phases and clear milestones and regular evaluations to assess progress [11].

Strengthening veterinary services

The subtitle of the Global FMD Control Strategy is 'Strengthening animal health systems through improved control of major diseases'. Although 'animal health systems' refers to the entire complex of stakeholders involved in improving and safeguarding animal health, including animal health professionals (veterinarians other professionals and para-professionals) and livestock producers and traders, the main focus within the context of this Strategy is on the VS, which associate public and private sector veterinarians and other animal health professionals 1. Support for the development of private-public partnerships (PPPs) is part of the Global Strategy and is an indirect way of promoting the role of other stakeholders, and especially livestock producers, in the animal health system [3].

The VS are the core component of a system that protects animal health and safeguards animal production. This, in turn, protects the livelihoods of those involved in agriculture and global food security and creates opportunities for economic development. To function effectively, VS require appropriate infrastructure, a clear organization and chain of command, trained and effective personnel and a sufficient budget to carry out their disease management activities. Unfortunately, in many developing countries these elements are of insufficient quality and the operating budgets are inadequate. Harmonization of control policies with neighbouring countries is often advisable and under some circumstances imperative, for instance in regions where there is cross-border nomadic animal movement [37].

The actions taken to control FMD correlate with effective VS and will have wider benefits. If a country can successfully control FMD it implies the establishment of more effective VS that will be better able to combat other major diseases of livestock and especially TADs. The OIE PVS Pathway (18a) will be used as a tool to evaluate the quality of the VS (PVS Tool) in terms of compliance with OIE standards, to monitor their improvement (PVS follow-up missions) and to identify and assess the level of investments a country must mobilize in order to eliminate its gaps in terms of OIE standards (PVS Gap Analysis). The PVS Gap Analysis takes into account the country's priorities, including the prevention and control of TADs [38].

Prevention and control of other major diseases of livestock

The cost-effectiveness of the Global FMD Control Strategy will be increased through appropriate linkages with other monitoring, surveillance and disease control activities or with production related activities. In addition, the activities undertaken to achieve progress in the field of FMD control will result in valuable information and capabilities useful for the control of other TADs. Diseases that may be considered for control alongside FMD include: in cattle: haemorrhagic septicaemia (HS); brucellosis; contagious bovine pleuro pneumonia (CBPP); anthrax and in some regions possibly blackleg and rabies. In small ruminants: peste des petits ruminants; sheep and goat pox and brucellosis. In pigs: classical swine fever and African swine fever [38].

The above list is not exhaustive – other diseases may be added according to the needs and priorities of individual countries and

regions. For example, in parts of Africa FMD vaccination could be applied alongside vaccination against CBPP, anthrax, blackleg or East Coast fever and in Asia it could be combined with vaccination against HS, anthrax and blackleg. The GF-TADs Regional Steering Committees are the appropriate fora to further investigate useful combinations of activities to fit the priorities of the regions they serve and to fine tune the activities. TADs other than FMD also have the potential to cause enormous economic damage and, as some are zoonotic, they can have considerable public health importance. In developed countries most TADs have been eliminated and their importance then relates to the cost of prevention. However, as in the case of FMD, it is in the interests of countries free from TADs to decrease the risk of reintroduction of the infection and hence they benefit from better control of TADs at source, which will also be more cost-effective [11].

Challenges in the prevention and control program of FMD

FMD virus and related challenges

The viral genome encodes for structural proteins (VP1, VP2, VP3, and VP4) and several non-structural proteins that play roles in virus replication, assembly of the virus particle, and control of the host innate and adaptive immune response. FMDV is genetically diverse, with seven distinct serotypes: type O, A, C, SAT 1, SAT 2, SAT 3, and Asia 1. Furthermore, subtypes within each serotype contain a large spectrum of genetic diversity due to high mutation rates during genome replication and many of these mutations can be accommodated while maintaining virulence. The broad genetic diversity between and within serotypes complicates identifying and protecting against disease. Specifically, the variability in the antigenic regions can reduce or effectively eliminate cross-subtype or -serotype protection from previous infection or vaccination as occurred in Iran in 2005 [23].

The ability of the virus to infect cross-species through sundry routes increases transmission opportunities, particularly where livestock agriculture is densely populated. Cattle and sheep are primarily infected through respiration of the virus in aerosol form, while swine are more likely to be infected through ingestion or subcutaneous wounds. Shedding of the virus may occur through multiple routes including in aerosol form, urine, feces, and bodily fluids. Excreted virus can retain infectivity for significant durations in aerosol form, with examples of some strains naturally traveling as far as 300 km. The extent of FMD transmission can be further

amplified by incidental transport on vehicles, humans, water, and animal products. The diverse routes of shedding and transmission coupled with the diversity of host species provide myriad opportunities for spread of the disease [13].

In certain hosts, including cattle and buffalo, the virus can persist and these asymptomatic, persistently infected animals can remain potentially contagious for up to 5 years. Infected animals are thought to reach a maximum transmission potential within 12 days of infection. In a dead host, the virus may remain stable, and persist in an infectious form for as long as 11 days in muscle tissue, and 4 months in the liver. Also, infectious virus can persist within many other animal products such as milk and cheese for differing durations [13].

Predominant vaccine technology

The risk of virulent virus contamination or insufficient inactivation during vaccine production requires that production facilities maintain rigorous biosafety standards. This restricts the locations where production facilities can be successfully constructed, maintained, and operated. Furthermore, these facilities must operate at a high level of containment. The distance between production facilities and regions of FMD infections presents a logistical challenge of distribution, particularly where international borders are concerned. To help alleviate this challenge, in some parts of the world FMD vaccine banks have been established to increase vaccine accessibility [7].

FMD vaccine banks decide how much vaccine they will store for any given serotype, and regularly test these stored vaccines for efficacy. These tests are essential as a concern with the current technology for inactivated virus vaccine production is the possible selection of antigenic variants during virus replication. It has been found that the selected variants for vaccines may not always be protective against current virus strains circulating in the field. In addition, the choice of which vaccines to store is complicated by limited cross-subtype and cross-serotype protection, requiring individual vaccines against each subtype that is currently circulating for effective protection. Vaccines must also be periodically replaced due to a shelf life of 1-2 years for conventional FMD vaccines. Storage of vaccines as concentrated antigens in liquid nitrogen improves shelf life. However, these concentrated antigens must be shipped to manufacturers for formulation with an adjuvant when needed, thus delaying their use in the field [7].

Administration of the vaccine also presents its own set of complexities such as proper handling, correct dosage, and optimal time of vaccination. All of these variables can significantly impact the efficacy of the vaccine. For example, a higher dosage of vaccine generally results in increased number of animals protected and reduces the time from administration to protection. As a consequence, during outbreaks in previously disease-free countries, emergency vaccination of animals with 6 protective dose 50 (PD50) is recommended by the OIE. Complexities of administration make it desirable for trained persons to administer the vaccine. Also, persons administering vaccines to multiple herds may inadvertently act as disease carriers. Furthermore, regions with inadequate veterinary services face the added challenge of increasing competency among those administering vaccination [24].

Economic considerations for FMD-enzootic regions

Although vaccines are currently available, they can be cost prohibitive and be limited in availability for many enzootic regions. In a cost-benefit summary of FMD eradication in Sudan it was estimated that 81% of the eradication costs were attributed to purchasing the vaccine. The price of a current vaccine hinders economically developing countries from disease eradication efforts because each vaccine cost between \$0.40 and \$3.00 USD to manufacture and ship. It is a challenge to reduce the cost of the traditional vaccine due to the stringent conditions needed to prevent contamination or insufficient inactivation and costs associated with testing, distribution, and storage. Future developments in vaccine technology must consider cost when attempting to produce alternative candidates for developing countries [26].

Social and political challenges surrounding eradication

Globalization of animal trade and animal product commerce further amplifies the difficulty to contain FMD. Both legal and illegal animal trade and animal product commerce have had FMD outbreaks in the past. This was epitomized by outbreaks occurring in Albania in 1996 due to lax trade policy and outbreaks in the island nation of Taiwan in 1997 where the suspected origin of the outbreak was illegally imported feed or pigs disease transmission. The lack of education leads to ineffective FMD prevention and eradication programs. Providing proper information regarding FMD transmission and convincing skeptical populations to take proper precautions is no small task. This is especially challenging when a short-term individual economic gain could be realized by ignoring proper precautions [9].

The lack of cross-governmental cooperation has also played a role in delaying eradication efforts. The ease of transmission and variety of hosts promotes transmission across borders.

Conclusion

Therefore, the spread of an outbreak is better controlled when bordering countries communicate and cooperate. Failure of international cooperation can undermine eradication programs through cross-border reintroduction of FMD. Cross-border spread of the disease is further stimulated by burdensome trade restrictions imposed on countries who report FMD within their borders. To avoid these trade restrictions, countries with outbreaks will delay reporting in order to privately stamp it out and continue trade. These delays in reporting increase the risk of disease spread and transmission. Although challenging, cross-governmental cooperation has proven effective in the past resulting in eradication or minimizing FMD outbreaks in places such as the US, Mexico, Argentina, Venezuela, Brazil, the UK, and parts of Asia [26].

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