Review on Foot and Mouth Disease

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ABSTRACT
Ethiopia is a leading country in the number of livestock population in the African content and Livestock play a great role in the country economy. However, our country is not using from her livestock as much expected due to many animal diseases circulating in animal population. Therefore, the objective of this paper is to review on Foot and mouth disease. Foot and mouth disease (FMD) is one of the animal diseases which cause threat to our livestock; an acute systemic infection affecting cloven hoofed animal species. The main route of infection of ruminants such as cattle is the inhalation of airborne virus, but infection via alimentary tract or skin lesions is also possible. Some of the clinical symptoms of FMD include fever, anorexia, weight loss, lameness, salivation and vesicular lesions (mouth and skin). Larger host range always supports fast spread of disease with more chance of the antigenic diversity and hence makes the control programme a tedious task. Diagnosis of FMD is by Clinical signs, and in a laboratory by virus isolation, demonstration of the FMD viral antigens or nucleic acid in a sample tissue or fluid. 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 vaccination.

1. INTRODUCTION
Ethiopia is a leading country in the number of livestock population in the African content and the role of livestock is very notable in that it contributes 13-16% of the total gross domestic product (GDP), 30-35% of Agricultural gross domestic
product (GDP) and more than 85% of farm cash income (Tsedeke and Endrias, 2011). In addition to their direct role in generating food and income (Perry et al., 2003; Bonnet et al., 2011), livestock are a valuable asset, serving as a store of wealth, collateral for credit and an essential safety net during times of crisis throughout the developing world (MoA, 2006) and generally generate a livelihood for 1.0 billion poor people in the world (Naqvi and Sejian, 2011).

The livestock sector accounts for about 30% of the agricultural GDP in sub-Saharan Africa (SSA) and nearly 60% of the value of edible livestock products is generated by cattle. However, Ethiopia has high livestock population which provides drought power, milk, meat fiber, fuel and fertilizer and foreign currency from hide and skin, our country is not using from her livestock as much expected due to many animal diseases circulating in animal population (Bonnet et al., 2011).

Foot-and-mouth disease (FMD) is one of these animal diseases which cause threat to our livestock; an acute systemic infection affecting cloven-hoofed animal species (Bastos et al., 2003).

FMD generally involves mortality below 5% but it is considered the most economically important disease of farm animals since it causes significant decreases in livestock productivity and trade in livestock products (Domingo et al., 2002). The main route of infection of ruminants such as cattle is the inhalation of airborne virus, but infection via alimentary tract or skin lesions is also possible. Some of the clinical symptoms of FMD include fever, anorexia, weight loss, lameness, salivation and vesicular lesions (mouth and skin). An asymptomatic persistent infection can be established in ruminants for several years. Animals with this kind of infection are referred to as carrier animals and are important reservoirs of the causative virus. African buffalo (Syncerus caffer) are important carriers and are a possible source of FMD outbreaks by virus transmission to susceptible animals such as cattle (Bruckner et al., 2002). Although FMD rarely causes death in adult animals, mortality rates are high in young animals (Doel, 1996). Recent outbreaks of the disease in a number of once FMD free countries have significantly increased public awareness of this highly infectious disease (Lordwin, 2002).

Foot and Mouth Disease (FMD) is one of the most important livestock diseases in the world in terms of economic impact. The economic importance of the disease is not only limited to production losses, but also related to the reaction of veterinary services to the presence of the disease and to the restrictions on the trade of animals and animal products both locally and internationally (James and Rushton, 2002). Even though this is economically important disease in livestock production area, there is a shortage of information on it. Therefore the objective of this paper is to review on etiology, epidemiology, pathogenesis, diagnosis, treatment and control of Foot and Mouth disease.
2. LITERATURE REVIEW

2.1. Etiology
The causative agent of the FMD (FMDV) belongs to the genus Aphthovirus of the family Picornaviridae (King et al., 2000). The size of the FMDV is about 30 nm characterized by the presence of single-stranded positive-sense RNA which is non-enveloped and has an icosahedral symmetry. The virion has sixty copies of each VP1-4, of which VP1, VP2 encapsidate the genome and VP3 are exposed outside (Jackson et al., 2002) while VP4 is completely lies underneath (Belsham et al., 1991). The three surface exposed capsid proteins carry the antigenic sites. Production of antibodies in infected animals is induced by both structural and non-structural proteins. The VP1-4 forms the virion. Most immunogenic protein VP1 has got maximum exposure on the capsid surface (Xu et al., 2013) whilst VP3 contributes mostly towards the capsid stability (Jackson et al., 2003).

Lipid solvents like ether and chloroform are ineffective whereas sodium hydroxide and sodium carbonate are effective disinfectants against FMDV. The FMDV is resistant to common chemical disinfectants especially when it is mixed with other organic materials. Phenolic-type disinfectants, alcohol, acetone, and other organic solvents and detergents have little effect on the virus. Formalin, KMnO4, sublimate of mercury, lactic acid and ethylene oxide are effective sterilizers. The virus can also be inactivated by 0.4% β-propiolactone and 1-2% NaOH, which destroys the virus in 2 minutes. A solution containing 4% sodium carbonate soap is effective under field conditions. The virus is also sensitive to drying. The sustainability of the virus in the the environment depends upon the environmental conditions; low temperature and high humidity rate always support the survival and propagation whereas hot and dry conditions as well as direct sunlight inactivate the virus (Verma et al., 2008).

2.1.1. Antigenic and Genetic diversity
Antigenic variability and genetic diversity make FMDV difficult to eradicate through vaccination. Presence of variable antigenic type in different geographical area and even the concurrence of different antigenic type in same geographical area always put a need to acquire the knowledge of existing antigenic type prior to start a control and eradication program or for the selection of a vaccine (Rudreshappa et al., 2012). Antigenicity is mainly decided by the capsid coating proteins. Seven immunologically distinct serological types of FMDV have been classified namely serotypes O, A, C, Asia 1 and SAT (Southern African Territories) 1-3 based on the antigenicity of the capsid coating proteins (Rodriguez and Gay, 2011; Ding et al., 2013). Within each serotype, there are a considerable number of strains with antigenic diversity and hence enforce to incorporate more than one FMDV strain to attain a significant protection. All the FMDV serotypes are clustered into genetic lineages distinctly with about 30–50% differences in the VP1 coding gene (capsid region genes) (Xu et al., 2013). New subtypes occasionally arise.
spontaneously. There is no cross protection between serotypes. Infection with one serotype type is fully susceptible with another six. Antigenic diversity led to variation in cross-protectivity particularly evident within the serotype A. Vaccines prepared from a single strain of serotype A virus may not provide immunity against other strains (Jangra et al., 2005). Further, variant forms (quasispecies) having versatility in antigenicity evolves in the field at different times due to high error rate during genome replication (Raies et al., 2009). Like other RNA viruses, the FMDV has a high mutation rate as the RNA polymerase lacks the proof reading activity. The population size of FMDVs is large which is responsible for high antigenic variability together with continuous circulation of the field virus and plasticity of the major neutralizing sites on surface of the virion. They give rise to serious problems in spite of availability of good inactivated vaccine (Chakraborty et al., 2014).

2.2. Economic Consequences of FMD
FMD has very serious both direct and indirect economic effects including loss of productivity in terms of meat and milk, loss of weight, delayed conception (James and Rushton, 2002). Countries where FMD has occurred lose national trading status and markets for live animals and animal products hence losing a lot of revenue that would be generated from the livestock sector. The disease also interferes with agriculture and tourism. Additional costs include application of control measures such as quarantines, slaughter, compensation, vaccination as well as conducting scientific surveillance after an outbreak in order to prove that the disease and the virus have been eliminated (Prempeh and Robert, 2001). The devastating economic implication of FMD are exemplified by the 2001 FMD outbreak in the United kingdom in which up to £5 billion was spent to compensate farmers and stamp out the disease (John, 2002).

2.3. Epidemiology
2.3.1. Host Range/Species Affected
Host range always governs the existence of pathogen in environment. Larger host range always supports fast spread of disease with more chance of the antigenic diversity and hence makes the control programme a tedious task (Verma et al., 2010; Teifke et al., 2012). FMDV infects mostly cloven-hooved mammals (order- Artiodactyla) and many other species of different orders (Thomson et al., 1984). Susceptible livestock include a variety of domesticated animals viz. cattle, water buffalo, small ruminants like sheep, goats along with pigs and reindeer. Deer, antelope, elephant, and giraffe are also susceptible (Teifke et al., 2012). Camels have low susceptibility. The FMDV do not affect horses, pet animals and birds. Experimental infection can be reproduced in Ilamas as wells as alpacas and camels. At least 70 wild animals species to settle down permanently in (including African buffalo, bison, elk, moose, chamois, giraffes, wildebeest, members related to deer as blackbuck, impala, and several species of deer along with the animals like
warthogs, kudu, antelopes and gazelles) can also get infection (Michel and Bengis, 2012).

2.3.2. Morbidity and Mortality
Variation in the morbidity rate occurs and may depend on species, age, sex as well as the status of the immunity. Self recovery in the animals is the result of immunity against the infecting serotype of the virus. Mostly the disease occurs due to one type of virus and development of immunity also remains confined against specific serotype, thus no immunity develops to other serotypes, a reason behind occurrence of the disease in the endemic areas. The presence of a single serotype in an area or population lead to clinical disease that may be in mild form and mainly infects young animals because of loss of protection from antibodies from the dam. Presence of carriers are common in endemic areas (Chang et al., 2013) and the best example of the same is the presence of 50-70% and 15% to 50% of carrier animals in wild African buffalo/cattle and sheep respectively. Morbidity and mortality rate may go up to 100% in such areas. There is also a report on the involvement of a single host i.e. pig involvement during one Asian epidemic. A mortality rate of <1% in adult animals has been observed in non-endemic areas with morbidity a rate of 100%. However, young animals may suffer severe losses as 40-94% mortality rates in lambs have been observed (OIE, 2009).

2.3.3. 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 (OIE, 2009). 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 Africa all the different serotypes of the virus are present with the exception of Asia 1 (Rweyemamu et al., 2008). In the eastern parts of Africa however serotypes: O and A; along with South African Territory (SAT–1 and 2) are still circulating (Ayelet et al., 2009; Balinda et al., 2010).

2.3.4. 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 (Woodbury, 1995). 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 10^8 infectious virus units per ml. 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 tyres or wind can play important role for spread of the disease (OIE, 2009).

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 (Tomasula and Konstance, 2004). Inhaled aerosolized virus may also serve as cause infection (Alexandersen et al., 2003), 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 (Alexandersen et al., 2003). Less obvious symptoms are seen in sheep compared to other species and in certain outbreaks they are important in disseminating the virus. The SAT type viruses in African buffalo populations may spread significantly though sexual contact. Infection in cattle can occur by breathing in the virus in small quantity.

Cool and damp climate always supports the spread of the FMD virus when animals are penned or housed especially in cold weather (Bhattacharya et al., 2005; Verma et al., 2008). The virus survives well below 40°C temperature, 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 (Donaldson et al., 2001). 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. Drying-off of the virus is prevented by organic material which also enhances virus survival. At 4°C, the viability persists for two months on wool. There is enhancement in survivability of FMDV provided there is protection from sunlight. Alteration in pH as below 6.5 or above 11 can easily inactivate the FMDV. 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 (Klein et al., 2008). Pacheco et al. (2012) reported that different serotypes or strains of FMDV have different transmission characteristics and emphasized the need of research in this area, which may be helpful in understanding the pathogenesis and epidemiology of FMD.

2.4. Pathogenesis
The route of infection of cloven-hoofed animals, other than in pigs where it is generally oral, is thought to be respiratory. In cattle the tissues most consistently infected during the pre-viraemic phase of the disease are the epithelia of the naso-pharynx and larynx (Arzt et al., 2011). The tissues of the naso-pharynx and FMD viruses have a complex relationship because not only does initial infection of ruminants take place there but the naso-pharynx is also the site of viral persistence in chronically infected animals (so-called carriers). Vesicle formation, cell lysis and significant inflammation occur at secondary replication sites (oral mucosa, skin of the horn-hoof junction & skin of the teats) but not in the epithelium of the primary replication site.

The cells which support viral replication are located in the basal layer of naso-pharyngeal epithelium. However, the mechanism by which viral replication occurs in the naso-pharyngeal epithelium without causing cell lysis is unknown; nor is there an explanation as to why virus can be readily cultured from pharyngeal scrapings (obtained using probing cups) that, in recently infected animals, may contain high levels of antibody (mainly IgA) directed against the infecting virus. In pigs, delayed clearance of viral RNA from pharyngeal and lymphoid tissues has been observed but that has not been shown for infectious virus (Arzt et al., 2011).

One or two days before the onset of clinical signs, cattle and pigs develop viraemia which may endure for up to 3 days. The source of virus in the circulation remains a matter of conjecture (i.e. another knowledge gap) but viraemia ensures distribution of virus to all parts of the animal's body. In infected animals the vesicles which develop at the sites of secondary replication contain by far the highest levels of infectivity; however, high concentrations of virus can also be found in lymph nodes, myocardium, lungs and skin even in the absence of obvious lesions (Zhang & Alexanderson, 2004; Arzt et al., 2010). Virus may also accumulate in the spleen, liver, adrenals, myocardium, pancreas, thyroid and mammary glands. In mammary tissue and myocardium, however, viral replication occurs in secretory epithelial cells of the alveoli and myocytes respectively, resulting in clear microscopic lesions (Arzt et al., 2011).

Epithelial lesions at secondary replication sites are initiated by infection of single cells in the stratum spinosum. Following infection of these cells, bullae develop either by lysis of cells swollen as a result of ballooning degeneration and the release of intracellular fluid, or by the formation of areas of focal intercellular oedema.
The bullae then coalesce, rupture or, more rarely, the fluid seeps away resulting in desiccation of the lesion (Woodbury, 1995).

Development of characteristic vesicular lesions in FMD is dependent on persistent local irritation or friction. In transplantation studies in guinea pigs it was shown that epithelium from predilection sites grafted to other body areas lost that predilection and vice versa. This explains why the mouth, feet and teats are predilection sites for the development of lesions and why pigs often develop lesions on the dorsum of the snout, i.e. as a result of “snuffling”. Similarly, warthog which often “kneel” on their carpal joints while feeding tend to develop lesions on their “knees” (Rout, 2016).

In various parts of the world including South America, East Africa and India/Pakistan, a heat-intolerance syndrome (sometimes referred to as ‘hairy panters’) has been associated with previous infection or ‘chronic FMD’, with a putative endocrine-related pathogenesis. The limited information available on this syndrome has been reviewed recently indicating that the extent of the syndrome’s association with FMD remains speculative (Arzt et al., 2011).

2.4. Clinical Signs
The disease is more severe in cattle and pigs but the sheep and the goats may even some time undergo undiagnosed. Anorexia and fever (up to 41°C) may develop in the cattle as well as in pigs. The clinical signs appear within 2 to 3 days after FMDV exposure and may last for 7-10 days. Fever and vesicles on the feet, between the toes as well as on heels, around the mouth, particularly in lips as well as tongue and palate and on the mammary glands are noteworthy but characteristic lesions are observed in interdigital space and coronary bands of hooves (Teifke et al., 2012).

In rare cases, the external genitalia may also develop the lesions. Depending upon the severity, these vesicles may enlarge and swell. Blisters that rapidly rupture/erupt can leave painful and raw erosions and ulcers that may take up to 10 days to heal. Various clinical signs such as depression and anorexia; salivation in excess; lameness and reluctant movement and rising are observed due to pain and discomfort from the lesions (Yoon et al., 2012). Abortions in FMD may not be directly due to virus replication but rather due to high rise of temperature. Most adults recover within 2-3 weeks though it may prolong due to secondary bacterial infections. Depression and lethargy, rapid loss of condition, gradual or sudden drop in milk production either temporarily or permanently may be observed. Lameness or mastitis in chronic form, reduced growth rate, loss of weight, infertility and poor body condition are the common sequel of the disease.

Although mortality rate in adult animals is very low but the young animals may die due to multifocal myocarditis. Severity in symptoms of FMD may vary according to host species, and the serotype and strain of the virus involved. In pigs, the
mouth lesions are comparatively less severe but the hocks and elbows may progress to severe foot lesions. The temperature in pigs may remain normal during the disease. The morbidity rate is 100% but a mortality of up to 5% in adults and up to 75% in piglets less than 8 weeks of age has been observed (Yoon et al., 2012).

In sheep and goats, lesions are less pronounced with variable clinical signs. Foot lesions may not be recognizable. Dental pad lesions in sheep can be seen. Mouth lesions are often remains unnoticed in the form of shallow erosions. Healing of the severe vesicles in the mouth occur within 7 days. Presence of vesicles on teats, vulva or prepuce is rare. There may be frequent development of feet and mammary gland lesions whereas in advance cases secondary infections lead to severe mastitis. The under-running of the sole and painful blisters may lead to chronic lameness. There may be drop in milk production and reluctance of the rams for mating may persist. Abortions are rare but ewes may abort. Sheep may remain asymptomatic (25%) or lesion at one site (20%). The mortality in immature lambs as well as in the kids is mainly because of the heart failure without showing any obvious vesicular lesions (Viuff et al., 2002).

Wild animals show symptoms similar to that in domesticated livestock with the formation of vesicle especially on the feet and in the mouth. Both the acute disease and subclinical infection or mild disease may be seen; SAT-type virus infection in African buffalo mostly remains subclinical. However, many wild species as gazelles, impala, blackbuck, white tailed-deer and warthogs show acute lesion with high mortality. Sometime FMDV may leads to swollen tongue similar to the allergic diseases (Deb et al., 2012). Myocarditis, losses in reproductive ability, and chronic heat intolerance are some of the common squeal of FMD that have also received little attention (Arzt et al., 2011).

2.4.1. Post Mortem Lesions
The FMD is characterized by the formation of fluid-filled vesicles or bullae either in single or multiple varying in size from 2-10 mm in diameter. The initial lesions include the formation of tiny pale areas leading to vesicle and subsequently bullae formation. These vesicles lost in few hours leaving behind red, eroded areas or ulcers. Sometimes vesicles having fibrinous coat, gray in colour and surrounded by a distinct demarcating line of newly developing epithelium may form. “Dry” lesions, mainly in pigs, are formed due to the loss of vesicular fluid and many time lead to necrosis. In rare cases, lesions may extend to skin and further secondary infections may aggravate the condition. Presence of coronitis and vesicle formation in multiple organs viz., teats or udder; pressure points in legs, pillars of rumen and external genitalia are common in cattle. Involvement of heart in the form of cardiac degeneration and necrosis which mostly appear as gray or yellow streaks in
the myocardium (“tiger heart” lesions) are observed in young calves (Chakraborty et al., 2014).

2.5. Diagnosis of foot-and-mouth disease
Diagnosis of FMD is by Clinical signs, and in a laboratory by virus isolation, demonstration of the FMD viral antigens or nucleic acid in a sample tissue or fluid. Detection of virus specific antibodies can also be used. Additionally, antibodies to viral non structural protein can be used as indicators of infection irrespective of vaccination status (OIE, 2009).

2.5.1. Clinical diagnosis
Infection of susceptible animals with FMDV leads to the appearance of vesicles on the feet, in and lesion around the oral cavity and on the mammary glands (Barnett and Cox, 1999). Vesicles can also occur in other sites such as nostrils and pressure points on the limbs especially in pigs. The severity of clinical signs varies with the serotype and strains of the virus, the age, breed of the animals, the host species, and the degree of immunity (Barnett and Cox, 1999). Other signs include lameness, reduced milk production, salivation. These signs range from a mild infection to one that is severe and in some extreme cases death may occur.

For example mortality from multifocal myocarditis is most commonly seen in young animals. However, clinical signs alone are not sufficient since other vesicular diseases such as swine vesicular virus disease, blue tongue disease among others, may produce similar signs and a wrong diagnosis may be made. A wrong diagnosis will consequently lead to inappropriate FMD control measures and this leads to wastage of otherwise limited resources such as vaccines and equipment in resource constrained communities and countries. It cannot even help in identifying the serotype and strain which are very crucial in vaccination program and this requires a laboratory based diagnosis (OIE, 2009).

2.5.2. Laboratory diagnosis
Several laboratory techniques for the detection and confirmation of FMD have been developed and are described in the OIE Manual of Diagnostic techniques (OIE, 2004).

Serological assays
Viral antigens can be detected using Enzyme Linked Immunosorbent Assay (ELISA). The demonstration of specific antibodies to structural proteins in non vaccinated animals can be achieved by this technique (Crowther and Abu, 1979). Serological tests for the detection of antibodies against FMD viruses irrespective of the vaccination status have been applied some studies (Berger et al., 1990). Although these tests were serotype specific, they were tedious to use for screening purposes especially in areas where FMD is endemic. Serological tests to detect
FMDV non structural proteins (NSP) as well as FMDV structural protein of serotype O have been developed (Chenard et al., 2003; Sorensen et al., 2005).

**Virus isolation**

FMDV infection can also be demonstrated by isolating the virus by cultures (OIE, 2004; OIE, 2009). The epithelium sample should be taken from the PBS/glycerol, blotted dry on absorbent paper to reduce the glycerol content, which is toxic for cell cultures, and weighed. A suspension should be prepared by grinding the sample in sterile sand in a sterile pestle and mortar with a small volume of tissue culture medium and antibiotics.

Further medium should be added until a final volume of nine times that of the epithelial sample has been added, giving a 10% suspension. This is clarified on a bench centrifuge at 2000g for 10 minutes. Once clarified, such suspensions of field samples suspected to contain FMD virus are inoculated onto cell cultures or into unweaned mice. Sensitive cell culture systems include primary bovine (calf) thyroid cells and primary pig, calf or lamb kidney cells. Established cell lines, such as BHK-21 (baby hamster kidney) and IB-RS-2 cells, may also be used but are generally less sensitive than primary cells for detecting low amounts of infectivity (Clarke and Spier, 1980).

The sensitivity of any cells used should be tested with standard preparations of FMD virus. The use of IB-RS-2 cells aids the differentiation of swine vesicular disease (SVD) from FMD (as SVD virus will only grow in this cell type) and is often essential for the isolation of porcophilic strains, such as O Cathay. The cell cultures should be examined for Cytopathic effect (CPE) for 48 hours. If no CPE is detected, the cells should be frozen and thawed, used to inoculate fresh cultures and examined for CPEs for another 48 hours. Unweaned mice are an alternative to cell cultures and should be 2–7 days old and of selected inbred strains. Some field viruses may require several passages before they become adapted to mice (Alexandersen et al., 2003). In the case of OP fluids, pre-treatment with an equal volume of chlorofluorocarbons may improve the rate of virus detection by releasing virus from immune complexes. This may not be of use in identifying the serotypes involved.

**Nucleic acid detection**

The presence of viral genomic material can be detected using RT-PCR assays. RT-PCR can be used to amplify genome fragments of FMD virus in diagnostic materials including epithelium, milk, serum and probang samples (Amarel et al., 1993). RT combined with real-time PCR has sensitivity comparable to that of virus isolation and automated procedures enhance sample throughput (Reid et al., 2001; Reid et al., 2003). Specific primers have been designed to distinguish between each of the seven serotypes. In situ hybridization techniques have been developed for investigating the presence of FMD virus RNA in tissue samples. These techniques
are only in use in specialized laboratories, although simplified systems for potential field-use are under development. Nucleic acid tests can identify the serotype and strains involved in FMD outbreaks providing a tool for tracing the spread of the virus, more detailed characterization and vaccine selection (Callahan et al., 2002).

2.6. Treatment

Instead of specific treatment, depending on the clinical manifestations symptomatic treatment may be rendered. Potassium permanganate mixed antiseptic mouth wash, sodium carbonate, boric acid and glycerin may be applied over the lesion. Feet of the affected animals may be washed with 2% copper sulphate solution. Washing of the wounds with soda ash solution and topical application of honey and finger millet is found suitable in foot lesions (Gakuya et al., 2011).

2.7. Prevention and Control

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 vaccination (Ding et al., 2013). Timely determination of exact status of disease in ruminants, particularly in small ruminants, is considered as gauze 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 authorities (Rashtibaf et al., 2012).

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 (Dhama et al., 2010).
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 (Klein et al., 2008).

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 (Sobrino and Domingo, 2001).

Implementation 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 (Bangar et al., 2013).

3. CONCLUSION AND RECOMMENDATION
Foot-and-mouth disease (FMD) is one of these animal diseases which cause threat to our livestock. The economic importance of the disease is not only limited to production losses, but also related to the reaction of veterinary services to the presence of the disease and to the restrictions on the trade of animals and animal products both locally and internationally. To control this disease 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 vaccination. Therefore, based on the above conclusion, the following recommendations are forwarded:

- Governments should develop and implement Foot and Mouth disease prevention and control policies and strategies
- Animal health worker should train animal owner on the importance of control foot and mouth disease to take their role
- National Veterinary institute should produce Foot and Mouth disease vaccine with minimum cost
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