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A Review on Foot-and-mouth disease: pathology, diagnosis and its management

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ABSTRACT

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Foot-and-mouth disease (FMD) is a highly infectious, contagious and economically important viral disease of cloven-hoofed animals and > 70 wild species. FMD virus (FMDV) belongs to the genus *Aphthovirus,* family *Picornaviridae*. This review is dealt with the pathology, diagnosis and management of FMD by ethnoveterinary practice. The review also addresses the progress made in understanding the pathogenesis of the disease and persistence of FMD virus.

Keywords: Aetiology, diagnosis, foot and mouth disease, FMD virus transmission, management, pathogenesis.

INTRODUCTION

Foot and Mouth Disease (FMD) is an Office International des Epizooties Listed disease and is considered to be the most infectious and an economically devastating disease to livestock industry[1-4]. It is a highly contagious, clinically acute, vesicular, notifiable disease of the members of cloven-hoofed animals, *viz.* cattle, sheep, goats, pigs and other domestic animals and more than 70 wildlife species including elephant[5,6]. Direct economic losses due to FMD are ascribed to losses in the meat and milk production[7], mortality in the young animals and reduced wool production in sheep[8]. Indirect losses occur in the form of declined draught capacity, reproductive disorders including abortions, still birth in pregnant animals and infertility in the recovered animals. As a result, it is a major hindrance to international trade in animals and animal products. FMD causes considerable economic losses in livestock productivity, and were estimated at round Rs. 23,000 crore per annum[9] in India. Eighty per cent of the total direct loss caused by FMD is due to drop in milk production[10, 11].

ETIOLOGY AND HOST PATHOGEN INFECTION

The aetiological agent of this disease is FMD virus (FMDV) is a prototype member of genus *Aphthovirus* and belongs to family *Picornaviridae*[12]. FMDV is moderately steady but can readily be inactivated by suitable disinfectants and heat. In general, the majority of strains are stable at pH range 7.0–8.5[13,14]. pH in bone marrow, lymph nodes and certain organs and offal does not decline during rigor mortis; virus can therefore be found in such material (especially if refrigerated or frozen) for an extended period of time, and may cause new outbreaks if fed to livestock as unheated waste food[15]. Alexandersen *et al*.[16] reported in a review about survival times of FMDV are as follows: up to 20 weeks on hay or straw; up to 4 weeks on cow's hair at 18–20°C; up to 14 days in dry faeces; up to 39 days in urine; up to 6 months in slurry in winter; 3 days on soil in summer and up to 28 days in autumn. FMDV can survive on hay for at least 200 days and in faecal slurry for 6 months[17]. Lipid solvents like ether and chloroform are ineffective whereas sodium hydroxide and sodium carbonate are effective disinfectants against FMDV but it is infective when it mixed with the other organic materials. Environment protection agency has recommended 4% sodium carbonate solution against FMDV is its maximum effectiveness. The virus can also be inactivated by 0.4% β- propiolactone and 1-2% NaOH, which destroys the virus in 2 minutes[18]. Sunlight has little or no direct effect on infectivity; any loss is indirect and occurs mainly through the effects of drying and temperature[19].

Viral genome encoding four structural proteins VP1-4 like VP1, VP2, VP3 and VP4, and 10 non-structural proteins (NSPs) L, 2A, 2B, 2C, 3A; 3B1, 3B2, 3B3; 3C and 3D[20,21]. Most immunogenic protein VP1 has got maximum exposure on the capsid surface[4] whereas VP3 contributes mostly towards the capsid stability[22]. The first molecule recognized as a primary host cell receptor for FMDV infection was integrins[23,24]. Receptors αvβ1, αvβ3, αvβ6 and αvβ8 plays an important role in entering the FMDV in cell[23,25-27]. In cattle, the αvβ6 integrin receptor is expressed constitutively at elevated levels on the surfaces of epithelial cells during natural infection at the infection sites, but not at the sites where lesions are not observed[28]. Major receptor that determines the tropism of FMDV for expression of FMDV antigen is αvβ6 integrin receptor in

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infected animal tissues like tongue and coronary bands. This integrin receptor recognition site consist a highly conserved region of Arg-Gly-Asp (RGD) triplet on the G-H loop of the VP1 capsid protein[29,30] and this G-H loop play an important role in respect to receptor and antibody binding site. It has been reported that upon multiple passages of FMDV in cell culture, the RGD motif can become dispensable; this is associated with the use of alternative receptors for cell entry[31,32].

PATHOGENESIS

Clinical sings and lesions

FMD is characterized by pyrexia, drooling of saliva and development of vesicles in and around mouth, on tongue, gum, feet, mammary gland and teats in adults[6,33]. Viraemia may be present for up to 2-3 days before the manifestation of vesicular lesions[16]. Lesions are often observed initially as blanched areas, followed by development of vesicles and these fluid-filled vesicles are readily seen in cattle and rarely observed in the mouth of sheep and goats, probably this is because of the thinness of the lingual epithelium causes superficial lesions to rupture early, leaving shallow erosions which usually heal within a few days. The age of lesions can be assessed by examining the stage of their development according to the following established criteria: development of vesicles from days 0 to 2; rupture of vesicles on days 1–3 (initially having fragments of epithelia attached); followed by sharply marginated erosion (days 2–3); with the sharpness lost from day 3; serofibrinous exudation on days 4–6; and the beginning of repair with a marked fibrous tissue margin at 7 or more days. In sheep vesicular lesions occur in the interdigital cleft, along the coronary bands and on the bulb of the heels, oral lesions are less common than on the dental pad, tongue and gums[33-35]. Clinical disease is usually severe in pigs, and the early signs include acute lameness, reluctance to stand, adoption of a dog-sitting posture, depression, loss of appetite and fever. In mouth lesions are most often located on the tongue, either far back on the dorsum or as tiny lesions at the tip. Lesions of the feet may include the shedding of claws ("thimbling"), and the accessory digits may be affected, as well as pressure points on the knees and hocks.

Mortality in adult animals is generally low, but it may be high in young animals, including calves, lambs and piglets, due to acute myocarditis. Post mortem examination of the heart in these cases often reveals a soft, flaccid heart with white or greyish stripes i.e. "tiger heart" or spots[36], seen mainly in the left ventricle and interventricular septum[16]. In young animals, dying from hyper-acute disease, there may be no significant macroscopical lesions in the heart (and an absence of vesicular lesions), but virus can usually be isolated from the myocardium or from the blood, and lesions can be detected by histopathological examination[37]. In adults no such significant lesion observed in the myocardium or skeletal muscles except lesions on the ruminal pillar[38].

The significance of FMD acute myocarditis in young animals in the spread of the disease is not well understood. Possibly there is little or no excretion of virus, since death usually occurs early, before the development of vesicular lesions. However, although in such cases FMDV replicates mainly in the heart, it appears plausible that a significant viraemia occurs[37]; if so, virus may be present in breath, saliva, nasal fluid etc. FMD may also cause abortion and still birth in pregnant animals (Ranjan et al., unpublished). Lungs and associated lymphnodes were severely engorged and oedematous; the fundic and pyloric regions of the abomasum were congested and had paintbrush haemorrhages; intestinal wall was oedematous and had diffused to patchy congestion/ haemorrhages over the serosa; the large intestines and mesenteric lymphnodes were congested and had patchy haemorrhages; spleen was congested, haemorrhagic and edematous; liver had discrete foci of haemorrhages over the capsule and gall-bladder distended with greenish bile observed in cattle and buffalo[38]. Sudden death during the clinical course and even during convalescent period in cattle and buffaloes has been ascribed to the degeneration of the myocardium and the conducting system[39] as has been observed in the necropsied cases.

Route 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, faeces and semen[40,41]. Mechanical transfer of virus has been reported from infected to susceptible animals through various route[42], people, fomites and vehicles[43,44]. $10TCID_{50}$ of virus is sufficient to infect a ruminant experimentally through aerosol exposure; however, pigs are relatively resistant to aerosol exposure[45] but infected pigs release largest quantities of air-borne virus and act as a important source of FMDV for long distance aerosol spread[45]. 2-4 days prior to onset of symptoms, the infected animals usually start shedding the virus[46-48]. Ruminants excrete lower titres of virus in their breath but are highly susceptible to infection by the respiratory route through air-borne transmission. As clinical diagnosis is often difficult in sheep, the infection can go unnoticed and therefore sheep can play a major role in the spread of disease as has been widely implicated in the prolific spread during the 2001 outbreak in the United Kingdom. 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[49].

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[15,50].

Incubation period

The incubation period for farm-to-farm spread resulting from direct contact may range from 2 to 14 days and depends on dose and the strain of virus, transmission route, species and the husbandry practices[35,51]. For within-farm spread the period is generally 2–14 days but may be as short as 24 h, especially in pigs and under very high challenge conditions. When spread is occurring within a herd or flock, the typical incubation period is 2–6 days, although, as mentioned above, under certain conditions it may be as short as 1 day or as long as 14 days. These ranges in incubation period are supported by both field and experimental observations[42,52]. Under experimental conditions the mean incubation period were 3.5 days for continuous, direct cattle to cattle contact and 2 days for intensive sheep-to-sheep contact[42,53]. Pigs were readily infected by direct pig-to-pig contact exposure, with a mean incubation period of 1–3 days depending on the intensity of contact[42]. Animals are not infectious until 0.5 days after the appearance of clinical signs as previous worker reported that period of infectiousness in cattle is only 1.7 days[54].

Mechanism of pathogenesis

In cattle, the epithelial cells of the dorsal soft palate, the roof of the pharynx just above the soft palate and part of the tonsil are thought to play a unique role in the prime infection[16] and it would be the possible site in other host species. Modern studies reported that subsequent to aerosol inoculation, the FMDV infection is initiated at the epithelia of mucosal associated lymphoid tissue of the nasopharynx in cattle[46,55,56]. After initial phase of infection ('pre-viremic' phase), virus replicates in pulmonary alveolar septa, FMDV is replicated significantly within the pulmonary pneumocytes with a considerable decrease in virus load inside the pharyngeal tissues[56]. Several studies have also concerned the roles for nasopharynx and lungs acts as the primary sites of FMDV natural infection in cattle[57,58]. In pigs, palatine tonsil or lungs are considered to be the primary site of infection following oral or aerosol inoculation, respectively[59]. Earlier published works have concerned the pharyngeal tissues of cattle as the predilection site for FMDV persistence[46,57,60-64].

First FMDV is interacted with the host cell receptors[23] and initial replication is followed by a viraemic phase for a period of 3-5 days. During viraemic phase, the virus reach to epithelial tissues of secondary sites of replication through the bloodstream. Previous record said tissue-specific localization of FMDV persistence with dorsal soft palate and dorsal pharynx concerned as the most common and frequent sites in cattle post viraemic phase[61,65]. Replication of FMDV at secondary sites viz. oral cavity, skin of feet and mammary teat which consist of cornified stratified squamous epithelia[16]. Epithelium of external genitalia and rumen is least affected by FMDV. In second stage of infection, lesions which are primarily observed as a blanched area followed by vesicles development on the mouth, feet and teats[35,66,67]. During viraemic phase, myocardial infection is typically seen in young pigs, small ruminants, and wildlife[68]. Due to active and effective immune response, virus is cleared from blood stream and tissues, which is confirmed by the production of virus specific antibody and may be dependent on the interaction of virus-antibody complex with phagocytic cells of reticuloendothelial system[69-71].

Sites of infection, replication and persistence of FMDV

FMDV enters susceptible animals directly through inspiration, ingestion or through cuts or abrasions on the skin. In the case of inhalation and ingestion of contaminated air or feed, the most significant site of infection and initial replication of the virus are probably the dorsal surface of the soft palate and the root of the pharynx. RT-PCR and in situ hybridization studies showed that these are the primary infection sites in pigs infected by contact or by airborne virus and also for cattle infected by contact or by needle inoculation[72]. The reason why the pharyngeal epithelial cell is more susceptible to FMDV infection than that in the oral cavity is that the epithelia in the oral cavity are stratified squamous and cornified. Therefore the viral particle passes this region that is covered, or protected, by a layer of dead cells, to the non- cornified pharynx region where the virus attacks the uncovered live cells directly. On the other hand, FMDV enters the animals through damaged skin or tongue directly. In contrast, replication takes place at the site of entry and the virus may spread through regional lymph nodes. After initial replication, either in the pharyngeal region or the other sites, the virus enters the circulation and reaches eventually to the secondary replication sites, especially the skin including the feet and mammary gland and the epithelia of the tongue and mouth, where the main viral amplification occurs.

Following recuperation from the acute phase of disease, a 50- 60 percentage of the animals may become carrier that shed the virus for long period[16,73,74]. However, pigs usually clear the virus within 3 to 4 weeks of infection and do not become carriers[16,75] with an exception of a single report which showed pigs as carriers[76]. FMDV continue to be present in very high titres at primary infection sites (e.g. nasopharynx, particularly the dorsal soft palate) in a subset of infected animals[46,61,64]. A carrier animal is one from which it is possible to recover infectious FMD virus 28 days after infection. This is generally done by isolation of infectious virus from

oesophageal-pharyngeal scrapings using a probang cup[77-79]. The maximum reported duration of the carrier state in different species is as follows: cattle, 3.5 years; sheep, 9 months; goat, 4 months; African buffalo, 5 years; water buffalo, 2 months[16]. However, the majority of cattle and sheep appear to lose their carrier status within a relatively short period of time. A meta-analysis of persistence studies indicated that carrier cattle cleared infection at a rate of 0.115 per month[80]. The mechanisms for the establishment and maintenance of the carrier state are not well understood, since persistence can occur in both vaccinated and non-vaccinated cattle[81]. The risk of carrier cattle or sheep transmitting virus to uninfected animals is generally believed to be extremely low[82]. The only direct evidence of transmission of virus from a carrier to a susceptible animal is that of transmission from African buffalo to cattle during the outbreaks in Zimbabwe in 1989 and 1991[83].

The historic recognition of FMDV persistence in ruminants has been reviewed extensively[6,16,45,68,78]. Briefly, the recovery of infectious FMDV from convalescent cattle was first convincingly demonstrated by Van Bekkum *et al.*[84]. Another landmark was Burrows' demonstration of tissue-specific localization of persistence with dorsal soft palate and dorsal pharynx implicated as the most frequent sites of recovery of FMDV from post viraemic cattle[61,65]. Yet, the anatomical and cellular sites where FMDV persists and the origin of virus detected by probang sampling still remain incompletely elucidated. Burrows had additionally recovered FMDV from several other tissues of carrier animals including the oesophagus, ventral soft palate, pharynx, glosso-epiglottic space and tonsillar sinuses. These early studies were somewhat limited in that they detected FMDV by VI, a technique which may be compromised in carrier animals by the presence of high titers of neutralizing antibody. The limitations of applying conventional VI techniques for detecting the carrier state in tissue samples and the benefits of detecting viral RNA by the polymerase chain reaction method has been highlighted by Donn et al[85]. In that study, viral RNA was detected in the tonsil, ventral and dorsal soft palate and cranial oesophagus of contact challenged cattle; however, all the tonsillar and oesophageal samples were negative by VI. More recently, detailed time course experiments have characterized clearance of FMDV RNA from tissues during the immediate post-acute period in cattle[86]. This work demonstrated that viral RNA was detectable in various tissues for up to two days after cessation of viraemia, but was largely cleared from most tissues of cattle at 14 days post-challenge. However, the same study demonstrated FMDV RNA in pharyngeal tissues (carrier and non-carriers) and lymph nodes (carriers only) up to 72 dpi. Notably, only one tissue (dorsal soft palate) contained viral RNA in every animal from which the probang specimen was positive by VI. This correlation strongly suggested a dorsal palatal source of virus detected via probang. Other works have similarly described that viral RNA is detectable in pharyngeal tissues beyond 28 dpi[45,46,60,62,78]. Similarly, in sheep, viral RNA has been detected in tonsil, dorsal soft palate and nasopharynx up to 43 days post-needle or contact challenge[87]. A recent study in sheep showed that by 10 dpi, the only tissues where FMDV still replicated were the tonsil and soft palate[88]. Viral RNA of FMDV Asia1 detected in OP fluid on or beyond 28 days post infection in Indian buffaloes[89] and cattle[90]. The percentage of FMDV Asia 1-positive OPF samples per animal during the sampling period, referred as persistence score, varied from 20% to 70% among the carriers.

Various mechanisms have been proposed to explain the establishment and maintenance of FMDV persistence[45,91]; however, further elucidation is clearly required. The hypothesis that immune mechanisms play a role in persistent infection in ruminants is supported by the early observations that infected vaccinated cattle become persistently infected more consistently than unvaccinated ones[92] and observed that dexamethasone treatment decreases viral shedding from persistent cattle[93]. Unvaccinated cattle excrete significantly higher levels of virus for longer periods compared with vaccinated cattle and this is independent of whether or not they subsequently become carriers[94].

Histopathology

The first histopathological changes in the cornified, stratified squamous epithelium are ballooning degeneration and increased cytoplasmic eosinophilic staining of the cells in the stratum spinosum, and the onset of intercellular oedema within the dermis. These early lesions are detectable only by microscopical examination[95,96] and as indicated earlier, apparently normal skin may contain significant amounts of virus[97]. This early stage may be followed by necrosis and subsequent mononuclear cell and granulocyte infiltration; the lesions, now macroscopically visible, develop further into vesicles by separation of the epithelium from the underlying tissue and filling of the cavity with vesicular fluid. In young animals dying from acute disease, there is lympho-histiocytic myocarditis with hyaline degeneration, necrosis of myocytes and infiltration with mononuclear cells[16]. The heart muscles showed extensive damages (hyalinization) to the muscle fibers, engorgement/ haemorrhages and infiltration with large collections of mononuclear cells between the fibers. Mucosal epithelium showed microvesicles and necrotizing inflammation and underneath dermis had mononuclear cells infiltration around the engorged blood vessels and oedema of the connective tissue[38]. The lung

showed severe engorgement, oedema and inter-alveolar mononuclear cells infiltration. Juleff *et al*.[62], found in the light zone of germinal zone of germinal centres following primary infection of naive cattle by laser capture micro-dissection in combination with quantitative real-time reverse transcription polymerase chain reaction, immunohistochemical analysis and corroborate by in situ hybridization. In germinal centre, he found FMDV positive capsid by Immunohistochemical analysis of tissue 29 to 38 days post contact infection. In persistently infected animals, dorsal nasopharynx (80.95%) and dorsal soft palate (71.43%) are the highest prevalence of viral detection while laryngeal mucosal tissues, oropharyngeal mucosal sites, and lymph nodes draining the pharynx are less frequently detected as persistence of FMDV[98].

DIAGNOSIS

Early recognition Foot and Mouth Disease in the field coupled with rapid laboratory diagnosis of the viral agent is of prime importance for both control and eradication campaigns in FMD endemic areas and as a supportive measure to continue disease free zones. It is also imperative to differentially diagnose the disease having similarity in clinical signs from other vesicular diseases such as, swine vesicular disease, vesicular stomatitis, and vesicular exanthema of swine[99]. Apart from these vesicular diseases, other infectious diseases viz., rinderpest (RP), peste des petits ruminants (PPR), malignant catarrhal fever (MCF), blue tongue (BT) and epizootic haemorrhagic disease (EHD) as well as physical injury; chemicals and thermal burns may also leads to stomatitis and foot lesions[99]. In addition, FMDV infected sheep and goats lesions are often confused with those of bluetongue or contagious ecthyma and lip or leg ulceration and are difficult to diagnose clinically. The suspected cases showing symptoms for FMDV are generally confirmed by laboratory diagnosis either by detecting the viral antigen/genome or antibody.

Virus detection

Various methods have been described in the OIE Terrestrial Manual for the detection of FMDV[49] and these methods are antigen detection ELISA (Ag-ELISA), virus isolation (VI), and nucleic acid recognition (NAR) methods. In vitro method for the detection of live virus in clinical samples only carried out by VI in clinical samples. A variety of cell culture systems viz. bovine[100], ovine[101], caprine[102] and porcine[103] origin *Viz.* primary bovine thyroid cells[100,104] or primary pig, calf or lamb kidney cells[105], BHK-21 or IB-RS-2 cells[106-108] and foetal goat tongue cell i.e. ZZR 127[102] is used for VI for FMDV from different clinical samples based on the cytopathic effect (CPE) usually develops within 48 h. Antigen capture ELISA (Ag-ELISA) is more sensitive than complement fixation test and this test is used for antigen detection and serotyping of the virus[104,109,110]. Other advanced test based on the principle of Ag-ELISA and chromatography skill was developed for detection of FMD[111-114]. Another method for diagnosis of FMD is based on genome detection. Rapid detection of FMDV genome from diverse groups of biological specimens such as nasal swabs[115], vesicular epithelium[116-118], milk, serum and probang samples[118,119], semen[118] by using different molecular tools. Variety of reverse transcription-polymerase chain reaction (RT-PCR) procedures were developed for detection of FMDV genome: conventional RT-PCR[120,121], RT-PCR ELISA[122], nested RT-PCR[123], real-time RT-PCR[119], portable real time RT-PCR[124,125] and automated RT-PCR[126]. Other nucleic acid detection methods were also developed for FMDV genome detection, the nucleic acid sequence based amplification (NASBA) test[127,128], the RT loop-mediated amplification (LAMP) test[118], real time reverse transcription-polymerase chain reaction (RT-LAMP)[3,129], universal RT-PCR[4], gold nano-particle immuno-PCR (GNP-IPCR)[3]. Newer methods of typing have been developed and widely utilized now a day's based on genotype specific multiplex polymerase chain reaction (PCR)[130], lineage differentiating RT-PCR for serotype A[131] and Asia-1[132] for simultaneously test and gives serotype identification[133] also developed, and are in use in India for detection of circulating Indian strains. In this country, detection of FMDV serotypes is routinely carried out by a double antibody sandwich ELISA[110]. RT-PCR[121,131,132] is applied on ELISA negative samples. If the disease is reported late, liquid-phase blocking ELISA is used for diagnosis for FMDV.

Antibody detection

Detection of antibody against structural protein of FMDV: Antibody against structural protein of FMDV has been detected by various tests viz. virus neutralization test (VNT), liquid-phase blocking ELISA (LPBE) and solid phase competitive ELISA (SPCE) as per recommended by OIE[49]. The VNT is now largely used as a confirmation test for sera found positive by ELISA and for import/export certification when importing countries specify the use of the VNT. VNT is labour intensive, requires sensitive cell lines, live FMDV and containment laboratory facility. The advantages of ELISA over VNT are that the test is rapid, can use inactivated antigens, and requires smaller volumes of post-vaccination sera, which are often available in limited quantities[134]. LPBE based antibody detection system is quicker, more reproducible, less variable and the result correlates well with VNT[135-137]. However, the LPBE was criticised for the specificity and variable stability of inactivated antigen used in the test[138]. The SPCE was developed to overcome this problem, because it has higher specificity than LPBE[138,139]. Recently

an alternative assay (rP1 protein-based solid phase competitive ELISA, rP1-SPCE) to LPBE for the detection of antibodies to FMDV serotype O has been developed[140].

Detection of antibody against non-structural protein of FMDV: Presence of FMD-specific structural antibody could be useful for diagnosis for FMDV, but this requires the absence of any history of vaccination because purified vaccine elicits antibodies only against structural proteins (SPs) not against NSPs after the vaccination while natural FMDV infection elicits antibodies against both SP and NSPs. Therefore, an ELISA that evaluate antibodies to FMDV NSPs can be used for differentiating infection from vaccinated animals (DIVA). Though, this OIE-index test for NSP serology is only available from PANAFTOSA, Brazil to the South American laboratories. A number of 3ABC ELISA test kits have recently become available and their sensitivity and specificity were compared to one another and to the OIE-index screening method at an international workshop in Brescia in 2004[141]. It was concluded in the workshop that 2 tests performed comparably to the OIE-index method of which the Ceditest (currently known as PrioCHECK® FMDV NS) is the only one available as a commercial kit[142]. In addition to 3ABC ELISAs, a variety of NSP tests based on the detection of antibodies to the recombinant 2B[143], 2C[144], 3AB[145], 3D[146] were developed.

Mucosal antibody detection: IgA is the excretory and secretary antibody. IgA test has considerable potential for the detection of persistently infected cattle following the application of a vaccinate-to-live policyand oropharyngeal IgA responses in FMDV-vaccinated and infected cattle and demonstrated that parenteral administration of conventional FMD vaccine does not elicit any IgA antibody in saliva[147]. Vaccinated pigs do not elicit mucosal antibody whereas vaccinated and subsequently infected pigs produce high levels of mucosal antibody, as seen in cattle[148].

Other test which are also detect antibody level in serum by Lateral flow devices (LFD)[113,114], latex beads agglutination test, enzyme-linked immune electrotransfer blot assay, monoclonal antibody based ELISA, and multiplexed Luminex assay have been developed for FMDV[3]. A chromatographic strip assay (Pen-side test) has been developed to rapidly detect serum antibodies to FMDV-NSP[149,150].

MANAGEMENT OF FMD BY ETHNOVETERINARY PRACTICES

There is no specific treatment for FMD. The conventional method of treating affected animals mainly involves the use of antibiotics, flunixin meglumine and mild disinfectants[151]. FMD has been managed traditionally by use of natural soda ash solution for washing of the lesions, while some communities have applied honey and even finger millet flour to the lesions[11,152]. These traditional remedies have been reported elsewhere in the management of wounds and ulcers[153-155]. Application of cereals and honey for the treatment and control of livestock diseases has been documented in Kenya[156-159]. By topical application of paste of finger millet flour and honey (50%), the mouth lesions healed in 4-5 days, and affected animals started taking feed slowly from third day onward and cows resumed eating after 3- 4 days after application[11,152]. Honey has been employed for treatment of infected wound as long as 2,000 years ago, even before bacteria were discovered. Antibacterial properties of honey are due to production of hydrogen peroxide, even though the concentration of hydrogen peroxide in honey is little; it is still effective as an antimicrobial mediator[155]. Honey stimulates monocytes in cell culture to release cytokines, tumour necrosis factor-alpha (TNF-á), interleukin (IL)-1 and IL-6, which activate the immune response to infection when used at a concentration of 1%[160]. When honey used at a concentration of 0.1%, it stimulate proliferation of peripheral blood B-lymphocytes and T-lymphocytes in cell cultures and phagocytes are also activated at same concentration[161]. Therefore, the mobilization of blood cells which are crucial in the immune response to infection together with the production of hydrogen peroxide, which inhibit microbes, could have contributed to the fast healing of the lesions in this case. Traditional usage of raw honey, wheat flour, finger millet flour, whole rice and jaggery plays an important role in the management and control of FMD. Finger millet act as galactagogue and bestowed with many other medicinal properties[162]. Gruel feeding remitted in rapid recovery of FMD affected dairy cows and improved milk production to the tune of 80- 90 %, even up to100 in almost all cows affected with FMDV infection and this gruel was prepared by cooking of equal proportion of whole rice, wheat flour, and finger millet flour in adequate quantity of water, jaggery (10%) and mineral mixture[11].

CONCLUSIONS

Foot-and-mouth Disease (FMD) is an economically important, highly contagious multispecies viral disease, affecting mainly cloven hoofed animals including wild life. It can spread rapidly by a various routes. The disease is usually characterized by severe lameness and dullness in pigs and severe mouth lesions in cattle, but the signs may be mild, especially in sheep and goats. An important feature of FMD is persistent infection in ruminants, producing the so-called carrier state. This may occur in convalescent ruminant animals as well as in vaccinated ruminants following exposure to infectious virus. Although the amount of infectivity that can be recovered

from carriers is small, the virus continues to be present in some species for months and in others for years. The risk of transmission from carrier animals cannot be excluded, but it appears to be low and to require certain, as yet undefined, trigger factors. The severe and highly contagious nature of the disease and the recognition of a carrier state have had major adverse consequences for the international trade in livestock and animal products. New techniques show great potential for more rapid and effective diagnosis and surveillance, but much remains to be done to validate their performance before they can be adopted by regulatory authorities for routine use. To prevent the economic losses from FMD there is need to adopt ethnoveterinary practice for management of FMD. Traditional usage of raw honey, wheat flour, finger millet flour, whole rice and jaggery plays an important role in the management and control of FMD.

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