Foot and Mouth Disease: A Disease of Top Priority for Eradication in India

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Introduction

Foot and mouth disease (FMD), a highly contagious and fast-moving disease (FMD) affects all cloven-hoofed animals including cattle, buffalo, pig, sheep and goat as well as more than 70 wildlife species. The disease finds a position in the WOAH/OIE list A infectious diseases of animals that is considered to be the most important hurdle for international trade of animals. In the world, the countries free from FMD have adopted strong measures to retain their freedom status. The Smoot-Hawley Tariff Act of 1930 passed after the last outbreak of FMD in the United States in 1929 is an exemplary effort that imposed a strict restriction on import of susceptible livestock. Except in New Zealand the disease outbreaks have been reported in every region of the world. It is currently enzootic in all continents except in Australia and North America. FMD has its first historical description during 1514 by an Italian physician Girolamo Fracastoro who encountered a similar disease of cattle in Italy. Subsequently, it took nearly 400 years when Friedrich August Johannes Loeffler and Paul Frosch in 1897 made a ground-breaking discovery demonstrating that a filterable agent could cause FMD that became the first observation of an animal disease to be caused by a virus creating a milestone in the history of veterinary virology.

Etiology and Pathogenesis

FMD virus (FMDV) belongs to the *Aphthovirus* genus in the *Picornaviridae* family. The RNA genome of the virus is single-stranded, positive-sense having a size of approximately 8.5kb surrounded by four structural proteins forming an icosahedral capsid. Seven immunologically distinct serotypes of the virus e.g., O, A, C, Asia 1 and South African Territories (SAT) 1, 2, and 3 circulate globally. In India, three serotypes O, A and Asia 1 are prevalent with serotype O attributable to majority of outbreaks. The virion appears as round particle with 25 nm diameter in electron microscopy. FMDV has very high mutation rates in the range of 10^{-3} to 10^{-5} per nucleotide site per genome replication.

Cattle and pigs are the most studied animals for pathogenesis of FMD. Infection of cattle usually occurs through the respiratory route by aerosolized virus. Studies have suggested that virus takes its initial replication in the lungs or pharynx, from where the virus further disseminates to foot and mouth epithelial areas. Within first 24 hours of experimental infection in cattle, virus has been detected in lungs and bronchiole, while by 72 hours, it could reach tongue, soft palate, feet, tonsils and tracheobronchial lymph nodes. While respiratory route is important for infection in cattle, oral route seems to play a vital role for

infection in pig that becomes infected through FMDV-contaminated food. Despite being less susceptible to aerosol infection than cattle, pigs have been reported to excrete huge quantum of aerosol virus as compared to cattle or sheep. Foot lesions are the most common finding and tongue lesions are less noticeable in pigs than in cattle. Large amount of aerosol virus is excreted by pigs, where huge viral replication takes place in the nasal mucosa than in the lungs.

Transmission and Symptoms

FMD virus (FMDV) rapidly replicates and spreads very fast through aerosol within the infected animals and among in-contact susceptible animals. After 2-3 days of exposure of the animal to the virus, the clinical signs appear and continue for 7 to 10 days. The typical clinical signs of FMD in cattle are fever, lameness, development of blisters/vesicles on tongue, oral cavity, interdigital space, coronets, udder and teats. Ruptured blisters on foot and mouth lead to lameness and reluctance to eat. In sheep and goats, the disease expresses itself in a mild or subdued form. Because of such mild or less florid nature of the disease in these species, clinical diagnosis of FMD in sheep was felt very difficult, for which they played a major role in the spread of disease to other livestock in 2001 UK outbreak. It has been reported that one-fourth of the infected sheep fail to develop lesions, while an additional one-fifth of affected sheep may exhibit solitary lesion. The symptoms of FMD are very similar to that of swine vesicular disease (SVD), vesicular stomatitis (VS) and vesicular exanthema of swine (VES) that must be considered while making a differential diagnosis. Although the disease is not so fatal in adult animals, it has debilitating effects causing weight loss, low milk production and tremendous reduction in draught power thereby drastically influencing the productivity of the animals. Severe myocardial involvement of the virus in young animals lead to mortality.

Cryptic Carrier State

After FMDV infection, some ruminants enter into an asymptomatic persistent infection. Some vaccinated and subsequently infected animals may also enter this phase. Such animals are referred to as 'persistently infected' or 'carrier' animals. Van Bekkum and associates were the first to demonstrate live FMDV from oesophageal-pharyngeal fluid (OPF) of FMD-recovered cattle. Carrier animals are those from which live virus can be isolated at 28 days or later after infection. The carrier state has been observed in cattle, sheep, goat, but not in pigs. Despite the demonstration of carrier status in ruminants, their role in spread of infection to naïve animals in field/natural scenario is controversial or debatable. Researchers have not yet found any experimental evidence indicating that carrier cattle or sheep can transmit virus to healthy animals. In a nutshell, the exact mechanism for the establishment and maintenance of such carrier state and its real significance in FMD epidemiology is not well understood till date.

Diagnosis

Control strategy for any infectious disease depends upon appropriate diagnostics to detect the agent as early as possible. For FMD this is of particular importance, since other vesicular diseases also produce very similar clinical signs and lesions thereby necessitating their consideration in differential diagnosis. For such situation, sensitive diagnostic assays should be used for an early and prompt diagnosis. Currently, FMD is

diagnosed and confirmed by serotyping sandwich ELISA, RT-PCR, real-time PCR, LAMP assay etc. For antibody detection, many ELISAs have been developed targeting different NSP genes of FMDV. Virus isolation is attempted in BHK-21, LFBK, IBRS-2 cell lines.

Countries with Re-emergence of FMD

Taiwan was free from FMD for 68 years, while an FMD outbreak due to serotype O virus, O/Taw/97 (Cathay topotype) struck the country during March 1997 that compelled the authority to slaughter a tune of 4 million pigs (38% of the entire pig population of the country) costing approximately 6 billion US dollar. One interesting fact was that even though FMD is considered to affect cattle and pig, but this 1997 Taiwanese epizootic demonstrated a restricted host specificity/tropism only in pigs (considered porcinophilic) not in cattle or goats. In the UK, outbreak of FMD due to serotype O PanAsia lineage virus occurred in 19th February 2001 that also caused havoc in Taiwan, South Korea, Japan, Mongolia and Russia. South Korea and Japan were free from FMD for 66 years and 92 years, respectively. But in March 2000, the outbreak occurred in these two countries.

From the 20th century, FMD has been a disease of high concern to many developed and developing nations. The fear for its re-emergence and its tremendous ability to cripple the national economy of a country have compelled for establishment of several sophisticated laboratories/institutes to continue research and development works to control the disease. Some of such institutes established specifically for FMD research are the Insel Reims in Germany in 1909, the Pirbright Institute (formerly the Institute for Animal Health) in Surrey, United Kingdom in 1924, Lindholm Island in Denmark in 1925, the PanAftosa in Brazil in 1951, the Plum Island Animal Disease Center (PIADC) in the United States in 1953 and National Institute on FMD-International Centre for FMD at Bhubaneswar, Odisha, India in 2017.

Prevention and Control

Currently, inactivated trivalent FMD vaccine is being used in bovine population at six months interval in India for control of the disease as an initiative of Government of India under Livestock Health and Disease Control Programme (LHDCP). The country took such initiative to control FMD since 2003 under FMD control program (FMDCP). The implementation of the FMD control programme has drastically reduced the incidence of FMD. Strict biosecurity practices and movement restriction of animals undoubtedly help minimizing the chances of virus spread. Public awareness is of immense importance for such efforts.

National Animal Disease Control Programme

National Animal Disease Control Programme (NADCP), a flagship scheme initiated by hon'ble prime minister of India in September 2019 with a dream towards control of FMD and another bacterial disease Brucellosis through vaccination of 100% cattle, buffalo, sheep, goat and pig population for FMD and 100% bovine female calves of 4-8 months of age for brucellosis with a total estimated cost of Rs.13, 343 crore for five years (2019 to 2024). The programme itself is a true reflection of the importance of FMD and how Government of India (GoI) is serious with high concern. The overall aim and objective of the NADCP for FMD is to control the disease by 2025 with vaccination with its final eradication by 2030 that will augment

the production with increased exports of milk and livestock products. Intensive Brucellosis Control programme in animals was aimed towards controlling Brucellosis leading to effective management of the disease in animals and humans being a disease of zoonotic concern. The programme is a central sector scheme with 100% funds provision by GoI to the states and union territories.

Conclusion

FMD is a highly contagious disease affecting all cloven-hoofed animals including cattle, pig, sheep and goat. FMD virus belongs to the *Aphthovirus* genus in the *Picornaviridae* family and rapidly replicates and spreads very fast through air. In India, three serotypes O, A and Asia 1 are in circulation with serotype O responsible for majority of outbreaks. FMD in cattle produces frank clinical signs of lameness and vesicular lesions on the tongue, feet, snout, and teats. After FMDV infection, some ruminants enter into an asymptomatic persistent infection carrying the virus in the oropharyngeal region. Sensitive assays like ELISA, RT-PCR and real-time PCR platforms are used for diagnosis of FMD. National Animal Disease Control Programme is an initiative of Government of India towards control and eradication of FMD, where biannual vaccination of all bovine population is ensured so as to build a higher level of herd immunity.