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A Comprehensive Review on Epidemiology, Prevention and Control of FMD Virus in Pakistan

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Abstract: Foot-and-mouth disease (FMD) is a severely debilitating viral infection that affects cloven-hoofed animals and is seen as a major danger to the global cattle economy. The OIE has designated 70 nations as FMD-free zones, regardless of immunization status, whereas Pakistan and about 100 other countries are still classified endemic or sporadic zones. The infection is most common in cattle and pigs, although it also affects goats, lambs, buffaloes in Pakistan. External factors, such as common disinfectants and standard meat preservation methods, have no effect on the virus. After an acute infection, the virus is shed in all body secretions and excretions (including exhaled air), such as saliva, nasal and lachrymal fluid, milk, urine, faeces, and sperm. In the absence of infection, preventive measures such as national border control should be established to prevent major movement of animals and livestock products from non-free neighbors or trading partners. FMD is currently widespread and widespread throughout Pakistan, while the disease's prevalence varies significantly throughout the country's various farming systems and agro-ecological zones. Five of the seven FMDV serotypes have endemic distributions in the nation, with Serotypes O, A, C, SAT1 and SAT2 being responsible for FMD outbreaks from 1974 to 2007. The most common serotype is O, which accounts for 72% of all outbreaks studied in the nation. Control through eradication, strengthened veterinary services, and control and prevention of other infections are all part of the global elimination of FMD. The virus-related obstacles, economic considerations of FMD enzootic considerations, and social and political issues are the key challenges addressed during FMD eradication. Eradication; FMD; Pakistan are some of the terms that come to mind while thinking about eradication.

Keywords: Eradication, FMD, Pakistan

1. Introduction

Foot-and-mouth disease (FMD) is a severely debilitating viral infection that affects cloven-hoofed animals and is seen as a major danger to the global cattle economy [58]. Foot-and-mouth disease (FMD) is a clinically acute, infectious viral infection that affects domesticated ruminants, pigs, camels, and more than 70 wild animals, including elephants. It is a global danger to food security and causes substantial economic damage to livestock producers and industry. The causal agent, FMD virus (FMDV), belongs to the Aphthovirus genus in the Picornaviridae family [11]. The virus is divided into seven immunologically different serotypes: A, O, C, Southern African territories (SAT)-1, 2, 3, and Asia-1, with a large number of strains demonstrating varying degrees of genetic and antigenic diversity within each serotype. Fever, lameness, and vesicular sores on the lips, tongue, feet, snout, and teats of affected animals are all symptoms of the disease [2]. One of the virus's characteristics is that it is impossible to stop it from spreading, making it tough to control and eradicate the disease globally. Although the virus is rapidly inactivated at pH values less than 7.0 (below neutral pH), it may withstand high temperatures when protected by proteins, such as those found in milk, which limits virus inactivation and hence increases virus persistence in the environment [41]. Many of the known animal infectious are prevalent in Pakistan and are poorly managed. FMD has a significant influence on economic development, resulting in both direct and indirect losses. FMD is viewed as a key impediment to international commerce in Pakistani prospective cattle exports. This view is based in part on the misconception that national FMD-free status is necessary before exports may take place. The Pakistani government is now working to construct a disease-free zone for export purposes, which the World Organization for Animal Health (OIE) supports [30]. FMDV is prevalent in Pakistan, where it causes many outbreaks each year. Previous research has found evidence for the presence of five FMDV serotypes out of seven (O, A, C, SAT1, SAT2) in Pakistan samples obtained from distinct outbreaks. Currently, the frequency of FMD outbreaks in Pakistan is growing, and cattle are at danger of infection; however, there is no government policy in place to combat the disease. Lack of immunization tactics, unfettered animal mobility, high rates of interaction between animals at commercial markets, community grazing areas, and watering stations, and insufficient surveillance and diagnostic facilities have all been cited as explanations for the disease's rising occurrence [5]. As a result, the goal of this study is to discuss the epidemiology, as well as the prevention and control of food and mouth infection.

2. Epidemiology

The FMD was originally widespread throughout the world, but due to stringent control and eradication measures implemented by emerging nations, its incidence has decreased. The OIE has designated 70 nations as FMD-free, regardless of vaccination status, whereas Pakistan and nearly 100 other countries are still deemed endemic or sporadic zones [36]. With the exception of New Zealand, outbreaks have occurred everywhere there is cattle. The infection, however, is seen in enzootic form on all continents (except Australia and North America). Serotypes O and A, as well as South African Territories (SAT–1 and 2), are still circulating in eastern Africa [19]. FMD is endemic in many parts of Asia (including the Middle East), Africa, and South America. Europe has had sporadic outbreaks of FMD, but Canada and the United States are devoid of the disease [57]. Due to the virus's longevity in wild African buffalo, eradication is impossible. The most frequent serotype of FMDV is type "O," which is found all throughout the world among the seven serotypes. The pan-Asian outbreak of 1990, which caused substantial economic losses in several nations throughout the world, was also reported [64]. There have also been a few reports of FMD occasional seasonal recurrence at low levels in specific portions of Pakistan and northern India [36]. Many nations, including South Africa, Botswana, Namibia, Zimbabwe, Tunisia, and Morocco in Africa, and Chile, southern Argentina, Uruguay, Guyana, Surinam, and French Guiana in South America, have eliminated FMD and are said to be free of the infection. Iran, the former Soviet Union's southern states, and South-East Asia, including India and Pakistan, the Philippines and Malaysia, as well as Sub-Saharan Africa, Tanzania, Egypt, Ethiopia, and Eritrea [1, 44]. Many European nations claim to be free of FMD, although isolated outbreaks have been observed, such as in Greece in 2000 and the United Kingdom, Republic of Ireland, Netherlands, and France in 2001 [59]. The same strain was responsible for an epidemic in Asia. After the slaughter of over 4 million animals, the outbreak was eventually brought under control in the United Kingdom, but no vaccination programme was implemented [44]. Serotype that is most common:

South America, Europe, and Africa are the continents O, A, and C, respectively.

Asia 1 (O, A, C): Asia.

North and Central America, New Zealand, and Australia are all virus-free [27].

3. Risk Factors

3.1. Factors Affecting the Host

The infection is most common in cattle and pigs, although it also affects goats, lambs, buffaloes in Pakistan, and llamas in South America. The virus's infectivity is restricted to certain species in some strains. Although cattle, sheep, and goats can be carriers, they are not frequently infected, and early tests in Kenya revealed that goats were seldom carriers and sheep were not at all. Immature animals and those in high health are more sensitive, and genetic variations in susceptibility have been discovered [53, 54]. The infection does not affect horses [20]. Wildlife such as deer in England, water buffalo (Bubalus bubalis) in Brazil, and wild ungulates in Africa become infected on a regular basis, however they are thought to play little or no role as infection reservoirs for domestic animals. The African buffalo (Syncerus caffer) is a significant exception, since it is likely the natural host of the SAT forms of the virus and a major source of infection for cattle in southern Africa [56, 65]. Although the infection is minor in buffalo populations, infection rates are typically high and can last for years [55]. The tamed Asian buffalo, on the other hand, exhibits normal clinical infection and disease transmission from buffalo to other animals. In Europe, small rodents and hedgehogs, as well as capybaras in South America, might serve as reservoirs [11].

3.2. Environment and Pathogens Factors

External factors, such as common disinfectants and standard meat preservation methods, have no effect on the virus. It can survive contaminated premises for up to a year, 10-12 weeks on clothing and feed, and up to a month on hair. It's very sensitive to pH shifts away from neutral [66]. The virus is swiftly destroyed by sunlight, but it may survive on pasture for lengthy periods of time at cold temperatures [67]. When heat disinfection is utilized, boiling successfully eliminates the virus if it is devoid of tissue, but autoclaving under pressure is the safest approach. In bull sperm frozen at -79°C, the virus may persist for more than 60 days. In general, the virus is heat-susceptible but cold-resistant [68]. The majority of standard disinfectants have little impact, however sodium hydroxide or formalin (1-2%) or sodium carbonate (4%) will kill the virus in a matter of minutes [4]. Uncooked meat tissues, particularly bone, are likely to stay infectious for lengthy periods of time, especially if quickly frozen, and to a lesser extent, meat cooled or frozen slowly. The pH of the medium has a strong influence on the virus's ability to survive [75]. The virus is inactivated when it develops acidity in rigor mortis, but fast freezing prevents acid phonation, hence the virus is likely to survive [63]. However, when the virus is thawed, the paused acid generation resumes, and the virus is potentially killed [60]. Where acid production is lower, such as in the viscera, bone marrow, blood arteries, and lymph nodes, prolonged survival is more likely [51]. Meat that has been pickled in brine or salted using dry techniques may still be infectious. Fomites, such as bedding, mangers, clothes, motor tires, harness, feedstuffs, and skins, can be a long-term source of infection [69]. There are allegations that the virus may travel through the alimentary tracts of birds unaffected, allowing them to function as carriers and spread infection across great distances and through natural topographical barriers such as mountain ranges and the sea [7].

3.3. Mode of Transmission

After an acute infection, the virus is shed in all bodily secretions and excretions (including exhaled air), such as saliva, nasal and lachrymal fluid, milk, urine, faeces, and sperm [70]. Despite viral entrance via skin wounds or the gastrointestinal system, the predominant preference and replication location is the mucosa of the throat. Pigs, in particular, shed large amounts of viruses in aerosolized form Infected animals normally begin releasing the virus four days before symptoms appear. After recovery, some animals might continue to excrete the virus for months or even years. Vesicles in the buccal mucosa (particularly the tongue and dental pad), bulbs of heels, and inter-digital area break within 24 hours, producing vesicular fluid with up to 108 infectious virus units per ml [40]. Direct or indirect contact with diseased animals and contaminated fomites and fodder can transfer the infection, however the majority of transmission events occur due to the movement of infected animals. Many other routes of infection, such as diseased animals' wool and hair, contaminated grass or straw, animal handlers' boots and clothes trapped in mud or dung, livestock equipment or vehicle tires, or wind, can also play a part in disease dissemination [36]. Infected milk might infect newborn calves and spread disease between farms. The virus has also been discovered to be transmitted by milk trucks [45]. Inhalation of aerosolized virus, ingestion of contaminated feed, fodder, and exposure to contaminated utensils can all contribute to viral penetration through skin wounds and the mucosal barrier, spreading the infection [50]. However, there is species diversity in the importance of sources and chances of exposure through different pathways, since aerosolized virus affects cattle and sheep more severely than pigs [3]. The virus can live well below 40 degrees Celsius, but it can be readily inactivated by raising the temperature and lowering the relative humidity to less than 60%. Aerosol transmission of virus up to 250 kilometers has been documented under favorable environmental circumstances (high humidity) [75]. The virus may persist for up to a year at 4 degrees Celsius. By quickly heating the virus to 56°C, the virus loses its infectivity. Because FMDV is connected with animal proteins, a% age of FMDV in contaminated milk will survive pasteurization. In dry faeces, the virus may persist for 14 days, more than 6 months in slurry, and 39 days in winter. Virus survival in animal products, including meat, is dependent on pH; the virus thrives at pH>6.0, but is rendered inactive by rigor mortis, which causes muscle acidification [52]. Lymph nodes or bone marrow that have been frozen or refrigerated can potentially keep the virus alive for a long time. Carriers (particularly cattle and water buffalo), convalescent animals, and vaccinated animals exposed to the infection can all spread the disease [25].

3.4. Various Strategies for Prevention and Control

In the absence of infection, the following preventive actions should be implemented: National boundaries must be controlled to prevent major migration of animals and livestock products from non-free neighbors or trading partners. Imports of animals and cattle products from endemic nations are prohibited in officially free countries, in conformity with OIE criteria. In the case of an epidemic, take the following steps: To reduce the quantity of virus released, rapid slaughter of infected animals, in contact animals and herds considered to have received infection by contact, followed by cleaning and disinfection to reduce the risk of re-infection, strict movement controls, extending to movement of livestock products on and off farms. It's also vital to consider the possibility of an emergency vaccine [14]. Strong infrastructure, skilled veterinary professionals, well-equipped laboratories, good governance, prompt and accurate diagnosis, rapid reaction measures, ongoing monitoring and surveillance, and obligatory immunization are all required to successfully manage FMD [71]. The accurate diagnosis of infection status in ruminants, especially tiny ruminants, is used as gauze to monitor viral activity in a given region. Controls and monitoring in specified areas or zones are essential to safeguard FMD-free nations against imports and cross-border animal movement [72]. If FMD is suspected, it is critical to notify regulatory veterinary authorities as soon as possible so that a quick diagnosis may be made [49]. A timely reaction is critical for containing an FMD epidemic. If there is any indication of vesicular infection, the state and central veterinary authorities must be notified immediately [34]. Due to the negative economic repercussions of the existence of FMD, some steps have been implemented to maintain a country's disease-free status. To control FMD in a disease-free country, there is a requirement for the initial implementation of a test and slaughter policy of all infected as well as susceptible animals (in close proximity), as well as movement restrictions for susceptible animals, disinfection of infective premises, and increased surveillance to prevent further spread. Import restrictions on suspected livestock or animal products, including fresh meat, from countries where FMD is present are necessary [48]. Economic constraints and societal or religious taboos are preventing FMD-endemic nations like India from enacting test and slaughter policies. In endemic nations, vaccination followed by sero-monitoring is the greatest option for successful control [62]. In reality, in the past, numerous European nations, such as France, have implemented vaccination and then halted it [13]. It is critical to comprehend disease dynamics in order to establish an effective immunization strategy [73]. It identifies the best times to provide vaccines. Individual vaccination of huge ruminant populations becomes easier as a result [16]. It is important to remember that the bulk of the infections caused by this virus are subclinical in form and so unrecognized, necessitating the use of vaccinations of different quality and efficacy [25]. Emergency vaccination is not permitted in certain industrialized nations because the vaccine interferes with accurate diagnosis [22]. There has been a misconception about carrier animals and their involvement in FMD epidemiology; any animal with FMD viral antibodies is considered a possible carrier and hence cannot be traded internationally [35]. If an epidemic such to the one that occurred in the United Kingdom in 2001 occurs again, safe and efficient vaccination is required [15]. In India, a location-specific programme dubbed the 'Foot and Mouth Disease Control Programme' (FMDCP) has been implemented in more than 200 districts. This has helped cloven-footed animals build herd immunity and has saved huge economic losses [39]. The federal government is providing cash for vaccine purchases, cold chain maintenance, and other logistical support, as well as cooperation from state governments to supply personnel [12].

4. Vaccination

Vaccination, which includes FMD, is the most effective technique for preventing viral infections. Veterinary vaccines represent 26% of the worldwide vaccination industry [40]. However, vaccinations that can prevent infection and transmission are in short supply. The current vaccination protects against the infection but not against infection or viral replication. Furthermore, vaccinated animals may develop into asymptomatic carriers who release the virus for months or even years after vaccination. Vaccination reduces FMDV transmission to neighboring regions during outbreaks, in addition to giving protection. The decision to vaccinate is complicated and depends on a variety of scientific, economic, political, and social variables [13]. Although killed trivalent vaccinations (containing strains 0, A, and C) are widely used, the development of vaccines from locally isolated virus is becoming more prevalent due to the growing frequency of antigenic ally distinct sub strains. Infected tongue tissue, a cell culture of bovine tongue epithelium, or another cell culture are used to get the virus. BHK (baby hamster kidney) is a popular viral culture medium, and the BHK vaccine is currently widely used. Its main advantage is its capacity to adapt to deep suspension culture rather than monolayer culture, allowing large-scale viral production to be carried out within reasonable space constraints [74]. Formalin was once used to inactivate the virus and generate a dead vaccine, but it has drawbacks, thus more complex agents, such as binary ethylene immune (BEl), are now utilized. Only 6-8 months of serviceable immunity may be expected following a single vaccine [47]. Vaccines made from 'nature' viruses provide better protection than vaccines made from 'culture' viruses. Oil-adjuvant vaccines have the potential to provide extended protection and only require yearly revaccination in mature cattle, biennial revaccination in young stock, or every 4-6 months in pigs [46]. General immunization is advised as a control measure in countries where the infection is enzootic or where the risk of introduction is high, such as Israel. If an outbreak arises, a booster vaccine with the appropriate serotype will dramatically strengthen the population's resistance. The broad immunization technique, on the other hand, has a number of drawbacks. In animals whose susceptibility has been lowered by vaccination, hidden infections can develop, allowing for the formation of 'carrier' foci [61]. The number of carrier animals produced by vaccination is now widely acknowledged to be significantly higher than previously assumed. Apart from being a powerful means of propagating the infection, these animals also serve as a good medium for the mutation of existing viral strains, as the hosts are immune. The carrier condition in both vaccinated and unprotected cattle can last up to 6 months and can cause new epidemics in all species [4].

5. Eradication as a Method of Control

The completeness with which an eradication effort is implemented determines its success. All cloven-footed animals in the exposed groups should be killed and burnt or buried on site as soon as the diagnosis is made. Meat should not be reclaimed, and milk should be considered contaminated. Inert items that might be contaminated should not be left infectious areas without being properly disinfected. This is especially true with human apparel, automobiles, and farm machines. Bedding, feed, feeding utensils, animal products, and other items that cannot be sterilized properly must be disposed. Cleaning and disinfecting barns and small yards using 1-2% sodium hydroxide or formalin or a 4% sodium carbonate solution is required. Acids and alkalis are the most effective viral activators, and their action is substantially boosted when a detergent is present. The presence of organic debris can drastically affect the effective pH of a disinfection surface, thus it must be well maintained. The farm should be left unstocked for 6 months after all probable sources of infection have been eliminated, with restocking authorized only after 'sentinel' test animals have been introduced and have remained uninfected. International standards for verifying infection-free status are stringent. Outdoor location recommendations are tough to come by. According to observations in Argentina, polluted pastures and unsheltered yards that are kept unstocked for 8-10 days are free of infection. There can be no animal movement, and human and car traffic must be kept to a minimum. Persons working on the farm should wear waterproof clothes that can be cleansed easily with a spray and then removed as soon as the person departs the farm [10].

6. Quarantine

The diagnosis of FMD is enough to cause adjacent disease-free countries to close their borders and other countries to impose embargoes. Animals cannot be moved to or from the affected location, according to local veterinary officials. Only veterinary authorities' permission is required for movement of animals, supplies, and vehicles within a 10-kilometer radius of the contaminated site. Cleaning and disinfecting contaminated areas using acid or alkali chemicals at appropriate concentrations is the preferred method of decontamination. Veterinary authorities should not allow premises to be refilled until sentinel animals have remained disease-free and the premises have been deemed satisfactory [37].

7. The Disease's Current Status in Pakistan

In the outbreaks 62 serotype of O, 24 serotype of C, and 12 serotype of A were reported in Pakistan between 1957 and 1973, according to reports. Between 1982 and 2000, three serotypes of FMDV were detected in cattle epidemic investigations by the National Veterinary Institute [18]. FMD is currently widespread throughout Pakistan, while the disease's prevalence varies significantly throughout the countries various farming systems and agro-ecological zones. Previously, the infection was common in the pastoral herds of the country's fringe low-land zones. However, this pattern has shifted, and the disease is now often seen in the country's highlands [43]. Five of the seven FMDV serotypes have endemic distributions in the nation, with Serotypes O, A, C, SAT1 and SAT2 being responsible for FMD outbreaks from 1974 to 2007. The most common serotype is O, which accounts for 72% of all outbreaks analyzed in Pakistan, followed by A (19.5%), and Serotype C, which has not been detected in Pakistan since 1983 [6]. A serotype C specific antibody was found in cattle, suggesting that serotype C virus transmission in the nation may have gone undiscovered [42]. Serotypes O, A, SAT2, and SAT 1 were identified as the causative serotypes of outbreaks between 2007 and 2012 [21]. In the last seven years (2009-2015), MoLF has received 93 reports of FMD outbreaks on average. Every year, outbreaks occurred, however the most were recorded in 2011 and 2012, with 124 and 205 outbreaks reported, respectively. However, due to the endemic nature of the disease and the unreported cases by farmers, the estimates supplied are clearly low and do not reflect the reality of the epidemiological situation in the nation [32]. The disease's prevalence varies by location, and studies undertaken thus far have not included all parts of the country. However, recent serological investigations in the southern part of Pakistan [42], the central part of Pakistan [17], the northern and south-west parts of Pakistan [17], the northwest and eastern parts of Pakistan [31], and various regions of the country [6] revealed that FMD is a major threat in many parts of the country, resulting in significant economic losses due to morbidity, mortality, and trade restrictions. It was looked at the seroprevalence of FMD in three districts of Punjab [42]. A total of 193 (21%) of the 920 cattle tested were determined to be positive at the individual animal level. On the other hand, out of 116 herds tested for antibodies to the FMD virus's 3ABC non-structural protein, 68 (59%) had at least one positive animal. Furthermore, Rawalpindi district (61%), Lahore (59%), and DG Khan (52) districts had considerably greater herd seroprevalence. Similarly, the Rawalpindi district has the highest FMD sero-prevalence (26.1%), followed by Lahore (18.8%), and DG Khan (17.8%). Between November 2007 and February 2008 [17] conducted a sero-epidemological investigation in two districts of Punjab with the goal of determining the seroprevalence of Foot and Mouth Disease (FMD) in cattle and identifying potential risk factors associated with the disease. Using the 3ABC-ELISA, they collected sera samples from 273 cattle in 98 herds and found an overall sero-prevalence of 12.08%. When it came to sero-prevalence at the district level, they discovered that the Rawalpindi district had a substantially greater seroprevalence (20%) than the Lahore district (5.88%). They also looked at herds for the presence or absence of other species in terms of FMD prevalence and discovered that herds with other species had a prevalence rate of 15.52%, while those without any other species had a prevalence rate of 6.06%. [28] Used 3ABC ELISA to examine FMD in indigenous cattle in Southern Punjab between October 2007 and March 2008. At the animal and herd levels, seroprevalence was determined to be 9.5% and 48.1%, respectively. Furthermore, they found that Seroprevalence was substantially greater in Punjab than in Sindh [33]. Between October 2008 and May 2009, a sero-epidemiological investigation was conducted in seven districts of the South Punjab zone in south-western Pakistan. The 3ABC-ELISA was used to examine 770 cow serum, with an overall seroprevalence of 8.18% recorded. The district with the greatest incidence was DG Khan (30.2%), while the districts with the lowest frequency were Kashmor and Sukkar, each having a prevalence of 6.3%. A total of 496 cattle were tested for antibodies to the FMD virus's 3ABC non-structural protein, and 219 (44.2%) were declared positive. The highest level of seropositivity was found at Sindh Agriculture

University's dairy farm (80.0%), while the lowest was found in Kohat city (28.3%). Jenberu [21] used the 3ABC ELISA to investigate seroprevalence and related risk factors for seropositivity of cattle FMD in the Hyderabad from October 2007 to April 2008. Gewane (11.9%) had considerably greater seroprevalence than Karachi (4.2%), Thatta (2.9%), and TM Khan (2.9%) at the district level (5.2%). Person and herd seroprevalence were determined to be 5.6 and 48.4%, respectively, at the individual and herd level. Mohamoud [31] performed a seroprevalence investigation on indigenous cattle in Somalia Regional State, in the Awbere and Babille Districts in Jijiga zone, from October 2009 to March 2010. The 3ABC-ELISA was used to analyses 384 sera for antibodies against the FMD virus's non-structural protein, and the overall individual animal antibody seroprevalence was 14.05%. At the district level, 14.2% (n = 225) of animals in Awbere District were found, while 15.1% (n = 159) in Babille. From November 2007 to March 2008, Mekonen., et al. [29] conducted a seroprevalence research in the Borana plateau and Guji highlands of southern Ethiopia to evaluate the prevalence of Foot and Mouth Disease (FMD) in bovines. Using the 3ABC-ELISA approach, they found a prevalence of 24.6% (113/460). Furthermore, they found that Borana had a much greater frequency of 53.6% (82/153) than Guji, which had a prevalence of 10.1% (31/307). Bayissa, et al. [8] carried out a cross-sectional serological investigation in the Borana pastoral and agro-pastoral area to investigate seroprevalence and risk variables associated with foot and mouth disease infection, as well as to examine community opinions of the infection's relevance. A total of 768 cow sera were examined using the 3ABC ELISA test from 111 herds, yielding a seroprevalence of 23.0% at the individual level. A total of 65 (58.6%) of the 111 herds investigated had at least one positive animal.

8. Global Eradication or Control Programmes

8.1. Control by Eradication

For decades, some parts of the world, such as Central and North America and Australia-Oceania, have been able to maintain their FMD-free status. FMD prevalence has fallen significantly in other areas, most notably Europe, South America, and several South-East Asian nations. FMD, on the other hand, is still prevalent in many African, Middle Eastern, and Asian nations. Furthermore, due to increased worldwide mobility and commerce of cattle and animal products, the danger of FMD has grown even in nations where the infection is not present. In addition to the economic costs, FMD outbreaks and the methods used to manage them in affluent nations, such as mass culling, have caused widespread concern, not only among farmers but across society. Animal welfare, ethical problems, and potential dangers to domestic animal biodiversity are among the points raised [38]. Following the recommendations of the first international conference on FMD control, held in Asuncion, Paraguay, in 2009, the OIE and FAO have embarked on a Global Strategy and Global Action Plan for FMD control, under the umbrella of the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs). In May 2011, during the 79th General Session of the World Assembly of Delegates of the OIE, a first sketch was presented. The Global Strategy recommends the Progressive Control Pathway (PCP), a step-by-step strategy to improving a country's FMD control capability in a sustainable manner, which is also intended to have a favorable influence on the performance of the VS and, as a result, enhance animal health status in general. The strategy focuses on endemic infection areas across the world. A good resolution will help both nations where FMD is still prevalent, the majority of which are poor countries, and those where FMD is now absent [38]. Intervention will be prioritized at the national and regional levels, where the majority of actions will be carried out. The focus at the global level will be on international cooperation and overall progress monitoring. The programme will be long-term: a 15-year overall duration has been chosen, with 5-year stages, explicit goals, and frequent progress reviews [11].

8.2. Veterinary Services Are Being Strengthened

'Strengthening animal health systems via enhanced control of key infections' is the subtitle of the Global FMD Control Strategy. Although the term '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) as well as livestock producers and traders, the VS, which brings together public and private sector veterinarians and other animal health professionals, is the focus of this Strategy. 1. The Global Strategy includes support for the establishment of private-public partnerships (PPPs), which is an indirect means of boosting the engagement of other stakeholders, particularly livestock producers, in the animal health system [3]. The VS are a critical component of a system that guarantees animal health and production. As a result, the livelihoods of individuals working in agriculture are protected, as is global food security, and chances for economic development are created. To carry out its disease control efforts, VS need proper infrastructure, a clear organization and chain of command, educated and effective employees, and a sufficient money. Unfortunately, many developing nations' operational budgets are limited, and these elements are of poor quality. Harmonization of control regulations with neighboring nations is frequently recommended and in some cases required, such as in locations where cross-border nomadic animal migration occurs [37]. The steps made to combat FMD are linked to effective VS and will have a broader impact. If a country can effectively control FMD, it means that it will be able to create more effective VS that will be better equipped to tackle other serious cattle infections, including TADs. The OIE PVS Pathway (18a) will be used as a tool to evaluate the quality of the VS (PVS Tool) in terms of OIE standards compliance, 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 compliance (PVS Gap Analysis). The PVS Gap Analysis considers the country's priorities, which include TAD prevention and control [38].

8.3. Prevention and Control of Other Major Diseases of Livestock

Through suitable links with other monitoring, surveillance, and disease control operations, or with production-related activities, the cost-effectiveness of the Global FMD Control Strategy will be enhanced. Furthermore, the efforts carried out to make advances in the field of FMD control will yield significant knowledge and skills that may be used to the control of other TADs. In cattle, haemorrhagic septicaemia (HS), brucellosis, contagious bovine pleuro pneumonia (CBPP), anthrax, and, in some areas, blackleg and rabies may be considered for management with FMD. Peste des petits ruminants, sheep and goat pox, and brucellosis in small ruminants. In pigs, there are two types of swine fever: classical swine fever and African swine fever [38]. Other diseases may be added to the above list depending on the requirements and priorities of particular nations and areas. For example, in some places of Africa, FMD immunization might be paired with CBPP, anthrax, blackleg, or East Coast fever vaccine, while in Asia, it could be combined with HS, anthrax, and blackleg vaccination. The Regional Steering Committees of the GF-TADs are the proper fora to further research and fine-tune suitable combinations of activities to match the goals of the areas they serve. Other TADs, like FMD, have the potential to cause massive economic harm and, because some are zoonotic, they can have significant public health implications. Most TADs have been eradicated in affluent nations, and their relevance now depends on the cost of prevention. However, as with FMD, it is in the interests of TAD-free nations to reduce the danger of virus reintroduction, and so they gain from improved TAD management at the source, which is also more cost-effective [11].

8.4. FMD Virus and Related Challenges in the Prevention and Control Program of FMD

The viral genome encodes structural proteins (VP1, VP2, VP3, and VP4) as well as a number of non-structural proteins that are involved in virus replication, particle assembly, and modulation of the host's innate and adaptive immune responses. FMDV has seven different serotypes, including type O, A, C, SAT 1, SAT 2, SAT 3, and Asia 1. Furthermore, because to high mutation rates during genome replication, subtypes within each serotype include a wide range of genetic diversity, and many of these alterations may be tolerated while retaining virulence. The significant genetic variation between and among serotypes makes infection detection and prevention more difficult. Variability in antigenic areas, in particular, can diminish or effectively abolish cross-subtype or -serotype protection from earlier infection or vaccination, as was the case in Iran in 2005 [23]. The virus's capacity to infect cross-species through a variety of channels improves the virus's transmission potential, especially in areas where livestock agriculture is heavily populated. Cattle and sheep are infected largely by inhalation of the virus in aerosol form, but pigs are infected more frequently through ingestion or subcutaneous wounds. The virus can shed through a variety of ways, including aerosols, urine, faeces, and body fluids. In aerosol form, excreted virus can keep infectivity for long periods of time, with some strains naturally reaching up to 300 kilometres. Accidental transmission of FMD 13 on cars, persons, water, and animal products can amplify the disease's spread. The disease's propagation is complicated by the many methods of shedding and transmission, as well as the variety of host species [13]. The virus may survive in some hosts, such as cattle and buffalo, and these asymptomatic, chronically infected animals can be infectious for up to 5 years. Within 12 days of infection, infected animals are assumed to have reached their maximal transmission capacity. The virus can stay stable and infectious in a deceased host for up to 11 days in muscle tissue and 4 months in the liver. Infectious virus can also be found in a variety of different animal products, such as milk and cheese, for varying periods of time [13].

8.5. Predominant Vaccine Technology

The potential of pathogenic viral infection or inadequate inactivation during vaccine production necessitates strict biosafety regulations in vaccine manufacturing facilities. This limits the places where industrial facilities may be built, maintained, and managed successfully. These facilities must also maintain a high degree of confinement. The distance between manufacturing facilities and FMD-infected areas poses a logistical distribution issue, especially when international boundaries are involved. To assist address this issue, FMD vaccination banks have been formed in several regions of the world to boost vaccine accessibility [7]. FMD vaccine banks select how much vaccine to keep for each serotype and assess the effectiveness of such vaccinations on a regular basis. These studies are necessary because the possibility of antigenic variant selection during viral replication is a problem with present technology for inactivated virus vaccine manufacturing. It has been discovered that the chosen vaccination variations 1 may not always be protective against current viral strains in the field. Furthermore, inadequate cross-subtype and cross-serotype protection complicates vaccine selection, necessitating different vaccinations against each presently circulating subtype for optimal protection. Vaccinations must also be renewed on a regular basis because traditional FMD vaccines have a shelf life of 1-2 years. Vaccines stored as concentrated antigens in liquid nitrogen have a longer shelf life. These concentrated antigens, on the other hand, must be delivered to manufacturers for adjuvant formation when needed, delaying their usage in the field [7]. The vaccine's administration comes with its own set of challenges, including proper handling, dose, and immunization timing. All of these factors can have a substantial influence on the vaccine's efficacy. A larger vaccination dose, for example, often results in a greater number of animals protected and a shorter interval between injection and protection. As a result, the OIE recommends emergency vaccination of animals with 6 protection dose 50 (PD50) during outbreaks in formerly disease-free nations. The vaccine's complexity necessitates the need of qualified personnel to deliver it. In addition, individuals who provide immunizations to various herds may unintentionally function as disease carriers. Furthermore, locations with insufficient veterinary services confront the additional problem of expanding vaccination competency [24].

8.6. Economic Implications in FMD-Affected Areas

Although vaccinations are already available, they are sometimes prohibitively expensive and in short supply in many enzootic areas. In a cost-benefit analysis of FMD eradication in Sudan, it was estimated that procuring the vaccine accounted for 81% of the eradication expenditures. Because each vaccination costs between $0.40 and $3.00 USD to make and transport, disease eradication efforts in economically underdeveloped nations are hampered. Due to the tight conditions required to avoid contamination or inadequate inactivation, as well as expenditures associated with testing, distribution, and storage, lowering the cost of a typical vaccination is difficult. When creating alternative vaccination alternatives for impoverished nations, future improvements in vaccine technology must take cost into account [26].

8.7. Social and Political Challenges Surrounding Eradication

The difficulties of limiting FMD is exacerbated by the globalization of animal trade and animal product commerce. FMD epidemics have occurred in the past in both legal and criminal animal trade and animal product commerce 19. This was shown by outbreaks in Albania in 1996 as a result of liberal trade policies, and outbreaks in Taiwan in 1997, where the likely source of the epidemic was illegally imported feed or disease transmission from pigs. FMD prevention and eradication activities are inadequate due to a lack of information. It's no easy effort to provide accurate information on FMD transmission to take the necessary safeguards. This is especially difficult when neglecting adequate safeguards might result in a short-term individual economic advantage [9]. Eradication attempts have also been hampered by a lack of cross-government coordination. Transmission across borders is encouraged by the simplicity of transmission and the range of hosts available.

9. Conclusion

As a result, when neighboring nations communicate and cooperate, the spread of an outbreak is better managed. Through cross-border reintroduction of FMD, a lack of international collaboration might jeopardize eradication efforts. The disease's spread across borders is aided by trade restrictions imposed on countries that report FMD within their borders. To evade these trade limitations, nations having epidemics will postpone reporting in order to stamp out the disease discreetly and keep commerce flowing. The danger of disease dissemination and transmission increases as a result of these reporting delays. Although difficult, cross-governmental collaboration has already been beneficial in eradicating or reducing FMD epidemics in the United States, Mexico, Argentina, Venezuela, Brazil, the United Kingdom, and parts of Asia [26].

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