

A BRIEF REVIEW ON FOOT AND MOUTH DISEASE (FMD) IN IRAQ

HANA SHERZAD RAOOF

College of Veterinary Medicine, University of Sulaimani, New Sulaimani, Street 27, Sulaimanyah, Kurdistan Region, Northern Iraq.

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ABSTRACT

Foot-and-mouth disease (FMD) is a severe and extremely contagious viral disease. Cows, sheep, goats, deer, pigs, and other animals with divided hooves are among the animals infected by the FMD virus, which is a member of the Picornaviridae family and genus Aphtho virus. There are seven different serotypes of this virus: Asia-1, SAT1, SAT2, SAT3, A, O, and C. Heat, ultraviolet light, pH values of 6.5 or higher, gamma radiation, chemicals, and disinfecting agents all inactivate the virus; however, it remains virtually stable at below-freezing temperatures for a prolonged amount of time. Animals affected by this disease develop vesicular lesions on their tongue, dental pad, gums, cheeks, hard and soft palates, lips, nostrils, muzzle, interdigital region (between the hoof), and a coronary band. Viral infections can spread through the respiratory tract or via the oral cavity. Clinical manifestations of FMD are used to diagnose the disease, along with laboratory and epidemiological investigations. Due to the high morbidity linked to outbreaks, difficulties in the local adoption of more advanced production techniques, limitations on trade between countries, and expenses related to the implementation of control measures, FMD results in significant economic losses. FMD can be controlled and prevented through immunization, restrictions on animal migration, physical segregation from wildlife, and clinical therapy. However, FMD demonstrated challenges to control because of its complicated epidemiological nature, poor diagnostic capacity, and lack of cross-immunity between strains. Investigation is consequently essential to progressing the creation of a multivalent and effective vaccination.

Keywords: Foot and mouth disease, Aphthovirus, Vesicular lesions, Iraq.

INTRODUCTION:

The foot-and-mouth disease virus (FMDV) is the cause of the extremely contagious illness known as foot-and-mouth disease (FMD) (Zell *et al.*, 2017). Foot-and-mouth disease (FMD) affects cloven-hoofed

animals, including pigs, cattle, sheep, goats, and buffaloes (Jamal and Belsham, 2018). The virus is a positive-sense single-stranded RNA virus belonging to the family Picornaviridae and genus Aphthovirus (Woldemariyam *et al.*, 2021). The length of this RNA is 8,400 nucleotides (Belsham *et al.*, 2020). The four distinct structural proteins known as VP1, VP2, VP3, and VP4 enclose this RNA genome. The genome is encircled by a capsid made up of these four proteins. Because VP1, VP2, and VP3 are outwardly present but VP4 is present inside

Corresponding author: Hana Sherzad Raouf

E-mail address:

Present address: College of Veterinary Medicine, University of Sulaimani, New Sulaimani, Street 27, Sulaimanyah, Kurdistan Region, Northern Iraq.

the capsid, the virus is thought to possess antigenic features (Wubshet *et al.*, 2019). There are seven serotypes of FMDV (O, A, C, Asia 1, SAT 1, SAT 2, and SAT 3) that have been identified from various parts of this world (Brito *et al.*, 2017). Infected animals exhibit a variety of clinical symptoms, including anorexia, fever, and excessive salivation due to the vesicular formation of the tongue epithelium. Blisters with vesicles form on the nose, muzzle, lips, feet, snout, and various other parts of hairless skin areas, and erosion between the hooves causes lameness (Azeem *et al.*, 2020). Direct or indirect contact with infected animals or objects, as well as airborne transmission, can all quickly spread this disease (Zhang *et al.*, 2021). Furthermore, a new, vulnerable animal might acquire it by respiratory tract infection or oral transmission. Aerosol transmission is the most typical means of disseminating within a herd (Lee *et al.*, 2020). Due to its strong transmission capacity, high infectivity, and cross-border dissemination, FMD has been classified as a disease that must be reported by the Office International des Epizooties (OIE) (Knight-Jones and Rushton, 2013). The disease is diagnosed using esophageal-pharyngeal fluid or samples of the affected tissues. Virus neutralization, complement fixation, polymerase chain reaction, and enzyme-linked immunosorbent assay (ELISA) are several laboratory techniques that might be performed to confirm the illness (Souley Kouato *et al.*, 2018). The illness rate is 100% in the vulnerable population. There is a 100% mortality rate for young suckling calves, and the risk of dying from myocarditis might rise to 50% (Govindaraj *et al.*, 2021). Regarding its economic impact, FMD is considered to be the most important animal sickness. It results in massive losses for the animal industry because of the expenses associated with eradication or control methods like widespread immunization campaigns or devastation of livestock, as well as because of productivity declines in milk and beef because of clinical illness (Zewdie *et al.*, 2023). The objective of this article is to provide a thorough overview of FMD's

molecular epidemiology, economic impact, diagnosis, and control strategies in Iraq in relation to the international situation.

1. The FMD virus's etiology and taxonomy:

Aphthous fever, epizootic aphthae, and infectious aphthous stomatitis are other names for foot-and-mouth disease (Shebiah and Arivazhagan, 2023). During an epidemic close to Verona, Italy, in 1546, it was first found. In South Africa, it was identified in 1780. Although the disease was not well recognized until the end of the 19th century, it caused a serious risk to the cattle industry in earlier decades. The 20th century enabled extensive understanding of the FMD virus, including its genetic and structural nature (Admassu *et al.*, 2015). Following that, the International Committee on Virus Taxonomy made the initial identification of it in 1963. It is a member of the Aphthovirus genus in the Picornaviridae family. The Latin terms are the source of the name Picornaviridae. "Pico," which means small, and "rna," which stands for RNA (ribonucleic acid), which describes the kind and size of the virus's genome. 'Aphthovirus' is the genus name applied to the vesicular lesions that occur in the mouths and feet of the animals (Abd-Ellatieff *et al.*, 2023). The non-enveloped capsid and genetic material comprise the FMD virion (TIKUYE YALEW, 2019). Single-stranded positive-sense RNA in the FMDV genome has an extremely low molecular weight, ranging from 7.2 to 8.4 kb (Longjam *et al.*, 2011). When exposed to pH values below 6.5 or above 9, the virus might turn inactive. Its capsid is resistant to lipid solvents since it is made up of polypeptides instead of lipoproteins. Heat, UV and gamma radiation, chemicals, and disinfectants can all readily inactivate the virus; however, it remains stable for a very long time at temperatures below freezing. Heating at 70 °C for a minimum of 30 minutes can inactivate the virus found in milk and meat (Onodera *et al.*, 2023). The virus is classified into seven serologically and genetically different types: O, A, C, Asia1, SAT1, SAT2, and SAT3, with

more than sixty subtypes. FMDV has a high mutation rate because the virus's RNA-dependent RNA polymerase cannot

proofread. The strains do not have any cross-immunity (Paton *et al.*, 2021).

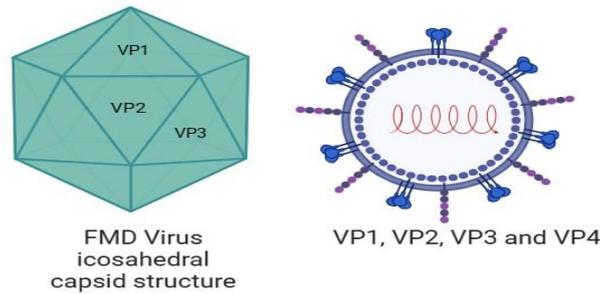


Figure 1: FMD virus structure. (Created by BioRender.com)

2. Epidemiology and Risk Factors:

2.1. Epidemiology of the Disease:

The seven diverse serotypes of the virus—A, O, C, SAT1, SAT2, SAT3, and Asia1—are found primarily in Asia, Africa, and the Middle East, but they are widespread throughout the world. Nonetheless, there is no FMD in Australia, New Zealand, Japan, or certain other countries. Serotype O is widely spread worldwide among the seven FMDV serotypes, although serotype C has a low report rate (Wondwossen, 2017). Globally, over one hundred countries are still impacted by FMD, and it's estimated that the illness still exists in approximately two-thirds of all countries (Betelihem, 2021).

3.2. The risk factors:

Animal species play a significant role in the transmission of disease and animal susceptibility. Cattle and pigs are more vulnerable, although goats, sheep, buffalo, and other species, including antelope, deer, and hedgehogs, can also get a mild illness with symptoms. Additionally, wildlife species are important reservoirs of infection for domestic animals making it challenging to remove diseases from them (Mesfine *et al.*, 2019). The risk of animal death is also influenced by the animal's age. FMDV rarely results in death in mature animals; however, in calves and piglets, the virus can seriously damage their hearts, leading to a significant

mortality rate in these young animals (Menda *et al.*, 2014). It was discovered that the dry season is when FMD is most prevalent. The incidence was lowest during the wet season. Moreover, there was more herd contact with wild animals in the dry season than in the wet season (Souley Kouato *et al.*, 2018). The aerosol transmission of foot-and-mouth disease may be inhibited during the rainy season by heavy rain, high relative humidity (60%) temperatures, and wet winds (Jamal and Belsham, 2013). Wintertime brings favorable weather circumstances, including low temperatures (weak sunshine), movement of animals, moderate humidity, and dry weather and winds that make FMD infections more common (Upadhayay and Ewam, 2012).

3. Global dissemination:

In many regions of Asia, the majority of Africa, the Middle East, and certain regions of South America, foot and mouth disease is endemic. FMD affects 77% of livestock worldwide. FMD-free regions at the current time include Australia, New Zealand, Indonesia, Central and North America, and continental Western Europe. However, FMD is a transboundary animal illness that might occasionally arise throughout a typically uninfected area (Pal, 2018). Reports of FMD outbreaks have been published in Iran. A phylogenetic study of the virus revealed that

Asia 1 and O and A serotypes were common (Gadir *et al.*, 2023). In Turkey, FMD is prevalent, and outbreaks occasionally occur there. There are reports of FMD serotypes O, A, and Asia 1. According to economic survey reports, production losses due to FMD are significantly high (İnce *et al.*, 2023). Three separate serotypes of FMD -O, A, and SAT 2 are prevalent in Egypt. In 2019, a novel sublineage of SAT 2 was found, which caused abrupt clinical symptoms in buffaloes (El Damaty *et al.*, 2021). The economy of Saudi Arabia has suffered due to the endemic presence of FMD, and reports of serotypes O, A, and Asia 1 originated from the region (Mahmoud *et al.*, 2021).

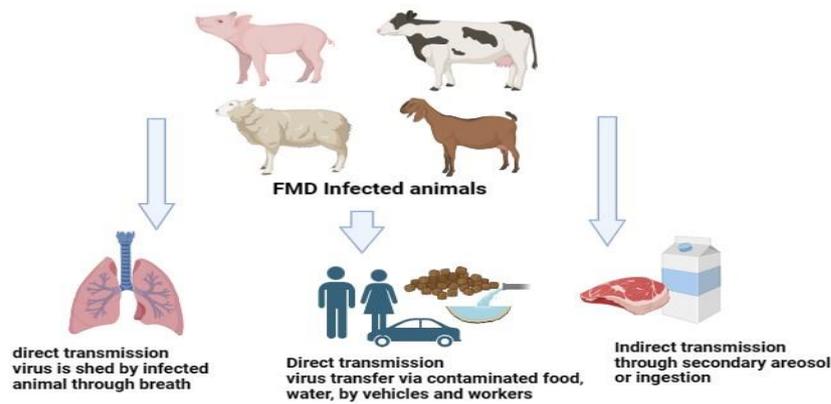
4.1. Occurrences and Present Situation in Iraq:

Iraq has an endemic case of FMD, which results in significant yearly losses for cattle owners. There have been reports of FMD since the late 19th and early 20th centuries. In 1937, the Sulaymaniyah/Bashder checkpoint on the Iraqi border reported the first known instance of the disease. Out of 202 cattle in the herd, 11 of them showed growing clinical indications of the illness (Al-Salihi, 2019a). In 1938, there was a reported case of FMD in bovine and buffalo in the Iraqi-Iranian borderlands towns of Basra, Missan, and Diala. Following that, there were widespread outbreaks of FMD in 1957 that affected the majority of the Iraqi governorates and affected buffalo, cattle, sheep, and goats. Records for the illness persisted into the 1960s, 1970s, 1980s, and 1990s. The epidemic of 1999 is regarded as the worst case of FMD to have struck Iraq during the economic sanctions period of 13 governorates in Iraq, it resulted in a significant loss of cattle and small ruminants (El Idrissi, 2003). Since 2010, the FMD epidemic has persisted. While the number of affected animals decreased, FMD outbreaks reappeared in 15 governorates in Iraq in 2012. Additionally, the veterinary services conducted a vaccination campaign in 2012,

immunizing 7,105,941 small ruminants and 1,798,074 cattle and buffalo, respectively (Al-Jobori, 2012). The Sulaymaniyah province reported a serotype of FMD in 2013 (Rashid *et al.*, 2014). The investigation conducted in 2017 was regarded as the first molecular characterization of serotype Asia1 in Iraq (Sheikh *et al.*, 2017). Molecular characterization and prevalence rates of FMD have been measured in 2019 from outbreaks in the Iraqi province of Nineveh through the use of ELISA and RT-PCR technologies. The prevalence rates were 46.95% (Salim *et al.*, 2020). In Sulaimani province, cattle were found to harbor FMDV serotype O (Sheikh *et al.*, 2021).

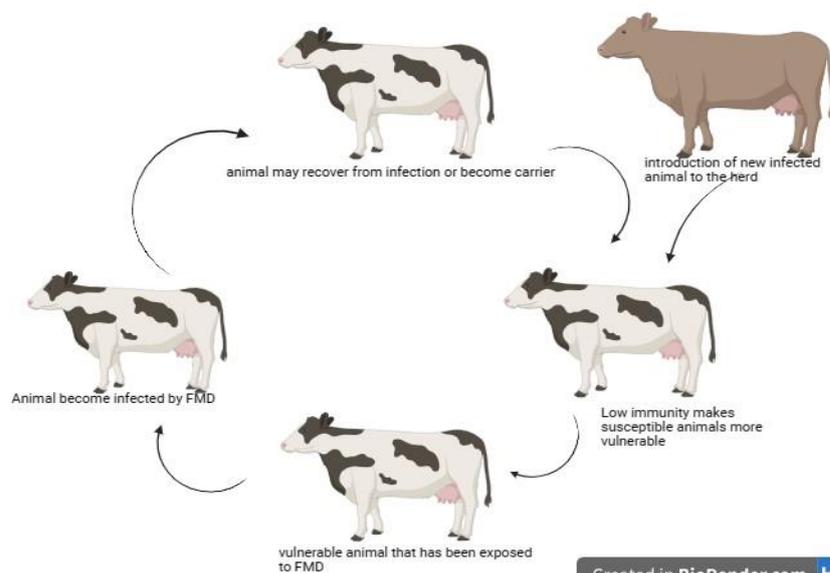
4. Transmission of FMD virus:

The virus was transmitted by infected animals in all bodily secretions and excretions, including blood, milk, urine, feces, nasal and lachrymal fluid, air, saliva, and semen, prior to the disease's clinical signs (Chakraborty *et al.*, 2014). The virus can spread easily through the air because of its extremely simple structure. There have been reports of airborne transmission cases up to 300 kilometers from the infection site (Sørensen *et al.*, 2001). Other potential mechanisms of infection include eating contaminated food, directly inoculating susceptible animals, and infecting skin sores. During acute infection, transmission is facilitated by virus shedding from ruptured vesicles and in bodily excretions and secretions, including breath, milk and semen. Susceptible ruminants can be infected by very low doses of inhaled virus through direct contact with the breath of other acutely infected animals, or indirectly by resuspension of aerosols from contaminated materials. Generally, direct contact, airborne, via fomites, or mechanical means are used to spread viruses (Figure 2). For cattle, inhaling an aerosolized virus is a typical method of transmission. Carrier cattle have the potential to spread the FMD virus to additional susceptible cattle (Stenfeldt *et al.*, 2016). The transmission cycle of FMDV in a herd is represented in (Figure 3).



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Figure 2: Transmission routs for FMD virus. (Created by BioRender.com)



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Figure 3: Transmission cycle of FMD virus. (Generated by BioRender.com)

5. Pathogenesis:

Through inhalation, skin abrasion, or mucous membrane erosion, the virus can enter the host cell by binding to cellular receptors through its capsid proteins (Dill and Eschbaumer, 2020). The cytoplasm of infected cells is where FMDV RNA replicates. The virus's principal location of replication is the respiratory tract. Adult epithelial tissue and young cardiac muscle are the main targets for the virus. After undergoing primary replication in the host's pharynx and mucous membrane, the virus travels through the circulation and lymphatic system to impact the mammary glands, lymphatic glands, and epithelial tissues surrounding the mouth and foot. After three

to five days of febrile viremia, the virus distributes within the body and causes a secondary illness (Upadhayay and Ewam, 2012). Virion continuous replication causes cell lysis, after which the particles leave the cell to infect surrounding cells (Rodriguez Pulido and Sáiz, 2017).

6. Clinical Manifestations:

There is species diversity in the clinical manifestations of FMD, which can range from moderate to severe. Numerous factors, including the kind of virus, exposure dose, animal age and their breed, host species, and immune status, influence the incubation period and clinical manifestations of food and mouth disease; in most cases, the incubation

period might extend from two days to fourteen days (Hossain *et al.*, 2023). The disease's symptoms in cattle are marked by a high fever (~40 °C) that causes vesicular lesions on the teeth pad, snout, hard palate, lips, gums, tongue, interdigital cleft, and teats. When they have an acute infection, animals tend to drool extensively, stamp their feet, and lie down. Ruptures of the oral vesicles consolidate to cause erosions in the mouth, which heal in around 11 days. Vesicles seen on the foot heal more slowly and are more vulnerable to bacterial infection, which can result in prolonged lameness. Mastitis is a common sequel of FMD in dairy cattle. Mastitis might result from a subsequent bacterial infection caused by teat lesions. The animals rapidly lose their ability to produce milk and condition after developing vesicular lesions, and this loss may last for a longer period of time (El Bagoury *et al.*, 2022). There is occurrences of classic vesicular/erosive lesions at the uncommon location of the horn corneum layer during Iran's outbreak of FMD (Mohebbi *et al.*, 2017). Virus-induced damage to the myocardium is sometimes seen upon necropsy in young calves that pass away without exhibiting any symptoms (Donaldson, 2019). Lameness is the initial clinical symptom in sheep and goats, followed by a high body temperature and vesicle development. Clinical symptoms of FMD in wildlife are similar to those in domestic animals (Muthukrishnan *et al.*, 2020).

7. Postmortem Lesions of the Disease:

Single or numerous fluid-filled vesicles, or blisters, ranging in diameter from 2 mm to 10 cm, are the hallmark lesions of foot-and-mouth disease. Vesicles usually only last a short time. Red, worn spots, or ulcers will appear after they burst. Depending on the species, FMD lesions differ in location and prominence. Cattle's oral cavity may have many vesicles, ulcers, or erosions (Sahoo *et al.*, 2023). These lesions might be more prevalent in sheep and goats on the interdigital cleft, coronary band, and heel of

the foot. Other places where vesicles can be noticed include the prepuce, vulva, udder, or teats. The myocardium of young animals may exhibit gray or yellow streaking due to cardiac degeneration and necrosis; these lesions are commonly referred to as "tiger heart" lesions (Tolawak *et al.*, 2023).

8. Morbidity and mortality:

Foot and mouth illness has a low mortality rate and a high rate of morbidity. Breed type, production manner, age group, lack of movement restriction, animal density, use of open pasture and watering places, and season are some of the main variables linked to the disease's morbidity and fatality rate (Chanchaidechachai *et al.*, 2022).

9. Differential diagnosis:

To differentiate between diseases that share similar clinical symptoms, differential diagnosis is necessary (Upadhyay and Ewam, 2012). The clinical manifestations of several diseases, including rinderpest, peste des petits ruminants, blue tongue, epizootic hemorrhagic disease, and vesicular stomatitis, are identical to those of FMD. Differentiating between these disorders requires a laboratory diagnosis (Wong *et al.*, 2020).

10. Diagnosis Techniques of Foot-and-Mouth Disease:

9.1. Clinical diagnosis:

An essential diagnostic method that can lead to a laboratory diagnosis or offer a preliminary diagnosis is the clinical examination. Clinical signs of the condition are used to diagnose it. The FMD examination entails taking the patient's temperature, checking for vesicles on the oral mucosa and other non-hairy areas of the body with palpation, and assessing the presence of salivation, auscultation, vision, and interdigital spaces (Admassu *et al.*, 2015).

9.2. Laboratory Diagnosis:

The significance of laboratory testing lies in its ability to distinguish FMDV from other kinds of vesicular diseases, which share similar clinical symptoms. Samples such as

blood, sperm, serum, milk, oropharyngeal fluid, epithelial samples, vesicular fluids, throat swabs, and so on can all be utilized for laboratory diagnosis. Virus isolation (VI), the most reliable method for diagnosing FMD, is a process that needs advanced biosafety facilities and is labor-intensive and slow (Cavalera *et al.*, 2024). The highly specific and sensitive viral neutralization test (VNT), which also requires live virus and cell cultivation equipment. ELISA has been utilized to diagnose a variety of infectious disorders, among them FMD. For FMDV detection, typing, quantification, and strain discrimination, ELISA and its many modifications were applied with great specificity and sensitivity. After 3–4 hours of receiving the sample at the lab, it is the recommended approach for identifying viral serotypes and detecting FMD viral antigen. Serological methods, such as viral neutralization and liquid-phase enzyme-linked immunosorbent assays, are quick tests; however, they are not always able to separate vaccinated animals from infected animals. Consequently, they are not the best option for identifying acute infections (Jafarsab *et al.*, 2022). One of the newest and most popular nucleic acid-based diagnostic tools for amplifying and finding FMDV genome fragments in genome-based approaches is PCR. RT-PCR amplification followed by nucleotide sequencing is a more dependable technique for diagnosing FMD. The identification of serotypes by traditional RT-PCR techniques is dependent on the magnification of the VP1 gene. Real-time polymerase chain reaction (PCR) has become widely used due to its increased sensitivity and speed (Amir *et al.*, 2023).

11. Treatment:

There is no particular medication for FMD. The use of supportive treatment arises when targeted treatments are not available. Classical treatment procedures involve the use of antibiotics in conjunction with mild disinfectants. In susceptible animals, ribavirin is one of the antivirals used as a prophylactic approach to avoid the disease. Sodium carbonate, boric acid, glycerin, and

an antiseptic mouthwash combined with potassium permanganate can be placed on the lesions (Yirgalem *et al.*, 2020). Tetracycline is a broad-spectrum antibiotic that is administered intravenously (IV) to prevent bacterial infections. Animals that are infected are kept separate and given supportive care, which includes wound care, antibiotics, and anti-inflammatory medications. This could decrease animal suffering and mortality, but it does not prevent the virus from continuing to exist and spread (Seyoum and Tora, 2023).

12. Control and prevention:

The adoption of disease control and prevention techniques helps stop animal diseases from spreading further. Due to its extremely contagious nature, ability to infect many hosts, stability of the virus, multiple antigenic kinds or subtypes, indefinite immunity, and remarkable genetic and antigenic complexity, FMD is a challenging disease to control (Tadesse *et al.*, 2017). Due to antigenic differences between the strains, immunization against a single strain of FMDV may fail to cross-protect against different strains, and there are currently no effective vaccination control methods. Additionally, one serotype of FMDV does not cross-protect against other serotypes, even within a single serotype. The most popular approach to preventing disease, both in endemic and disease-free areas of the world, is vaccination. The most popular approach to preventing disease, both in endemic and disease-free areas of the world, is vaccination (Heshmati *et al.*, 2021). The following requirements should be met by the perfect vaccine formulation: Safety, heat stability, affordability, multivalency, rapid and durable immunity with a single dose, and compliance with DIVA (difference between diseased and vaccinated animals) guidelines constitute key factors. The primary component of FMD vaccinations is the inactivated virus, which induces antibodies that defend against virus structural proteins (Kamel *et al.*, 2019). A variety of vaccine strategies are potentially available for immunization of livestock against FMD infection, the predominately

utilized FMD vaccine is based on inactivated FMDV in Iraq. Triple vaccine (Serotype A, O, and Asia 1) that met all Iraq's needs and surrounding areas and helped in the success of the FMD control plan in Iraq and the Middle East. Due to the disadvantages of inactivated vaccines there is an obvious increased demand for novel vaccines that feature higher potency, safety, improved DIVA capability and most importantly, adequate coverage of circulating and emerging FMD strain (Al-Salihi, 2019b).

CONCLUSION:

Foot-and-mouth disease remains a serious disease that impacts a variety of livestock animals and is extremely contagious, genetically, and antigenically different. Transboundary animal migration allows the virus, which exists in various strains and serotypes, to propagate. Vesicles on the foot and mouth are a symptom of FMD infection in ruminants, and young animals with tiger cardiac symptoms (myocarditis) have a high rate of mortality. Animals with FMD can get treatment for their symptoms, but there is no known cure for the disease. The disease results in a significant economic loss because of its high morbidity effect, limitations on the international trade of animals and animal products, and the expenses related to controlling disease outbreaks. As a result, the following recommendations are made considering the facts above:

- ❖ Enhancing the management of animal mobility is necessary to stop the spread of serotypes.
- ❖ It is important to perform comprehensive molecular characterization of the serotypes prevalent, particularly in rural situations.
- ❖ Since Iraq's vaccination is ineffective against all serotypes present there, vaccines should be created in accordance with the strains that have been most widespread.

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مرض الحمى القلاعية

هانا شيرزاد روؤف

Email: Assiut University web-site: www.aun.edu.eg

مرض الحمى القلاعية (FMD) هو مرض فيروسي شديد ومعد للغاية. البقر والأغنام والماعز والغزلان والخنزير والحيوانات الأخرى ذات الحوافر المقسمة هي من بين الحيوانات المصابة بفيروس الحمى القلاعية. وهو عضو في عائلة Picornaviridae و جنس Aphthovirus هناك سبعة أنماط مصلية مختلفة لهذا الفيروس Asia-1 و SAT1 و SAT2 و SAT3 و A و O و C. الحرارة والأشعة فوق البنفسجية ، pH ٦,٥ أو أعلى وأشعة جاما والمواد الكيميائية وعوامل التطهير كلها تعطل الفيروس ؛ ومع ذلك ، فإنه يظل مستقرًا تقريبًا في درجات حرارة أقل من درجة التجمد لفترة طويلة من الزمن. تصاب الحيوانات المصابة بهذا المرض بأفات حويصلية على لسانها ، وسادة الأسنان ، اللثة ، الخد ، الحنك الصلب واللين ، الشفتين ، الخياشيم ، الكمامة ، المنطقة بين الأصابع (بين الحافر) ، والشريط التاجي. يمكن أن تنتشر العدوى الفيروسية عبر الجهاز التنفسي أو عن طريق تجويف الفم. تستخدم المظاهر السريرية لمرض الحمى القلاعية لتشخيص المرض ، إلى جانب التحقيقات المخبرية والوبائية. ونظرًا لارتفاع معدلات المراضة المرتبطة بالفاشيات، والصعوبات التي تعترض الاعتماد المحلي لتقنيات إنتاج أكثر تقدماً، والقيود المفروضة على التجارة بين البلدان، والنفقات المتعلقة بتنفيذ تدابير مكافحة، فإن مرض الحمى القلاعية يؤدي إلى خسائر اقتصادية كبيرة. يمكن السيطرة على مرض الحمى القلاعية والوقاية منه من خلال التحصين والقيود المفروضة على هجرة الحيوانات والفصل المادي عن الحياة البرية والعلاج السريري. ومع ذلك، فقد ثبت أن مرض الحمى القلاعية يمثل تحدياً في السيطرة بسبب طبيعته الوبائية المعقدة، وضعف قدرته على التشخيص، ونقص المناعة المتقاطعة بين السلالات. وبالتالي فإن التحري ضروري للتقدم في إنشاء لقاح متعدد التكافؤ وفعال.