ŞIRNAK ÜNİVERSİTESİ FEN BİLİMLERİ DERGİSİ
SIRNAK UNIVERSITY JOURNAL OF SCIENCES

ISSN: 2667-7083
e-ISSN:2687-3796

Review

Clinical Manifestations and Preventive Strategies for Foot-and-Mouth Disease (FMD) in Türkiye: A Contemporary Review*

Şap Hastalığında Klinik Bulgular, Tanı Yaklaşımları ve Tedavi Stratejileri: Türkiye Örneği Güncel Bir Derleme

Ayşe Özge DEMİR[1], Sinan HAKAN[2*]

[1]Van Yuzuncu Yil University, Faculty of Agriculture, Department of Animal Science, 65080 Tuşba/VAN
aodemir@yyu.edu.tr
[2] Provinceal Directorate of Agriculture and Forestry of Ministry of Agriculture, 65040 Tuşba/VAN
shk851@hotmail.com
*Corresponding author: shk851@hotmail.com

Article Information / Makale Bilgisi

Citation / Atıf: Demir A. Ö. & Hakan, S. (2025). Clinical Manifestations and Preventive Strategies for Foot-and-Mouth Disease (FMD) in Türkiye: A Contemporary Review. *Sirnak University Journal Of Science*, *9*, 98-119. / Demir A. Ö. & Hakan, S. (2025). (2025). Türkiye'de Şap Hastalığının (FMD) Klinik Görünümleri ve Önleyici Stratejiler: Güncel Bir İnceleme. *Şırnak Üniversitesi Fen Bilimleri Dergisi*, *9*, 98-119.

Date of Submission (*Geliş Tarihi*)	10. 09. 2025
Date of Acceptance (*Kabul Tarihi*)	08. 11. 2025
Date of Publication (*Yayın Tarihi*)	23. 12. 2025
Article Type (*Makale Türü*)	Derleme (*Review*)
Peer-Review (*Değerlendirme*)	Double anonymized – At Least Two External (*Çift Taraflı Körleme / En az İki Dış Hakem*).
Ethical Statement (*Etik Beyan*)	It is declared that scientific, ethical principles have be followed while carrying out and writing this study, a that all the sources used have been properly cited. (*çalışmanın hazırlanma sürecinde bilimsel ve etik ilkele uyulduğu ve yararlanılan tüm çalışmaların kaynakça belirtildiği beyan olunur*).
Plagiarism Checks (*Benzerlik Taraması*)	Yes (Evet) – Ithenticate/Turnitin.
Conflicts of Interest (*Çıkar Çatışması*)	The author(s) has no conflict of interest to declare (*Çık çatışması beyan edilmemiştir*).
Complaints (*Etik Beyan Adresi*)	sufbd@gmail.com
Grant Support (*Finansman*)	The author(s) acknowledge that they received external funding in support of this research. (*araştırmayı desteklemek için dış fon kullanılmamıştır*).
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* This study was presented as an oral presentation at the ASES V. International Çanakkale Scientific Studies Congress, Çanakkale/ Türkiye, August 29–31, 2025.

ABSTRACT

Foot and mouth disease (FMD) remains one of the most economically serious transboundary animal diseases worldwide, affecting cloven hoofed animals including cattle, sheep, goats and pigs. Türkiye, due to its strategic geographical position bridging Europe with Asia, continues to face periodic challenges from FMD outbreaks. This review, aims to provide a comprehensive overview of the clinical symptoms, diagnostic procedures, treatment protocols and prevention strategies currently employed against FMD in Türkiye. Emphasis is placed on the species specific clinical presentations, the importance of differential diagnosis and the integration of molecular diagnostics such as RT-PCR and ELISA in rapid disease confirmation. Supportive treatment options, including anti-inflammatory therapy, nutritional support and secondary infection control are discussed in light of field realities. Furthermore, Türkiye's vaccination strategies and regional control programs are evaluated for their current effectiveness. The findings underscore the need for continuous veterinary training, improved surveillance systems and enhanced awareness among livestock owners to ensure timely response and reduce the socioeconomic burden of FMD.

Keywords: Foot and mouth disease (FMD); Türkiye; ELISA; RT-PCR

ÖZET

Şap hastalığı (FMD), sığır, koyun, keçi ve domuz gibi çift tırnaklı hayvanları etkileyen, dünya genelinde en ciddi ekonomik sonuçlara yol açan sınır aşan hayvan hastalıklarından biri olmaya devam etmektedir. Avrupa ile Asya arasında stratejik bir köprü konumunda bulunan Türkiye, dönemsel olarak şap salgınlarıyla karşı karşıya kalmaktadır. Bu derleme, Türkiye'de şap hastalığına karşı kullanılan klinik bulgular, tanı yöntemleri, tedavi protokolleri ve korunma stratejilerine kapsamlı bir bakış sunmayı amaçlamaktadır. Çalışmada özellikle türlere özgü klinik tablolar, ayırıcı tanının önemi ve RT-PCR ile ELISA gibi moleküler tanı yöntemlerinin hızlı hastalık doğrulamasındaki yeri vurgulanmıştır. Destekleyici tedavi seçenekleri arasında anti-enflamatuvar uygulamalar, beslenme desteği ve sekonder enfeksiyon kontrolü saha koşulları ışığında tartışılmıştır. Ayrıca, Türkiye'nin aşılama stratejileri ve bölgesel kontrol programlarının güncel etkinliği değerlendirilmiştir. Bulgular, veteriner hekimlerin sürekli eğitimi, sürveyans sistemlerinin güçlendirilmesi ve yetiştiricilerin farkındalığının artırılmasının, hızlı müdahale ve şap hastalığının sosyoekonomik yükünün azaltılması açısından hayati önem taşıdığını ortaya koymaktadır.

Anahtar Kelimeler: Şap hastalığı (FMD); Türkiye; ELISA; RT-PCR

1. INTRODUCTION

Foot-and-mouth disease (FMD) represents a persistent global threat to livestock health, food security and international trade. Its rapid transmissibility across borders and species has necessitated coordinated international efforts to contain its impact. FMD remains one of the most economically disruptive transboundary animal diseases, primarily due to its ability to spread quickly among cloven hoofed animals, including cattle, sheep, goats, pigs and various wildlife species (Alexandersen et al., 2003; Grubman and Baxt, 2004; Jamal and Belsham, 2013).

The global response to FMD is spearheaded by leading institutions such as the World Organisation for Animal Health (WOAH), the Food and Agriculture Organization of the United Nations (FAO) and the World Reference Laboratory for FMD (WRLFMD). These entities, in collaboration with national institutions, focus on surveillance, diagnostics, vaccine development and coordinated emergency responses to mitigate the disease's socioeconomic burden (FAO, 2021; WRLFMD, 2023; WOAH, 2024). The integration of these activities reflects a multidisciplinary strategy aimed at strengthening preparedness and resilience against outbreaks worldwide.

Türkiye occupies a critical geographic position bridging Europe and Asia, which places it at the intersection of endemic and non endemic FMD zones. This strategic location, combined with extensive livestock movement, transhumance practices and trade activities, significantly increases Türkiye's exposure to transboundary incursions and the introduction of multiple serotypes (Di Nardo et al., 2011; İnce and Kanat, 2015; WRLFMD, 2023). Although comprehensive control measures such as ring vaccination, movement restrictions, surveillance systems and awareness campaigns have been implemented by the Ministry of Agriculture and Forestry, sporadic outbreaks persist, particularly in border regions and high density livestock areas (DEFRA, 2023).

To facilitate comprehension across disciplines, this review incorporates a glossary of key institutional terms, diagnostic methods and molecular techniques in Table 1. This glossary, aligned with both global institutional frameworks and Türkiye specific veterinary infrastructure, provides readers with a structured reference to navigate the technical terminology that underpins FMD prevention and control.

Table 1. Glossary of scientific and institutional terms related to FMD

Abbreviation	Full name (English)	Country of origin	Description / Role
FMD Institute	Foot-and-Mouth Disease Institute	Türkiye	Türkiye's FMD vaccine production and diagnostic center
WRLFMD	World Reference Laboratory for FMD	United Kingdom	Global FMD surveillance and strain characterization
WOAH	World Organisation for Animal Health	France	International animal health authority
FAO	Food and Agriculture Organization	Italy	Global food and animal health coordination
EUFMD	European Commission for the Control of FMD	Italy	FAO coordinated European initiative for FMD
DEFRA	Department for Environment, Food and Rural Affairs	UK	UK government disease control authority
WAHIS	World Animal Health Information System	France	WOAH's global disease monitoring system

2. ETIOLOGY AND PATHOGENESIS OF FMD

2.1. Etiology and pathogenesis of FMD in the World

FMD is caused by the Foot-and-Mouth Disease Virus (FMDV), a highly contagious, non-enveloped, single stranded, positive sense RNA virus belonging to the genus *Aphthovirus* within the family *Picornaviridae* (Grubman and Baxt, 2004; Jamal and Belsham, 2013). The virus affects cloven hoofed animals, including cattle (*Bos taurus*), pigs (*Sus scrofa domestica*), sheep (*Ovis aries*), goats (*Capra hircus*) and several wildlife species (e.g., *Sus scrofa, Cervus elaphus*).

FMDV exhibits seven distinct serotypes O, A, C, Asia-1, SAT-1, SAT-2 and SAT-3 none of which confer cross protective immunity, necessitating serotype specific surveillance and vaccination (Grubman and Baxt, 2004; Jamal and Belsham, 2013). Its high mutation rate accelerates antigenic drift, thereby complicating vaccine matching and requiring constant updates to immunization strategies.

The infection process begins when the virus enters the host primarily through the respiratory route, targeting the pharyngeal epithelium as the primary site of replication. It subsequently spreads systemically via viremia, infecting multiple tissues (Jackson et al., 2000; Golde et al., 2008). Viral entry is mediated by interactions with integrin receptors such as αvβ6 and αvβ3, and to a lesser extent by heparan sulfate proteoglycans.

The virus displays strong epithelial tropism, particularly in the oral cavity, tongue, feet and teats, leading to the characteristic vesicular lesions. These lesions result from virus induced cytolysis and inflammation, manifesting clinically as fever, drooling and lameness. Importantly, persistent infections are common, especially in ruminants, where animals may remain asymptomatic carriers for months, silently spreading the virus and complicating eradication efforts (Salt, 1993).

2.2. Etiology and pathogenesis of FMD in Türkiye

Türkiye occupies a critical epidemiological position due to its bridge location between Europe and Asia, making it highly vulnerable to FMD incursions. The disease is endemic in many regions of the country and constitutes a continuous threat to livestock productivity, trade and regional biosecurity.

The predominant circulating serotypes in Türkiye are O and A, with occasional detection of Asia-1 in earlier decades (İnce and Kanat, 2015; Sareyyüpoğlu, 2022). The pathogenesis in Türkiye mirrors global mechanisms: initial replication in the pharyngeal epithelium, systemic dissemination via viremia and the development of vesicular lesions. However, local studies underscore the role of integrin mediated entry (αvβ6, αvβ3) and highlight the potential influence of host genetic resistance factors, particularly among native breeds (Dinçel et al., 2019).

Furthermore, persistent infections and silent carrier states have been well documented in cattle populations, especially in the Aegean and Eastern Anatolia regions (Sareyyüpoğlu, 2022). These carriers present a serious challenge to eradication programs, as they can sustain viral circulation despite mass vaccination.

Türkiye's unique husbandry practices, including transhumance and smallholder livestock systems, contribute to heterogeneous spread patterns and complicate disease control. This underlines the need for region specific surveillance, risk based vaccination and targeted outbreak response protocols.

2.3. Similarities and differences between global and Turkish FMD

Understanding the similarities and differences between global and national patterns of FMD serotype circulation is essential for developing effective regional control strategies. Comparative analysis enables the identification of Türkiye's distinct epidemiological characteristics while situating them within the broader landscape of global viral diversity.

Table 2 summarizes the approximate global emergence of the seven FMDV serotypes and the years in which they were first reported in Türkiye. Although all serotypes have been documented worldwide since the early 20th century, Türkiye's historical profile is characterized primarily by the early detection and long term circulation of serotypes O (first reported in 1957) and A (1958), alongside the sporadic and limited detection of Asia-1 (1973). In contrast, serotype C was last recorded in 1959, while SAT-1 was investigated but only reported from sample submissions between 1962 and 1965 without confirmed sustained circulation and SAT-3 has never been recorded in the country. A significant epidemiological transition occurred with the first confirmed detection of SAT-2 on 3 March 2023, representing a newly emerging serotype within Türkiye's FMD landscape (DEFRA, 2023; WOAH, 2023; WRLFMD, 2023).

This shift highlights the dynamic nature of FMD viral evolution and emphasizes the importance of strengthened cross border surveillance, timely genomic monitoring and regular updates to vaccine strain composition to ensure continued effectiveness of national and regional control programs.

Table 2. Emergence and distribution of FMDV serotypes: Global trends vs. Türkiye specific detection

Serotype	**Estimated global emergence**	**Year first reported in Türkiye**	**References**
O	~1900s	1957	Samuel and Knowles, 2001; Knowles and Samuel, 2003; Grubman and Baxt, 2004; Klein et al., 2006; Jamal and Belsham, 2013; WRLFMD, 2023
A	~1870s	1958	Klein et al., 2006; Di Nardo et al., 2011; Mahapatra et al., 2016; WRLFMD, 2016; WRLFMD, 2023
Asia-1	~1930s	1973	Jamal and Belsham, 2013; İnce and Kanat, 2015; WRLFMD, 2023
C	~1935s	1959	WRLFMD, 2023
SAT-1	~1600s	1962-1965	Vosloo et al., 2002; WRLFMD, 2023; Wasfy et al., 2025
SAT-2	~1600s	March 3, 2023	DEFRA, 2023; WOAH, 2023; WRLFMD, 2023
SAT-3	~1940s	Never recorded	Vosloo et al.,2002; WRLFMD, 2023; TUSEDAD, 2025; Wasfy et al., 2025

This comparative overview underscores the need for continuous regional serotype monitoring, tailored vaccine strategies and integration of genomic data to anticipate and prevent future incursions.

3. CLINICAL MANIFESTATIONS

3.1. Clinical manifestations in the World

FMD presents a broad spectrum of clinical signs influenced by host species, immune status, age and environmental conditions. Typical clinical features include high fever, excessive salivation, vesicular eruptions in the oral cavity, interdigital spaces of the feet and varying degrees of lameness. Severe cases may result in myocarditis, particularly in young calves, sometimes leading to sudden death (Alexandersen et al., 2003; Grubman and Baxt, 2004).

These clinical signs cause significant reductions in productivity, mobility and reproductive efficiency, making FMD one of the most economically disruptive livestock diseases worldwide. Importantly, clinical expression varies among species: cattle and pigs often present overt and severe signs, whereas sheep and goats may remain subclinical, contributing to the silent spread of infection (Thomson et al., 2003; Radostits et al., 2007). To provide a structured reference, Table 3 summarizes species specific clinical signs based on global literature, including both domestic and wild cloven hoofed animals.

Table 3. Comparative clinical signs of FMD in global and Turkish contexts with species specific References

Species (Common name)	Scientific name	Clinical signs global perspective	References (Global)	Clinical signs Türkiye	References (Türkiye)
Cattle	*Bos taurus*	High fever, drooling, vesicles in mouth and feet, lameness, myocarditis in calves	Alexandersen et al., 2003; Grubman and Baxt, 2004	Identical signs observed; myocarditis related deaths and milk drop reported in outbreak zones	İnce and Kanat, 2015; Sareyyüpoğlu, 2022
Sheep	*Ovis aries*	Often subclinical; mild oral and interdigital vesicles; occasional lameness	Thomson et al., 2003; Radostits et al., 2007	Lameness and mild vesicles during outbreaks; often underdiagnosed	İnce and Kanat, 2015
Goats	*Capra hircus*	Similar to sheep; minimal lesions; vesicles may not form; potential silent spread	Radostits et al., 2007 Arzt et al., 2011	Clinical signs often absent or mild; oral erosions and limping in outbreaks; molecular confirmation required	Dinçel et al., 2019; Sareyyüpoğlu, 2022
Pigs	*Sus scrofa domestica*	Snout, foot and coronary band vesicles; severe lameness; hoof sloughing; high piglet mortality	Domingo et al., 2002; Brown and Torres, 2008	No clinical cases documented; pig production negligible	Wilson and Yilmaz, 2020; Ministry of Agriculture and Forestry, 2025
Wild boar	*Sus scrofa*	Experimental infection shows vesicles and virus shedding; can act as amplifiers	Bastos et al., 2001; Thomson et al., 2003	No surveillance or field reports; wild populations not included in official monitoring	Albayrak et al., 2013; İnce ve Kanat, 2015
Red deer	*Cervus elaphus*	Vesicles, lameness, fever in challenge studies	WOAH-WAHIS, 2022; Vosloo et al., 2002	No monitoring program or confirmed cases; epidemiological role unknown	Ministry of Agriculture and Forestry, 2025; Nature Association, 2021
Carrier	–	Long term carriers possible in ruminants	Salt, 1993; Arzt et	Carrier state confirmed in local cattle (*Bos taurus*); not	Dinçel et al., 2019;

Species (Common name)	Scientific name	Clinical signs global perspective	References (Global)	Clinical signs Türkiye	References (Türkiye)
Status		(especially cattle and buffalo)	al., 2011	monitored in sheep/goats or wildlife	Sareyyüpoğlu, 2022

As shown in Table 3, cattle are consistently the most clinically affected species in both global and Turkish contexts. In contrast, sheep and goats frequently present with mild or subclinical symptoms, complicating early detection and facilitating silent transmission. The epidemiological role of wild species remains poorly defined in Türkiye due to insufficient monitoring, despite international evidence supporting their susceptibility. By contrasting Türkiye specific outbreak data with international findings, Table 3 illustrates both parallels and critical gaps, particularly concerning wildlife surveillance. This comparative framework highlights the urgent need for enhanced diagnostic vigilance and the systematic integration of wildlife monitoring into national FMD control strategies.

3.2. Clinical manifestations in Türkiye

In Türkiye, clinical presentations of FMD largely parallel global patterns but are strongly influenced by local husbandry practices such as transhumance, mixed species rearing and limited biosecurity measures. Cattle represent the most clinically affected species, frequently displaying fever, excessive salivation, vesicular lesions on the tongue and feet and myocarditis related mortality, often accompanied by decreased milk yield (İnce and Kanat, 2015; Sareyyüpoğlu, 2022). In contrast, sheep and goats typically exhibit subclinical or mild clinical forms, which complicates timely diagnosis and facilitates silent viral transmission within herds (Dinçel et al., 2019). Pigs, although highly susceptible in global contexts, have negligible epidemiological importance in Türkiye. National livestock data indicate that Türkiye's domestic pig numbers fell to around 1,200 by 2017, with annual production remaining under a few tonnes (Wilson and Yilmaz, 2020). Moreover, the 2025 national disease control program did not list pigs among key target species, suggesting their minimal role in FMD surveillance and control strategies (T.C. Tarım ve Orman Bakanlığı, 2025).

Wildlife species especially wild boar (*Sus scrofa*) and red deer (*Cervus elaphus*) are not yet incorporated into structured FMD specific surveillance activities in Türkiye, which creates certain gaps in understanding their potential epidemiological role. Evidence from neighbouring regions provides helpful context for this issue. For example, a study conducted in Southeast Bulgaria demonstrated that wild boar and deer may experience subclinical FMD infections, with seropositive cases observed in proximity to livestock outbreak areas

(Alexandrov et al., 2013). Although these findings do not indicate long term wildlife reservoirs, they illustrate that wildlife can be involved in local transmission dynamics under particular ecological conditions.

In Türkiye, available wildlife research has focused on other viral infections of wild boar rather than FMD. Notably, a serological survey reported exposure to several multi host pathogens and highlighted the broader importance of wildlife monitoring for disease ecology (Albayrak et al., 2013). While this study does not address FMD directly, it underscores that wildlife surveillance remains limited and that expanding monitoring to include FMD would contribute valuable insights. Taken together, international experience and national wildlife data suggest that integrating wild boar and deer into FMD surveillance frameworks would strengthen Türkiye's overall capacity to detect, interpret and respond to potential transmission pathways.

4. DIAGNOSTIC APPROACHES

FMD diagnosis relies on the integrated use of clinical evaluation, laboratory confirmation and molecular detection, supported by differential diagnosis procedures relevant to endemic regions such as Türkiye. Clinically, suspicion arises when fever, excessive salivation and characteristic vesicles/erosions on the tongue, dental pad, feet or teats are observed; however, mild or subclinical infections in small ruminants frequently require laboratory confirmation (Anonymous, 2025).

Laboratory diagnosis in Türkiye routinely includes virus isolation (VI) using bovine thyroid (BTY) or IBRS-2 cell cultures and a series of ELISA based assays: Solid-Phase Competition ELISA (SPCE) for serotype specific antigen detection, Liquid Phase Blocking ELISA (LPBE) for post vaccination antibody assessment and vaccine matching and Non Structural Protein ELISA (NSP-ELISA) for differentiating infected from vaccinated animals (DIVA), an essential component of Türkiye's national control strategy (Şevik and Öztürk, 2013; Anonymous, 2025).

Molecular confirmation is primarily achieved through reverse transcription polymerase chain reaction (RT-PCR) and real time RT-PCR, which provide rapid, sensitive detection and serotype identification (WOAH, 2021). Türkiye's national reference laboratory (Anonymous, 2025) routinely performs VP1 gene sequencing for molecular epidemiology and tracing of circulating strains (İnce et al., 2023).

5. CONTROL STRATEGIES AND EPIDEMIOLOGICAL PERSPECTIVES

5.1. Global and regional FMD control approaches

Efforts to control and prevent FMD vary significantly across world regions, shaped by differences in endemicity, livestock density, veterinary infrastructure, wildlife interactions and geopolitical constraints. Some countries particularly in Western Europe have achieved FMD free status through strict biosecurity measures, surveillance programs and movement controls without routine vaccination (WOAH, 2023). By contrast, regions such as Sub-Saharan Africa and Southeast Asia continue to struggle with persistent endemicity, due to the circulation of multiple serotypes, porous borders and the presence of wildlife reservoirs such as African buffalo (*Syncerus caffer*) and wild boar (*Sus scrofa*) (Vosloo et al., 2002; Rweyemamu et al., 2008). In South America, regional cooperation coordinated by Pan American Foot-and-Mouth Disease Center (PANAFTOSA) and the FAO has led to significant improvements, with risk based vaccination campaigns playing a key role in reducing incidence (FAO, 2021). In Southeast Asia, Southeast Asia and China Foot-and-Mouth Disease Campaign (SEACFMD) programs have provided a structured framework for vaccination and monitoring, though challenges remain in surveillance consistency (WOAH, 2023). This global variability is critical for benchmarking Türkiye’s strategies. Comparative lessons show that successful regional approaches integrate vaccination with surveillance, rapid outbreak response and wildlife monitoring. Table 4 summarizes these diverse strategies, providing a comparative framework for Türkiye’s positioning in the global control landscape.

Table 4. Comparative overview of FMD epidemiology, wildlife reservoirs and control strategies by region

Region / Country	Endemic status	Dominant serotypes	Control strategy	Wildlife reservoirs	Surveillance intensity	Vaccination policy	References
Sub-Saharan Africa	Endemic	SAT-1, SAT-2, O	Variable, limited control	African buffalo (*Syncerus caffer*)	Low	Sporadic, localized vaccination	Rweyemamu et al., 2008; WOAH, 2023
Southeast Asia	Endemic	O, A	SEACFMD campaigns	Wild boar (*Sus scrofa*)	Medium	Regular mass vaccination	Rweyemamu et al., 2008; WOAH, 2023
South America	Controlled	O, A	PANAFTOSA coordinated programs	Minimal significant wildlife reservoirs	High	Risk based vaccination	Rweyemamu et al., 2008; FAO, 2021
Western Europe	FMD free (no vaccine)	–	EU-regulated surveillance and movement control	None significant	Very high	No routine vaccination	European Union, 2016; WOAH, 2023

Region / Country	Endemic status	Dominant serotypes	Control strategy	Wildlife reservoirs	Surveillance intensity	Vaccination policy	References
Türkiye	Partially endemic	O, A, Asia-1; SAT-2 detected 2023	Mass vaccination + stamping out + border control	Wild boar (*Sus scrofa*), red deer (*Cervus elaphus*)	Medium–High	Biannual vaccination in high risk zones	DEFRA, 2023; WRLFMD, 2023; Anonymous, 2025)
Middle East	Endemic	O, A, Asia-1	National programs, variable success	Wild ungulates	Low–Medium	Inconsistent coverage	Di Nardo et al., 2011; WOAH, 2023

5.2. Türkiye's position in the global control landscape

Türkiye's FMD control program has evolved into a multi tiered approach comprising vaccination, surveillance, border control and international collaboration. Positioned at the interface of endemic and non-endemic zones, Türkiye faces recurrent incursions of serotypes O and A, and most recently the emergence of serotype SAT-2 in Eastern Anatolia in 2023, marking a critical epidemiological shift (DEFRA, 2023; WOAH, 2023; WRLFMD, 2023).

Although Türkiye has relatively limited research on the spatial temporal clustering of FMD, existing studies demonstrate meaningful analytical progress. Among these, the work of İnce et al. (2023) represents one of the few but valuable national examples, providing empirical evidence on regional clustering patterns, temporal variability and outbreak hotspots. Thus, this study should be viewed not as contradicting an absence of research, but rather as an illustration of the limited yet emerging analytical capacity in Türkiye regarding FMD spatial epidemiology.

Vaccination: The cornerstone of Türkiye's program is its biannual mass vaccination strategy, primarily targeting cattle in high risk regions. This is supported by antigen matching, risk mapping and strategic vaccine stockpiling. Field studies confirm that antigenic drift often reduces vaccine effectiveness, necessitating frequent updates (Knight-Jones et al., 2014).

Surveillance: The surveillance system integrates passive reporting of vesicular diseases and active post vaccination monitoring through serological testing and risk based sampling. Limitations remain, particularly in detecting subclinical infections in small ruminants and wildlife (WOAH, 2023).

Border control: Porous frontiers with endemic regions represent a major vulnerability. Although quarantine and movement restrictions are in place, enforcement inconsistencies and transhumant livestock practices compromise efficacy (Di Nardo et al., 2011).

Institutional role: Şap Enstitüsü (Ankara) is central to Türkiye's response, conducting molecular diagnostics, vaccine formulation, and outbreak management. It collaborates with WRLFMD and contributes data to international serotype databases. However, molecular surveillance in non cattle species remains underdeveloped, creating epidemiological gaps (Dinçel et al., 2019; Sareyyüpoğlu, 2022).

6. MOLECULAR EPIDEMIOLOGY AND GENETIC EVOLUTION OF FMDV

6.1. Genetic diversity and phylogenetic patterns

FMDV is an RNA virus of the genus Aphthovirus, characterized by its lack of proofreading activity in RNA dependent RNA polymerase, which results in a high mutation rate and substantial genetic variability. The virus comprises seven immunologically distinct serotypes (O, A, C, Asia-1, SAT-1, SAT-2, SAT-3), with no cross protective immunity between them, making continuous molecular monitoring and serotype specific vaccination essential (Grubman and Baxt, 2004; Jamal and Belsham, 2013).

Global phylogenetic analyses of the VP1 gene have revealed the presence of multiple topotypes and lineages within each serotype (Knowles and Samuel, 2003; WRLFMD, 2023). For example, serotype O is subdivided into Middle East–South Asia (ME-SA), East Africa and Cathay lineages ("A unique O serotype lineage predominantly identified in China and neighboring regions).

In Türkiye, the O/ME-SA/PanAsia-2 lineage has been predominant since the 1990s, accompanied by intermittent incursions of A/Iran/2005-like strains (İnce and Kanat, 2015; WRLFMD, 2023).

A significant recent development was the detection of SAT-2 in Eastern Anatolia in 2023, representing a novel incursion and a major epidemiological shift in Türkiye's FMD landscape (DEFRA, 2023; WOAH, 2023; WRLFMD, 2023).

Molecular tools such as maximum likelihood phylogenetic trees, recombination analysis and molecular clock dating are widely employed to track viral evolution and spatiotemporal spread (Di Nardo et al., 2011).

6.2. Molecular surveillance in Türkiye

Türkiye's molecular surveillance efforts are spearheaded by the FMD Institute (Ankara), which plays a central role in molecular diagnostics, VP1 sequencing, antigenic cartography, and vaccine matching. The institute collaborates with international agencies, including

WRLFMD and EUFMD, contributing to global serotype databases and vaccine strain selection efforts (Dinçel et al., 2019).

Current molecular surveillance capacity in Türkiye includes VP1 sequencing of field isolates, antigenic cartography for vaccine strain matching and genome based approaches to evaluate vaccine compatibility. Despite these advanced tools, several limitations remain. Molecular surveillance in small ruminants and wildlife is highly restricted, raising concerns about the existence of cryptic lineages that may go undetected. Furthermore, evidence of recombination events in viral genomes isolated from eastern regions suggests potential inter lineage exchanges facilitated by porous borders. These findings underscore the urgent need for strengthened cross border genomic surveillance and improved regional data sharing mechanisms. Overall, although Türkiye’s infrastructure for molecular surveillance is well developed, it remains disproportionately focused on cattle, while sheep, goats and wildlife are underrepresented despite their potential role in viral persistence and transmission (Klein et al., 2006). Obtaining data on the spatial and temporal spread of cases and identifying FMD clusters may be useful for clarifying changes in risk areas, identifying new risk areas, and implementing more effective control strategies during outbreaks (Alkhamis et al. 2009).

To our knowledge, no studies have been conducted in Türkeye to evaluate the spatial-temporal clustering of FMD outbreaks in cattle and small ruminants. Furthermore, there is limited information on the molecular epidemiology of FMDV in Türkeye. Between 2010 and 2019, İnce and colleagues (2023), sought to determine the temporal patterns and spatiotemporal clusters of FMD by analysing retrospective FMD outbreak data. A spatial-temporal analysis of FMD virus (FMDV) outbreak data occurring in Türkeye between 2010 and 2019 has been conducted. The spatial temporal analysis was performed using a total of 7,796 FMD outbreak data points and the space-time scanning statistic. A space-time analysis was performed using a total of 7,796 FMD outbreak data points. The SDE analysis indicated that direction of FMD transmission was northeast to southwest. A significant decrease in the number of outbreaks and cases were observed between 2014 and 2019 compared to 2010–2013 ($p = 0.010$). Most of the serotype A, serotype O and serotype Asia-1 associated FMD outbreaks were observed during the dry season (April to September). Among FMD cases, cattle and small ruminants accounted for 80.75% (180,932 cases) and 19.25% (43,116 cases), respectively. Among the serotypes detected in the cases, the most frequently detected serotype was serotype O (50.84%), followed by serotypes A (35.67%) and Asia-1 (13.49%) (İnce et. al., 2023).

7. WILDLIFE INTERFACE AND ECOLOGICAL RISK FACTORS

7.1. Global evidence on wildlife-linked FMD transmission

The interface between wildlife and domestic livestock is a critical yet often underexplored dimension of FMD epidemiology. Multiple wild ungulate species have been identified as potential reservoirs or amplifiers of the virus, with varying roles across regions (Vosloo et al., 2002; Thomson et al., 2003).

In Southern Africa, the African buffalo (Syncerus caffer) is recognized as a long term maintenance host, sustaining SAT serotypes and facilitating spillover into domestic herds (Bastos et al., 2001).

In Eastern Europe, wild boar (*Sus scrofa*) and red deer (*Cervus elaphus*) have shown serological evidence of subclinical infection in populations located near domestic outbreaks (WOAH-WAHIS, 2022).

In Asia, experimental studies confirmed the susceptibility of wild pigs and deer, demonstrating that these species can develop vesicular lesions and shed virus, potentially acting as silent amplifiers (Thomson et al., 2003).

Despite this evidence, systematic wildlife surveillance for FMD remains limited globally, constrained by logistical challenges, lack of standardized sampling frameworks and lower prioritization compared to domestic livestock health systems.

7.2. Türkiye’s wildlife landscape and surveillance gaps

Wild boar (*Sus scrofa*): Experimental data suggest that infected animals can shed virus and contribute to transmission dynamics, yet no systematic monitoring exists in Türkiye (Thomson et al., 2003).

Red deer (*Cervus elaphus*): Challenge studies confirm susceptibility, but Türkiye has no field based monitoring programs to assess their epidemiological role (Vosloo et al., 2002).

Silent carriers in wildlife remain an unquantified risk, particularly in eastern and southeastern Türkiye, where transboundary animal movements overlap with transhumant livestock routes, raising the risk of undetected viral circulation.

7.3. Policy implications and recommendations

To address these gaps, Türkiye's national FMD control program must adopt a One Health aligned approach by systematically integrating wildlife into surveillance and risk modeling frameworks (Knight-Jones and Rushton, 2013; WOAH, 2023).

8.VACCINATION TECHNOLOGIES AND EFFICACY ASSESSMENT

8.1. Conventional vaccines and regional applications

Conventional FMD vaccines are formulated as multivalent, oil adjuvanted, inactivated virus suspensions, which remain the global standard for immunization (Knight-Jones et al., 2016). A meta analysis from Africa demonstrated that vaccination can reduce FMD transmission by approximately 69% when properly implemented (Wubshet et al., 2024). Global context: Multivalent vaccines targeting multiple serotypes (O, A, Asia-1, SAT lineages) are widely used, but their effectiveness is heavily dependent on antigenic match between vaccine strains and circulating viruses (Wubshet et al., 2024).

Türkiye: Triple vaccines containing O, A and Asia-1 are administered twice a year, in spring and autumn, using a double-dose schedule in high-risk areas. These vaccines generally achieve potency levels of ≥3 PD_{50}. However, field protection varies, reflecting antigenic mismatch challenges (Knight-Jones et al., 2014).

8.2. Challenges in vaccine matching and antigenic drift

FMDV's high mutation rate, particularly in the VP1 coding region, results in antigenic drift, which can undermine vaccine effectiveness (Hardham et al., 2020).

In Türkiye, antigenic mismatches have been documented for the A/Iran-05 lineage and the O/ME-SA/PanAsia-2 lineage, leading to reduced vaccine effectiveness (Knight-Jones et al., 2016).

Such mismatches highlight the importance of routine sequencing of field isolates and the use of antigenic cartography to inform strategic vaccine updates (Ludi et al., 2022).

8.3. Future perspectives: novel platforms

Next generation vaccine platforms are being developed to overcome the limitations of conventional inactivated vaccines:

mRNA vaccines: A serotype O mRNA vaccine has induced strong neutralizing antibody and $CD4^+/CD8^+$ T-cell responses in murine and porcine models, maintaining protection for over four months (Zhao et al., 2025).

Virus like particle (VLP) vaccines: Peptide based VLP vaccines have shown promising immunogenicity in mice and guinea pigs (Lu et al., 2024).

Novel adjuvant systems: Adjuvants such as furfurman have been associated with enhanced mucosal immunity and prolonged T-cell memory (Kim et al., 2024; Li et al., 2025).

These innovative platforms offer scalable, biosafe and rapidly adaptable alternatives, particularly relevant for emerging and transboundary FMD variants.

8.4. Türkiye's vaccine production capacity and strategic gaps

Türkiye's vaccine production is centralized at the FMD Institute (Ankara), which oversees trivalent vaccine production, antigenic matching and field efficacy testing. Despite the implementation of biannual vaccination campaigns, several structural challenges persist. Vaccination coverage in small ruminants remains low, thereby limiting the development of adequate herd immunity. In addition, gaps in cold-chain logistics, particularly in rural areas, compromise vaccine potency and delivery efficiency. Another critical limitation is the insufficient integration of molecular surveillance data into vaccine updates, which hinders timely adjustments to evolving viral lineages. Finally, Türkiye's high throughput sequencing capacity remains underdeveloped, restricting the effective monitoring and detection of emerging escape mutants (Knight-Jones et al., 2014).

9.CONCLUSION

FMD remains one of the most contagious and economically devastating viral diseases affecting cloven hoofed animals worldwide. The present review has synthesized knowledge from multiple disciplinary perspectives, including clinical manifestations, molecular epidemiology, wildlife livestock interfaces, vaccination technologies and national control strategies. By integrating global evidence with Türkiye specific data, this analysis underscores the complexity of managing FMD in regions characterized by porous borders, heterogeneous husbandry practices and continuously evolving viral serotypes.

The recent emergence of serotype SAT-2 in Türkiye, in parallel with the endemic circulation of serotypes O and A, illustrates the dynamic epidemiological landscape and highlights the necessity of continuous surveillance, routine serotyping and frequent vaccine strain matching to ensure adequate immunological protection.

Türkiye's FMD control strategy centered on biannual vaccination campaigns, centralized vaccine production, and expanding molecular surveillance capacity reflects a structured and determined national effort. Nevertheless, persistent challenges remain, particularly with respect to low vaccination coverage in small ruminants, the absence of systematic wildlife surveillance and limited genomic monitoring for antigenic drift.

Future progress will require the adoption of a One Health oriented framework, integrating ecological and genomic data with veterinary surveillance, while strengthening regional collaboration and cross border information sharing. The development and implementation of novel vaccine platforms (e.g., mRNA and virus like particle technologies), alongside improvements in cold chain logistics and field based genomic diagnostics, represent critical priorities.

By aligning national control measures with international risk models and eradication initiatives, Türkiye can enhance its resilience to future outbreaks and contribute substantially to the global goal of FMD eradication.

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