Research article

Emerging of SAT-2 foot-and-mouth disease strain in the Middle East region, the risk of its incursion into Iran, and future measures in the region

Amir Javadi[1*], Mohammad Nouri[2]

1. *DVM, DVSc, Deputy Director General of Qazvin province office of Iran Veterinary Organization, Qazvin, Iran.*
2. *Emeritus professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.*

Amirjavadivet@gmail.com

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Home Messages

- The immunity to one FMD serotype does not confer immunity to other serotypes, so vaccines that used currently in our country does not immune animals against SAT-2 virus.
- Serotype SAT-2, topotype 14 has entered the Middle East region in December 2022 and officially confirmed in Iraq in January 2023.
- On the 8th of March, in the northeast of Turkey, on the border with Armenia, in the region of Agdir, Iğdır/Tuzluca/Merkez, in an epidemiological unit with 21 cows, the first report of the disease was detected in Turkey.
- SAT-2 virus also in Bahrein and Oman are detected after occurrences of this strain in Turkey.
- The SAT-2 virus has not had occurred in Iran form beginning of emerging until December 2023.

Keywords: Foot and Mouth Disease, SAT-2, Emerging, Middle east, Iran.

Introduction:

The foot-and-mouth virus is a significant and highly contagious disease affecting domestic and wild animals. It has been considered a critical disease in different countries due to its economic, social, and occasionally political impacts. In the field of livestock, it serves as a key indicator when evaluating the efficacy

and performance of veterinary services in disease control.

FMD is caused by an Aphthovirus of the family Picornaviridae, which is a non-enveloped, double-stranded, positive-sense RNA, and seven strains (A, O, C, SAT1, SAT2, SAT3, and Asia1) are endemic in different countries worldwide. The disease affects cattle, swine, sheep, goats and other cloven-hoofed ruminants. It is a transboundary animal disease (TAD) that greatly affects the production of animals and disrupts regional and international trade in animals and animal products. The FMD virus is estimated to circulate in 77% of the global livestock, in endemic countries. The clinical presentation of foot-and-mouth disease is characterized by several characteristic signs. Infected animals typically show fever, accompanied by a loss of appetite and a decrease in milk production. One of the most notable signs of the disease is the formation of blisters and ulcers in the epithelial tissue, predominantly appearing in and around the mouth, feet, and udder. These lesions can be painful and cause discomfort for the affected animals. Secondary infections can arise, leading to complications such as growth retardation and in severe cases, fatalities. Newborns are particularly vulnerable to the disease, as it may result in myocarditis, further increasing the severity and potential long-term injuries. This disease is highly contagious and endemic in many Asian and African countries, posing a significant threat to livestock populations. Periodically, new strains of the virus emerge due to the consecutive virus replication and circulation in susceptible animals. These replication errors and mutations in the virus genome give rise to different lineages and sub-lineages in seven currently known serotypes. It is essential to note that these serotypes are not cross-immune to each other, which further complicates the control and prevention of the disease. The impact of foot-and-mouth disease on the global economy is remarkable, with estimated annual losses ranging from 8 to 22.5 billion dollars. Measures for controlling and preventing foot-and-mouth disease involve rigorous biosecurity measures, punctual and appropriate vaccination campaigns, and surveillance programs to detect and manage outbreaks.

Historically, serotypes O and A were the first serotypes identified in France and Germany, followed shortly by serotype C, but they became extinct in 2017. Afterwards, the serotypes of the southern African territories (SAT 1-3) were detected, and in 1957, the Asia-1 serotype was recognized in the Indian subcontinent.

In total foot-and-mouth disease virus has seven serotypes, namely O, A, C, Asia-1, and the three serotypes collectively known as Southern African Territories (SAT). The Euro-Asia serotypes (O, A, C, and Asia-1) have mainly circulated in Europe, Asia, and South America, while the SAT serotypes have mostly been isolated in Africa. By means of strict hygienic and biosecurity measures, as well as mass vaccination plans in some cases, foot-and-mouth disease has been successfully eradicated from North America, Australia, Europe, and most South American countries. Despite genetic diversity, all serotypes cause similar diseases in terms of clinical presentation. Hence, differences in host specificity and virulence between virus strains may lead to diversity in disease manifestations. The viral genome sequence is analyzed and evaluated to trace the evolution and emergence of new lineages based on sequencing and especially based on the coding sequences of the VP1 capsid protein. The data obtained from the genetic sequences along with the geography and the virus isolation region are the base for the classification and naming of this virus. The epidemiology of foot-and-mouth disease (FMD) in the Middle East and Asia is complicated due to the concurrent circulation of endemic viruses and the sporadic incursions of emerging virus strains from other pools mostly pools 2 and 4 for instance from East Asia and the Indian subcontinent and North Africa.

SAT-2 serotype properties:

According to a meta-analysis study of 919 sequences with serotype records, 91.19% of the sequences belonged to Euro-Asian serotypes (O, A, Asia1 and C) and 8.81% to strains from South African territories (SAT 1-3). All SAT strains have been originating from Africa, except one (AY593839.1; SAT-1; collected in 1970), whose origin was unclear.

According to phylogenetic analysis, serotypes of the South African Territories arose in Uganda and later spread to Botswana and the Gaza Strip. SAT-1 appears to be the ancestor of the entire group, offering drift to SAT-2, SAT-3, and serotype A, which later separated into serotypes Asia-1, O, and C. Recent molecular epidemiologic analyses have indicated that serotype O is the most recent, diverse, and widespread lineage. In addition, regarding the number of outbreaks, serotype A and Asia-1 rated second and third respectively, followed by all SAT serotypes.SAT-2 and SAT-3, are endemic in African countries south of the Sahara region, and the prevalence of SAT-3 in domestic animals is limited to a few countries in southern Africa. SAT-2, which is elaborated on

in this review, has often occurred in domestic animals and is widely, spread across the African continent, reaching from West to Senegal, East to Ethiopia and South to South Africa. This serotype is categorized into 14 topotypes, designated by Greek numbers from I to XIV, between them, the nucleotide homology in the VP1 region is about 80%. This serotype was spread from Botswana to Ethiopia, Zimbabwe, and Zambia, and then extended to neighboring countries, including the eastern region of the African continent.

Emerging of SAT-2 in the Middle East:

It has crossed the Sahara region and has spread to North Africa and the Middle East in recent years. The Middle East outbreak first occurred in North Yemen in 1990, followed by Saudi Arabia and Kuwait in 2000, and in North Africa in Libya in 2003, which reappeared after an apparent absence in the region for about 50 years. In 2012, outbreaks occurred in Egypt, Libya, and Bahrain (9). It has been suggested that changes in the region since 2011 ("Arab Spring") may have contributed to this increase in outbreaks, such as forced displacement of people and their animals due to conflict or change of governments following changes in trade. The epidemiology of SAT serotypes in sub-Saharan Africa varies from that of other serotypes in Africa and other regions because the wildlife reservoir, African buffalo (Syncerus caffer), is also present in areas where that serotype is present. The disease is rarely symptomatic in buffalo, and animals can be persistently infected for a period of several years. Monitoring for the incursion of the new strain by surveillance in the region has significant importance, although vaccination programs may be effective for controlling endemic strains also it is one of the main pillars of disease control, local strains of vaccines confer absolutely no protection against newly emerged and exotic strains. It is clear that vigilant and close monitoring of the FMD disease status in the region is necessary to evaluate the risk of future outbreaks and likewise to ensure the appropriateness of control measures for this virus. In addition to the national impact of this outbreak on the country's livestock industry, the spread of the SAT-2 strain in the region can be a threat to the eastern and northern border countries and even to European countries in the future. Due to the fact that serotype SAT-2, like Asia-1, is restricted to its geographic region, it mainly circulates in African countries.

Serotype SAT-2 and topotype 14 entered the Middle East region in December 2022 and was officially confirmed in January 2023. According

to the latest information, until the end of the summer of 2023, 36 outbreaks have been reported in Iraq (Figure 1). 150 outbreaks of this serotype have been reported in Turkey, which has led to the fact that the FMD outbreaks in Turkey have increased to 326 outbreaks of two circulating strains (O and SAT-2) from the beginning of January until November.

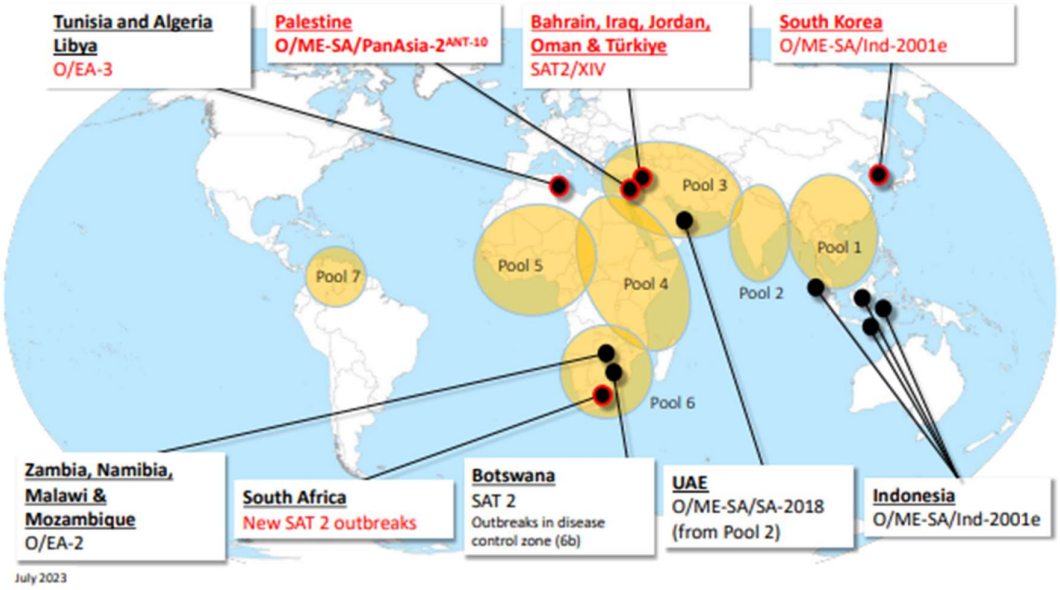

Figure 1: Recent FMD global outbreaks (new headline events reported April to June 2023 are highlighted in red) with endemic pools highlighted in orange. Source: WRLFMD. Map conforms to the United Nations World Map, June 2020.

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Following an unexpected increase in the number and clinical severity of foot-and-mouth disease cases, especially in animals vaccinated with endemic strains of foot-and-mouth disease, a new strain of the virus was suspected in Iraq. The first cases of these outbreaks were detected in Iraq in December 2022. The clinical presentation of the disease was similar to the typical form of the disease with blistering and ulcerative lesions in the mouth and feet, the severity and morbidity of the disease were reported in buffaloes more than in cows. The detection of this strain in Iraq was officially confirmed on January 15, 2023, through the WAHIS website.

Subsequently, samples were sent to Turkey's foot-and-mouth disease institute (SAP) according to an agreement between countries established by the European Commission for the Control of Foot-and-Mouth Disease (EuFMD), and on the third of February 2023, it was reported that the causative virus belongs to the serotype SAT- 2, and topotype XIV which is closely linked

with the sequence of Ethiopian SAT-2 strains that has been detected in 2022.

As claimed by Iraq veterinary service estimations, from December 2022, more than 70 to 80 per cent of large ruminant herds in the country have been affected by the new SAT-2 strain. High morbidity with more than 90% morbidity, plus mortality in cows and buffalo calves, also the disease in adult animals were observed. Most of the losses and clinical manifestations were due to secondary infections as a consequence of Enterotoxemia (Clostridium Perfringens), Pasteurellosis (Pasteurella Multicida) and retardation of proper growth of animals. It is declared that the Outbreaks had been limited to small ruminants, and according to the reports of the Iraqi Veterinary Service, perhaps the confirmation of the serotype of the new strain in small ruminants has not been done properly.

The initial foci in Iraq started from the Baghdad region, which later involved other provinces, especially in the central and northern regions, and still no foci of the diseases have been recorded in Basra and southern Iraq.

At the same time and since the beginning of 2023, outbreaks of this virus were also reported in Jordan. The reason for the simultaneous incident and whether Iraq was involved in Jordan or vice versa is still unclear. However, it should be considered that the number of trades between the two countries was extensive last year. Following the occurrence of the disease in Jordan, the disease has been controlled and diminished within a few months with widespread vaccination.

Despite the efforts made by the Iraqi veterinary service, a vaccine containing the SAT-2 strain has not been implemented in this country yet. The situation was towards stability in the outbreaks of the disease, which increased again from the beginning of September 2023, hence, again alarmed and formed a threat in the region.

On the 8th of March, in the northeast of Turkey, on the border with Armenia, in the region of Agdir, Iğdır/Tuzluca/Merkez, in an epidemiological unit with 21 cows, the first report of the disease was detected in Turkey, then four other epidemiological units showed clinical symptoms of the disease. After that, active surveillance teams have been activated in Turkey. This strain was also similar to the Iraqi strain and from topotype 14. In the beginning, no deaths from the disease were recorded and the number of disease deaths in Turkey was limited. Despite the limited number of disease outbreaks in Turkey with endemic strains, which made this country ready to enter the third stage of FMD control, this

incursion leads a delay in the programs to increase the level of disease control at least for a few years. A few days after the first outbreaks of the disease, on 10 March in Turkey, the first batch of SAT-2 vaccine was produced and distributed by SAP Institute based on the virus received from Iraq. Another batch of half a million doses of Monvalant Eritrea 98 strain was donated to Turkey about 10 days later by the EU Vaccine Bank in the form of EuFMD cooperation for implementation in the border region with the European Union.

In Turkey, the restriction of livestock movement was implemented a few days after the official approval of the outbreak until Eid al-Adha, which coincided with the full coverage of vaccination in large ruminants in Turkey. The fact that whether the virus was transmitted from the center or even the north of Iraq to the north of Turkey is an unanswered question, but it seems that the transmission may have occurred through wild animals or from the livestock market. According to Turkish veterinary reports, these animals are indigenous and belong to Turkey, and there was no history of purchasing animals in those epi units. As you can see in Figure 2, most of the occurrences in Turkey have been reported in the Anatolian region and the east of this country

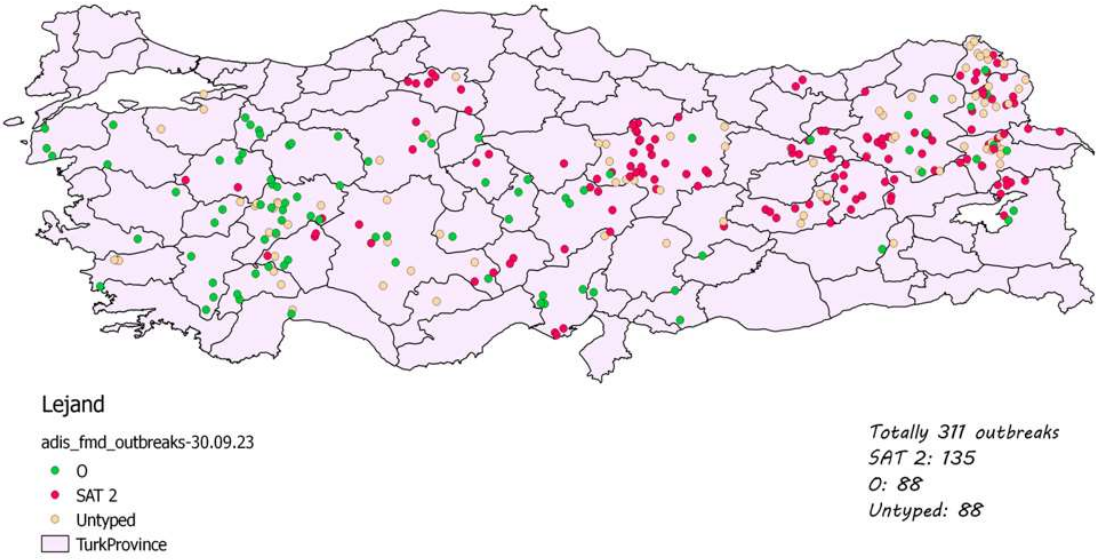

Figure 2: FMD outbreaks in Türkiye in 2023 (until 30 Sep.): geographical distribution and serotypes.

Since the countries of the Persian Gulf region are not prolific countries regarding population of indigenous livestock and animal husbandry industry, mainly live livestock are imported from countries such as

Somalia, Ethiopia and other African countries as well as India and Sri Lanka. Owing to the arrival of live livestock from different and mostly high-risk areas, the emergence of new strains of FMD conceivable in these countries, especially in quarantine sites. Therefore, from the samples sent from Bahrain and Oman in late 2022, whose sequence results have been recently prepared and reported by Perbright accordingly, this virus was SAT-2 and topotype 14. This new strain belongs to a separate lineage in comparison to the strains that circulated in Turkey, Iraq and Jordan.

On First of January 2023, this strain was officially announced in the WAHIS for Oman. Interestingly, the strain isolated in Oman is more closely related to the Ethiopian 2022 strain compared to the strain circulating in Iraq, and there is a significant genetic difference between the two samples obtained, so it can be concluded that the strains isolated in Oman are from Livestock is imported and has no mutual origin.

In addition, following the outbreak of FMD in Qatar, samples were sent to the reference laboratory. Although, in the samples sent from Qatar to Perbright the SAT-2 was not isolated, the SAT-1 strain was isolated, which is close to the strain circulating in Kenya.

Prevention measures in Iran:

In Iran, following the warning of the disease in Iraq on 20th February 2023, the standstill for movement of ruminants, including the entry and exit of livestock from the western provinces of the country, including West Azerbaijan, Kurdistan, Kermanshah, Ilam, and Khuzestan, was announced. Subsequently response plan for the exotic strain in the country was prepared. In this plan, different disease outbreak scenarios with exotic strains and their required measures are described. Then, on 13th March 2023, due to the outbreak of SAT-2 in Turkey, livestock transit from Turkey was also stopped in the country. Also, on 19th March 2023, following the report of a suspicious outbreak in Gilan province, the livestock movement standstill was implemented, for 24 days until 12th April 2023, following the definitive ruling out of the SAT-2 strain in the laboratory. Subsequently, due to the stable status of the disease in the region, after about 50 days of limitation on the movement of livestock, on 7 May 2023, the ban on the movement of live livestock was lifted for the western provinces.

Additional other executive measures are the establishment of risk based active surveillance in the western provinces and the obligation to take samples from all FMD suspicious cases. Strict control in livestock farms

and milk collection unions and the need for the presence of permanent official staff in the livestock market of the border provinces, holding a round table simulation exercise at the national and provincial levels, the requirement for fulfilling the investigation form in any FMD outbreaks and subsequent notification and warning to other stakeholders.

Further points that should be mentioned are that in any conceivable outbreaks according to the response plan, provided that the incursion of an exotic strain of FMD is confirmed, the movement of livestock within a 50-kilometer radius would be suspended and animals would be sent to slaughterhouse within a 50-kilometer radius of the foci.

The economic impact of SAT-2:

The estimation identified likely pathways for an SAT2 incursion for most countries in the region. Illegal movements of live animals and common grazing are the ways of greatest concern because direct live animal contact is a very effective way of FMD transmission, particularly in the scarcity of hygienic standards. The increase of animal movements associated with events such as Eid al-Adha (qurban), as well as seasonal grazing, boost the possibility of FMD spread.

The other pathways analyzed were assessed to have a lower likelihood of SAT2 introduction and spread. Cross-border spread of FMD via animal products is usually associated with pigs consuming contaminated products. However, many countries in the region have limited or no domestic pig populations and wild boars are present in only some of the countries. The other routes (cross-border movements of wildlife, hay, vehicles and people) are also possible in some countries. Furthermore, FMD transmission via indirect contact (fomites) is less effective.

An incursion of FMD SAT2 would have a significant negative consequence in all countries considered in this risk assessment, with the production losses and cost of control measures estimated at USD 3.6–6.5 billion, depending on the extent of spread within the region. Outbreaks of FMD also have a negative impact on food security, the economy, labor markets, and the livelihoods of vulnerable people.

Conclusion:

Since the outbreak of the disease, several measures have been implemented in Iran, including holding multiple meetings regarding the newly appeared virus at the national and organizational levels, risk base active surveillance and

virological surveillance, restriction of the movement of livestock, suspending the transit of livestock from Turkey and exporting livestock to Iraq due to the risk of the disease entering through Livestock dealers and the announcement of the response plan following the occurrence of any conceivable exotic strain in the country. Moreover, it was decided to provide and order the conditions and attributes for the purchase of a monovalent vaccine of this strain through holding a tender.

The emergence of this serotype in any countries is crucial from various aspects, which includes the economic impact caused by the occurrence of disease, extra cost of controlling a newly emerged strain in the country, restriction and standstill in the movement of livestock and obstacle for export of livestock to countries free of this strain.

Since the newly appeared strain in Iraq, Turkey, Jordan, Bahrain and Oman is SAT-2 serotype, topotype 14, currently none of the vaccines has the ability to protect animals against this new strain.

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