Acta Scientific Veterinary Sciences (ISSN: 2582-3183)

Volume 5 Issue 7 July 2023

Review Article

Evaluation of SAT-2 Serotype Foot and Mouth Disease and Use of One Health Tripartite as Solution

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Received: April 18, 2023

Published: June 09, 2023

Abstract

Foot and Mouth Disease is a viral infection of cloven-footed animals with multiple serotypes which are further divided into topotypes and genotypes. The disease is economically important because it is the major trade barrier for livestock around the globe. WOAH declares endemic, non-endemic and disease free regions. FMD has 7 distinct serotypes (O, A, C, Asia-1, SAT-1, 2, 3). SAT-2 is one of its most diverse strains which escaped its natural endemic pool and caused outbreaks in different parts of the Middle East and North America. Different strains reported causing endemic in past. Major endemics of SAT-2 were witnessed in Egypt, Libya, and Ethiopia. Recently a new strain of SAT-2 caused an outbreak in Iraq, Jordan, and Israel from where the virus migrated to Turkey. Effective quarantine measures and Vaccination campaigns against virus are started. These measures will halt the virus temporarily but cannot eradicate virus. The only effective solution is seeking help through One Health by linking human, animal and environmental professionals and other stakeholders to work together for early detection and investigation of disease and make plans to stop future outbreaks.

Keywords: FMDV; FMD; SAT-2 Serotype; One Health

Introduction

Foot and Mouth Disease is a highly contagious viral disease of cloven-footed animals [11]. The disease is the main trade barrier for livestock and livestock products across the world. It is the 1st virus to be filtered in the 18th century. FMD causative agent is *Aphthovirus* of the family Picornaviridae, a single-stranded, positive- sense, non-enveloped, RNA virus [1,16]. WOAH ranks it 1st in Infectious Diseases of Animals [13]. Molecular weight is low from 7.2 to 8.4 kb. Due to its small size, wind dispersal is possible. Its endemic outbreaks are caused due to novel genetic and antigenic variations, its multiple modes of transmission (wind, fomites), contagious nature, and a wide range of host preferences (70+ cloven-footed species) [1,14].

FMD virus has 7 recognized serotypes that are O, A, C, Southern African Territories [SAT-1], SAT-2, SAT-3, and Asia 1, all around the world. Serotypes are further divided into temporarily and spatially distributed topotypes [1]. Antigenic variants continue to emerge within each of the seven observed serotypes of the virus,limiting the strength of cross-protective immunity between some strains [20], even within the same serotype and topotypes [13]. The disease is most commonly spread across Asia, Africa, the Middle East, and certain regions of South America [16]. On the whole, it is estimated to affect around 77% of global livestock population. It is endemic in most countries with sporadic outbreaks. Morbidity rate is 100% in exposed animals. Mortalityrate is based on strains moreover further affected by the age, breed, and sex of the animal [11,14].

In recent years SAT-2 strain has been detected to cause outbreaks around the globe. In 2012 it was detected outside its usual geographic region i.e. Sub-Sahara. This upsurge affected countries; Libya and Egypt in North Africa and Palestine Autonomous Territories [PAT] and Bahrain in the Middle East. Genomic analysis has made it evident that SAT-2 has at least 14 topotypes [12]. SAT-2 has also caused endemic outbreaks in Ethiopia and Egypt [2,3]. The most recent endemic outbreak of SAT-2 is in Iraq and Jordan which then made its spread to Turkey [4].

Turkey is the most recent endemic country with its eastern part affected mostly. Based on WOAH (World Organization of Animal Health) notice main cities affected are Agri, Kars and Elazig [7,8]. According to media reports, there are cases from other parts of the country that have not yet been notified by WOAH. FMD outbreak causes economic influences so safety measures are taken strictly [8,15]. Authorities urge caution against symptoms of disease with an emphasis on the surveillance system [16], early detection and traceability, quarantine and movement control, infection management measures, and vaccination [5,7,8,16]. Infected animals can infect other animals as well through pens, materials, vehicles, buildings, and clothes, etc. Infected animals also shed a large amount of aerosolized virus while breathing out which can infect other animals through air. It is difficult to differentiate FMD from other vesicular diseases [1] so methods like RT-PCR, Lateral Flow Devices (LFD), ELISA, and virus isolation are needed. Although virus does not render milk and meat unfit for human consumption so there is no risk of zoonosis and it readily decreases the milk yield.

The economic influence of FMD varies significantly between endemic and non-endemic countries and also between developed and developing countries [15]. FMD outbreak can seriously affect a country's economy in terms of loss of production, vaccination cost, export bans, and loss of tourism in exposed regions [8]. Markets are closed in Turkey [5]. Intercity animal transport is prohibited. TVMA (Turkish Veterinary Medical Association) printed that there are 14 million animals in earthquake region that requires vaccine so vaccine should not be interrupted in any case [4].

The only solution to this problem is routine Vaccination. Another important factor that can reduce the frequency and magnitude of FMD outbreaks is the One Health program. One Health promotes collaboration among public health, veterinary and environmental health professionals, and other stakeholders to work together for the early detection of disease. It will also help in rapid response. It will improve vaccination programs and Biosecurity measures. It will help reduce environmental factors and will produce public health response [24].

Global serotypes and strains of FMD virus

FMD is one of the major trade barriers for livestock across the world. Restrictions put strains on the economy of an endemic country. Moreover country bears loss in terms of loss of milk and meat production, vaccination cost, export ban, and losses of tourism in exposed regions. WOAH divided the world into 7 endemic pools [12]. Each pool represents the region where specific FMD viral strains are maintained [1,6].

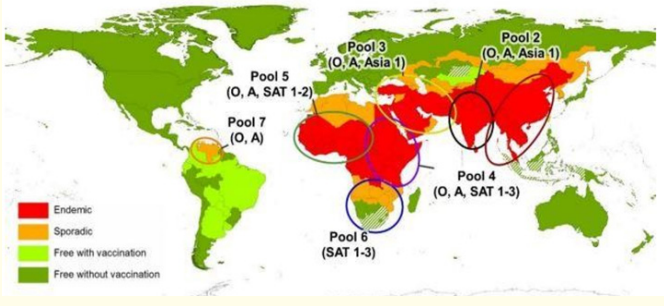


Figure 1: Map showing WOAH FMD status and historic endemic Pools of foot-and-mouth disease where FMD virus serotypes circulate independently. Some countries may have WOAH-free status with or without vaccination, for example, Russia. Striped coloring indicates areas that currently have FMD-free status suspended.

FMD type-O virus

It's the most commonly found serotype of FMD Virus serotype present in the World that's why most extensively studied too. It has 8 topotypes (Cathy, Middle East South-Asia [ME-SA], South East Asia [SEA], Europe South America [Euro-SA], Indonesia-1 [ISA-1], Indonesia-2 [ISA-2], East Africa [EA] and West Africa]). Almost all are found in different regions of world regardless of their naming except ISA-1 and 2 which are totally restricted to Indonesia. EA1-4 and ME-SA are most commonly found in Africa and EA3 and 4, particularly in Ethiopia [2]. This serotype has 5 neutralizing-antigenic strains found on the external surface of Viral Protein1 (VP-1) and the carboxylic end of VP-1.

FMD type-A virus

This is the most antigenically diverse novel strain of Euro-Asia present mostly in Western Asia that lacks cross-protection [20]. Type-A is identified in 3 distinct topotypes named Africa, Asia, and Europe-South America [EUR-SA] [9]. This serotype has more recombination than any other. 4 antigenic sites are found in Type-A viruses which are located on VP-1 and VP-2 [9].

FMD type-C virus

Type-C virus is not found to cause endemic since 1983 in Africa and 2004 in Kenya. Genetic divergence and antigenic divergence is a common features.

FMD type SATs viruses

There are 3 South African serotypes 1, 2, and 3 that have a significantly higher diversity of sequence, within each other, than type-O. There is more variation in SAT types i.e at the nucleotide or amino acid level [11].

SAT-1 has 8 topotypes, which are highly geographically localized. SAT-2 has total 14 topotypes and 3 serologically subtypes. SAT-3 is rarely detected in African buffalo and has less epidemiological coverage. It has 6 topotypes with 25 genotypes [9].

Evaluation of FMD type SAT-2

According to OIE (now WOAH), SAT-2 was the predominant serotype in Africa (47%, 2000-2010). SAT- 2 Virus mostly comes from wild and African buffalo. It was detected in 1990 and 2000 in Middle East._24_ Its multiple topotypes caused endemics and outbreaks in regions out of Sub-Sahara range. Most outbreaks are reported south of Sahara, North Africa, and the Middle East [12]. Those outbreaks became a latent risk to European Nations in mostly FMD-free countries which are densely populated with pigs [10].

Different topotypes of SAT-2 are related to each other in different ways. Some are homologous, others are geographically clustered. The genetic relationship of the isolates can be represented in the form of a Phylogenetic Tree.

History of SAT-2 outbreaks

SAT-2 strain mostly affects bovines and ovine. Endemic in pigs are rare. In 2012 this virus caused great economic loss to Egypt, Libya, and Palestinian Autonomous Territories [PAT] [12]. This again appeared in Ethiopia and banned its trade since [2,13]. Most recently SAT-2 infected bovines and ovine in Iraq, Jordan, and Israel [4]. Viruses spread from Iraq through stray or wild animals to Turkey [4]. Serotype SAT-2 was most recently reported in Egypt between 2014 and 2018 (Egypt WRLFMD, 2023) [3,6]. and previous SAT2 outbreaks in the Middle East have affected animals in Kuwait (in 2000), Oman (in 2015), Palestine (in 2009 and 2013) and Saudi Arabia (in 2000) (Western and 3 Central Asia WRLFMD, 2023) [6].

2018-19 Outbreak in Egypt

A new strain of FMDV SAT-2 was found in Egypt that was closely related to the one found in Libya (2012) [3]. Having 92-93% amino acid similarity with SAT2/GVII/Gharbia-Egy/2012 and SAT2/GVII/Alex- Egy/2012 [10,18,20]. This new strain can be distinguished clearly. The local vaccine against SAT- 2/EGY/2/2012 was not effective against new topotype that was similar to VII, Lib-12 [3,20]. The strain of vaccine should match the strain of virus in the field so a newly modified vaccine was needed. A high antigenic variation is identified as a main hurdle in vaccination [10].

SAT-2 circulation in Ethiopia

The agricultural sector makes up 45% of total GDP in Ethiopia and animal nurturing is a major part ofit. Domestic food supply and about 85% of job opportunities come from the Agriculture sector [13]. Livestock production and productivity are very low in Ethiopia because prevalence of disease. A study from Sept 2015 to May 2016 isolates and characterizes the FMD virus, assessing potential risks, the seroprevalence of antibodies against the disease, and the seroprevalence of the disease [11,13]. Outbreaks in different regions were due to different serotypes. SAT-2 topotype VII genotype IV Most frequent off serotypes found in Ethiopia outbreak 2015 [2,18].

The seroprevalence of antibodies in different age groups, sex groups, and breeds was found different. Older dairy cattle > 3 years have a hogher seroprevalence of antibodies than younger cattle. Like this seroprevalence of antibodies against FMD is higher in female dairy cattle [11].

Recent FMD outbreak in Iraq, Jordan, and Israel

FMD serotype SAT-2, is identified by the World Organization for Animal Health (WOAH) in Iraq (WOAH, 2023). On January 3, 2023, the first of nine outbreaks in Iraq took place in the north of the country [4,6]. Additional outbreaks were reported across the month in the country's center and subsequently in the south, close to the Iranian and Kuwaiti borders.

The WRLFMD, The Pirbright Institute (World Reference Laboratory for FMD) confirmed on February 2 that these outbreaks were brought on by a new viral topotype, known as SAT 2/XIV, which is closely related to SAT-2 viruses collected from Ethiopia in 2012 [2,4,6].

The Jordanian Ministry of Agriculture has confirmed the first occurrence of FMD SAT-2 in Jordan, andsequences from the Jordanian University of Science and Technology (JUST) provided to the WRLFMD share a close genetic relationship with the Iraqi SAT2/XIV sequences [6]. This raises concerns about the possibility of further spread to other countries in the region, as these are the first reports of the SAT-2 serotype in these nations. There have been recent vaccine campaigns in the area to reduce the prevalent serotype O, but it is unlikely that they will cover serotype SAT-2 [6].

On January 3, 2023, domestic buffaloes, cattle, and sheep in northern Iraq experienced the first outbreaks of FMD serotype SAT-2. Similar outbreaks happened in Sulaymaniyah and Diyala Province on January 30 and 31, as well as in Ninawa, Basrah, Najaf, Dihok, and Baghdad on February 1. At this time, there have been no reports of FMD serotype O in Iraq.

The Jordanian Ministry of Agriculture has reported 7 outbreaks of FMD serotype SAT-2 in domestic cattle, sheep, and goats since March 2022. Of these, 4 occurred in November and December 2022, and 3 in November and December 2022. Official authorities have closed livestock markets in all regions of the country for 14 days, and a committee has been formed to facilitate the setup of movement restrictions. The Jordanian Veterinarians Association has criticized the Ministry of Agriculture for potential negligence of quarantine procedures and allowing entry of cows and sheep into the country without testing. The Jordanian Ministry of Agriculture has also facilitated the import of vaccines against FMD, but the efficacy of the vaccine for serotypeSAT-2 is yet to be reported [6].

The Israeli Government has issued guidance on preventive measures, for FMD SAT-2, includingmaintenance of stringent biosecurity. They are also raising awareness amongst all personnel of the importance of maintaining this biosecurity. The veterinary services in Israel hold an emergency supply of frozen FMD SAT-2 vaccine, but the quantity is limited, highlighting the need for vigilance and biosecurity measures [6].

Outbreak in turkey

In March, Turkey's MinAF (Ministry of Agriculture and Forestry) informed the WOAH (World Organization for Animal Health) that they identified the SAT-2 strain of FMD in bovine for 1st time [4,6,8] so the entire Livestock is unprotected and should be vaccinated as soon as possible [19]. This virus is reported in animals from various sites in the eastern half of Turkey, and there may be more cases in other regions that arenot yet reported [7]. The Ministry says uncontrolled and illegal trade of animals from Iraq is the main reason of the outbreak [8].

To FMD virus spread, MinAF implemented several measures e.g. cordon-quarantine, traceability and movement controls, vaccination and disinfection procedures [7,8]. They have also closed animal markets andrestricted the movement of animals across the country susceptible to FMD [5,7]. Exemptions from these only apply to animals that are being sent to slaughterhouses directly or those designated for official export or import channels [7,8].

Livestock producers are concerned about the impact of this FMD strain on meat and milk yields, whichmay cause retail prices for these items to rise even further. The livestock industry is already suffering from the effects of recent earthquakes and tough economic conditions that forced many farmers to sell their livestock [4,7,8].

Turkey has dealt with FMD cases in past and had difficulty eradicating the virus due to intensive livestock movements within the country and illegal movements from bordering countries. The detection of the SAT-2 strain of FMD comes from its territory [8].

Thrace region of Turkey is considered an FMD-free region with vaccination since 2010. The region is home to a large dairy industry. The FMD-free status allows Turkey to ship dairy products to the European Union. To preserve this status strict measures and testing controls are applied in Thrace [8].

MinAF notified in early March that they have developed (research carried out by Turkey's Şap Institute Directorate) a vaccine against new topotype and would immediately start vaccination of suspected animals [4,7]. It is critical to complete the vaccination campaign before the upcoming holidays (Islamic Holiday i.e., Eid al Adha) [7,8]. otherwise Livestock industry will suffer even greater financially.

The Ministry immediately took action to stop the further spread of the disease, such as increasing border surveillance and road control activities. When the 1st case of FMD serotype SAT-2 was identified all necessary measures (cordon-quarantine) were taken immediately in infected enterprises [19]. All animal movements during the vaccination campaign are stopped in the country, except for those which are direct to be sent to the slaughterhouse and import/export purposes [7]. The Ministry is done with the production of a vaccine against this new strain and is working to vaccinate all cattle in the country [10]. The Ministry is closely following all developments related to FMDV SAT-2 and taking necessary precautions [4].

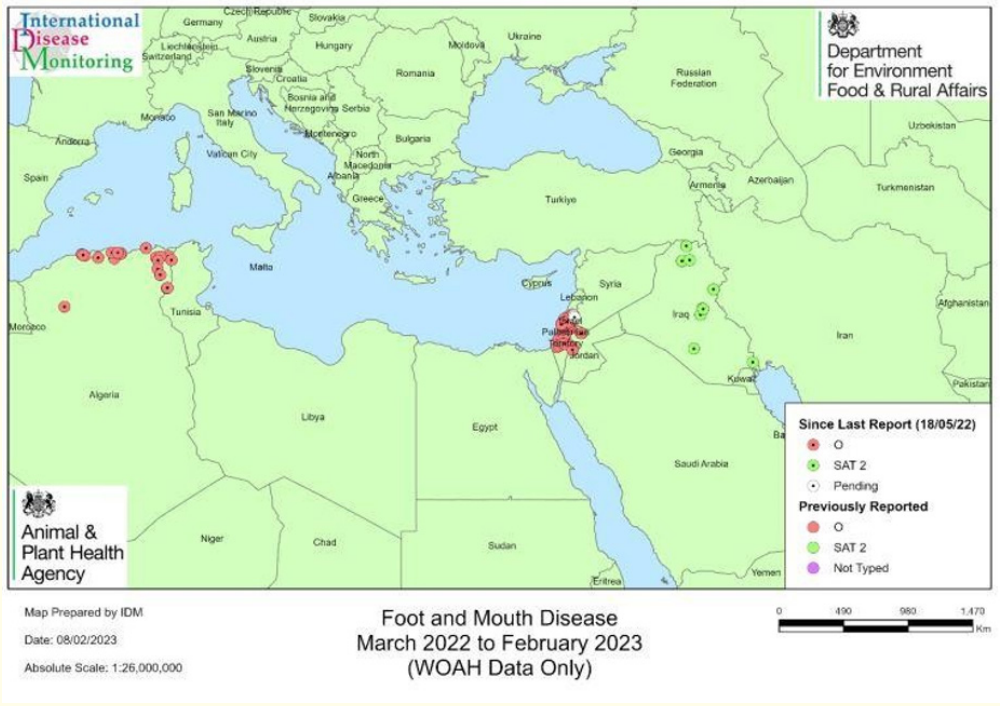


Figure 2: Map showing outbreaks of FMD in Middle East & North Africa between March 2022 and February 2023.

One health

One Medicine was a concept that advocates combining human and veterinary medicine to respond against zoonosis, the "One World or One Health" concept was suggested in 2004 [23].

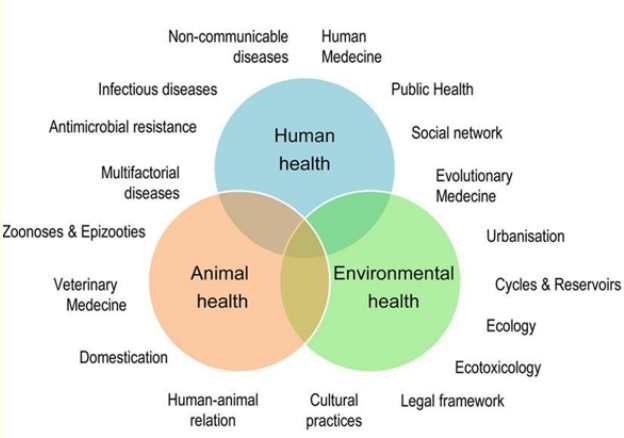


Figure 3: Linkage of Human, animal and environmental health and scope of One Health in on picture.

World Health Organization (WHO) regional director for Europe recognized that "environmental factors that could be avoided and/or eliminated cause 1.4 million deaths per year" in the WHO European Region. This paved the way for Ecohealth in One Medicine and created a combined concept of One Health [23].

Human health, animal health, and environmental health are examined as closely linked to control intra- disciplinary problems like emerging infectious diseases, food safety, and antimicrobial-resistant pathogens and In particular, emerging zoonotic disease problems. Controlling these complex problems often requires interdisciplinary approaches such as One Health [21].

The Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (WOAH), the United Nations Environment Program (UNEP) and the World Health Organization (WHO)welcome the newly formed operational definition of One Health from their advisory panel, the One Health High Level Expert Panel (OHHLEP), whose members represent a broad range of disciplines in science and policy- related sectors relevant to One Health from around the world [22].

The four organizations are working together to mainstream One Health so that they are better prepared to prevent, predict, detect, and respond to global health threats [22].

The One Health definition developed by the OHHLEP states

"One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent [22].

The approach mobilizes multiple sectors, disciplines, and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development [25].

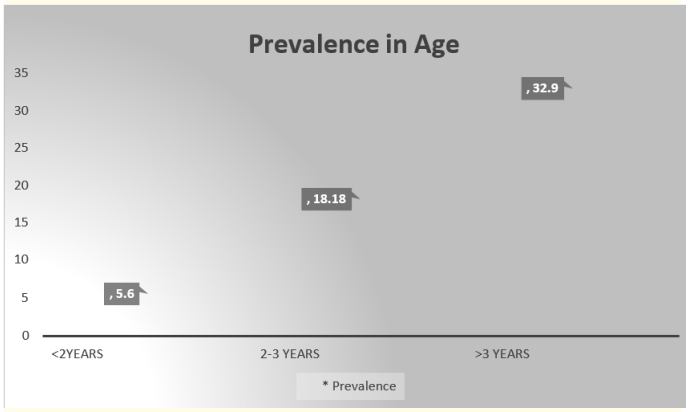
Resolving FMD through one health

There are numerous ways that FMD can spread, and most of them are influenced by the surroundings. Human safety management is necessary to prevent transmission through objects like clothing and cars. For both prevention and response management, it is essential to comprehend the causes of higher FMD transmission rates and how they are related to the environment and people. Understanding and reducing the effects of climate change and FMD outbreaks require a One Health approach, which takes into account all human, animal, and environmental components as well as other stakeholders [24].

The One Health approach can help in reducing FMD (Foot-and-Mouth Disease) outbreaks in several

ways

- Early Detection and Rapid Response: One Health encourages collaboration between veterinary experts, public health experts, environmental health experts, and other stakeholders to quickly identify and address FMD outbreaks. Together, they can immediately locate the outbreak's origin, gauge the degree of its spread, and put control measures in place to stop future transmission.
- Vaccination Programs: One Health understands the value of vaccination in preventing FMD epidemics. Veterinary practitioners can minimize the occurrence and spread of FMD in animals by supporting vaccination programs, hence reducing the financial effect of outbreaks.
- Enhanced Biosecurity: To stop the introduction and spread of FMD, One Health emphasizes the necessity for enhanced biosecurity measures. The danger of FMD transmission can be decreased by enacting stringent biosecurity measures, such as disinfecting equipment, restricting animal movement, and keeping an eye on visitors.
- Environmental variables: One Health acknowledges the critical role that environmental variables playin the FMD epidemic. Environmental health specialists can assist in lowering the risk of FMD transmission by addressing environmental issues like water quality and land use.
- Public Health Response: One Health is aware that FMD has the potential to transmit from animals to people, having a severe negative impact on public health. Public health experts can aid in lowering the risk of human illness by supporting public health initiatives like hygiene practices and awareness campaigns.



Graph 1: Sero-prevalence against FMDV among different age groups in Dairy Cattle and in and around Adama and Asella Towns.

Site of OutBreaks			No.of Samples	CPE positive	Sandwich ELISAresult (Positive)	RT-PCR	Topotype
Region	Zone	District					
Oromia	Arsi	Guna	12	8	A (8)	GDa	Africa
		Ludehitosa	6	5	SAT-2 (5)	GDa	VII
	East Shewa	Adama	4	4	SAT-2 (4)	GDa	VII
		Boset	5	4	SAT-2 (4)	NT	NT
Addis Ababa	Addis Ababa	Kolfe	7	7	O (3), A (2) and SAT-2 (2)	NT	NT
Total			34	28			

Table 1: FMDV serotypes and their topotype identified.
CPE: Cytopathic Effect; GD: Genome Detected; ELISA: Enzyme-Linked Immuno-Sorbent Essay; NT: Not Tested; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction
*One representative isolate sequence.

Sex	Sera Tested	Test (+) %	95%CI	X2	P-value
Female	479	121 (25%)	0.21-0.29	1.8	0.179
Male	95	18 (19)	0.09-0.38		
Total	574	139 (24.1)	0.21-0.28		

Table 2: Sero-prevalence of antibodies against FMDV between sex groups in dairy cattle in and around Adama and Asella Town.
(+) Positive, CI Confidence Interval.

Conclusion

FMDV is endemic in many regions of the world and causes outbreaks which are major obstacles in the growing livestock industry. It divulges adverse effects on the production and trade of livestock. FMD is like cancer for Agricultural Lands. SAT-2 strain of FMD virus is significantly diverse strain that is causing more economical loss than any other strain. Every year SAT-2 is causing endemic outbreaks in different countries worldwide with a new mutated genotype. The epidemiology of FMD virus causes problems due to its vast host range, both domestic and wild, and its survival in any of them. If we eradicate FMD from all domestic animals there is no guarantee that it will not break out again from the wild. The only apparent solution to this issue is vaccination, but the lack of prophylactic vaccines and veterinary infrastructure that can effectively handle the dynamic pattern of outbreaks on a large scale each year significantly contributes to the disease's frequent occurrence. As a result, prevention and control of FMD are quite difficult. An organized national FMD control strategic plan is therefore absolutely necessary.

It is challenging to control the spread of FMD between different herds of livestock and between livestock and migratory species. Natural resources like water sources are depleting, forcing domestic and wild animals closer together. Climate change has made this problem worse. To address this issue, a One Health program is necessary. One Health research draws on the opinions of a wide range of professionals due to its interdisciplinary nature; nevertheless, trans-disciplinary approaches-which consider the perspectives of people and other actors in society often go unnoticed.

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