Indonesia Medicus Veterinus Mei 2024 13(3): 296-312
pISSN: 2301-7848; eISSN: 2477-6637 DOI: 10.19087/imv.2024.13.3.296
online pada http://ojs.unud.ac.id/php.index/imv

Serotype of Foot-and-Mouth Disease Virus in Cattles Circulated in Asia Region Including Indonesia: A Literature Review

(*KAJIAN PUSTAKA: SEROTIPE VIRUS PENYAKIT MULUT DAN KUKU PADA SAPI YANG TERSEBAR DI KAWASAN ASIA TERMASUK INDONESIA*)

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ABSTRACT

Foot-and-mouth disease virus (FMDV) is a highly contagious infectious disease that poses significant economic and agricultural threats to the livestock industry worldwide. It primarily affects animals with split hooves. The disease is endemic in various regions, where livestock farming, particularly of cattle and other split-hooved animals, plays a vital role in the regional economy. The distribution of the seven Foot-and-mouth disease virus (FMDV) serotypes is not uniform. Foot-and-mouth disease virus exhibits wide antigenic variability and is classified into seven serotypes. Serotype A virus comprises 32 subtypes, while Asia 1 virus is characterized by three antigenic subtypes. For instance, 44 strains of Asian serotype 1 showed genetic variations. Serotype C viruses isolated in Europe and South America were classified into five antigenic subtypes. Among the different serotypes, the SAT-1 serotype demonstrated six topotypes, the SAT-2 serotype contained eleven topotypes, and the SAT-3 serotype contained six topotypes. Multiple topotypes within the serotypes indicate the diverse nature of FMDV strains circulating in various regions. This literature review aims to provide an analysis of the serotypes of FMDV prevalent in Asia with a specific focus on Indonesia. Understanding the genetic and antigenic diversity of FMDV is crucial for developing effective control measures and vaccines. Ongoing surveillance and research efforts are essential to combat the spread of FMD and protect global livestock populations from its devastating impact on agriculture and economies.

Keywords: foot and mouth disease; serotype; topotype

ABSTRAK

Penyakit Mulut dan Kuku (PMK) adalah penyakit hewan menular yang menimbulkan ancaman ekonomi dan pertanian yang signifikan terhadap industri peternakan di seluruh dunia. Penyakit ini memengaruhi hewan berkuku belah. Penyakit Mulut dan Kuku endemik di berbagai wilayah, di mana peternakan, khususnya sapi dan hewan berkuku belah lainnya, memainkan peran penting dalam perekonomian regional. Distribusi tujuh serotipe virus penyakit mulut dan kuku tidak seragam. Penyakit Mulut dan Kuku menunjukkan variabilitas antigenik yang luas dan diklasifikasikan menjadi tujuh serotipe. Virus serotipe A terdiri dari 32 subtipe, sedangkan virus Asia 1 ditandai oleh tiga subtipe antigenik. Studi genetik telah mengungkapkan karakteristik berbeda dari berbagai strain virus PMK. Terdapat 44 galur serotipe Asia 1 yang menunjukkan variasi genetik. Selain itu, virus serotipe C yang diisolasi di Eropa dan Amerika Selatan diklasifikasikan menjadi lima subtipe antigenik. Di antara serotipe yang berbeda, serotipe SAT-1 menunjukkan enam topotipe, serotipe SAT-2 berisi sebelas

topotipe, dan serotipe SAT-3 berisi enam topotipe. Kehadiran beberapa topotipe dalam serotipe menunjukkan sifat beragam strain virus PMK yang beredar di berbagai daerah. Penulisan kajian pustaka ini bertujuan untuk memberikan analisis serotipe virus PMK yang lazim di Asia dengan fokus khusus di Indonesia. Memahami keragaman genetik dan antigenik virus PMK sangat penting untuk pengembangan tindakan pengendalian dan vaksin yang efektif. Upaya pengawasan dan penelitian yang berkelanjutan sangat penting untuk memerangi penyebaran PMK dan melindungi populasi ternak global dari dampaknya yang merusak pertanian dan ekonomi.

Kata-kata kunci: penyakit mulut dan kuku; serotipe; topotipe

INTRODUCTION

Foot-and-mouth disease virus (FMDV) is a highly contagious viral infection disease that infects animals with split hooves such as cattle, buffalo, pigs, sheep, goats, and other animals (Alexandersen *et al*., 2003b; Jamal *et al*., 2013). Foot-and-mouth disease virus does not have an envelope and has an icosahedral structure which is one of the *Aphthovirus* genus and the *Picornaviridae* family (Alexandersen *et al*., 2003b).

Foot-and-mouth disease virus has the characteristics of being able to infect healthy animals with fast replication and with a high rate of virus excretion through direct contact with infected animals, droplets, saliva, and vomit (Alexandersen *et al*., 2003a; Alexandersen *et al*., 2005). In addition, indirect transmission can also occur through feed, equipment, transportation, animal deception, and humans contaminated with viral agents. Foot-and-mouth disease virus can form vesicles and erosions on the skin mucosa and hairless areas such as the mouth and nails. In endemic countries, FMDV causes death in young animals and decreases the productivity of these animals (Brehm *et al*., 2008). This characteristic causes FMDV to become one of the most important viral diseases in the world. Foot-and-mouth disease virus is an endemic disease in many countries in Asia, Africa, South America, and Europe. Which makes FMDV is an animal health problem that is still a concern in the world. The Asian region is one of the regions that has various economic levels that influence the direction of trade in many sectors including the trade in livestock and their products which increases the opportunity for the spread of FMDV (James *et al*., 2002). This literature review aims to examine FMDV virus serotypes that are spread in several countries in the Asian region including their effects on livestock, especially cattle and their products.

WRITING METHODS

The literature was carried out by searching data from related journals, books, and articles from several database sources such as Google Scholar and PubMed using the keyword

"Foot-and-mouth disease virus". The criteria for the selected articles were articles written within the last 20 years, the object of the case was the FMDV virus in the Asian region. However, the authors do not rule out the possibility of using literature such as books written outside the last 20 years, to enrich the information in this literature review.

RESULTS AND DISCUSSION

Serotypes and Species of FMD Virus

The virus that causes FMDV is a single-stranded positive RNA virus. The RNA virus from FMDV is surrounded by a protein capsid consisting of 60 capsomeres. Each capsomere is composed of four structural proteins, i.e., virion protein (VP)-1, VP2, VP3, and VP4 (Klein, 2009). The structural proteins VP1, VP2, and VP3 are located on the surface of the virus and associated with the antigenic factors of the virus, whereas VP4 is located on the internal parts of the virus. Among these four structural polypeptides, VP1 is the protein considered to have the most important role in viral attachment, protection of host immunity, and serotype specificity (Alexandersen *et al*., 2003b; Ma *et al*., 2011). The nucleotide sequence of the VP1 coding region is used to identify the characteristics of the FMDV strain because VP1 has a very important role in virus attachment. Phylogenetic analysis based on VP1 sequencing was also used to identify epidemiological relationships among FMDV virus genetic lineages and to trace the origin of the strain and its movement in outbreak cases (Jamal *et al*., 2013). Foot-and-mouth disease virus is caused by seven immunologically distinct serotypes, namely serotypes O, A, C, Asia 1, South African Territories (SAT) 1, SAT 2, and SAT 3, which belong to the FMDV virus species (genus *Aphthovirus*, family *Picornaviridae*). Phylogenetic studies showed that there were at least ten genotypes from serotype A, ten topotypes from serotype O, and six genotypes from serotype Asia 1 (Le *et al*., 2012).

Serotype O. This serotype has ten known topotypes namely Europe-South America (Euro-SA), Middle East-South Asia (ME-SA), Southeast Asia (SEA), Cathay (CHY), West Africa (WA), East Africa 1 (EA-1), East Africa 2 (EA-2), East Africa 3 (EA-3), Indonesia-1 (ISA-1) and Indonesia-2 (ISA-2). There are three separate topotypes in SEA, namely O/SEA, O/ME-SA, and O/CHY (Khounsy *et al*., 2008). The Indonesian topotypes O/ISA-1 and O/ISA-2 were isolated from outbreaks in 1962-1983 and 1972-1974 (Samuel and Knowles, 2001), and are now said to be extinct (Knowles *et al*., 2005). The O/SEA topotype is characterized by two lineages, namely O/SEA/Mya-98 and O/SEA/CAM-94, which have a dominant genetic lineage with a common ancestor from 35 years ago (Abdul-Hamid *et al*., 2011). In 1999 the O/ME-

SA/PanAsia lineage entered parts of Southeast Asia and in April 2000 all countries experienced an outbreak (Knowles and Samuel, 2003). The O/ME-SA/PanAsia lineages are divided into PanAsia and PanAsia-2 with the latter only being reported in Malaysia in 2003, 2005, and 2009 (Di-Nardo *et al*., 2011; Brito *et al*., 2017). The O/ME-SA/Ind-2001 lineage is the original lineage from the Indian subcontinent which caused outbreaks in North Africa, the Middle East, Southeast Asia, the Far East, and the FMDV-free island of Mauritius from 2013 to 2017 The O/ME-SA/Ind-2001 subtype first appeared in Southeast Asia causing outbreaks in Laos and Vietnam in 2015 and Myanmar in 2016 (Vu *et al*., 2017; Qiu *et al*., 2017; Arzt *et al*., 2017). The O/ME-SA/Ind-2001 subtype was further divided into two growing sub-breeds, namely Ind-2001d and Ind-2001e, both of which caused outbreaks in Southeast Asia.O/ME-SA/Ind-2001e entered Myanmar in 2017, then spread to other countries, which are Thailand, Vietnam and Malaysia (Bachanek-Bankowska *et al*., 2018). The emergence of the hog-adapted O/CHY strain topotype was associated with the movement of pigs across the Chinese border to North Vietnam in 1997 and presumably to the Philippine Island of Luzon in 1994 by pork products as "swill" via Manila Airport, with limited deployment to Thailand and Malaysia in 2005. The O/CHY topotype was detected in Thailand in 2012 and Vietnam in 2015–2017. It is still uncertain whether this virus is endemic in Southeast Asia or reappears through the movement of animals or animal products (Blacksell *et al*., 2019; Madin, 2011).

Serotype A. Antigenic historical studies during the 1960s with serotype A virus distinguished 32 subtypes (Davie, 1964). Subsequent studies of the FMDV virus serotype A originating from Asia in 1980 found that the A22 lineage (Isolate A22/IRQ/24/64) was dominant and the A15 lineage (Isolate A15/Bangkok/TAI/60) was also found to cause disease (Rweyemamu *et al*., 1984; Doughty *et al*., 1995). Recently, a comparison of approximately 300 serotype A viral VP1 sequences demonstrated three major geographically restricted topotypes: (i) Euro-SA, (ii) Asian, and (iii) African (Knowles *et al*., 2005). The Asian topotype consists of the A15, A22, Iran-05, Thai-87, Sea-97, and G-VII lineages and all A virus serotypes found in Southeast Asia belong to the Asian topotype (Rweyemamu *et al*., 2008; Abdul-Hamid *et al*., 2011; Knowles and Samuel, 2003; Khounsy *et al*., 2009). Closely related serotype A viruses circulate within and between Southeast Asian countries. For example, samples from outbreaks in Malaysia in 2002 (A/MAY/2/2002) and 2009 (A/MAY/9/2009) were grouped with isolates obtained in the same years from Thailand and Vietnam (Abdul-Hamid *et al*., 2011). The serotype A virus from the outbreak that occurred in Laos in 2003 was 99.84% similar to the Malaysian isolate A/MAY/4/2003 which showed the same origin

(Khounsy *et al*., 2009). Cambodian isolates from 2006 and 2008 and those collected between 2008 and 2010 from Thailand and 2009 in Malaysia, were grouped with viruses originating from Vietnam (Vu *et al*., 2017). The serotype A virus that was discovered in Myanmar for the first time in 2015 came from buffalo samples collected in 2008/2009 and this virus is close to the virus that was reported in Thailand in 2014/2015. Data from this viral relationship is strong evidence to show that the virus moves in an area, especially related to the ruminant animal trade.

Serotype Asia 1. Asia 1 virus has three antigenic subtypes (Knowles *et al*., 2005) and genetic studies of 44 strains of Asia 1 serotype from Bangladesh, Bahrain, Bhutan, Myanmar, Cambodia, Greece, Hong Kong, India, Israel, Kuwait, Lebanon, Malaysia, Nepal, Oman, Pakistan, Saudi Arabia, Tajikistan, Thailand, Turkey, and Yemen collected between 1954 and 1992 showed all isolates belonging to a single topotype (Abdul-Hamid *et al*., 2011). A study investigated the Asia 1 virus responsible for outbreaks that occurred in Asia from 2003 to 2007 and classified it into six groups based on the VP1 sequence. Viruses in group IV belong to a larger and more diverse group of viruses found only in Southeast Asia and Hong Kong from 1974 to 2006, and interestingly, only two viruses originating from Southeast Asia emerged from this supergroup, namely, Bangkok/ Thailand/60 (Thai old viral vaccine strain) and ASIA1/MYA/2/2001. In group IV, the Asia 1 virus that caused outbreaks in Yunnan province of the People's Republic of China (adjacent to Laos, Myanmar, and Vietnam) and Vietnam in 2005 and 2006 has similarities to viruses originating in Thailand in 1998 and Myanmar in 1998 (Valarcher *et al*., 2009). Separate studies further confirmed and described outbreaks (homologous <95%) that occurred in Myanmar in 2005 and 2006. The 2005 outbreak in Myanmar is closely related to the Asia 1 virus that was reported in the 2005 outbreak in the People's Republic of China, while the in 2006 was closer to the outbreak that occurred in Vietnam in 2005-2006 (Madin, 2011). There was no other evidence of this serotype seen in other areas until the outbreak in Rakhine State, Myanmar in 2017, and sequencing data indicated that the outbreak was caused by a new lineage, namely G-VIII from Bangladesh.

Serotype C. Serotype C viruses isolated in Europe and South America were classified into five antigenic subtypes namely, C1-C5 (Davie, 1962). Comparison of VP1 sequences of FMDV viruses classified into three topotypes namely Euro-SA, Africa and Asia (Knowles and Samuel, 2003). This C serotype entered the Philippines in 1976 (C-Philippines) and this virus is closely related to the South American vaccine strain, C3/Resende/Brazil/55 (Knowles and

Samuel, 2003). There were no outbreaks reported worldwide in the last 14 years up to 2019 (Paton *et al*., 2021; Blacksell *et al*., 2019).

Serotype *Southern African Territories* (SAT) 1, 2 and 3. Found mainly in Sub-Saharan Africa. The genetic characteristics of the FMDV virus, which originates from African buffalo, are evolutionarily different from existing viral lineages. Three lineages of SAT-1 were detected and two East African topotypes were detected. Virus studies from West Africa found two topotypes of SAT-1 bringing a total of six topotypes of SAT-1 that have been detected in Africa. For the SAT-2 serotype, there are 11 topotypes, four topotypes from South Africa, two topotypes from East Africa, two topotypes from Central Africa, one topotype from the Horn of Africa region, and two topotypes from West Africa. For the SAT-3 serotype, there are six different topotypes which are only limited to seven countries such as South Africa, Zimbabwe, Zambia, Namibia, Botswana, Malawi, and Uganda. Three of the five existing topotypes are found in Zimbabwe (Vosloo *et al*., 2002).

FMDV Serotype Circulated In Asia Region

FMDV Serotype in Malaysia. In Peninsular Malaysia, FMDV was reported as early as the 1860s when it became sporadic and resulted in annual outbreaks. Since then, Malaysia has become an endemic area for FMDV. In a study of FMDV outbreaks from 2001 to 2007 in Malaysia, 89.95% were from serotype O and 7.7% were from serotype A (Zubaidah *et al*., 2017). In a subsequent study of FMDV outbreaks from 2012 to 2016, out of 110 positive samples, it was Serotype O (80%) followed by Serotype A (20%) (Singanallur *et al*., 2020).

FMDV Serotype in the Philippines. In the Philippines, serotypes of FMDV that have been reported are serotypes O and A. Buffaloes are suspected to be carriers of the virus in the Philippines and may carry the risk of further outbreaks in the future (Windsor *et al*., 2011). Rweyemamu *et al*. (2008) stated that events in the last decade have demonstrated the vulnerability that the Philippines has received from the virus through illegal pork imports. However, in 2015 the Philippines officially received recognition from the World Organization Internationale des Epizootics (OIE) as a non-vaccinating FMDV-free country and the Philippines maintains this status by routinely carrying out disease surveillance, livestock monitoring, and strict eradication measures from countries with cases.

FMDV Serotype in Singapore. Singapore has only ever reported an outbreak with serotype A in 1973. Pal (2018) also revealed that Singapore, Australia, and New Zealand are included in countries free of FMDV. So far there have been no reports of FMDV outbreaks in Singapore.

FMDV Serotype in Thailand. Thailand is an endemic country for FMDV cases. Foot-and-mouth disease virus outbreaks occur in almost all parts of Thailand except for eastern Thailand which is an FMDV-free zone. In 2017, there were 126 cases of FMDV outbreaks reported. The serotypes found in Thailand are serotypes O and A. The South-East Asian and PanAsian topotypes of serotype O have been reported to have been found in Thailand (Gleeson, 2002; Premashthira, 2018).

FMDV Serotype in South Korea. South Korea was a country that was free of FMDV since 1934 and 1908. However, outbreaks were found to occur again in 2002 and 2010. The outbreak in 2002 was caused by the O virus serotype, which belongs to the PanAsian lineage, not only the O serotype (topotype SEA, MYA-98 lineage) and A (ASIA topotype, SEA genotype, MYA-97 lineage) were also the cause of the outbreaks that occurred in 2010-2011 (Yoon *et al*., 2011). South Korea has three viruses that entered in 2010. South Korea was first hit by FMDV with serotype A (A/SEA/MYA/97) in January 2010. The incident was handled well. The next hit occurred in April 2010, namely serotype O (O/SEA/MYA/98). South Korea was declared free of FMDV by the OIE on September 27 2010 without having been vaccinated. The next hit was caused by O/SEA/MYA/98, in November 2010 and it spread throughout South Korea (Jamal *et al*., 2013).

FMDV Serotype in Vietnam. The endemic FMDV serotypes in Vietnam are O (1956, 1967, 1969, 1997, 1999-2018), A (2004-2007, 2009-2010, 2012-2017), and Asia 1 (1992, 2005-2007). The topotypes and lineages that have existed, and existed in Vietnam are ME-SA (PanAsia), SEA (Mya-98), ME-SA (Ind-2001d), CHY, and ME-SA(Ind-2001e) (Blacksell *et al*., 2019).

FMDV Serotype in Cambodia. During the last 10 years until 2002 outbreaks of serotype O and Asia 1 have been reported, but there have been no reports of serotype A. The last four years up to 2002 reported two strains of serotype O in Cambodia. The strain belonging to the South-East Asian topotype was replaced by the PanAsian topotype in 2000 which probably entered Cambodia from Vietnam (Gleeson, 2002). Foot-and-mouth disease virus serotypes that are endemic in Cambodia are O (1989, 1992, 1994, 1998-2000, 2004-2008, 2010-2013, 2015-2016), A (2006-2008, 2015-2016), Asia 1 (1980- 1981, 1988, 1990-1991, 1993-1994, 1997), and unidentified (2006, 2009, 2011). The topotypes and lineages that have existed and existed in Cambodia are ME-SA (PanAsia) and ASIA (SEA-97) (Blacksell *et al*., 2019).

FMDV Serotype in Myanmar. In recent years, type O FMDV has been the most frequently reported serotype circulating in Myanmar, apart from that, outbreaks of Asian type 1 have also been reported every year. There has never been a report of type A virus in Myanmar in recent years, except for a localized outbreak in an area bordering Thailand in 1999. Myanmar is a country that has an important epidemiological role against FMDV because it has a very large ruminant population potential as a source of disease from parts of the Indian continent (Gleeson, 2002). Foot-and-mouth disease virus serotypes that are endemic in Myanmar are O (1956-1958, 1971, 1977-1978, 1982, 1989, 1996, 1998-2011, 2015-2017), A (1971, 1978, 2010, 2015), and Asia 1 (1958, 1971, 1977-1978, 1982, 1989, 1991, 1997, 2000-2001, 2005, 2017). The topotypes and lineages that have existed and existed in Myanmar are SEA (Mya-98), ME-SA (Ind-2001d), and ME-SA (Ind-2001e) (Blacksell *et al*., 2019).

FMDV Serotype in Laos. Only Asian types 1 and O have been detected causing outbreaks in the field in the last ten years until 2002, from the results of serological studies it appears that there is circulation of serotype A which is localized in certain areas. Often, in animal trading transactions, sick animals are used because they have lower prices in areas experiencing outbreaks and are transported to other areas for slaughter so that they can spread the disease to other areas. Laos is also a major trade route for pigs and ruminants from Vietnam to Thailand, large ruminants from Cambodia to Thailand (via South Laos), and from China to Thailand (via Northwest Laos). This movement of traded animals is very important for epidemiological studies of FMDV because Asian strains enter Thailand from all three routes (Gleeson, 2002). FMDV serotypes that are endemic in Laos are O (1978, 1981-1982, 1984, 1987-1990, 1993, 1998-2001, 2003-2013, 2016-2017), A (2003, 2006-2008, 2014-2015), and Asia 1 (1984, 1991-1993, 1996, 1998). The topotypes and lineages that have existed in Laos are ME-SA (PanAsia), ME-SA (Ind-2001d), SEA (Mya-98), and ASIA (Sea-97) (Blacksell *et al*., 2019).

FMDV Serotype in Timor Leste. Timor-Leste has no reported cases of FMDV, will, or has not yet been detected but still needs an official FMDV-free certificate from the World Organization for Animal Health. This led to the fact that in 2010 Indonesia banned and tightened imports of cattle from Timor-Leste.

FMDV Serotype in India. Serotype O is the most common in India and causes the most outbreaks. There are currently three different lineages of serotype O viruses, named Ind2001, PanAsia, and Ind2011 circulating in India. Most outbreaks (80%) of FMD are caused by serotype O viruses, the vaccine used to control serotype outbreaks is O/IND/R2/75

(Mahapatra *et al*., 2015). Foot-and-mouth disease virus outbreaks in India are recorded to occur throughout the seasons and the influence of seasons as well as environmental conditions plays a significant role in the spread of the virus. There are counted four seasons in India. FMDV incident outbreaks generally occur at the end of the monsoon season and after the monsoon due to relatively dry weather, which is very conducive for virus transmission (Subramaniam *et al*., 2011).

FMDV Serotype in Bangladesh. In Bangladesh, FMDV is known in the local community by the name *"Khura Rog"*. FMD occurs as an endemic disease and has a very high incidence throughout the country since 2009. Only serotype O virus has been reported circulating in Bangladesh since 2000 (Loth *et al*., 2011). However, there were previous reports of FMDV serotypes O, A, and Asia I outbreaks in Bangladesh in 1958 and 1996. It is possible that out of several FMD serotypes, only three serotypes A, O, and Asia 1 were circulating in Bangladesh with a prevalence of 10-10% each, 15%; 80-85%; and 5% (Nandi *et al*., 2015) therefore, the FMD serotype O is the predominant serotype compared to the other two serotypes (Giasuddin *et al*., 2016; Siddique *et al*., 2018). Every year many epidemics occur in Bangladesh, and these outbreaks cause huge economic losses (Ali and Giasuddin, 2020).

FMDV Serotype in Iraq. Serotype A was reported for the first time in 1952. Subsequently, different serotypes were found, i.e., Asia 1 in 1975, 1983, and 1984; O-1 in 1985 and 1993; O Manisa in 1998 and 1999; and A-IRN-96 in 2000 and 2002 (Mohammed, 2013). Another serotype called A/IRN/2005 hit Iraq in 2009, 2010, 2011, 2012 and 2013. The other serotypes that hit Iraq were FMDV-O, FMDV-A, FMDV-Asia1, FMDV-SAT1, FMDV-A ASIA Iran05^{BAR-08}, FMDV-A ASIA Iran05^{AFG-07}, FMDV-O ME-SA PanAsia2^{ANT-10}, FMDV-A Asia 1 Sindh-08, and FMDV-A Asia1 Iran05^{SIS-10} (Al-Salihi, 2019).

FMDV Serotype in Pakistan. Serotypes O, A, and Asia-1 are FMDV serotypes that cause outbreaks in livestock in Pakistan and Afghanistan. The Asia-1 serotype was detected in Pakistan and Afghanistan since 1998 and was detected again in 2008/2009. Then it was found that the O-PanAsia and A-Iran05 virus serotypes were found in Pakistan (Abubakar *et al.*, 2022; Jamal *et al*., 2011).

FMDV Serotype in Afghanistan. Outbreaks that occurred from 1995 to 2016 in Afghanistan from samples collected were caused by serotypes A, O, and Asia-1. Serotype O was reported in 1957, 1965, 1971-1972, 1974-1975, 1996, 2004, 2007, 2009-2011, 2013-2014, 2016, and 2017. Serotype A was reported in 1956, 1959, 1964, 1970, 1975, 2004-2005, 2007, 2009-2011, 2013, 2016, and 2017. Asia-1 serotypes were reported in 1957, 1963, 1971-1972,

2001, 2003-2004, 2009, 2011, 2013-2014, 2013-2014 and 2017. Serotype C was only ever reported in 1957 (Osmani *et al*., 2019).

FMDV Serotype in Saudi Arabia. Serotypes O, A, C, Asia 1, SAT 1, and SAT 2 have been reported in Saudi Arabia. Serotype A classified as A/IRN/2005 was first reported in Iran in 2005 and spread to Turkey and Saudi Arabia in 2006 and to Jordan in 2007. The same virus subtype was reported to also circulate in Bahrain and is the predominant subtype in Georgia and Turkey in 2008. In 1988 to 1991 serotype O and Asia 1 viruses were found. The isolated Asia 1 serotypes looked similar with Asia 1/Tadzhikistan/64 which had been reported in Russia, and Asia 1/TUR/15 /73 ever reported in Turkey. Furthermore, the SAT 2 serotype was reported to be found in Saudi Arabia in 2001 which was similar to that which had been isolated in Eretria. The O/ME-SA/Ind-2001 strain was also reported in Saudi Arabia and Libya in 2013 (Hemida *et al*., 2018). Outbreaks by serotype O occurred in 1970-1973, 1978, and 1980-1998; serotype A in 1973, 1976, 1984, 1986-1987 and 1991-1993; serotype C in 1984, serotype Asia-1 in 1982 and 1992; serotype SAT 1 in 1962-1970 (Baky *et al*., 2005).

FMDV Serotype in China. Foot-and-mouth disease virus in China was first reported in 1958 (Bai *et al*., 2011). In the same year, serotypes O and A isolates were identified from the Xinjang Uygur Autonomous Region and Asian serotype 1 isolates were identified from Yunnan province. The seasonal distribution of FMDV in China peaks primarily in spring and summer and secondary peaks in autumn (Hu *et al*., 2022). In January 2012, the OIE and the World Food and Agriculture Organization (FAO) jointly developed a global FMDV control roadmap, releasing a global control strategy and proposing FMDV control goals for the next 15 years.

FMDV Serotype in Iran. Serotype O, A, and Asia 1 FMDV have been detected circulating in Iran since 2011 (Ilbeigi *et al*., 2018).

FMDV Serotype in Japan. Serotype O FMDV appeared in Japan in 2000 isolated from various host species including cattle, buffalo, pigs, sheep, goats, and deer. The number of cases usually peak in the summer (Knowles *et al*., 2005).

FMDV Serotype in Indonesia. The FMDV that has occurred in Indonesia is serotype O (1952, 1956-1958, 1962, 1972-1974, 1983, 2022) while the topotypes and lineages is Indonesia-1 (ISA-1) and Indonesia-2 (ISA- 2).

FMDV that is Hitting Indonesia in 2022

The Director General of Livestock and Animal Health of the Ministry of Agriculture of the Republic of Indonesia stated that the Ministry of Agriculture is still investigating the

possible origins of FMDV entering Indonesia. Therefore, it is not certain where the FMDV that spread in Indonesia came from. However, some guesses came from experts. The possibility of transmission of the FMDV, which comes from the *Picornaviridae* family, is due to the opening of the animal import faucet by Indonesia. The transmission of this infection can be in the form of direct contact or through animal/agricultural products imported from countries infected with FMDV from animal to animal, so it is necessary to place restrictions on the movement of livestock especially in the outbreak area so as not to further spread the FMDV outbreak. Foot-and-mouth disease virus transmission happens through aerosols and direct contact with animals affected by FMDV. The foot-and-mouth disease virus that is currently sweeping in Indonesia is the O/ME-SA/Ind-2001e serotype (Department for Environment, Food and Rural Affairs, 2022; Blacksell *et al*., 2019). There is a strong suspicion that the serotype O FMDV which will be epidemic in 2022 is different in subtype from the FMDV outbreak virus before 1990. This new genus of FMDV for Indonesia entered Indonesia through imports of meat during *Hari Raya* (Ied al-Fitr) which increased beef consumption. It is suspected that the subtype of the virus currently in Indonesia is similar with the FMD virus circulating in India and Cambodia.

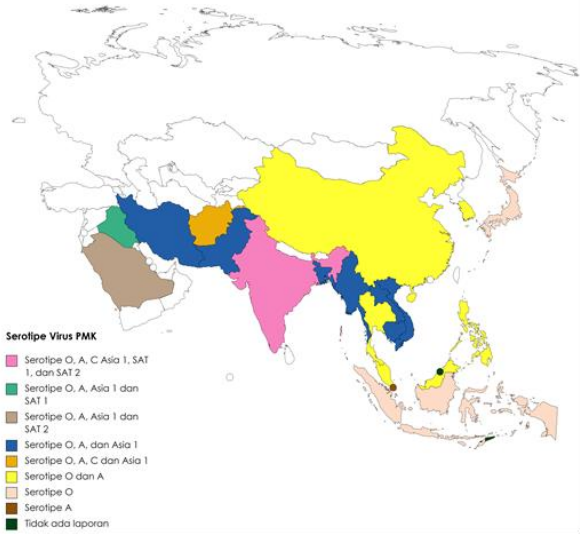

Figure 1. Distribution of FMD virus serotypes in Asia

Effect of FMDV on Cattle and Their Production

Foot-and-mouth disease virus is a highly contagious disease of all cloven hooves. The disease is endemic in Africa, South America, and Asia, but only in Northern Europe is it considered an epidemic sporadic disease (Haydon *et al*., 1997). Foot-and-mouth disease virus outbreak in the UK in 2001 demonstrated how severe and invasive the consequences of this disease could be in areas previously free of FMDV. Mass culling was implemented, resulting in the slaughter of over a million animals on affected holdings, three million more animals

(mostly sheep) for disease control objectives, and an additional of 2.5 million animals for welfare reasons. (Woolhouse, 2003). The virus strain can be quickly identified by nucleotide sequencing as a PanAsian topotype of serotype O virus FMDV. This particular strain is known to exist in most parts of Asia, i.e., Japan, South Korea, South Africa, Mongolia and Eastern Russia (Knowles, *et al*., 2001). In 2002, an experimental study with FMD disease viruses showed that the FMDV O/UKG/2001 strain, belonging to the PanAsian topotype of FMDV, infects sheep, cattle, and pigs as the main livestock targets (Knight-Jones and Rushton, 2013).

The transmissibility of the FMDV in terms of transmission and survival is related to its diverse hosts (PanAsian strains have been isolated from cattle, sheep, goats, pigs, buffaloes, deer, antelopes, and camels), its ability to transmit quickly to cause new infections and mild symptoms allowing a large number of animals to be infected before the virus can be detected. In the UK livestock and food losses from the FMDV outbreak in 2001 were estimated at £3.1 billion, while £100 million is spent annually on FMDV control measures in cattle (Thompson *et al*., 2002).

Production losses due to FMDV directly include decreased milk production, affecting both humans and calves. Although in some cases FMDV has a short-term effect on animal health, chronic FMDV usually reduces milk production by up to 80% (Bayissa *et al*., 2011). Growth rates are also suppressed and mortality among young animals is usually 2-3%, and sometimes much higher. Foot-and-mouth disease virus can result in miscarriage/abortion, which is detrimental to the farmer because the farmer has to pay to keep the cow without producing calves for a year or more or unalive the animal. The most pronounced disadvantages can be seen in pigs in intensive production systems and dairy cows. These systems are the main sources of animal protein in poor countries and their demand for protein is increasing (Delgado *et al*., 2005).

CONCLUSION

Foot-and-mouth disease virus is caused by seven immunologically distinct serotypes, O, A, C, Asia 1, South African Territories (SAT) 1, SAT 2, and SAT 3. Historical antigenic studies since the 1960s reveal that viral serotype A differentiated into 32 subtypes. Asian 1 virus has three antigenic subtypes and genetic studies of 44 Asian serotype 1 strains. Serotype C viruses isolated in Europe and South America were classified into five antigenic subtypes namely, C1-C5. The SAT-1 serotype has a total of six topotypes, while the SAT-2 serotype has eleven topotypes and the SAT-3 serotype has six topotypes. Understanding the genetic and

antigenic diversity of FMDV is crucial for the development of effective control measures and vaccines. Ongoing surveillance and research efforts are essential to combat the spread of FMDV and protect global livestock populations from its devastating impact on agriculture and economies. By closely monitoring and studying the virus's characteristics, international cooperation can facilitate improved prevention and control strategies to minimize the risk of FMDV outbreaks and safeguard the livestock industry.

SUGGESTION

It is necessary to carry out continuous surveillance considering that new lineages of the FMDV continue to evolve, making it difficult to eradicate through vaccination. All the endemic countries of FMDV need to continue to be monitored systematically to monitor the possibility of this disease continue spreading.

ACKNOWLEDGMENTS

On this occasion, the author would like to thank the Co-assistance for Veterinary Internal Medicine, Faculty of Veterinary Medicine, Udayana University who has been willing to assist the author in facilitating and guiding until the completion of this literature review.

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