



UNIVERSITI PUTRA MALAYSIA

**DESCRIPTIVE EPIDEMIOLOGY OF LUMPY SKIN DISEASE IN
MALAYSIA**

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DESCRIPTIVE EPIDEMIOLOGY OF LUMPY SKIN DISEASE IN MALAYSIA

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CERTIFICATION

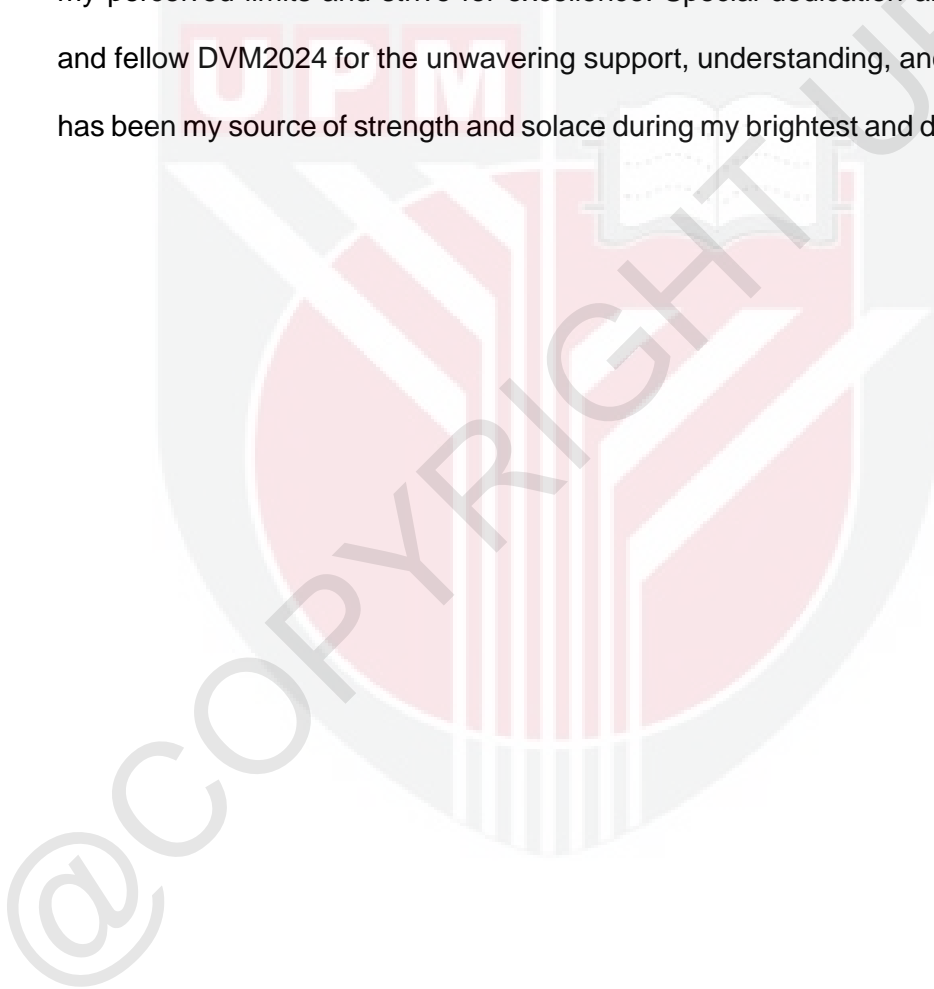
It is hereby certified that I have read this project paper entitled “Descriptive Epidemiology of Lumpy Skin Disease in Malaysia”, by Chong Xin Hui and in my opinion, it is satisfactory in terms of scope, quality, and presentation as a partial fulfilment of the requirement for the course VPD 4901 - Final Year Project.

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DEDICATION

This thesis is dedicated to my beloved family, whose boundless love and support have been the guiding light throughout my DVM journey. I would also like to dedicate this thesis to my wonderful supervisor, Prof. Dr. Latiffah Hassan for your patience, guidance, encouragement, and constructive input which inspired me to reach beyond my perceived limits and strive for excellence. Special dedication also to my friends and fellow DVM2024 for the unwavering support, understanding, and empathy which has been my source of strength and solace during my brightest and darkest moments.



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CONTENTS

	Page
TITLE	i
CERTIFICATION	ii
DEDICATION	iii
ACKNOWLEDGEMENTS	iv
CONTENTS	v
LIST OF TABLES	vii
LIST OF FIGURES	vii
ABSTRAK	viii
ABSTRACT	x
1.0 INTRODUCTION	
1.1 Background.....	1
1.2 Objective.....	2
1.3 Justification.....	2
2.0 LITERATURE REVIEW	
2.1 Causative agent.....	2
2.2 History and Geographical Distribution.....	3
2.3 Transmission.....	4
2.4 Susceptible Host.....	6
2.5 Pathology.....	7
2.6 Diagnosis	
2.6.1 Detection of Virus.....	9
2.6.2 Detection of Antibody.....	10
2.6.3 Differential Diagnosis.....	10

2.7 Control and Prevention.....	11
2.8 Economic Significance.....	12
3.0 MATERIALS AND METHODS	
3.1 Data collection and management.....	13
3.2 Data analysis	
3.2.1 Descriptive Statistics.....	13
3.3.2 Spatial Analysis.....	14
3.3.3 Temporal Analysis.....	14
3.3.4 Spatiotemporal Analysis.....	14
4.0 RESULTS	
4.1 Descriptive Statistics.....	16
4.2 Spatial Analysis.....	18
4.3 Temporal Analysis.....	19
4.4 Spatiotemporal Analysis.....	23
5.0 DISCUSSION.....	26
6.0 CONCLUSION.....	32
7.0 RECOMMENDATIONS.....	32
8.0 REFERENCES.....	33
9.0 APPENDICES.....	39

LIST OF TABLES

	Page
Table 1: Descriptive statistics of Lumpy Skin Disease, by states.....	17
Table 2: Descriptive Statistics of Lumpy Skin Disease in Malaysia.....	18
Table 3: Spatiotemporal cluster by discrete Poisson model on Lumpy Skin Disease Outbreaks in Malaysia.....	25

LIST OF FIGURES

	Page
Figure 1: Spatial distribution of Lumpy Skin Disease outbreaks in Malaysia.....	19
Figure 2: The epidemic curve of Lumpy Skin Disease outbreaks in Malaysia.....	21
Figure 3: The epidemic curve of Lumpy Skin Disease cases in Malaysia...	21
Figure 4: The epidemic curve of Lumpy Skin Disease outbreaks, by states.....	22
Figure 5: The epidemic curve of Lumpy Skin Disease cases in Malaysia, by states during the Northeast Monsoon from November to March.....	23
Figure 6: Distribution of Lumpy Skin Disease outbreaks based on the epidemic day in Malaysia.....	24
Figure 7: Mapping of spatiotemporal cluster identified by discrete Poisson model.....	26

ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 - Projek Ilmiah Tahun Akhir.

EPIDEMIOLOGI DESKRIPTIF *LUMPY SKIN DISEASE* DI MALAYSIA

Oleh

Chong Xin Hui

2024

Penyelia: Prof. Dr. Latiffah Hassan

Lumpy Skin Disease (LSD) yang disebabkan oleh Capripoxvirus, merupakan penyakit lintas sempadan yang mudah dijangkiti, wajib dilaporkan dan memberi kesan ekonomi kepada industri ternakan di Malaysia sejak Mei 2021. Walau bagaimanapun, tiada kajian dilakukan untuk menerangkan ciri epidemiologi wabak LSD di Malaysia. Kajian ini bertujuan untuk menerangkan ciri epidemiologi dan taburan LSD di Malaysia antara 1 Mei 2021 dan 31 Mei 2023. Data diperolehi daripada *World Animal Health Information System-WAHIS* portal telah dianalisis untuk menyiasat penyebaran LSD menggunakan analisis deskriptif, lengkung epidemik, pemetaan, dan pengkelompokan. Sepanjang tempoh kajian, 321 wabak telah dilaporkan dari 11 negeri, yang terdiri daripada 14987 lembu yang rentan, 717 kes, empat kematian, dan 220 lembu yang disembelih. Analisis lengkung epidemik menunjukkan corak propagasi, dan bukannya corak bermusim yang biasanya dilihat bagi penyakit bawaan vektor, mungkin disebabkan oleh kelimpahan vektor,

pergerakan haiwan yang tidak terkawal, dan potensi kemunculan strain rekombinan LSDV. Arah penyebaran adalah dari utara ke selatan, yang mencadangkan bahawa wabak LSD di Malaysia mungkin disebabkan oleh pergerakan haiwan yang dijangkiti dari negara jiran yang terjejas. Kelompok berisiko tinggi yang dikenal pasti menggunakan model diskret Poisson adalah di bahagian utara Semenanjung Malaysia dengan tempoh risiko tinggi dari 1 Jun 2021 hingga 31 Oktober 2021 dan risiko relatif sebanyak 27.95. Secara keseluruhan, LSD mempunyai kadar morbiditi yang tinggi iaitu 18.14% dan kadar kematian yang rendah iaitu 0.04%. Walau bagaimanapun, kadar morbiditi yang tinggi dilaporkan di Kelantan dan Terengganu pada 45.08% dan 56.48% masing-masing, menunjukkan kewujudan faktor risiko yang boleh disiasat secara lebih lanjut. Penemuan dalam kajian ini akan menyediakan maklumat asas untuk kajian epidemiologi selanjutnya dan membantu dalam pelaksanaan langkah kawalan yang lebih baik untuk mengekang penyebaran LSD di Malaysia.

Kata kunci: Epidemiologi deskriptif, Lumpy Skin Disease, lembu, Malaysia, WAHIS.

ABSTRACT

An abstract of the project paper presented to the Faculty of Veterinary Medicine in partial fulfilment of the course VPD 4999- Final Year Project.

DESCRIPTIVE EPIDEMIOLOGY OF LUMPY SKIN DISEASE IN MALAYSIA

By

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2024

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Lumpy Skin Disease (LSD), caused by Capripoxvirus, is a transboundary, contagious, and notifiable disease affecting the cattle industry in Malaysia since May 2021. However, limited studies have been conducted to describe the epidemiological features of the outbreak in Malaysia. This study aims to describe the epidemiological characteristics and distribution of LSD in Malaysia between 1st May 2021 and 31st May 2023. The data were obtained from the World Animal Health Information System-WAHIS portal and were analysed to investigate the spread using descriptive analysis, epidemic curves, mapping, and clustering. During the study period, 321 outbreaks were reported from 11 states affecting domestic cattle in Peninsular Malaysia, which comprised 14987 susceptible cattle, 717 cases, four deaths and 220 cattle culled. Epidemic curve analysis indicates a propagated epidemic pattern, instead of a seasonal pattern which is common in vector-borne diseases, likely due to vector abundance, uncontrolled animal movement and the potential emergence of a new recombinant LSDV strain. The direction of spread is from north to south, suggesting

that the possible source of the outbreak in Malaysia is the movement and smuggling of infected animals from affected neighbouring countries. The most likely cluster identified using the discrete Poisson model is in northern Peninsular Malaysia with high-risk period from 1st June 2021 to 31st October 2021. Overall, LSD has a morbidity rate of 18.14% and a low mortality rate of 0.04%. However, high morbidity rates were reported in Kelantan and Terengganu at 45.08% and 56.48% respectively, suggesting the presence of underlying risk factors that should be investigated further. The findings in this study have provided the baseline information for further epidemiological studies and aid in the implementation of better control measures to curb the spread of LSD in Malaysia.

Keywords: Descriptive epidemiology, Lumpy Skin Disease, cattle, Malaysia, WAHIS.

1.0 INTRODUCTION

1.1 Background

Lumpy Skin Disease (LSD) is a transboundary, contagious, notifiable disease affecting Malaysia since May 2021. The causative agent is the Lumpy Skin Disease virus (LSDV), under the genus Capripoxvirus of the family Poxviridae.

LSD is highly host-specific, causing debilitating disease in cattle and water buffalo (WOAH, 2017). LSD can be acute or inapparent and the classical signs are lacrimation, fever of 40-41 °C, enlarged subscapular and precrural lymph nodes, and skin nodules of different sizes (1-5cm) and numbers (Tuppurainen and Oura, 2012). Ulcerative lesions may also be seen in the mucous membrane of the eyes, and oral and nasal cavity in severe cases, leading to excessive lacrimation, salivation, and nasal discharges. In general, LSD is reported to have a low mortality rate, but a high morbidity rate and the clinical severity of the disease depends on the age, breed, immune status, and production status (Namazi and Tafti, 2021).

LSD has expanded its geographical range rapidly from the African continent and the Middle Eastern countries to Southeast Europe, the Balkans, Russia, and Asia from 2012 to 2022, suggesting transboundary transmission (WOAH, 2023). This disease causes devastating economic loss through a drop in milk yield, temporary or permanent infertility, decreased growth rate, decreased value of hide, global trade restriction and costly control measures (Tuppurainen and Oura, 2012). Historically, Malaysia has been free from LSD, but samples of unknown skin disease in dairy cattle presented in May 2021 were confirmed to be positive for LSDV through Polymerase Chain Reaction (PCR) (Khoo et al., 2022).

1.2 Objective

To describe the epidemiological characteristics and distribution of LSD in Malaysia between May 2021 and May 2023 using the officially reported outbreak data to the World Animal Health Information System – WAHIS portal.

1.3 Justification

LSD is listed as one of the notifiable diseases under the World Organisation of Animal Health (WOAH) due to its socio-economic significance. LSD has spread beyond its geographical range from Africa and the Middle East to Asia in a decade, suggesting the transboundary nature of the disease. LSD has never been reported in Malaysia. WAHIS (2023) reported Malaysia as being free from LSD but since May 2021, LSD outbreaks occurred in Malaysia affecting cattle from multiple states in Peninsular Malaysia. There are currently no studies done to describe the epidemiological characteristics of the first LSD outbreak in Malaysia because the disease is locally new. Hence, this study is important to identify the area of focus for the follow-up studies and to allocate resources for effective control.

2.0 LITERATURE REVIEW

2.1 Causative Agent

LSDV is a large double-stranded linear DNA of approximately 151kbp in length with 156 open reading frames (ORF), from the genus Capripoxvirus in the subfamily Chordopoxvirinae within the family Poxviridae (Tulman, 2001). The ORFs located in the central area of the LSDV genome exhibit high similarity with the genome of other mammalian poxvirus and are likely to encode for protein needed for viral replication and morphogenesis, while the ORFs located in the outer area of the LSDV genome exhibit lower resemblance and are likely to encode for protein required in

viral virulence and determination of host range (WOAH, 2023). Other closely related virus includes sheep pox virus (SPPV) and goat pox virus (GTPV). They are from a similar genus but are different phylogenetically, and there is only one serotype of LSD found, in which it can cross-react with SPPV and GTPV serologically (Tuppurainen et al., 2017). Immature virions are spherical or brick-shaped, measuring 365 x 470nm with a poorly defined envelope and electron-dense core, while matured virions are ovoid, measuring 295 x 452nm with double-membraned envelope, two lateral bodies, and a core (Khalafalla et al., 1995).

The phylogenetic study of LSDV isolates shows that strains sequenced currently are divided into two subgroups, which are subgroup 1.1 and subgroup 1.2 (Biswas et al., 2019). Subgroup 1.1 is comprised of the vaccine strains related to the original Neethling vaccine strain and the wild-type strain from past outbreaks in South Africa (van Schalkwyk, 2020). Subgroup 1.2 is comprised of wild-type LSDV strains from Southern Africa, Kenya, the northern hemisphere, and LSDV KSGP strains (Flannery et al., 2022; Wang et al., 2021; WOA, 2023). There were also reports of recombinant LSDV strains obtained from the field clinical cases of LSD in Russia and Central Asia, where they contain segments of both wild-type and vaccine LSDV strains (Flannery et al., 2022; Sprygin et al., 2020; WOA, 2023). The emergence of recombinant strain is likely due to the poorly manufactured Neethling-based Lumpivax live attenuated homologous virus vaccine used in the mass vaccination program in Kazakhstan (Vandenbussche et al., 2022).

2.2 History and Geographical Distribution

In 1929, a disease found in cattle, known as “pseudo-urticaria” before the aetiology of LSD was identified, thought to be caused by insect bites and subsequently convinced to be caused by plant poisoning, was noticed in the region

known then as Northern Rhodesia, which is known now as Zambia (Weiss, 1968). To date, LSD is said to be endemic throughout Africa, excluding Algeria, Morocco, Tunisia, and Libya, which is still unaffected by this disease (Tuppurainen et al., 2017). Since 2013, There have been LSD outbreak reports in many Middle Eastern countries, including Israel, the Palestinian Autonomous Territories, Jordan, Lebanon, Kuwait, Saudi Arabia, Iraq, Iran, Oman, Yemen, United Arab Emirates and Bahrain. In 2013, this disease spread to Turkey, which is now endemic (Tuppurainen et al., 2017). Turkey is a crucial junction linking the Eurasian continent, which aids the spread of LSD to the Balkans and some parts of the European countries (Liang et al., 2022). According to the WAHIS, the first LSD report in Asia and the Pacific region was in 2019, in northwest China, Bangladesh, and India. LSD then continued to spread throughout the Asia continent, with many countries in South and Southeast Asia reporting outbreaks during the northern summer of 2020. The first reported outbreak in Southeast Asia, according to the WAHIS database, was in Vietnam (5th October 2020), followed by Myanmar (9th November 2020), Thailand (29th March 2020), Malaysia (10th May 2021), Laos (22nd May 2021) and Cambodia (26th May 2021) (Wilhelm & Ward, 2023).

2.3 Transmission

The mode of transmission of LSDV is mainly indirectly through arthropods (Tuppurainen and Oura, 2012). A study in Israel conducted by Klausner et al. (2017) indicated that wind may be responsible for the long-distance dispersion of infected vectors.

Currently, LSDV is detected on stable flies such *Stomoxys calcitrans* (Chihota et al., 2003; Issimov et al., 2020; Issimov et al., 2021), *Stomoxys sitiens* (Issimov et al., 2020; Issimov et al., 2021) and *Stomoxys indica* (Issimov et al., 2020; Issimov et

al., 2021); Mosquitoes such as *Aedes aegypti* (Chihota et al., 2001; Sanz-Bernardo et al., 2021; Sanz-Bernardo et al., 2022; Paslaru et al., 2022), *Aedes japonicus* (Paslaru et al., 2022), *Anopheles stephensi* (Chihota et al., 2003), *Culex quinquefasciatus* (Chihota et al., 2003; Sanz-Bernardo et al., 2021; Sanz-Bernardo et al., 2022) and *Culex pipiens* (Paslaru et al., 2022); Biting midges such as *Culicoides nubeculosus* (Chihota et al., 2003; Sanz-Bernardo et al., 2021; Sanz-Bernardo et al., 2022; Gubbins et al., 2019; Paslaru et al., 2022) and *C. punctatus* (Şevik and Doğan, 2017); Horseflies such as *Haematopota spp.* and *Tabanus bromiums* (Sohier et al., 2019; Orynbayev et al., 2021); Non-biting flies such as *Musca domestica L.* and *Muscina stabulans* (Sprygin et al., 2018; Wang et al., 2022) which was linked to LSD outbreak caused by vaccine-like LSD strain in Russia and the West border of China; Ticks such as *Amblyoma hebraeum* (Tuppurainen et al., 2011; Lubinga et al., 2013; Lubinga et al., 2014; Lubinga et al., 2015), *Rhipicephalus appendiculatus* (Lubinga et al., 2013; Lubinga et al., 2014; Tuppurainen et al., 2011; Tuppurainen et al., 2013), *Rhipicephalus decoloratus* (Tuppurainen et al., 2011; Lubinga et al., 2014) and *Rhipicephalus annulatus* (Rouby et al., 2017) which were proven experimentally to exhibit intrastadial infection (Tuppurainen et al., 2011), transstadial persistence (Tuppurainen et al., 2011; Lubinga et al., 2013; Lubinga et al., 2014), transovarial persistence (Lubinga et al., 2013), transovarial transmission (Lubinga et al., 2013), mechanical /intrastadial transmission (Lubinga et al., 2015; Tuppurainen et al., 2013; Lubinga et al., 2014), and transstadial transmission (Lubinga et al., 2014; Lubinga et al., 2015; Tuppurainen et al., 2013).

Direct transmission is an inefficient way of transmission, as demonstrated by a study by Carn and Kitching (1995), which showed that no animals developed clinical signs or neutralizing antibodies even though the uninfected animals were housed in contact with the infected animals for one month. Aleksandr et al. (2020) showed novel

recombinant LSDV transmission in insect-proof facilities, possibly through shared resources and direct contact. Infective saliva may play a role, supported by successful transmission via shared drinking troughs (Haig, 1957; Weiss, 1968).

Infectious LSDV is found in saliva and nasal discharge for up to 18 days post-infection (Tuppurainen et al., 2017). Viable LSDV persists in cutaneous lesions protected inside crusts, and field experience suggests environmental persistence after stamping out (Tuppurainen et al., 2017). LSDV can be detected for up to 33 days in skin nodules (Weiss, 1968), and viable virus persists for up to 18 days in air-dried hides, up to months in a shed without sunlight, and up to 6 months in tissue culture fluid at 4°C (CFSPH, 2008).

Semen has been implicated in LSDV transmission, detected 22 days post-infection (Weiss, 1968). Viable LSDV can be isolated for up to 42 days in severely affected bulls, with viral DNA detectable for up to 159 days (Irons et al., 2005). Annandale et al. (2010) identified testes and epididymis as sites of persistence, with viral DNA in all semen fractions. Both Irons et al. (2005) and Annandale et al. (2010) noted that subclinical animals may shed the virus in semen, but the shedding is preventable by live attenuated Neethling vaccine (Osuagwuh et al., 2007).

In-utero transmission is supported by pre-colostral antibodies in a premature calf from a cow with clinical LSDV in the mid-trimester (Rouby and Aboulsoud, 2016). LSDV can be isolated from milk for infected and vaccinated animals up to 21 days post-vaccination (Katsoulos et al., 2018; Bedeković et al., 2018).

2.4 Susceptible Host

LSD is highly host-specific, causing natural infection of lumpy skin disease in cattle and Asian water buffalo (*Bubalus bubalis*) (Tuppurainen et al., 2017). The authors also mentioned that some LSDV strain is capable of replicating in sheep and

goat, but there was no proof that small ruminant can act as a reservoir of LSD. Buffalo is less susceptible to the disease, with reported lower seropositivity (Bianchini et al., 2023) and lower morbidity at 1.6% (Tuppurainen et al., 2017). *Bos taurus*, especially the thin-skinned breed, develops a more severe lesion, with high-producing lactating cows posing the highest risk (WOAH, 2023). This might be explained by Weiss (1968), who indicated that animals with intravenous inoculation of LSDV tend to develop more generalized and severe diseases in his paper. Tuppurainen and Oura (2012) noted that there was limited data on the role of wild ruminants in the epidemiology of this disease and also the susceptibility of wild ruminants to LSD. To date, there have been reported LSDV infections in African buffalo (Davies, 1982), Egyptian buffalo (Ahmed et al., 2021), Arabian oryx (Greth et al., 1992), Banteng (Porco et al., 2023), and giraffe (Dao et al., 2022), as well as Southern eland, springbok, impala and wildebeest (Barnard, 1997). Serum antibodies against LSD are detected in African Buffalo, Egyptian Buffalo, southern eland, springbok, impala, and wildebeest (Davies, 1982; Ahmed et al., 2021; Barnard, 1997). The detection of antibodies might indicate exposure to LSDV or challenge, but it could not imply that the species mentioned is responsible in the transmission and excretion of the virus. A study by Dao et al. (2022) revealed that LSDV is successfully isolated in giraffes with the clinical disease of LSD in Vietnam. LSD is not a zoonosis (Tuppurainen et al., 2017).

2.5 Pathology

According to the Food and Agriculture Organisation Field manual by Tuppurainen et al. (2017), the incubation period of animal infected experimentally is between four to seven days, whereas animals infected naturally can be up to five weeks.

Clinical signs of LSD, as outlined in the WOAHA Terrestrial Manual 2023 and the FAO field manual, include high fever exceeding 41°C lasting about a week, ocular nasal discharges, hypersalivation, and enlarged superficial lymph nodes. The discharges harbour LSDV. Additionally, there is a sharp drop in milk yield, potential abortions in pregnant animals, and temporary or permanent infertility in bulls. Skin nodules, varying in number, can coalesce into large irregular plaques, predominantly on the head, neck, perineum, genitalia, udder, and limbs. Limb oedema may cause reluctance to walk. Recovery from severe infection is slow, with common complications such as mastitis, pneumonia, myiasis, and emaciation. Subclinical infections of LSD are also common in field settings.

LSD exhibits characteristic gross lesions, including 10-50mm nodules with ulceration and scab formation on the head, neck, perineum, genitalia, udder, and limbs, which is deep, involving the skin, subcutaneous and potentially muscle (Tuppurainen et al., 2017). Oronasal necrotic plaques result in oronasal discharge with a high viral load. Bulls may develop lesions around the scrotum, prepuce, and testes, causing acute orchitis, while cows may experience lesions on the udder and teat, leading to mastitis (Coetzer et al., 2018). Histopathologically, acute-phase LSD shows vasculitis, perivascular fibroplasia, ballooning degeneration of keratinocytes in the epidermis, and inflammatory cell infiltration in the dermis and subcutis, while old lesions display coagulative necrosis, fibrosis, and thrombosis. Eosinophilic intracytoplasmic inclusions are diagnostically significant and found in endothelial cells, pericytes, and epithelial cells of mucus and serous glands during acute and subacute phases (Coetzer et al., 2018; Tuppurainen et al., 2017; Weiss, 1968).

It was suggested that upon entry into animals, LSDV replicates in the keratinocytes in the epidermis, and fibroblasts and endothelial cells and pericytes of blood vessels in the dermis (Weiss, 1968) which may lead to vasculitis and

lymphangitis following damage to the endothelial cell present in blood vessels and lymphatic vessels. This may lead to infarction and thrombosis in severe cases (Al-Salihi, 2014), presumably causing oedema and, eventually, necrosis of the tissue (Weiss, 1968).

2.6 Diagnosis

According to Tuppurainen et al. (2017), the recommended sample type is skin lesion with scabs, saliva or nasal swab, EDTA blood for Polymerase Chain Reaction (PCR), and whole blood for serum sample.

2.6.1 Detection of Virus

The methods outlined by WOAHP Terrestrial Manual 2023 are virus identification using transmission electron microscopy, fluorescent antibody test, immunohistochemistry, and molecular methods such as PCR.

For virus identification using electron microscopy, the general feature of a Poxviridae virion can be seen, and it is not possible to differentiate a Capripoxvirus virion from an Orthopoxvirus virion. However, in cattle, Orthopoxvirus is generally uncommon and is not usually associated with generalized disease, except for the vaccinia virus and cowpox virus. Meanwhile, in Buffalo, Orthopoxvirus is a common cause of skin lesions in domestic buffalo (WOAHP, 2023). This method can be used as a primary diagnostic test, but it is uncommon (Tuppurainen et al., 2017).

For conventional or real-time PCR, it is unable to distinguish LSDV, SPPV, and GTPV, and it is unable to detect the infectious status of the virus (Tuppurainen et al., 2017). To distinguish between vaccine strain and virulent field strain, we can use a PCR assay system comprising three different tests developed by Menasherow (2014) or sequencing on RP030 and G-protein-coupled chemokine receptor (GPCR)

genes (Gelaye et al., 2015). To distinguish between LSDV, SPPV, and GTPV, species-specific assays utilizing GPCR (Le Goff et al., 2009; Lamien et al., 2011) and snapback primer with the dsDNA intercalating EvaGreen dye (Gelaye et al., 2013) can be used.

2.6.2 Detection of Antibodies

The methods outlined by WOAHP Terrestrial Manual 2023 are viral neutralization test, enzyme-linked immunosorbent assay, indirect fluorescent antibody test, and western blot analysis. It is also worth noting that all Capripoxvirus share the same antigen for neutralizing antibodies, so it is not possible to differentiate between different strains of Capripoxvirus using serology (WOAHP, 2023). Generally, antibody level can neither differentiate between infection or vaccination nor identify if the animal is having an active infection, as it can merely tell if the animal has been exposed to the agent. According to Tuppurainen et al. (2017), the antibody level starts increasing about one week after the onset of clinical signs, peaks at about two to three weeks later, and then decreases eventually to an insignificant level. The authors noted that serological surveillance during the inter-epizootic period is difficult due to long-term cell-mediated immunity, and the serological test available to date might not be sensitive enough to identify mild, chronic LSD infection. They also mentioned that most infected animals will have seroconversion during active outbreaks, so serological tests can be used during the period.

2.6.3 Differential Diagnosis

Some differential diagnosis highlighted by Tuppurainen et al. (2017) includes bovine herpes mammillitis / pseudo-lumpy-skin disease, Insect bites, urticaria, photosensitization, pseudo cowpox, dermatophilosis, demodicosis, bovine papular

stomatitis, besnoitiosis, onchocerciasis and adverse reaction to live attenuated vaccine which mimics the clinical disease. Some other differential diagnosis suggested by WOA (2023) with the mucosal lesions includes foot and mouth disease, bluetongue, infectious bovine rhinotracheitis, and malignant catarrhal fever.

2.7 Control and Prevention

In endemic regions like Africa, LSD control involves voluntary vaccination, without movement control or stamping out, aiming to reduce clinical disease (Coetzer et al., 2018). During epidemics in non-endemic countries, measures include vaccination, stamping out, movement control, and vector control (Coetzer et al., 2018). Live vaccines, including attenuated LSDV, SPPV, and Gorgon GTPV vaccines, are commonly used, with 80% coverage recommended for effective protection using attenuated LSDV vaccine (Tuppurainen et al., 2017). They also noted that regional vaccination is preferred over ring vaccination. The Neethling strain is a common live LSDV vaccine, associated with the "Neethling response" (Tuppurainen et al., 2021). The attenuated SPPV vaccine is used in areas with LSD and SPV which offers partial protection, and the Gorgon GTPV vaccine is suitable for regions with LSD and GTP which offers similar protection to the LSDV vaccine (Tuppurainen et al., 2017). A minimum 50km radius restricted zone is recommended, with surveillance and protection zones covering the vector movement range for ring vaccination (Tuppurainen and Galon, 2016). Antibodies will be observed within 15 days and peak in 30 days post-vaccination, but seroconversion may be absent in some vaccinated and fully protected animals (Coetzer et al., 2018; Weiss, 1968).

EFSA (2016) concludes that vaccination is more effective in reducing LSD spread than stamping out policies, but it is recommended to cull severely affected animals to prevent transmission (Coetzer et al., 2018). According to the WOA

Terrestrial Code 2023, a country is considered free from LSD if historically disease-free, or if vaccination has been prohibited for three years with no infections detected in surveillance. Recovery of freedom status through stamping out requires waiting periods post-culling or vaccination. In preventive vaccination scenarios in a country free from LSD as a result threat, freedom from disease can be achieved eight months after the last vaccination with no infections detected in surveillance (WOAH Terrestrial Code 2023).

2.8 Economical Significance

LSD is listed as a notifiable disease under WOAHA due to its economic significance, and the economic losses are mainly due to reduced milk yield from the fever and secondary mastitis, temporary infertility in cows and bulls, emaciation of infected animals, the decreased growth rate in beef cattle, reduced value of hide due to deep skin lesion leaving permanent scars, global trade restriction of live animal and its products, and costly control measures such as vaccination and movement control (Tuppurainen and Oura, 2012).

The direct and indirect production losses due to LSD in intensive cattle farming are estimated to be 45 to 65% (Tuppurainen and Oura, 2012). The economic loss due to LSD in South, East, and Southeast countries is estimated to be USD 1.45 billion through direct losses of livestock and production, and the losses might be even higher because of the severe global trade restrictions (Roche, 2020). In Ethiopia, the median total economic loss due to an LSD outbreak at the herd level is USD 489 in subsistence farms and USD 2735 in commercial farms, and most of the economic loss was due to mortality, followed by milk loss (Molla et al., 2017). In Thailand, the estimated total economic losses over the LSD outbreak period is USD 68943, in which dairy farmers face loss between 8.23 to 9.96 tons of milk each month, equating to

between USD 119,43 to USD 412.57 in monthly income (Vinitchaikul et al., 2023). In Pakistan, a study by Haider et al. (2023) shows the consumption of milk and meat has reduced from 60-70% in Karachi, Pakistan, due to LSD, and it was also reported that the reported drop in milk production due to LSD can range from 10-85%.

3.0 MATERIALS AND METHODS

3.1 Data Collection and Management

WAHIS interface (<https://wahis.woah.org/#/home>) was used to identify the location and dates of reported LSD outbreaks in Malaysia which represents validated data reported by the veterinary service of each country. LSD outbreaks reported in WAHIS were chosen if they occurred in Malaysia between 1st May 2021 and 31st May 2023. The LSD cases were diagnosed based on Polymerase Chain Reaction. From the WAHIS report, the information collected included: the report date, outbreak start and end dates, location, number of susceptible animals, cases, death and culled. The data collected were imported into Microsoft Excel for further analysis. The outbreaks and cases involving domestic cattle and wild ruminants were analysed separately.

3.2 Data Analysis

The data analysis is divided into 4 parts, which are descriptive statistics, spatial analysis, temporal analysis, and spatiotemporal analysis.

3.2.1 Descriptive statistics

Descriptive statistics were done using Microsoft Excel v16.0. Morbidity (number of cases ÷ susceptible animals), mortality (number of deaths ÷ susceptible animals), case fatality (number of deaths ÷ number of cases) and the culled rate (number of culled ÷ susceptible animals) estimates were calculated for each reported

outbreak. “Culled” was interpreted as the animals slaughtered for consumption due to infection. The number of outbreaks, susceptible, cases, deaths, and culls for each state were also recorded. The mean, median, and interquartile range (IQR) of the number of cases was calculated.

3.2.2 Spatial analysis

This method is adapted with modifications from Wilhem and Ward (2023). The spatial distribution of LSD in Malaysia was examined by mapping the locations of the reported outbreaks (latitude and longitude) in Malaysia using a geographic information system (ArcGIS Pro v3.0.1). A colour ramp, from yellow to red was used to represent the number of cases from each reported outbreak (1 to 25 cases).

3.2.3 Temporal analysis

This method is adapted with modifications from Wilhem and Ward (2023). The temporal distribution of the outbreak and cases in each state in Malaysia is examined through the epidemic curve. The first reported outbreak or case in the region was assigned day 1 and the daily number of outbreaks or cases for each state was plotted for the duration of the outbreak on a normal scale to make the epidemic curve using Microsoft Excel v16.0.

3.2.4 Spatiotemporal analysis

A colour ramp, from green to red, applied to the mapped location of the reported outbreak was used to represent the epidemic day that each outbreak was reported to happen (Day 1 to Day 381) to monitor the direction and trend of the spread

of LSD in Malaysia. This method is adapted with modifications from Wilhem and Ward (2023).

This study also utilized a discrete Poisson model for retrospective space-time statistical analysis, which is adapted with modifications from Kulldorff et al. (1998), Yang et al. (2022), and Ma et al. (2021). SaTScan v10.1.2 was employed to identify statistically significant clusters of LSD cases in both space and time within the WAHIS reported data, which is identified when there are more cases observed than expected in the scanning cylindrical window. This method is widely used in epidemiological studies to help identify potential locations for investigation, to reveal common risk factors, and to aid in more targeted measures to control disease spread. Under the discrete Poisson distribution model, the null hypothesis states that there is a constant risk of LSD or LSD incidence over space and time inside and outside of all the cylinders. Meanwhile, the alternative hypothesis states that there are different risks of LSD or LSD incidence inside and outside of at least one of the cylinders.

The cylindrical windows, representing potential clusters, have circular bases for geographical areas and variable heights for time intervals. The cylindrical window is then moved in space and time to enable us to observe each possible time interval for each possible geographical area and size. The study scanned for areas with high attack rates, setting the scanning time in months and maximum spatial and temporal cluster sizes at 20% and 50%, respectively, by default. The likelihood ratio was calculated for each cylinder, based on observed and expected cases. Statistical significance was determined using Monte Carlo simulation (with 999 iterations). The null hypothesis of no statistically significant clusters was rejected if the p-value was < 0.05 . The most likely cluster had the maximum likelihood ratio, with other significant clusters identified as secondary spatiotemporal clusters. Relative risk (RR) was used

to assess epidemic risk in each cluster. The results were visualized using ArcGIS Pro v3.0.1.

4.0 RESULT

4.1 Descriptive statistics

There was a total of 321 LSD outbreaks in domestic cattle reported to WAHIS, comprising 717 cases, 14987 susceptible cattle, four deaths, 220 culled cattle, and 1712 vaccinated animals between 1st May 2021 to 31st May 2023. During this period, there was also one reported outbreak of LSD occurring in Seladang (*Bos gaurus*) in Pahang, involving 1 case, 25 susceptible animals, and one death. However, the LSD outbreak involving Seladang was not considered in the calculation of the descriptive statistics of the LSD outbreak in Malaysia. The affected population was the herd at a farm reared in an intensive system.

Most of the outbreaks (n=81), cases (n=231), and susceptible (n=4130) cattle were reported in Perak. The mean morbidity was high at 18.14%, but the mortality was low at 0.04%. A higher morbidity rate was reported in Kelantan and Terengganu at 45.08% and 56.48%, respectively. The case fatality rate was generally low at 0.63%, but a higher rate was recorded in Pulau Pinang at 19.05%. The culled rate for LSD is 4.48%, but out of 717 cases, only 220 were culled, and only four deaths were reported, which is inconsistent with the control measure implemented by the Malaysia Department of Veterinary Service. The vaccination status was not available for most of the outbreak reports submitted to WAHIS. Hence the vaccination rate was not calculated.

Table 2: Descriptive statistics of Lumpy Skin Disease in Malaysia.

Parameters	
Mean Morbidity Rate (%)	18.14
Mean Mortality Rate (%)	0.04
Mean Case Fatality (%)	0.63
Mean Culled Rate (%)	4.48

4.2 Spatial analysis

The spatial distribution of LSD outbreaks in Malaysia (**Figure 1**) shows a more concentrated outbreak occurring in Kelantan, Perlis, Perak, and Melaka. Meanwhile, a more scattered outbreak occurred in Pahang, Negeri Sembilan, Selangor and Johor. The maximum number of cases in a single outbreak was highest in Perak (n=25), as indicated by the red plot. Perak also had the highest number of reported cases (n=231). The first outbreak occurred in Kedah on 9th May 2021, as indicated by the green star in **Figure 1**, while the last outbreak occurred in Perlis on 24th May 2022, as indicated by the red star in **Figure 1**. The final outbreak in Perlis is a sporadic case happening three months after the last outbreak in Selangor on 23rd February 2022.

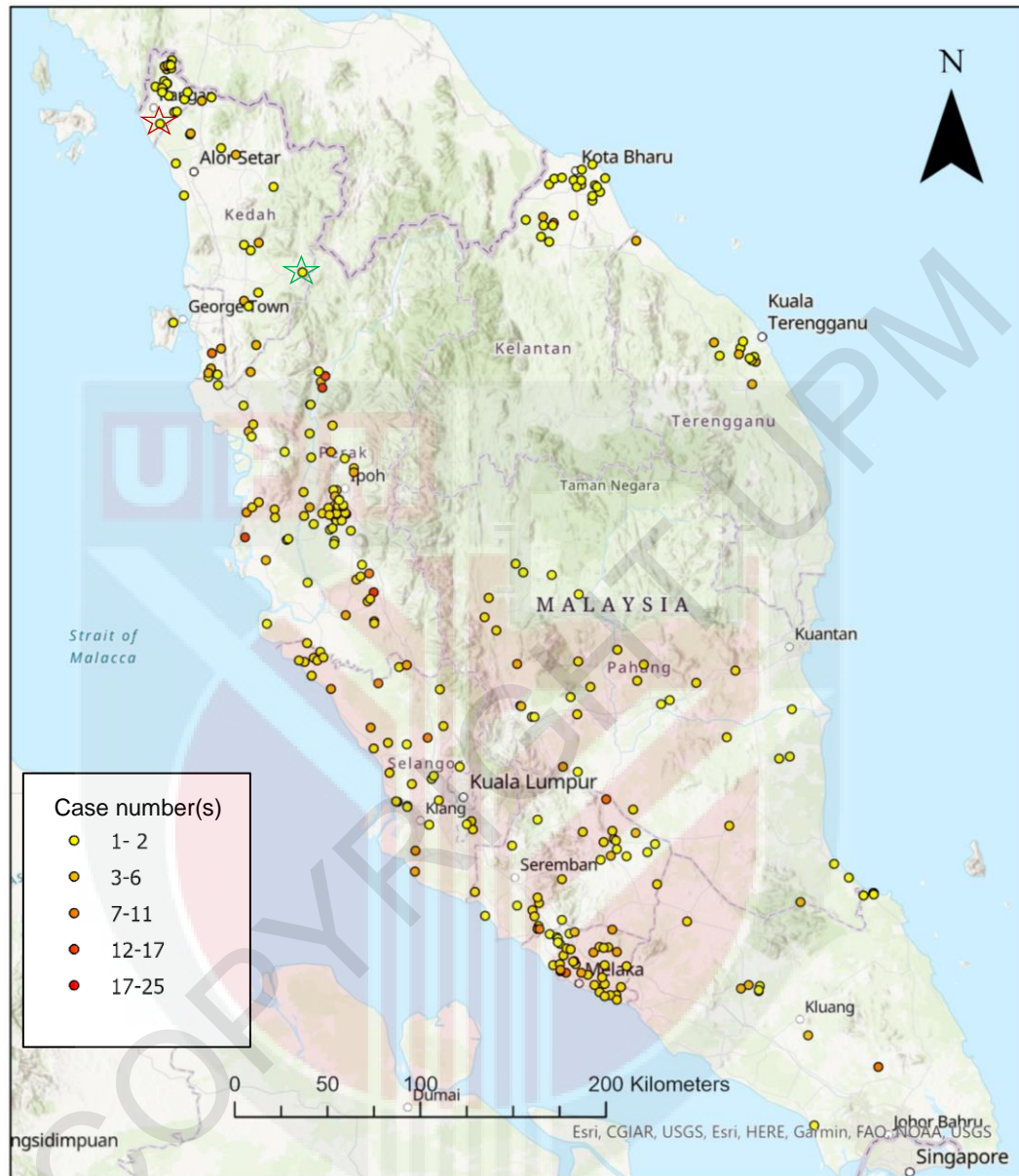


Figure 1: Spatial distribution of Lumpy Skin Disease outbreaks in Malaysia.

4.3 Temporal analysis

The epidemic curve of LSD outbreaks and cases in Malaysia (**Figure 2 and Figure 3**) shows a propagated pattern with several peaks. Day 1 represents the first reported LSD outbreak on 9th May 2021, whereas Day 381 represents the last reported LSD outbreak on 24th May 2022.

From the epidemic curve of LSD outbreaks in Malaysia (**Figure 2**), three peaks were observed. The first peak was on day 32 (9th June 2021), in which of the nine outbreaks, five were from Perak and four were from Perlis. The second peak was on day 58 (5th July 2021), in which of the nine outbreaks, six were from Perlis, and one was reported each in Kelantan, Negeri Sembilan, and Pahang. The third peak was on Day 121 (6th September 2021), in which of the nine outbreaks, eight were from Perak, and one was from Melaka. From Day 121 onwards, the number of outbreaks reduced, and the last outbreak was recorded on Day 381 (24th May 2022).

From the epidemic curve of LSD cases in Malaysia (**Figure 3**), three peaks were observed. The first peak was on day 58 (5th July 2021), in which of 24 cases, nine were from Kelantan, three were from Negeri Sembilan, one was from Pahang, and 11 were from Perak. The second peak was on day 100 (16th August 2021), in which of 40 cases, 31 cases were from Perak, six cases were from Negeri Sembilan, and three cases were from Selangor. The third peak was on day 151 (6th October 2021), in which from 31 cases, 25 cases were from Perak, one case was from Johor, four cases were from Melaka, and one case was from Negeri Sembilan. Similarly, the cases started to reduce from day 151 onwards.

The epidemic curve of LSD outbreaks by states (**Figure 4**) shows that Kelantan, Perak, and Perlis have more concentrated outbreaks at earlier epidemic days.

The epidemic curve of LSD cases in Malaysia during the Northeast Monsoon, from November to March (**Figure 5**) shows that the northern monsoon is not associated with a higher number of cases, which is commonly observed for most vector-borne diseases.

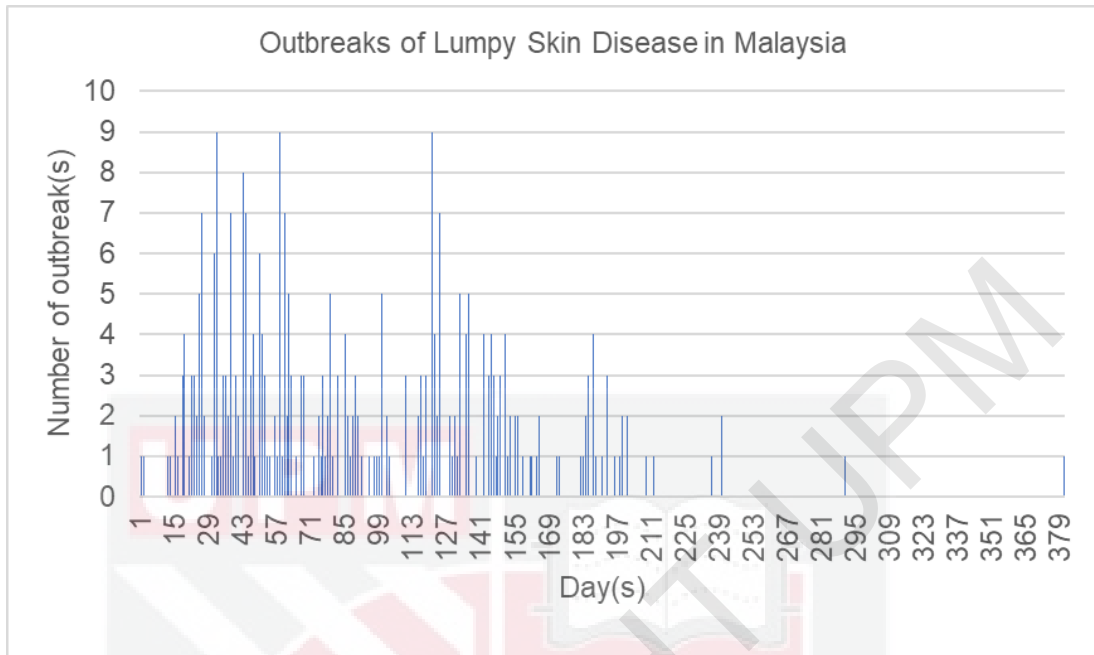


Figure 2: The epidemic curve of Lumpy Skin Disease outbreaks in Malaysia.

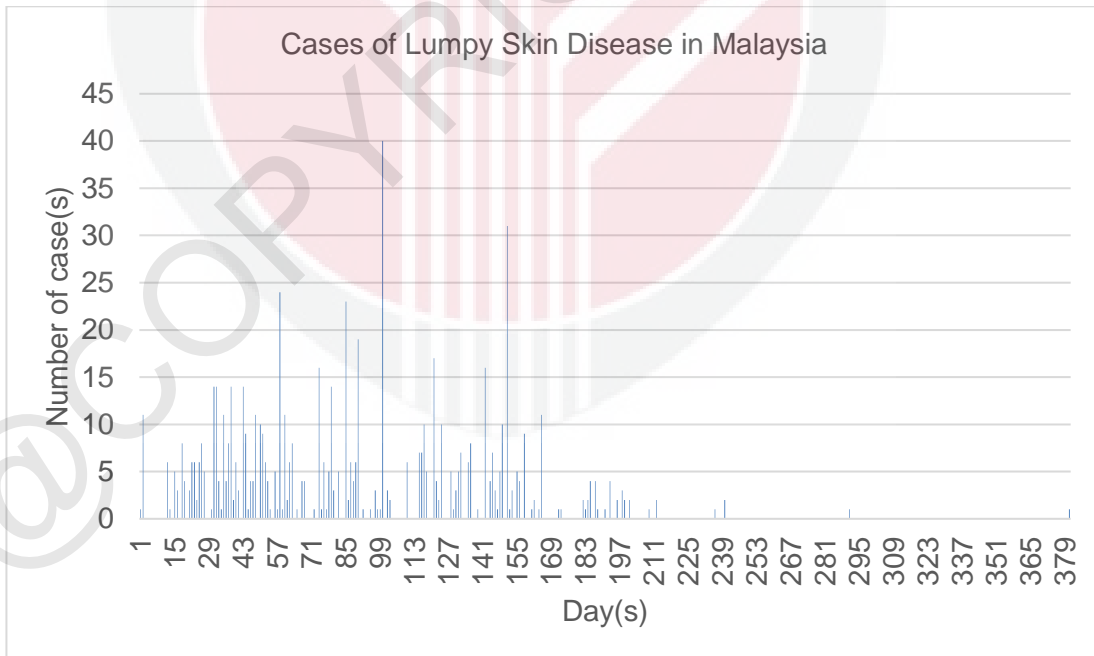


Figure 3: The epidemic curve of Lumpy Skin Disease cases in Malaysia.

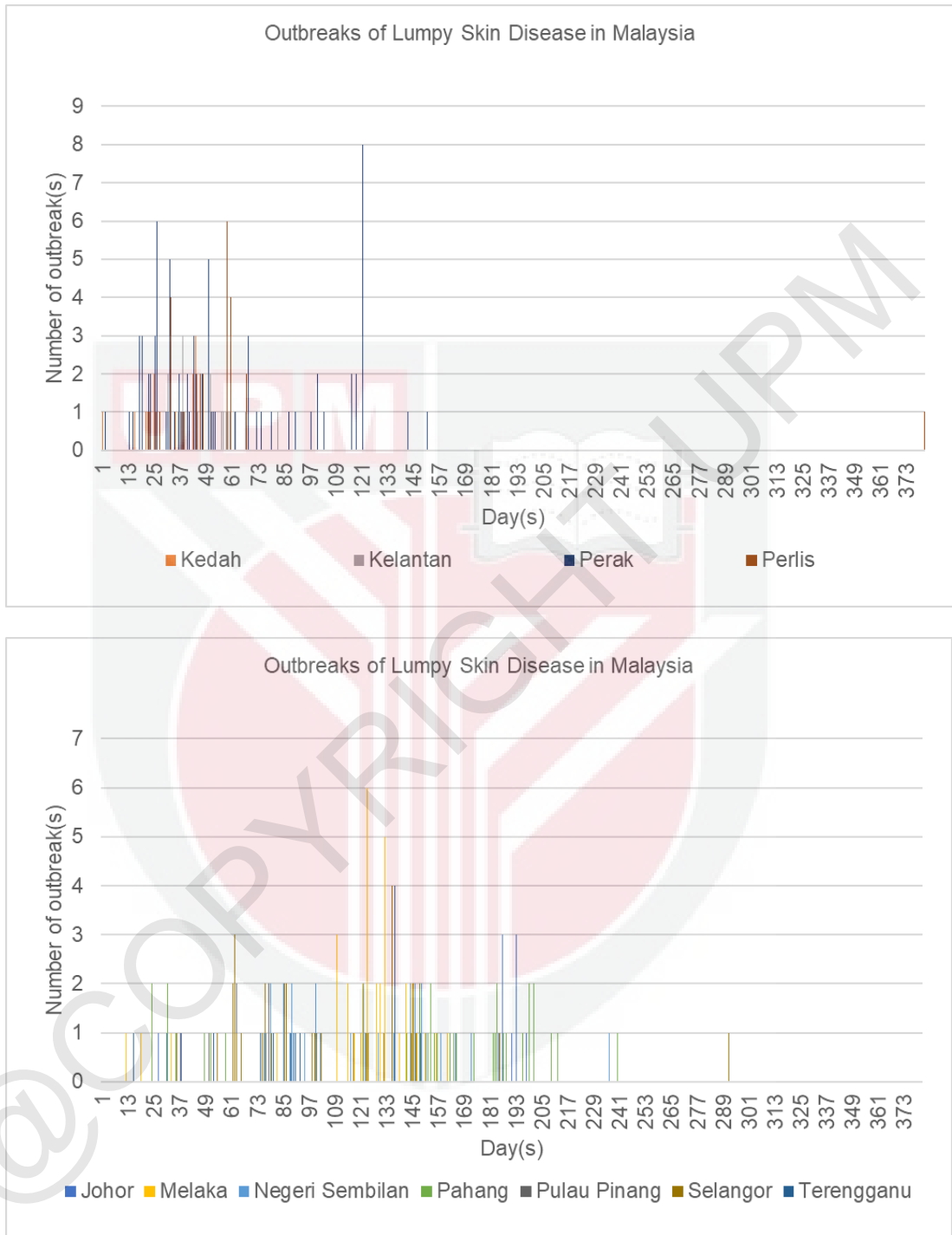


Figure 4: The epidemic curve of Lumpy Skin Disease outbreaks in Malaysia, by states.

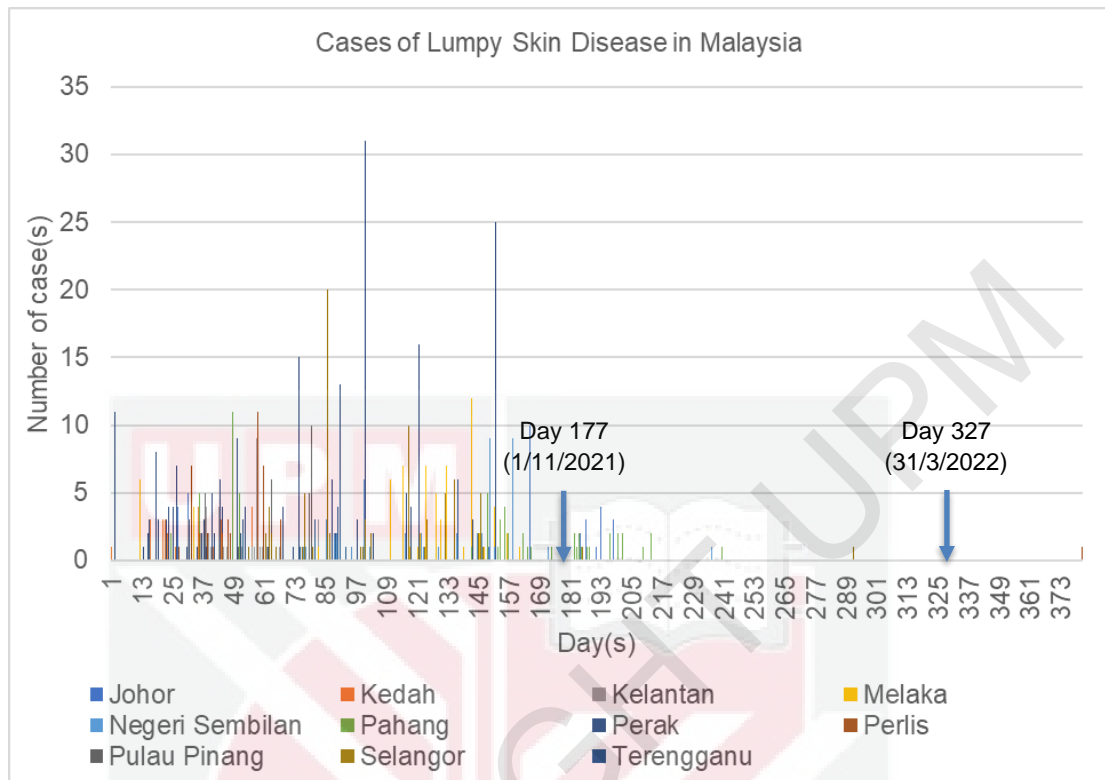


Figure 5: The epidemic curve of Lumpy Skin Disease cases in Malaysia, by states during the Northeast Monsoon from November (Day 177, 1st November 2021) to March (Day 327, 31st March 2022).

4.4 Spatiotemporal analysis

The spatial distribution of the outbreaks based on the epidemic day (**Figure 6**), showed that the direction of spread was from North to South.

Five statistically significant spatiotemporal clusters were identified using the discrete Poisson model in retrospective space-time analysis (**Table 3**), and the mapping of the spatiotemporal cluster (**Figure 7**) showed the location of the most likely cluster and four secondary potential clusters. The most likely cluster area is in Northern Peninsular Malaysia, which covers Kedah, Perak, Pahang, Kelantan and Terengganu, with a radius of 185.11km, an observed to expected ratio of 23.1 and a

relative risk of 28. The high-risk period identified was from 1st June 2021 to 31st October 2021.

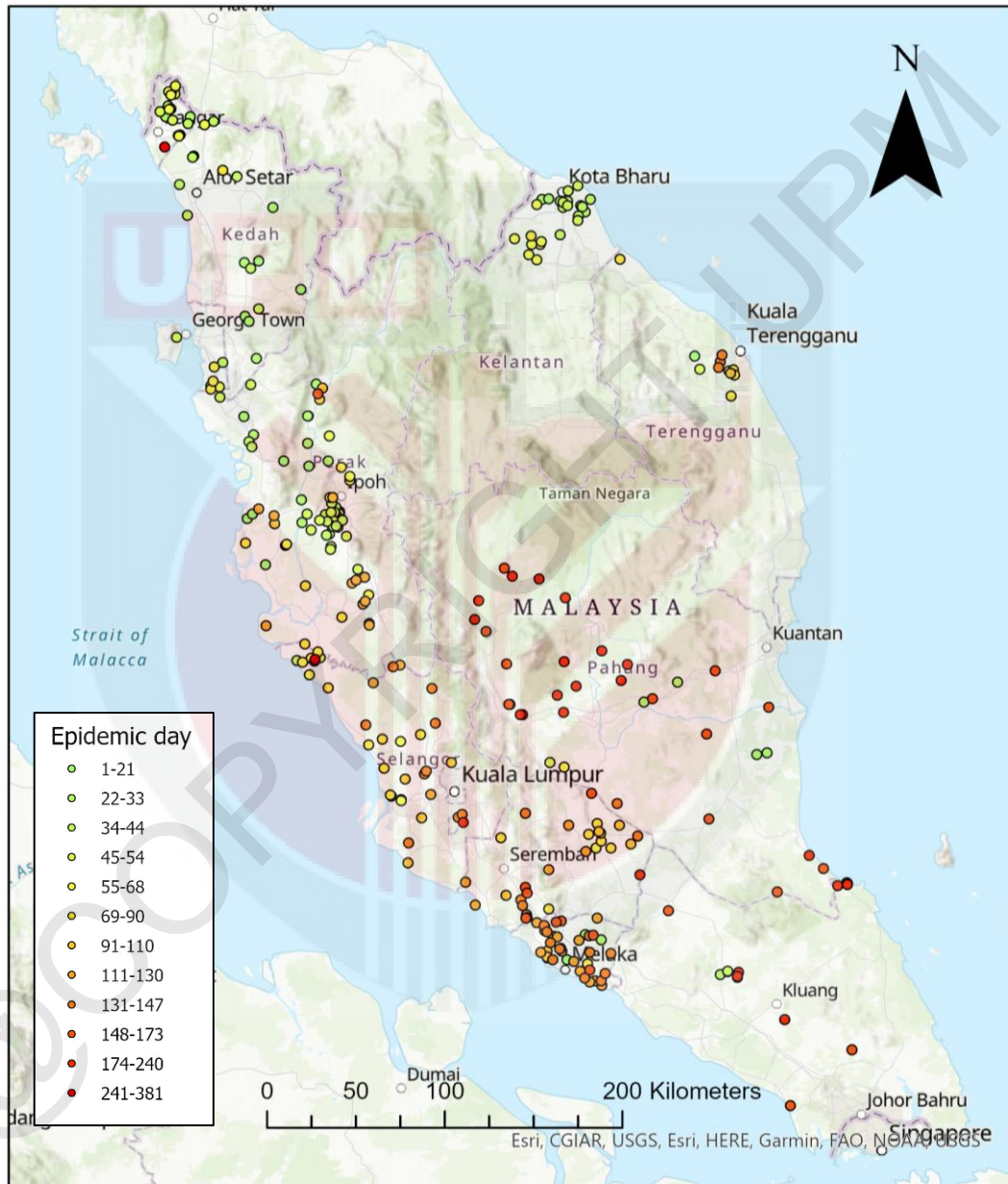


Figure 6: Distribution of Lumpy Skin Disease outbreaks based on the epidemic day in Malaysia.

Table 3: Spatiotemporal cluster by discrete Poisson model on Lumpy Skin Disease outbreaks in Malaysia

Clusters	Coordinate	Radius (km)	Time Frame	Observed	Expected	O/E ratio	Relative Risk	LLR	p-value
1	6.141419 N, 102.266948 E	185.11	1/6/2021 to 31/10/2021	130	5.6	23.1	28.0	295.2	0.001
2	3.441420 N, 101.243400 E	85.01	1/6/2021 to 30/9/2021	139	14.5	9.6	11.7	201.8	0.001
3	4.517970 N, 101.112250 E	33.60	1/5/2021 to 30/6/2021	70	6.0	11.7	12.9	111.3	0.001
4	2.708498 N, 102.169553 E	50.45	1/8/2021 to 31/10/2021	95	14.4	6.6	7.4	103.2	0.001
5	2.716190 N, 103.558361 E	103.00	1/10/2021 to 30/11/2021	34	5.1	6.7	6.9	36.1	0.001

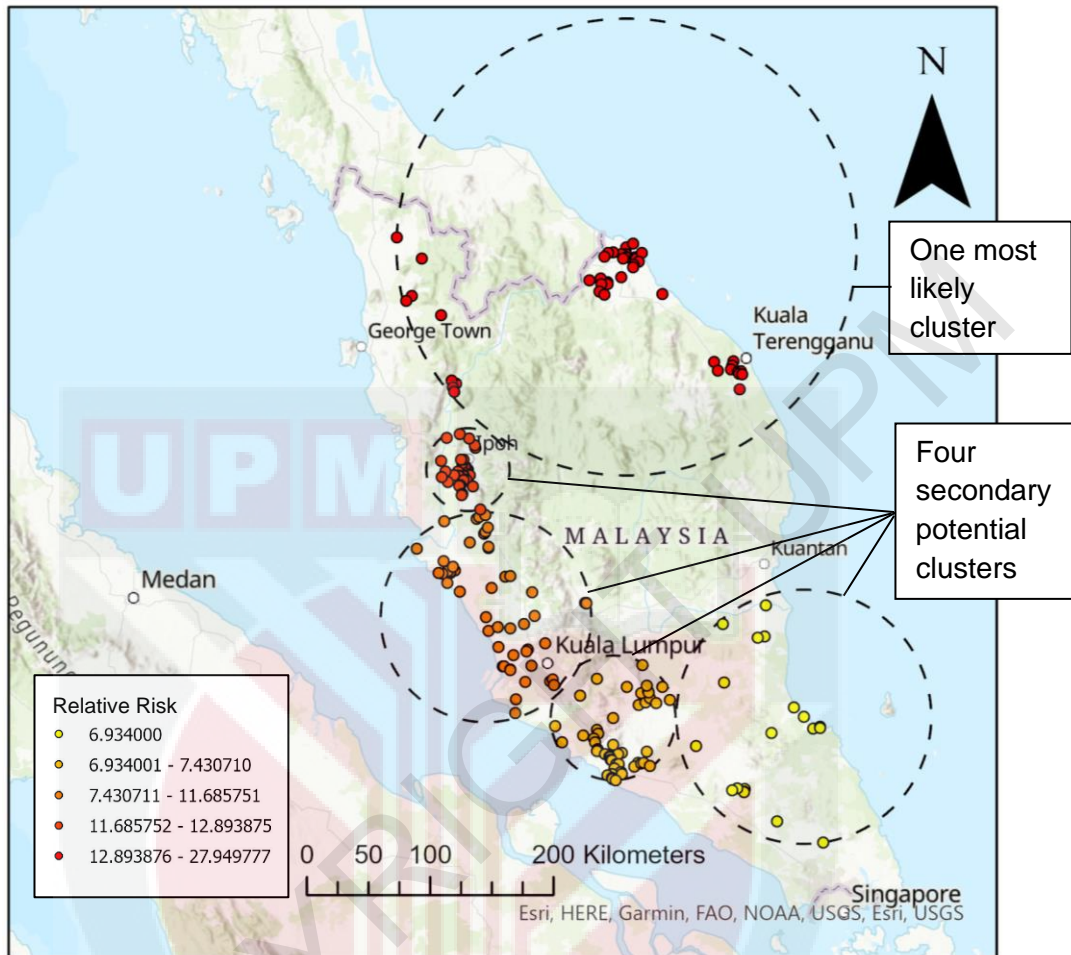


Figure 7: Mapping of the spatiotemporal cluster of Lumpy Skin Disease identified by discrete Poisson model.

5.0 DISCUSSION

Through the data from WAHIS, there is one report of wildlife transmission in Malaysia, involving Seladang (*Bos gaurus*) in Pahang. However, it is less likely for them to play a role in the LSD outbreak in Malaysia because the affected population is a small herd reared on a farm practising intensive system. The data on the diagnostic test used is unknown but the diagnostic method reported to be used in Malaysia is conventional gel-based PCR (Abdullah, 2021), which could not differentiate between Capripoxviruses, which comprised SPPV, GTPV and LSDV.

However, it was reported that SPPV and GTPV affect mainly small ruminants (Zewdie et al., 2021) while LSDV is more commonly associated with large ruminants (Tuppurainen et al., 2017). In the outbreak reported to WAHIS, we assumed that LSDV was isolated from the one case found in the clinically affected Seladang through PCR. Hence, this finding highlights the susceptibility of wild ruminants to LSDV and also the spillover of domestic animal disease to wildlife which poses a significant threat to conservation.

According to the protocol for LSD in Malaysia (*Protokol Veterinar Malaysia* 2021), positive or suspected cases should be isolated immediately and sent for slaughter. However, out of the 717 cases, only 220 were culled and four deaths were reported when all 717 cases should have been culled. Hence, it is suspected that there might be illegal slaughtering or movement of animals during the outbreak period which could have helped in spreading this disease throughout Peninsular Malaysia (WAHIS, 2023). The report on WAHIS which recorded 1712 vaccinated animals also did not tally with the report submitted by the Malaysian Department of Veterinary Service to the updated Lumpy Skin Disease (LSD) coordination meeting for Southeast Asia in 2022, which recorded a total of 91124 heads of cattle and buffalo vaccinated (Hamidah, 2022). This possibly indicates that there might be an error in reporting, which is one of the key limitations of this study that will be further discussed here.

LSD in Malaysia has a high morbidity rate of 18.14% but a low mortality rate of 0.04%. This result is consistent with the report by WOAHA in 2017 which states that the morbidity rate usually ranges between 10-20% while the mortality rate ranges between 1-5% (WOAHA, 2017). A higher morbidity rate is reported in Kelantan and Terengganu at 45.08% and 56.48% respectively, suggesting the potential presence of risk factors that should be investigated further. Thomas and Mare (1945) stated

that the morbidity rate can differ in a disease outbreak, depending on the host's immune status and the abundance of mechanical arthropod vectors. Some of the risk factors influencing the disease prevalence are herd size, distance to the water bodies and common food and water source (Sevik and Dogan, 2017; Ince et al., 2016; Gari et al., 2010; Namazi and Tafti, 2021). Other risk factors include warm and humid climates which promote the abundance of vectors and the introduction of new animals to the herd (Namazi and Tafti, 2021). Air current (Klausner, 2017; Rouby and Aboulsoud, 2016; Chihota et al., 2003) and mean annual rainfall (Ochwo et al., 2019) are also the risk factors influencing the transmission of LSD.

The case fatality rate is generally low at 0.63% but a higher rate is recorded in Pulau Pinang at 19.05% which could be related to the species, breed, immune status and stage of production as suggested by Tuppurainen et al. (2017) which observed that those factors mentioned can affect the severity of the clinical disease. *Bos taurus*, especially the thin-skinned Channel Island breeds tend to develop a more severe lesion, with high-producing lactating cows posing the highest risk (WOAH, 2023). However, these data are not available from the reports submitted to WAHIS, so it is not possible for us to identify the risk factors associated with LSD deaths in Malaysia.

The spatial distribution of LSD outbreaks in Malaysia shows a more concentrated outbreak occurring in Kelantan, Perlis, Perak, and Melaka, while a more scattered outbreak occurs in Pahang, Negeri Sembilan, Selangor and Johor. The scattered distribution might indicate the spread of disease through the movement of animals as vectors are not able to travel that far. According to an epidemiology study of LSD outbreaks in Albania by Gubbins et al. (2020), most transmission occurring over a short distance (less than 5 km) is likely associated with vector dispersal, while transmission over a longer distance is likely associated with animal movement. Most

blood-sucking insects can only fly a maximum of 100m if not assisted by air currents (Greenberg et al., 2012). However, we cannot rule out the possibility of vector involvement as research indicates that the direction and strength of air current might also aid in a longer distance spread of LSD via vector dispersal (Klausner, 2017; Rouby and Aboulsoud, 2016; Chihota et al., 2003). The final outbreak in Perlis is a sporadic case happening three months after the last outbreak in Selangor on 23rd February 2022, involving only one case in a farm with five susceptible cattle. This suggests that there might be undetected asymptomatic animals within the region or perhaps there are uncontrolled animal movements across the border.

The epidemic curve shows a propagated pattern with several peaks. This is in contrast with the seasonal pattern often reported in most vector-borne diseases (Gubler et al., 2001). This might be attributed to the vector abundance and uncontrolled animal movement. LSD outbreaks are typically seasonal but may occur at any time because no season is completely vector-free in many affected areas (Tuppurainen et al., 2017). LSD outbreaks tend to happen mainly during hot and rainy months, which is originally linked to higher vector abundance (Mafirakureva et al., 2017; Namazi and Tafti, 2021) and direct transmission is proven by Carn and Kitching (1995) to be inefficient in spreading the disease as no animal developed clinical signs or antibody despite being house with infected animal for a month. However, a recent study by Aleksandr et al. (2020) demonstrated that novel recombinant LSDV can be transmitted to in-contact animals in an insect-proof facility, possibly by sharing food and water troughs and direct contact with mucosa with adjacent animals. The phenotypic ability of indirect transmission through vectors and direct transmission through contact in recombinant LSDV provides extra benefit in terms of the spread of the disease over the wild-type, field strain which only has the ability of indirect transmission (Sprygin et al., 2022). Hence, sequencing may be necessary to examine

the strain present in Malaysia to implement suitable control measures. The presence of the recombinant LSDV strain may indicate the need to consider the possibility of direct transmission in the control measure since the current measures were more focused on minimising indirect transmission.

From the epidemic curve, the reduction and the subsequent halt in the number of outbreaks and cases is likely due to effective control measures implemented by local authorities. The control measures practised by Malaysia are movement control, voluntary vaccine, culling the clinical and suspected cases, followed by ring vaccination 10 km radius around the positive farm. Also, from the epidemic curve, Kelantan, Perak, and Perlis have more concentrated outbreaks at earlier epidemic days. This suggests that these areas could be the origin of the LSD outbreak in Malaysia before it spread throughout the other states in Peninsular Malaysia. It was also clear from the epidemic curve that the northern monsoon is not associated with a higher number of cases, which is commonly observed for most vector-borne diseases. In this case, since the case starts reducing on day 151, it is likely that this phenomenon occurs due to the effective control measure implemented. However, we cannot rule out that the short study duration can also be attributed to this.

Mapping of the outbreaks based on the epidemic day which shows that the direction of spread is from North to South, may suggest that the outbreak of LSD in Malaysia may have occurred due to the uncontrolled movement of animals from Thailand, considering the chronological spread of LSD in Southeast Asia from North to South (Wilhem and Ward, 2023) and the porosity of the border.

Spatiotemporal analysis reveals a most likely cluster and four secondary potential cluster areas. The most likely cluster area is in Northern Peninsular Malaysia, which covers Kedah, Perak, Pahang, Kelantan and Terengganu. The high-risk period identified was from 1st June 2021 to 31st October 2021. From here, we

can conclude that the LSD outbreaks were not randomly distributed over space and time. The high-risk period which was during the early epidemic days and the high-risk area which was located near the inter-country border, further suggest that the elevated incidence detected might be due to the uncontrolled movement of infected animals from Thailand. There was also no statistically significant increased attack rate during the Northeast monsoon from November to March, likely due to effective control measures or short study duration. This finding can help allocate resources for a more targeted intervention to curb the spread of disease in the future.

There are several limitations in this study. First, not all data is available about LSD in Malaysia. The species, breed, age, and stage of production of the cattle which might be important to study the risk factor, or the economic impact of the disease are not well documented in the WAHIS database. Secondly, the data used in this study is prone to information bias due to incomplete or inaccurate data or reporting bias. The third limitation is that there was heavy reliance on the country's reporting and surveillance system. Fourthly, underdiagnosis or under-reporting of cases might happen due to subtle signs, unobservant farmers, lack of knowledge among farmers and non-compliance among farmers. The fifth limitation is that the disease control practised in each farm can affect the spatiotemporal distribution of the disease. For instance, vaccination can result in fewer reported outbreaks or cases because it can reduce the number of animals with clinical diseases. This limitation is highlighted since Malaysia practices both ring vaccination during outbreaks and voluntary vaccination.

6.0 CONCLUSION

The LSD outbreak in Malaysia, occurring between 1st May 2021 to 31st May 2023 has a high morbidity rate of 18.14% but a low mortality rate of 0.04%. The outbreak of LSD in Malaysia likely occurred due to uncontrolled animal movement. A propagated epidemic curve pattern, instead of a seasonal pattern is observed, possibly due to vector abundance in Malaysia which is hot and humid in general, uncontrolled animal movement and potential emergence of new recombinant LSDV strain. The high-risk area is identified in Northern Peninsular Malaysia, which covers Kedah, Perak, Kelantan and Terengganu from 1st June 2021 to 31st October 2021. There was no seasonal trend observed during the Northeast monsoon, which is commonly associated with vector-borne disease, which is likely due to effective control measures, short study duration or the emergence of recombinant LSDV. The findings in this study can help policymakers to implement effective control measures.

7.0 RECOMMENDATIONS

Follow-up studies should be done to examine the risk factors associated with LSD outbreaks and the economic impact of LSD on farmers in Malaysia. Collaboration with local vet authorities is recommended to obtain more up-to-date and complete data about LSD in Malaysia. More research on wild ruminants should be done to examine their role in the epidemiology of LSD. Serological surveillance may also help to establish if the wild ruminant could act as a maintenance host. Sequencing to examine the LSDV strain present in Malaysia might be needed, especially because the novel recombinant LSDV strain is capable of both indirect and direct transmission.

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9.0 APPENDICES