Lumpy skin disease is expanding its geographic range: A challenge for Asian livestock management and food security

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Abstract

In recent years, lumpy skin disease virus has extended its geographical range outside of endemic sub-Saharan countries to the Middle East and Asia indicating transboundary spread. Recently, lumpy skin disease (LSD) outbreaks have been reported in Asian countries such as Bangladesh, India, China, Nepal, Bhutan, Vietnam, Myanmar, Sri Lanka, Thailand, Malaysia, Laos and for the first time and represent a cause of serious concern for their livestock and dairy industries. This report summarizes information on the recent outbreaks of LSD in southern Asia and emphasizes the threat it poses to neighbouring countries. Various strategies and actions needed to control outbreaks of this emerging disease in Asia are also suggested.

Abbreviations: LSD, Lumpy skin disease; LSDV, Lumpy skin disease virus; FAO, Food and Agriculture Organization; OIE, Office Internationale deś Epizooties (World Organization of Animal Health); PCR, Polymerase chain reaction; GPCR, G protein-coupled chemokine receptor; RPO30, RNA polymerase subunit-30; NCBI, National Centre for Biotechnology Information; ELISA, Enzyme Linked Immunosorbant Assay; DIVA, Differentiating infected from vaccinated animals.

Keywords: Cattle; Capripoxvirus; Control; Skin; Transboundary spread

Introduction

Lumpy skin disease (LSD) is a highly host-specific, debilitating disease of all cattle breeds and water buffalo (*Bubalus bubalis*) (Badhy et al., 2021). The causal agent, lumpy skin disease virus (LSDV), belongs to the genus *Capripoxvirus* of the family *Poxviridae.*[1] Disease presentation varies from acute or subacute, to inapparent in infected cattle. The outcome of infection includes abortion in cows, infertility in both bulls and cows, loss of body mass, and a sharp decline in milk production (Tuppurainen and Oura, 2012, Tageldin et al., 2014). The natural incubation period of LSDV is believed to be 1–4 weeks, and the clinical disease is well described. Clinical signs include a fever of 40–41 °C, reluctance to move, inappetence, salivation, lachrymation, and nasal discharge. The superficial lymph nodes (subscapular and pre-crural) of infected cattle are enlarged. Also, skin nodules varying in number and size are the classical manifestations of LSD (Tuppurainen et al., 2005, Tuppurainen and Oura, 2012). Recent reports from epidemic areas in the Middle East and Europe have indicated a disease morbidity of 5–45%, and mortality usually <10% in cattle[2] (FAO, 2017). The ulceration of nodular lesions can lead to the formation of permanent scars that decrease the value of hides (Chaudhry et al., 2011).

Due to the impacts of global climate change and changes in trading patterns of animals and animal products, LSD has become an emerging disease threat. In the Middle East and Asia, civil conflict hampering veterinary services and disrupting livestock movement patterns aids in the increased spread of the virus. Increased illegal trade of animals leads to further spread (Tuppurainen and Oura, 2012). Several outbreaks of LSD, once endemic only to the African continent, have sporadically occurred outside Africa, in Madagascar (1929), Israel (1989), and the Middle East (e.g., Kuwait 1991) and more recently in the United Arab Emirates (2000), Bahrain (2003), Oman (2009), Bangladesh[3] (2019), India[4] (2019), China[5],[6] (2019, 2020), Nepal[7] (2020), Sri Lanka[8] (2020), Bhutan[9] (2020), Vietnam[10] (2020), Myanmar[11] (2020), Thailand[12] (2021), Malaysia[13] (2021), Laos[14] (2021) and Cambodia[15] (2021) (Odend'hal, 1983, Shimshony, 1989, Tuppurainen and Oura, 2012, Tageldin et al., 2014). The disease has now become firmly established in Asia and has emerged as a challenge for Asian livestock management and a threat to food security.

The mechanical transmission of LSDV by blood-feeding vectors (Carn and Kitching, 1995), mainly biting flies of the genus *Stomoxys* and mosquitoes of the genus *Aedes,* is considered to be the most significant mode of transmission (Chihota et al., 2001, Issimov et al., 2020). Ticks may also play an important role in the transmission of LSDV as the virus has been detected in the saliva of ticks fed on LSDV-infected cattle (Tuppurainen et al., 2011, Lubinga et al., 2013). Additionally in ticks, transovarial transmission may occur, as well as overwintering of the virus by transstadial persistence (Lubinga et al., 2014a, Lubinga et al., 2014b). The prolonged excretion of LSDV in bovine semen, even in asymptomatic bulls, raises concerns for venereal spread (Irons et al., 2005). Transmission of the virus by artificial insemination has also been confirmed (Annandale et al., 2014). A recent study suggested that contact transmission of LSDV can occur in the absence of insect vectors. Using a virulent viral strain resulting from recombination between a live-attenuated vaccine and a field strain (Saratov/2017), Aleksandr et al. (2020) experimentally infected bulls and showed that in-contact animals in an insect-proof environment were found to be infected with this LSDV strain.

Although variable LSDV antibody responses have been detected in blue wildebeest (*Connochaetes taurinus*), eland (*Taurotragus oryx*), giraffe (*Giraffa camelopardalis*), impala (*Aepyceros melampus*), greater kudu (*Tragelaphus strepsiceros),* and African buffalo (*Syncerus caffer*), the role of wildlife in the transmission of the disease is still unclear (Hedger and Hamblin, 1983, Barnard, 1997, Fagbo et al., 2014).

LSD control in countries free from capripoxviruses is by strict regulation of imported animals and animal products from countries in which the virus is present. Should the disease be introduced in a non-endemic country, stamping out of infected animals, movement controls and improved biosecurity would need to be implemented. In an endemically-infected country, vaccination using a live attenuated vaccine strain is commonly recommended as a control measure, in addition to vector control (Tuppurainen et al., 2014, Haegeman et al., 2021). The use of live-attenuated vaccines is not without the risk of the emergence of hybrid viruses with novel transmission abilities. Recombination between vaccine and field viruses has been reported to cause some outbreaks (Sprygin et al., 2020). Therefore additional or alternate control strategies including improved vaccines are required. The need for rapid, improved and sensitive diagnostic techniques was further highlighted in the light of recently-reported contact transmission of the virus by Aleksandr et al. (2020).

Epidemiology of recent outbreaks

LSD was recently reported for the first time in Bangladesh, China, India, Nepal, Sri Lanka, Bhutan, Vietnam, Myanmar, Thailand, Malaysia, Laos and Cambodia (Fig. 1), mainly affecting Asian breeds of cattle (*Bos indicus*) and Asiatic (water) buffaloes (*Bubalus bubalis*), although in some countries (such as Nepal) *Bos taurus* breeds were also affected.

Fig. 1. Chronological order of lumpy skin disease virus (LSDV) outbreaks in Asian countries (2019–2021). Year of LSD emergence: blue markers (2019), orange markers (2020), red markers (2021).

Bangladesh

The first outbreak in Asia occurred in Bangladesh, in mid-July 2019, affecting 66 cattle in Chittagong/Chattogram (Badhy et al., 2021). A second outbreak occurred in Dhaka in October 2019 and affected 16 cattle. A third outbreak occurred in Khulna in March 2020 and affected 33 cattle, while a fourth outbreak occurred in Rajshahi in March 2020 and affected 60 cattle. No deaths were reported in any of the outbreaks and morbidity rates were variable in each.[3]

China

The first outbreak in the People's Republic of China occurred in Xinjiang Province in the first week of August 2019 and affected 65 cattle, with all affected animals slaughtered. By July 2020, eight outbreaks in seven Chinese provinces were reported, affecting 156 cattle and resulting in the death of seven[6] (Lu et al., 2020).

India

An outbreak occurred in India in the second week of August 2019, affecting nine cattle in the state of Orissa/Odisha. Two other outbreaks occurred later in August, in the same state affecting 79 cattle. Overall the apparent morbidity and mortality rates in the country were 8.48% and 0%, respectively[4] (Sudhakar et al., 2020).

Nepal

The first Nepalese outbreak occurred in the fourth week of June 2020 (Acharya and Subedi, 2020), affecting 500 Jersey crossbred, Holstein Friesian crossbred, and local cattle of various age groups (4 months to 8 years old). Within a week, several areas of Koshi Province were affected leading to the death of 12 cattle. The second and third outbreaks in July 2020 affected 700 Jersey crossbred cattle of various age groups in the Narayani Province and 20 Jersey crossbred cattle of various age groups in two regions of Province No. 2. In the Bagmati Province, 175 Jersey crossbred cattle were affected and no deaths were reported in the latter outbreaks. Four more outbreaks occurred in July and August, two in the Gandaki Province, also affecting Murrah buffaloes. However buffaloes that were not in direct contact with cattle appeared unaffected. A total of 1220 animals were affected including 12 deaths. Overall the apparent morbidity and mortality rates in the country were 14.52% and 0.14%, respectively.[7]

Sri Lanka

Six outbreaks occurred from the first week of September 2020 in Kopay town near Jaffna City in the Northern Province affecting 36 cattle. The second outbreak occurred in Chavakachcheri, a large town in Jaffna in the same province affecting nine cattle, and three further outbreaks occurred in the same province affecting 36 cattle. The last outbreak occurred in the Vavuniya area in the Northern Province affecting two cattle. No deaths were reported in any of the outbreaks.[8]

Bhutan

Seven outbreaks occurred in the fourth week of September 2020 affecting 147 cattle, and leading to three deaths. Overall the apparent morbidity and mortality rates in the country *were 11.86% and 0.24%, respectively.*[9]

Vietnam

In the second week of October 2020, the virus was detected in cattle and buffaloes in Vietnam. By March 2021, 163 communes in 65 districts of 18 cities and provinces were affected, with LSD found among 2748 susceptible cattle and buffaloes; there were 137 cases, two deaths and nine animals were destroyed.[10]

Myanmar

In an initial outbreak in the second week of November 2020, six cattle were affected in the Me Thei and Nyein Chan, Tabayin and Shwebo areas of Sagaing Region. The morbidity rate was 9.52% and no deaths were reported in any of the outbreaks.[11]

Thailand

The first outbreak in Thailand was reported in the second week of April 2021 in the Saen Suk and Panom Phrai districts of Roi Et Province. This affected 10 beef cattle, which were culled.[12]

Malaysia

From the second week of May 2021, 23 outbreaks occurred in the states of Perak, Kedah, Pahang, Perlis, Melaka and Terebgganu affecting 54 cattle and disease appeared to be confined to these states in the Malaysian peninsula.[13] No deaths were reported in any of the outbreaks, although six affected animals (from small-holder farms in villages) were culled.

Laos

After the initial outbreak in the third week of May 2021, a total of nine outbreaks occurred in the provinces of Savannakhet and Vientiane affecting 369 cattle. No deaths were reported in any of the outbreaks.[14]

Cambodia

An outbreak which started in the last week of May 2021 (World Organisation for Animal Health [OIE], 2021e) affected 103 cattle in backyard farms in the Akphivoath Village in the Preah Vihear Province. No deaths were reported.[15]

Phylogeny and possible sources of LSDV introduction

Based on the above reports to OIE of LSD incursions in Asian countries, the presence of LSDV in all countries was confirmed using real-time PCR assays. The analysis of the first official country outbreak reports indicated that most cases occurred in Nepal, followed by Laos and Bangladesh with most incursions in summer (Fig. 2). This emphasized the seasonality of outbreaks that coincided with the abundance of insect vectors during those periods.

The source of the first outbreak in Bangladesh as well as the origin of infection in other Asian countries is unknown. There is regular movement of cattle and buffaloes between India, Bangladesh and Nepal (Roche et al., 2020). From China, the virus may have spread to Bangladesh, as Bangladesh imports live animals from China. The chronology of outbreaks also supports this hypothesis (Fig. 1).

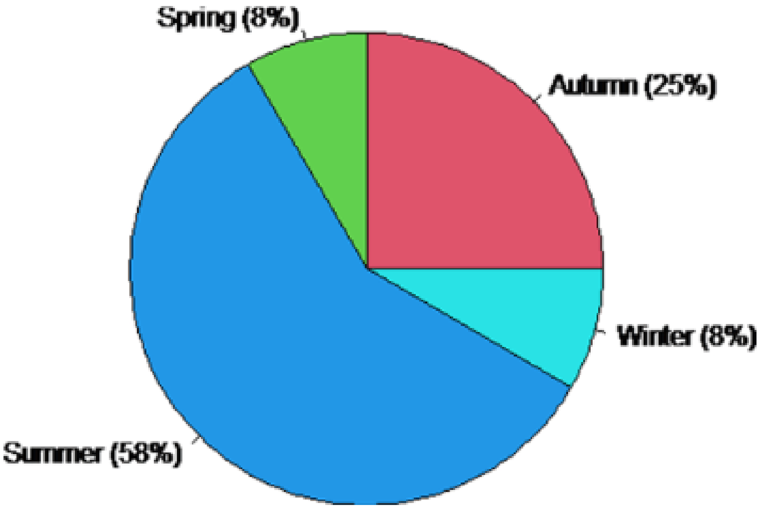

Fig. 2. Season-wide incidence of lumpy skin disease (LSD) in cattle in Asian countries, showing highest incidence in summer and lowest in spring and winter. Incidence is calculated based on the first official country report to the World Organisation for Animal Health (OIE).

To understand the epidemiological links and infer possible means of the introduction of LSDV in Asian countries, phylogenetic analyses were undertaken on samples obtained from the countries that recently reported LSD, using two LSDV genes: the G protein-coupled chemokine receptor (GPCR) and RNA polymerase subunit (RPO30) genes. LSDV gene sequences from Russia, Kazakhstan, Bangladesh, India and China submitted between 2018–2021 were obtained from the public database NCBI[16] (Table 1). LSDV isolates from Russia were included because a recent report has also indicated that the virus in China originated in Russia (Lu et al., 2020).

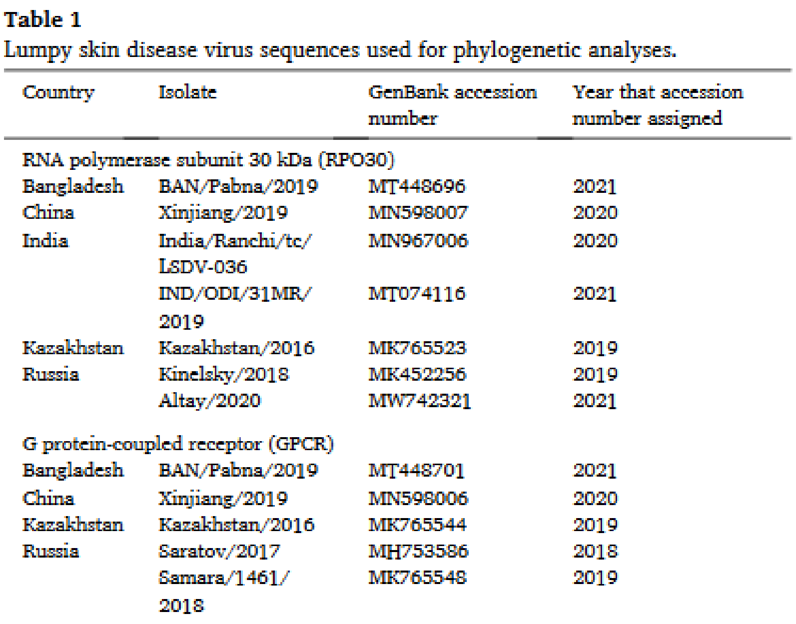

Table 1

Lumpy skin disease virus sequences used for phylogenetic analyses.

Country	Isolate	GenBank accession number	Year that accession number assigned
RNA polymerase subunit 30 kDa (RPO30)			
Bangladesh	BAN/Pabna/2019	MT448696	2021
China	Xinjiang/2019	MN598007	2020
India	India/Ranchi/tc/LSDV-036	MN967006	2020
	IND/ODI/31MR/2019	MT074116	2021
Kazakhstan	Kazakhstan/2016	MK765523	2019
Russia	Kinelsky/2018	MK452256	2019
	Altay/2020	MW742321	2021
G protein-coupled receptor (GPCR)			
Bangladesh	BAN/Pabna/2019	MT448701	2021
China	Xinjiang/2019	MN598006	2020
Kazakhstan	Kazakhstan/2016	MK765544	2019
Russia	Saratov/2017	MH753586	2018
	Samara/1461/2018	MK765548	2019

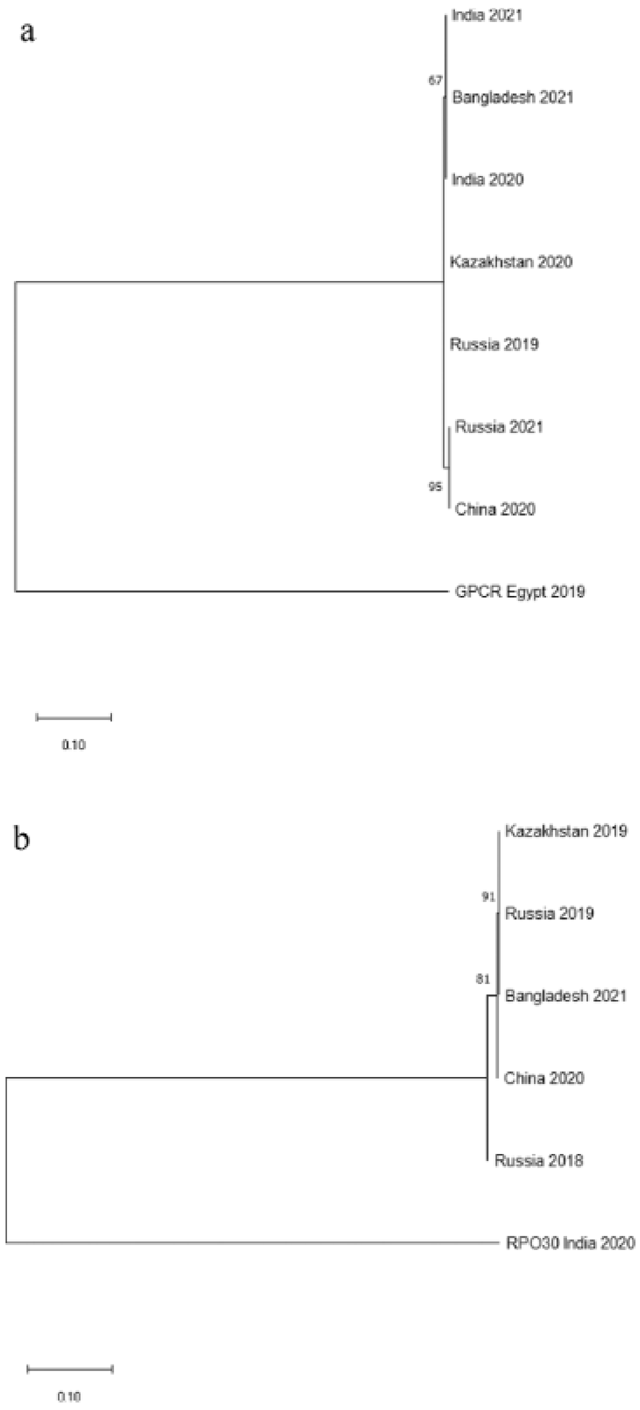

Fig. 3. Phylogenetic analyses of available lumpy skin disease virus (LSDV) sequences in the public database (2018–2021) based on (a) RPO30 gene and (b) G protein-coupled receptor (GPCR) gene. For both trees the evolutionary history was inferred by using the Maximum Likelihood method and Tamura-Nei model (Tamura and Nei, 1993). The tree with the highest log likelihood (-1571.96) is shown. The percentage of trees in which the associated taxa clustered together is shown next to the branches. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the Tamura-Nei model, and then selecting the topology with superior log likelihood value. The tree is drawn to scale, with branch lengths measured in the number of substitutions per site. This analysis involved eight nucleotide sequences. Codon positions included were 1st + 2nd + 3rd + Noncoding. Evolutionary analyses were conducted in MEGA X (Kumar et al., 2018).

The RPO30 gene sequences were from cattle and included sequences from India, Russia, Bangladesh and China. The source of the sequence from Kazakhstan is not known. Another sequence from Russia used in this report was obtained from *Stomoxys calcitrans* (Fig. 3a). Sequences from the GPCR gene were from cattle and included samples from Russia, Bangladesh and China. The source of the gene sequences from Kazakhstan and Russia is unknown (Table 1; Fig. 3b).

Alignments were performed using Clustal W method and Lasergene software (version 11, DNASTAR) and phylogenetic trees were constructed using the maximum likelihood method with 1000 bootstrap replicates using MEGA X software version 10.1.8. Overall the GPCR and RPO30 gene sequence alignments and phylogenetic analyses indicated a high percentage identity (GPCR, 98.4–100%; RPO30, 99.1–100% identity) among LSDV sequences across countries suggesting the LSDVs circulating in Asian countries are the same (Fig. 3a and b).

Phylogenetic analyses performed in another study with isolates obtained from Bangladesh indicated a resemblance (100% nucleotide identity) to the KSGP-0240, NI2490, and Kenya strains of LSDV (Badhy et al., 2021). The LSDV isolates also clustered with LSDVs of Indian field isolates, recombinant field isolates from Russia, Russia/Udmurtiya/2019, and Russia/Sara-tov/2017. However, these strains are different from the African, Middle Eastern, and European strains of the virus as well as from the recently emerged LSDV variants from Russia and China (Badhy et al., 2021).

Two routes of transmission are hypothesized: either the virus moved from Russia or/Kazakhstan to China through the import of live cattle, or by the movement of insect vectors across the border from Russia/Kazakhstan to China. This is well supported by phylogenetic analysis of the RPO30 gene (Fig. 3a) and is consistent with published data by Lu et al. (2020).

Another possibility for the introduction of LSDV in the region is through migratory wild birds infested with LSDV-infected ticks. While migratory birds spend summer in Russia/Siberia, they fly southwards in winter. The northern part of Bangladesh is a potential migratory wild bird habitat. Specifically, in a recent study, a total of 30 species of migratory aquatic wild birds were identified in the char-lands of the Padma River[17] . Therefore, it is possible that LSDV reported from Bangladesh was previously circulating in Kazakhstan. This is supported by the phylogenetic analysis of the GPCR gene (Fig. 3b). The close association of the recent Indian/Bangladeshi LSDV isolates with 2019 isolates from Russia and Kazakhstan, based on sequence data of the RPO30 genes, suggests that the virus present in Russia/Kazakhstan may have been introduced to India first via migratory wild birds (Fig. 3a). It is possible that once introduced to India, LSDV spread eastward via cattle movements to Nepal, Bhutan, Bangladesh, Myanmar, Vietnam, Laos, Thailand, Cambodia and Malaysia (Fig. 1).

Although the outbreaks in China occurred at the same time as outbreaks in India and Bangladesh, the Chinese outbreaks were in regions geographically distant to other Asian countries and thus seem unlikely to be the source of those outbreaks. However, despite the recent outbreaks in Vietnam being geographically distant from those in China, the LSDV isolates from each showed a close molecular relationship. The sequence data of the p32 and RP030 genes of the Vietnamese LSDVs were 100% identical to the 2019 Chinese LSDV isolates (Tran et al., 2021) suggesting those outbreaks may be linked.

The low mortality rate of LSD in animals in Asia compared to outbreaks in Africa might be attributed to the virulence of the strains of LSDVcurrently circulating in Asia but this should be further investigated.

Control measures used

Based on recent reports to OIE, the disease in Asian countries was controlled by zoning and movement restriction, surveillance outside of the containment zone, official disposal and destruction of animal carcasses, products and waste, surveillance, quarantine, disinfection of the premises, vector control and vector surveillance was practiced.

While the use of vaccines for LSDV control is well documented (Tuppurainen and Oura, 2012, Tuppurainen et al., 2017), no vaccination programmes were practiced in any of the countries except China[6] and Vietnam (Tran et al., 2021). Stamping out could not be implemented in Nepal as laws prohibited the culling of animals (Anonymous, 2017).

Economic losses and impact on food security

LSD could cause huge economic losses in affected Asian countries, with direct livestock and production losses estimated to be worth up to $US 1.46 billion[18] (Roche et al., 2020). Indirect losses resulting in trade barriers including the export of live animals, meat and meat products, dairy products, and hides are likely to be higher than direct losses and are estimated at US$ 5.51 billion[18] (Roche et al., 2020). A Jordanian study indicated that the treatment of an LSD-affected animal could cost approximately US$ 38.40[19] (Abutarbush et al., 2015). In Ethiopia, the annual economic losses per animal due to LSD were estimated to be US$ 6.40 for indigenous cattle and US$ 58.00[20] for Holstein Friesian cattle (Gari et al., 2011). A study in Kenya estimated the economic impact of LSD on farm-level to be US$123.00[18] for indigenous and US$755.00[18] for exotic cattle (Kiplagat et al., 2020).

In milking cows, a sharp drop in milk yield in an LSD outbreak can cause considerable economic losses to farmers. In Asian countries, an estimated 400 million women and children are impacted by milk production both for domestic consumption and their livelihood (Roche et al., 2020, Kumar et al., 2011). LSD could thus threaten the livelihood of poor farming communities.

Risk to Pakistan

No LSD outbreaks have yet been reported in Pakistan, which has approximately 85 million cattle and buffaloes and the third largest cattle and buffalo populations in Southeast Asia (Roche et al., 2020). In Pakistan, livestock is the largest subsector in agriculture that contributes approximately 12% to the national GDP. Pakistan also produces almost 62 million tons of cattle and buffalo milk and 18,751 hides annually. Over 8 million rural farmers and their families are engaged in livestock production and they obtain approximately 40% of their income from livestock (Anonymous, 2021).

Since Pakistan borders with China, India, and Iran, all of which have reported LSD, and the presence in Pakistan of some of the competent vectors (*Rhipicephalus appendiculatus* and *Rhipicephalus decoloratus* ticks) of LSDV further increases the risk of an LSDV incursion into the country (Lubinga et al., 2014a, Lubinga et al., 2014b, Hussain et al., 2021). This will have a major economic impact on the livestock and export industry and will put neighboring countries such as Afghanistan also at risk, as Afghanistan imports live cattle from Pakistan (Roche et al., 2020).

Conclusions

The recent outbreaks of LSD in South Asian countries raise concerns for the transboundary spread of LSDV in the region. Although cattle movement is considered the main source of virus transmission, it is worth noting that the outbreak in Nepal occurred during the COVID-19 lockdown, when legal cattle trade declined. However, transmission of LSDV by insect vectors including ticks may have been responsible for such spread. With the possibility of LSDV infection of various life stages of ticks as well as the overwintering of the virus in tick vectors (Lubinga et al., 2014b), LSDV could be introduced into a country and circulate in the field for more than a year before an outbreak occurs. Migratory birds, which can disperse ticks, as well as their nymphal and to a lesser extent larval stages across national borders, are also a risk (Molin et al., 2011).

Countries bordering LSDV-infected countries should evaluate the potential of a transboundary incursion of the disease and prepare an emergency response plan. Countries should raise their biosecurity standards for cattle imports, prevent transboundary movement of animals including cattle smuggling, strengthen insect control programs and veterinary services for early disease detection, and monitor wild bovids for the presence of LSDV. Transboundary cattle trade should necessitate LSDV-free status, and animal quarantine should be enforced before allowing entry into a country. Molecular tools such as real-time PCR can be used to monitor the spread of the virus in carrier livestock. Pen-side or field-deployable diagnostic tests such as loop-mediated isothermal amplification could be useful for rapid detection of LSDV in cattle before importation (Batra et al., 2015). The surveillance of LSDV in insect vectors using molecular tools may also predict a potential incursion. Based on the recent reports to the OIE vector surveillance was practiced only by 25% of the affected countries but should be expanded across the region.

Additionally, countries at risk of LSDV introduction should conduct a comprehensive risk assessment and risk analysis followed by preparation of contingency plans in case of disease introduction. For example, such plans could include compartmentalization and zoning to prevent disease spread, the use of modern disease reporting systems, strategies for culling and vaccination, incentives to farmers for disease reporting and compensation when culling is needed.

Once LSD is introduced, it is very difficult to control and eradication will be difficult or impossible. In most Asian countries, stamping out is not possible either because of economic constraints or laws that prohibit animal slaughter. The phylogenetic analyses of circulating strains of the virus could shed light on the possible origin of outbreaks of LSD. This will also assist in strain-specific vaccination campaigns.

Livestock authorities in Pakistan should embark upon a comprehensive plan of farmer education and awareness about LSD. This can be done by reaching farming communities with free of charge LSDV vaccinations or by announcing 100% compensation for culling LSDV-affected animals as was done in Turkey. Turkey and Israel both enforced mandatory LSDV vaccination that helped in curtailing the disease in those countries (Calistri et al., 2020).

Farmers in Pakistan should be informed of possible disease incursions, and advised to promptly report skin disease resembling LSD in cattle or buffaloes to animal health authorities. Additionally, passive surveillance by veterinarians could assist in diagnosis and confirming increased frequency of skin diseases as was practiced in Azerbaijan (Zeynalova et al., 2016). Since some LSDV-infected animals can be asymptomatic (Tuppurainen et al., 2005), passive surveillance is not very effective in detecting LSD in all animals. Active surveillance based on clinical examination, real-time LSDV-specific PCR and ELISA testing could help in early detection (Roche et al., 2020). Capacity building for laboratory testing, staff training, and proficiency should be available. The identification of local vectors and the control of known LSDV vectors such as *Stomoxys calcitrans* should be addressed. Furthermore, experimental and field studies at the wildlife-livestock interface could inform the role of possible novel reservoir hosts in the epidemiology of the disease.

If LSD is introduced into a country such as Pakistan, a Government-approved policy on how mass vaccination will be conducted in locally relevant conditions would facilitate timely control of the disease. The development of improved vaccines with a DIVA approach containing local circulating strains should be considered (Byadovskaya et al., 2020). The cost of vaccination can be justified and is less than the economic damage caused by LSD (Roche et al., 2020). Possible trade issues and how to approach these issues should also be outlined.

In summary, LSDV continues to spread in Asian countries and concerted efforts involving experts from multiple disciplines such as virology, parasitology, pathology, epidemiology along with veterinary clinicians in the field, will be required to curtail losses by this emerging disease. Additionally, the role of international agencies, such as OIE and FAO, will be crucial in bridging technical gaps by linking experts across countries. Experience and resource sharing among the affected and at-risk countries will be required to address this transboundary challenge.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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[18] US$1 = approx. £0.76, €0.90 at 1 January 2020.

[19] US$1 = approx. £0.65, €0.83 at 1 January 2015.

[20] US$1 = approx. £0.65, €0.75 at 1 January 2011.