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Risk factors associated with lumpy skin disease in cattle in West Kazakhstan

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ABSTRACT

Lumpy skin disease is an important emerging disease posing a threat to the livestock industry worldwide. Moreover, factors involved in disease transmission in the field and at farm level remain unidentified. This research was based on a cross-sectional study using a questionnaire administered through face-to-face interviews with affected farmers. From January 2021 to July 2021, 543 households were visited in four provinces of the West Kazakhstan region to assess the prevalence of LSD and its associated risk factors. Animal and farm level risk factors were examined using univariable and multivariable mixed effect logistic regression. At animal level, the factors associated with LSD outbreaks include herd size Medium OR = 0.68, (95% CI: 0.54–0.84); large OR = 0.63, (95% CI: 0.49–0.81), purchasing animals OR = 11.67, (95% CI: 8.87–15.35), and selling animals during LSD outbreak OR = 1.24, (95% CI: 1.06–1.45). The overall animal level and herd level LSD prevalence were 10.2% (95% CI: 9.6 –0.10.9) and 49.2% (95% CI: 45.0 – 53.4) respectively. Our study demonstrates the dissemination of LSDV from primary outbreaks to new areas and risk factors associated with LSD in Kazakhstan. This finding will enhance knowledge on disease epidemiology and help develop coordinated actions in prevention and control of the possible LSD outbreaks.

1. Introduction

Lumpy skin disease virus (LSDV) belongs to the Capripoxvirus genus of the Poxviridae family. It is a highly contagious infectious disease of cattle. It is characterised by fever, skin nodules, enlargement of superficial lymph nodes, salivation, lacrimation, nasal discharge, and oedema and swellings of the joints and the dewlap (Davies, 1991). The World Organization for Animal Health classifies Lumpy Skin Disease (LSD) as a notifiable disease due to its significant economic impact (Tuppurainen and Oura, 2012).

LSD was first discovered in Zambia, where it was recorded in 1929. Subsequently, LSDV has become endemic across almost the entire African continent and in the Middle East, Turkey, and Azerbaijan, and is continuing to spread north, posing a threat to Europe and the Central Asia region. In 2015, LSD outbreaks were documented in Greece (Tasioudi et al., 2016), from where it spread to the Balkans. Similarly, in 2015, the disease was clinically confirmed in North Caucasus in Russia, where it became epidemic and spread throughout the country (Zeynalova et al., 2016; Sprygin et al., 2018). In 2016, LSD re-emerged in several regions of Southern Russia, including Astrakhan oblast bordering Atyrau oblast in West Kazakhstan.

An incursion of LSD in Kazakhstan was first recorded in July 2016, in Makash village in Atyrau oblast, located 49 km from the borderline with the Russian Federation. At that time, Russian veterinary authorities had already reported seven outbreaks of LSD in border farms located near the Kigash River Delta, which serves as a natural border with common pastures on both sides of the river. On 7 July 2016, the owner of a small cattle farm practicing mixed dairy and beef management reported that

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several animals at the holding were showing novel clinical signs. The unusual behaviour of the cattle within the herd was combined with multiple skin lesions similar to those reported by Davies (1991) and Weiss (1968); fever; nasal discharge; superficial lymphadenitis; anorexia; emaciation lameness; and reluctance to move, feed, and drink. Several animals within the herd demonstrated high fever followed by abortion and death. The post-mortem investigation revealed extensive haemorrhage of the uterus. Moreover, skin lesions in the form of multiple convex indurations were visible in aborted fetuses, similar to those described by Rouby and Aboulsoud (2016). The Office International des Epizooties (OIE) World Animal Health Information System (WAHIS) was notified as soon as LSD suspicion was confirmed by positive laboratory results on 22 July 2016.

According to the State Veterinary Control Service report, the current LSD status in Kazakhstan is negative, and no outbreaks have been reported since 2017. However, little is known about the magnitude of LSD occurrence and its predisposing factors.

A similar cross-sectional study in Ethiopia indicated LSD prevalence of 8.1% (95% CI: 7.3–8.9) at the animal level and 42.8% (95% CI: 37.5–48.3) at the herd level (Gari et al., 2010).

Thus, the aim of this study was to determine the prevalence of lumpy skin disease at individual and herd levels and risk factors associated with disease in West Kazakhstan.

2. Materials and methods

2.1. Ethics statement

The protocol was approved by the Human Ethics Committee of the Marat Ospanov West Kazakhstan State Medical University (permit number: 01-05-07-21-2020). The purpose and methods of the current study were thoroughly explained to all participants, and informed oral consent was obtained and documented in the questionnaire.

2.2. Study area

The study area was located in the west part of Kazakhstan (51° 38’ 55° 57’N, 46° 9′ −46° 4′*E*)– Atyrau, Aktobe and West Kazakhstan region. The entire study area borders with the Russian Federation (Fig. 1). The map was generated using ArcGIS Pro 2.8 (ESRI, CA, USA). The coordinate system used was WGS 1984 Web Mercator (Auxiliary Sphere). The basemap was developed using Land use/cover map (Abdi, 2020).

2.3. Study design and study population

This research was conducted in Kazakhstan, where a LSD outbreak was documented for the first time in 2016 (Orynbayev et al., 2021). A questionnaire based cross-sectional study was conducted between January and June, 2021, in three districts of Kurmangazy, three districts of Oiyl, three districts of Syrym and three districts of Zhanibek province.

A comprehensive questionnaire was designed to assess the magnitude of LSD occurrence and the risk factors associated with it. The questionnaire contained thirty-five questions grouped into two main sections. The first section contained questions related to herd size, breed of animals, contact with other domestic animals, year and month of LSD occurrence. The second section contained questions regarding herd management including feeding and watering management, animal movement, vaccination, treatment.

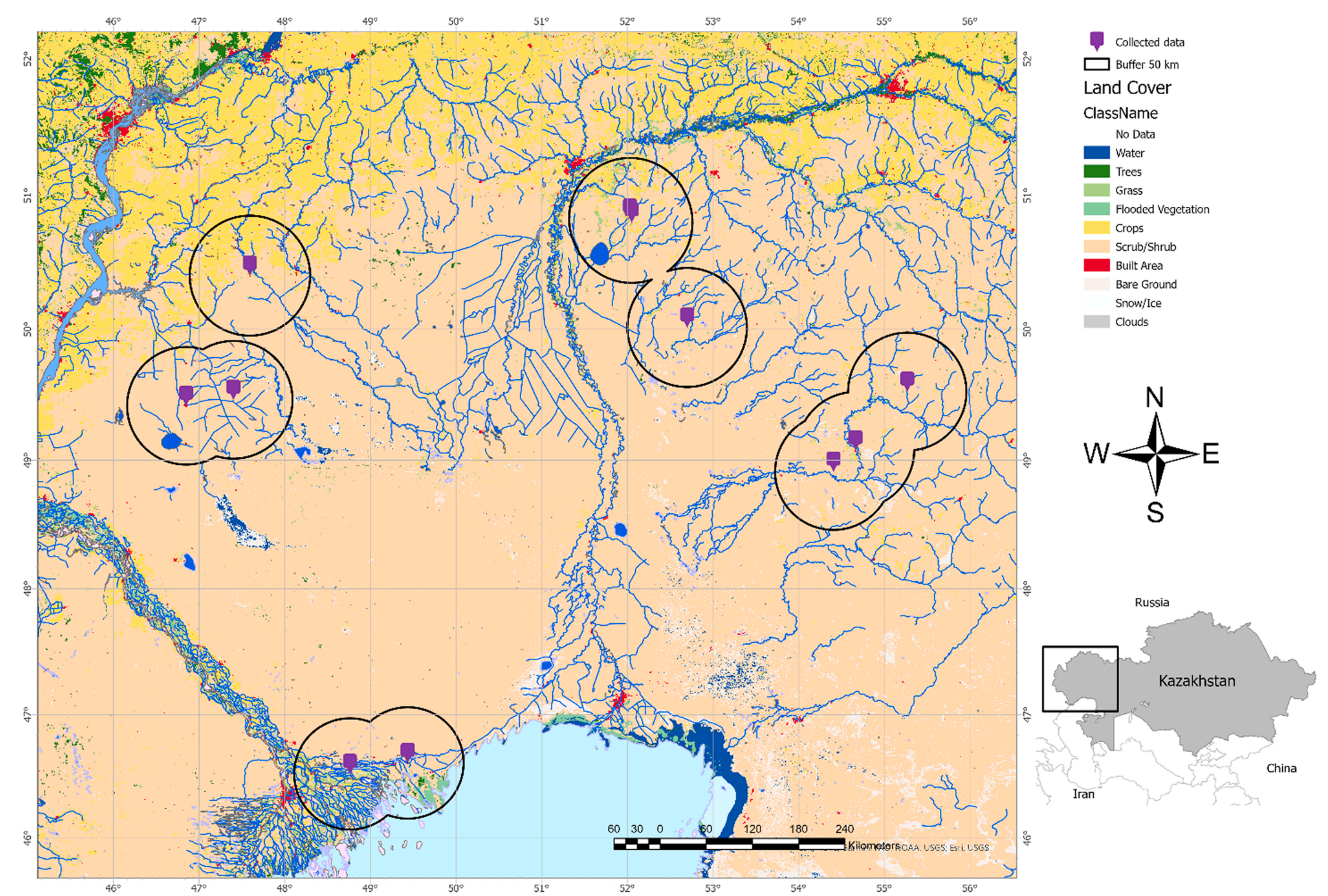

Fig. 1. The location of the lumpy skin disease (LSD) outbreak in West Kazakhstan oblast. The black box is an overview map of cattle distribution ((FAO) Food and agriculture organisation).

The questionnaire was pretested and modified after ten interviews to improve clarity of questions. Herd owners were interviewed using Kazakh and Russian languages depending on participants' native background.

According to the national census, the population of the West Kazakhstan region made up about 3 million people in an area of 736 241 km2. The cattle population in the same region is approximately 1.5 million heads. Most of the farms practised sedentary management. People with cattle farms were the participant of this study.

2.4. Sample size determination and sampling

The sample size was determined by considering an expected prevalence of 50%, a confidence level of 95% and required precision of 5% using the formula in Thrusfield (2018). Accordingly, the total households required for the study was 384; however, about 70% of the.

sampling units were added for consideration of clustering and non-response rates, which gives a total sample size of 543 smallholder farmers. The study districts were selected due to the high concentration of livestock and occurrence of disease within the study area. Information on the occurrence of confirmed LSD outbreaks in the selected districts between July 2016 and August 2017 were obtained from the District Veterinary Offices (DVO). The survey data were collected from a total of 543 smallholder farmers. These farms were selected randomly from LSD affected districts. Categorisation of farms into affected or non-affected farm was done based on presence or absence of LSD affected animal in the farm. A farm was considered affected if LSD-characteristic clinical signs such as numerous firm nodules, hyperaemia, excessive salivation and lacrimation were observed in at least one cattle in the herd. Each enroled farm owner was given a thorough description of LSD clinical signs to avoid confusion with other possible skin diseases such as, dermatophilosis, demodecosis, ringworm and bovine herpes mammilitis. Farmers were enroled and interviewed based on their willingness to participate in the study. When the selected farm owner declined to participate in the study, another farm owner was selected to replace them. The participation rate was 90%. Interviews were conducted on the farm and all interviewers were trained in using the survey.

2.5. Data management and statistical analysis

The collected data were entered into a Microsoft Excel spreadsheet, edited and analysed using STATA 14 software package. No personal information was collected or stored to protect privacy of participants.

Descriptive statistics such as table was used to summarise and present the data collected. The animal level or herd level prevalence of LSD was calculated as percentage by dividing the number of animals or herd positive for LSD to the total number of animals or herds examined.

Multilevel mixed effect logistic regression model taking herd/farm as a random effect was employed to assess the presence of association between LSD positive results (dependent variable) and independent variables (herd size, presence of other animals in the farm, using common grazing area, tick infestation, types of grazing, purchasing animals, where animals purchased, knowledge on LSD transmission, and selling animals during LSD outbreak). Following the univariable analysis, variables with P values < 0.25 were checked for multicollinearity between each other and those not collinear with each other were fitted into a multivariable multilevel mixed effect logistic regression model. The final model was obtained by a backward stepwise elimination procedure while checking for confounding. Confounding was considered present if there is at least a 25% change in the coefficients of any of the remaining variable after removing a non-significant ($p > 0.05$) variable from the model.

3. Results

3.1. General description of herd management

According to data collected, all households reported breeding local Kazakh crossbreed as the main cattle species. Similarly, all households reported using bulls for herd reproduction. Herd size varied differently from 3 to 47 heads among households, averaging 18 heads per heard. Daily cleaning of animal dung was performed in all farms interviewed, whereas 64 (12%) farms do not practice cleaning animal feeding troughs. Nearly two-thirds (65,7%) of households reported tick infestation in their herds. From the 543 households interviewed, 239 (44%) reported new cattle introduction to their herd, totalling 414 head. Animals were mainly purchased from the same village farms, nearby villages, and Town animal markets. A significant portion of newly introduced animals (67.1%) were purchased from neighbouring villages. Cattle purchased from the same village farms and town animal market accounted for 30.6% and 1.4% respectively. A great portion of herd owners (79%) reported presence of sheep and goats in their farms.

3.2. LSD occurrence

Data from the $n = 543$ questionnaires showed that, to a varying degree, all selected provinces were affected by LSD incursion between 2016 and 2017 (Table 1). The primary outbreak of LSD occurred in 2016 in the Western parts of the country in Atyrau oblast. Subsequently, LSD incursion was traced in most neighbouring districts spreading all over West Kazakhstan oblast. At animal level, the highest LSD prevalence was reported in Oiyl province, accounting for (11.3% (95% CI: 10.1 – 12.6)) and at herd level the highest LSD prevalence was reported from Zhanibek (51.5% (95% CI: 43.0–60.0)) (Table 1).

Ninety-seven per cent of respondents reported they had not heard about LSD prior to outbreak commencement in 2016. Affected herd owners reported that skin nodules were a clinical sign, which alerted them first. Two-thirds (68%) of those who reported symptoms peculiar to LSD declared that skin nodules were present on the head, the neck, and the back parts of the animal body, whereas 32% of those interviewed reported their animals having had lesions on the neck, the back and the udder. Of the study population, 40% of participants reported that they had been involved in animal trading (selling) during the outbreak, and about a quarter of interviewees (21%) reported that they had sold cattle exhibiting signs of LSD. A large portion of herd owners (47.3%) reported sending animals exhibiting LSD signs to a common grazing area.

Only 6 (1%) respondents were certain about the possible mode of transmission of LSD, and a small portion (3%) of those interviewed stated the importance of vaccination as a preventive tool. An overwhelming majority of households (98%) used broad-spectrum antibiotics to treat LSD. The average cost of antibiotic treatment varied considerably and averaged 15 USD per sick animal.

3.3. Risk factors for lumpy skin disease occurrence

Summary of the univariable mixed effect logistic regression at herd level is demonstrated in Table 2. Variables with P values < 0.25 in the univariable analysis, herd size, using common grazing area, and type of grazing were fit to the multivariable model and all of them were found insignificant.

At animal level, the variable herd size, presence of other animals, using communal grazing area, purchasing animals, and selling animals during LSD outbreak were found with P values < 0.25 in the univariable mixed effect logistic regression analysis taking herd/farm as random effect and these variables were fitted to the multivariable model. The final multivariable mixed effect logistic model identified herd size, purchasing, and selling animals during LSD outbreaks as the most important risk factors in relation to LSD occurrence at animal level

Table 1
Descriptive statistics of animal and herd level LSD prevalence by province in Kazakhstan during an outbreak of LSDV in 2016.

Province	Animal level			Herd level		
	No. of animals examined	No. of positive animals	Prevalence (95% CI)	No. of herds examined	No. of positive Herds	Prevalence (95% CI)
Kurmangazy	1852	190	10.3 (9.0 – 11.7)	109	51	46.8 (37.6–56.2)
Oiyl	2581	292	11.3 (10.1 – 12.6)	159	76	47.8 (40.1–55.6)
Syrym	2189	193	8.8 (7.7 – 10.1)	143	72	50.3 (42.2–58.5)
Zhanibek	1985	206	10.4 (9.1 – 11.8)	132	68	51.5 (43.0–60.0)
Overall	**8607**	**881**	**10.2** (9.6 - 10.9)	**267**	**543**	**49.2 (45.0 – 53.4)**

Table 2
Univariable analyses of potential risk factors for LSD at herd level (n = 543) using mixed effect logistic regression model including district as random effect during an outbreak of LSDV in Kazakhstan in 2016.

Risk factors	Category	Number of herds examined	Number (%) of positive herds	Odd ratio	Overall P-value
Herd size	Small	161	85 (52.8)	Ref	
	Medium	320	148 (46.3)	0.67	0.047
	Big	72	34 (47.2)	0.70	0.398
Presence of other animals	None	63	30 (47.6)	Ref	
	Horse and/ or sheep	480	237 (49.4)	1.11	0.710
Using common grazing area	No	23	15 (65.2)	Ref	
	Yes	520	252 (48.5)	0.51	0.142
Tick infestation	No	186	94 (50.5)	Ref	
	Yes	357	173 (48.5)	0.92	0.645
Type of grazing	Communal pasture	104	45 (43.3)	Ref	
	River plains	439	222 (50.6)	1.33	0.221
Purchasing animals	No	304	144 (47.4)	Ref	
	Yes	239	123 (51.5)	1.18	0.353
Where animals purchased	None	304	144 (47.4)	Ref	
	Same village	77	42 (54.5)	1.34	0.259
	Nearby village	158	80 (50.6)	1.14	0.523
	Town animal market	3	1 (33.3)	0.53	0.609
	Other	1	0 (0.0)		
Knowledge on LSD transmission	No	512	253 (49.4)	Ref	
	Not sure	25	11 (44.0)	0.80	0.600
	Yes	6	3 (50.0)	0.89	0.895
Selling animals during LSD outbreak	No	322	157 (48.8)	Ref	
	Yes	221	110 (49.8)	1.05	0.801

Table 3
Final multivariable model of risk factors related to lumpy skin disease at individual animal level using mixed effect logistic regression model including herd as random effect during an outbreak of LSDV in Kazakhstan in 2016.

Risk factors	Coefficients	Standard error	Odds ratio (95% CI)	P-value
Herd size: Small	Ref			
Medium	-0.39	0.11	0.68 (0.54–0.84)	0.001
Large	-0.46	0.13	0.63 (0.49–0.81)	0.000
Purchasing animals: No	Ref			
Yes	2.46	0.14	11.67 (8.87–15.35)	0.000
Selling animals during LSD outbreak: No	Ref			
Yes	0.22	0.08	1.24 (1.06–1.45)	0.006
Inter-herd variance	0.401	0.099		

(Table 3). The inter-herd variance was estimated as 0.401 (Table 3) resulting in an ICC of 0.109.

4. Discussion

The present study provided additional information regarding LSD dissemination in Kazakhstan. Initially, a survey study was planned to be conducted in two provinces of Atyrau oblast, as these districts were reported to OIE as LSD positive. However, from personal communications with local veterinarians, it was found that LSD outbreaks occurred in several other neighbouring provinces as well. To understand the scale of LSD spread in West Kazakhstan, it was decided to expand our study area and visit those farms suspicious of LSD outbreak in 2016.

In the current study, the knowledge and experience of farmers was assessed to identify LSD cases in their herds based on clinical manifestations. Veterinary service practitioners were involved for a consultation to confirm the information about the outbreak cases declared by the farmers in these districts. In addition, skin diseases, such as bovine herpes mammilitis, ringworm, dermatophillosis and demodicosis were taken into account as differential diagnoses during the survey.

Almost all respondents demonstrated a lack of knowledge on LSD transmission and prophylaxis methods such as vaccination. Instead, antibiotic treatment (300 mg oxytetracycline, 20.0 mg flunixin meglumine, Nitox Forte, NITA-FARM, Russia) was used to treat symptomatic LSD. Moreover, antibiotics were used as preventive tools to combat disease spread. The mass use of antibiotics by farmers may be explained by the reported rapid recovery of cattle with LSD where nodules reportedly disappeared after 1–2 days. From personal communication, herd owners who did not use antibiotics to treat their animals reported severe disease manifestation, secondary complication cases, slow recovery process. They stated that systemic antibiotics and anti-inflammatory drugs were given to affected animals for skin infections, mastitis and pneumonia. Pneumonia is a common complication in animals with lesions in the oral and respiratory tract.

In Oiyl and Zhanibek provinces, the LSD prevalence was higher than in other nearby regions. According to the local veterinary practitioner's report, this is highly likely due to the herd size, utilisation of common watering and grazing lands and free animal movements (Sultankul, 2021). Mixing animals from different herds can accelerate the infection spread between animals (Ocaido et al., 2009; Gari et al., 2010; Tuppurainen and Oura, 2012).

It is also noteworthy that new animal introductions to a herd is one of the main risk factors in the LSD outbreak within the herd. This implies an infected animal might be introduced to the herd owing to the negligence of herd owner purchasing LSDV positive animal without proper veterinary examination (Gari et al., 2010; Salib and Osman, 2011; Kiplagat et al., 2020). In line to this, in our study, the variables purchasing of new animals, herd size and selling animals during LSD outbreaks are significantly correlated with LSD occurrence at animal level. As smallholding farms are mostly market oriented in Kazakhstan, cattle and their products are the only source of income. Farmers reported that selling animals during the outbreak was a critical measure to get rid of sick or LSD suspicious animals from their herds, whereas others reported that they were afraid their animals could lose value if infected. This in turn, could greatly contribute for disease propagation in animals with mild and asymptomatic LSD.

Furthermore, it was established that in 2018 LSD reached Northern (Kostanay oblast) and Southern (Almaty and Zhambyl oblasts) parts of Kazakhstan (Amirgazin and Ragatova, 2020). However, this was not officially reported, and the consequences remain uncertain. For instance, in North Kazakhstan, the State Veterinary Control Service has referenced that the LSD case identified was mainly attributed to post-vaccination reactions that in some circumstances caused a generalised LSD. In South Kazakhstan, on the contrary, there was no understanding of the aetiology of LSD. Most farmers believed that the reasons for LSD occurring on their farm were mixing of affected cattle with unaffected during communal grazing. However, the current study did not measure LSD occurrence in these oblast's, and this observation needs to be analysed with caution, as detailed vaccination history was not available during the study period. On the other hand, in a more recent study, LSD emergence was reported in Ili Kazakh Autonomous Prefecture in China (Lu et al., 2020). LSD foci were reported 20 km from Kazakhstan borders, and the source of infection is unknown. Moreover, Wang et al. (2021) stated that there were no activities detected in transboundary regions between Kazakhstan and China in animal trading and illegal animal movements. Given these circumstances, it can be assumed that insect vector involvement may play a crucial role in LSDV introduction to new areas. In several recent studies, LSDV transmission has been experimentally demonstrated using haematophagous flies (Issimov et al., 2020; Sohier et al., 2019). Moreover, the flight range of some blood-feeding insects can cover large territories; in addition to this, it can be amplified by environmental and technical factors such as wind and transportation importing animals (Sprygin et al., 2018; Saegerman et al., 2018). This could also be supported by the previous findings into LSDV retention in *Stomoxys* fly species, where the virus could survive in infected flies up to 48 h if the midgut barrier breached (Issimov et al., 2021).

There are several limitations to this retrospective study that should be acknowledged. Firstly, the most important constraint was the reliability of data obtained from households. Farmers could distort data and like other businessmen, they might have the tendency to exaggerate their losses. Secondly, farmers interviewed on case herds remember events differently, whereby it was not feasible to ascertain causation while recall bias. As a result, the information provided cannot be ruled out. Notwithstanding these limitations, the findings of this study have demonstrated the significance of future qualitative studies, which in turn will shed light on the knowledge gap toward LSD, which was found among smallholding farms in Kazakhstan.

Additionally, from personal communication, it was found that herd management system among farms surveyed had not altered after outbreak. Therefore, it is suggested that implementing nationwide training programmes is essential to improve the preparedness and awareness of farmers and veterinary personnel to withstand future emerging diseases, including LSD. Presumably, this could be performed by a distribution of leaflets outlining the following epidemiological aspects of infectious diseases: prophylaxis and treatment methods; potential routes of disease transmission; shared use of grazing and watering points; introduction of new animals. Such measures, if taken, will promote biosecurity consciousness of the population and navigate the control and prevention of infectious diseases in herds in Kazakhstan. Moreover, risk maps of potentially epidemiologically disadvantaged areas could also be built based on existing knowledge of risk factors associated with LSD to target disease surveillance and control activities.

5. Conclusion

The propagation of the disease over such a large territory requires further study. In Kazakhstan, LSD was recorded mostly among emaciated animals, lactating cows. In the primary outbreaks, the morbidity rate of the herds varied from 50% to 100%. Introduction of new animals, herd size and selling animals during LSD outbreaks are substantial factors for the LSD occurrence. The overall animal level and herd level LSD prevalence were 10.2% (95% CI: (9.6 - 10.9) and 49.2% (95% CI: 45.0 – 53.4) respectively. Given the fact that there is a significant density of livestock in the West Kazakhstan region, the data obtained will enhance insight of disease epidemiology as well as examine the risk factors relating to LSD and will guide the development of prevention strategies suitable for use in the Central Asian region.

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Ethics statement

The protocol was approved by the Human Ethics Committee of the Marat Ospanov West Kazakhstan State Medical University (permit number: 01-05-07-21-2020).

CRediT authorship contribution statement

Arman Issimov: Supervision, Conceptualization, Methodology, Writing – original draft. **Wassie Molla**: Data analysis, Validation. **Kaissar Kushaliyev, Nurzhan Abekeshev**: Funding acquisition, Validation, Resources, Conceptualization, Methodology, Investigation. **Nurkuisa Rametov**: Software, Formal analysis. **Svetlana Bayantassova, Assylbek Zhanabayev, Assel Paritova, Malik Shalmenov, Altay Ussenbayev, Zhomart Kemeshov**: Resources, Conceptualization, Methodology, Funding acquisition, Data curation, Formal analysis, Validation, Investigation. **Peter White**: Investigation, Writing – review & editing.

Declaration of interest

None.

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