Review Article

Review on Lumpy Skin Disease and its Emerging Threat to Livestock in Nepal

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Abstract | Lumpy Skin Disease (LSD) is an economically important transboundary viral disease of livestock belonging to the genus *Capripoxvirus* was reported which was said to have originated from Zambia in Africa. LSD can be transmitted by both the vector and non-vector routes and is mainly seen in the rainy season. It mainly affects cattle and buffalo manifesting nodules in skin and mucous membrane with a high fever. Since the first report of this disease from the Morang district of Nepal in 2020, the disease has been spreading in various parts of the country. Cattle are comparatively more affected in Nepal than buffalo. Though this disease has less mortality rate it causes great economic losses by decreasing milk production, abortion, infertility, and other complication. The disease is comparatively new to Nepal but has already covered a wide geographical range but vaccination is yet to be introduced. The disease doesn't have any specific treatment only treatment after infection is supportive therapy but it is reported that control and prevention are possible by immunization, maintaining biosecurity in the herd, controlling the vector, and isolating the infected animals.

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Introduction

Lumpy skin disease (LSD) is an infectious viral disease caused by the lumpy skin disease virus (LSDV). The disease is called by various names such as LSD, pseudo-urticaria, Neethling virus disease, exanthema nodularis bovis, etc. (Al-Salihi, 2014; OIE, 2017). It is classified as a transboundary disease with only a few hosts mainly ruminants (cattle and buffalo), sheep, and goats even in close contact with infected cattle were found unaffected in Africa (Davies, 1991). The younger animals are found to be more susceptible to the virus (Tageldin *et al.*, 2014). The non-ruminants are not affected by the virus (Shen *et al.*, 2011). As the disease cause economic loss, reduction in production, poor skin quality, reduced growth, infertility, and even death of animal so it is listed as a notifiable disease under the World

organization for Animal Health (OIE) guidelines (OIE, 2021; Tuppurainen *et al*., 2017). This disease manifests high fever with nodules on the skin and mucous membrane similarly, lesions in respiratory and digestive tracts, and swollen lymph nodes as characteristic features (Sevik *et al*., 2016). Being a vector-borne disease too, insects like mosquitoes, flies, and ticks are mainly responsible for transmission but other sources like contact, water, and feed can also cause the virus transmission (EFSA Panel, 2015) . As the disease causes a high fever and immune compromise, several complications like mastitis and metritis arise, causing serious production and reproduction of cattle (Tuppurainen and Oura, 2012).

It is classified as a notifiable disease by the OIE due to its magnitude of spreading nature and economic impact after the outbreak. LSD was first reported in Zambia, Africa, and then reported throughout Southern Africa and North Sudan. Outside of Africa, it was from Israel in 1989 followed by Bahrain, Kuwait, Oman, Yemen, Lebanon, and Jordan in the Middle East (FAO, 2013). In the context of the sub-continent, LSD was reported in August 2019 from India, and from there the open border, cattle smuggling nexus brought the disease to Nepal where in June of 2020 it was reported in Morang district of Eastern Nepal (Gupta *et al*., 2020; OIE-WAHIS, 2021). In a very short time, it spread to many districts mostly those that had a concentrated commercial cattle population (Acharya and Subedi 2020). The disease is comparatively new and the information regarding the status of the disease in Nepal is scarce, despite being economically important. The appearance and re-appearance of the disease have pointed out the importance in the context of Nepal. This review aims to give an idea about the scenario of disease in Nepal based on the OIE database, possible risk factors, and outcomes to the livestock and the economy.

Etiology and mode of transmission

Lumpy skin disease virus is the causative agent of lumpy skin disease which belongs to the poxviridae family, sub-family Chordopoxvirinae, and genus *Capripoxvirus* (Gumbe, 2018). Only one serotype of LSDV is reported (Sevik *et al*., 2016). The virus is closely related to sheep and goat pox virus and is morphologically enveloped by a lipid bilayer (covalently-linked) with brick-shaped, has double-stranded DNA as genome and the matured virions have large lateral bodies with an oval profile (Aleksandr *et al*., 2020; Yehuda *et al*., 2008). The virus is arranged with a 151-kbp genome consisting central coding region surrounded by inverted terminals and has 156 putative genes, however, in terminal regions, the collinearity of the genome is disrupted with low or absent amino acid identity (Tulman *et al*., 2001). The virus is stable and can withstand ambient temperature for a comparatively long time, survive in organic matter, and can be detected from the nodules of skin even after 30 days or more. Although the titer of the virus doesn't change with exposure to the pH range from 6.6-8.6 for 5 days at 37 °C it is susceptible to even moderate chemical changes with both alkaline or acidic pH and may reduce the virus load and the chemicals like ether, chloroform, formalin, phenol, per oxygen compounds, the essential oil may decrease the virus load (OIE, 2017).

LSD is reported to be transmitted by various routes like direct and indirect contact, arthropod transmission, and seminal transmission (Tuppurainen, 2015). Various arthropod is known to be a vector for transmission of the LSDV and the presence of the virus in those vectors was seen (Chihota *et al*., 2003). Sexual transmission was observed with LSD virus through infected semen of bull to the heifer and even congenitally to the fetus (Annandale *et al*., 2014; Irons *et al*., 2005). The infected bull may transfer the virus to adult females as well through natural insemination or artificial insemination and the infected female may give birth to calves with skin lesions (Tuppurainen *et al*., 2017). Sharing common grazing areas, feeding, watering method, and reduced movement of the animal were reported as a risk factors for LSD transmission (Gari *et al*., 2010). The various routes of possible transmission of LSDV in cattle can be summarized in Figure 1, as explained by Das *et al*. (2021), thus proving that biosecurity can play an important role in its control.

Risk factors

The morbidity rate ranges from 10 and 20% whereas mortality rates are generally 1 to 5% (OIE, 2017). The incubation period is generally 1 to 4 weeks (Tuppurainen and Oura, 2012). Das *et al*. (2021) in their review have classified the risk factor of disease into three categories as host-associated factors, agent-related factors and environment, and management factors and have stated that LSDV can be isolated from various exudations of body, saliva, blood, milk, and semen. For conditions like that of Nepal, similar risk

factors can play role in the spread of the virus. Open borders with India and warm climatic conditions can be important risk factors for Nepal. With the increase in demand for milk products in Nepal, the population of high yielding cross breed cattle is also increasing in trend and it has increased the risk of spread of the diseases, many studies have suggested that cross-breed animals are more susceptible to the infection (Paudel *et al.*, 2021; Das *et al.*, 2021). And same is with the cross-breeds of Nepal which can be understood from Table 1. The diseases are susceptible to all breeds and sex of cattle and buffalo but Bos taurus which generally has thin skin and is high milk-producing animals are more vulnerable (Gumbe, 2018; OIE-WAHIS, 2021). As the rainy season supports the increased population of different arthropods, the season is favorable for LSD and the cases may reduce virtually in the winter season (Mulatu and Feyisa, 2018). However, Machado *et al.* (2019) observed the spread of the disease in more temperate and colder regions than the disease was previously seen. It was observed that female animals were more infected with the LSD virus than male animals (Gharban *et al.*, 2019) which was similar to the investigation by Ayelet *et al.* (2014) who found more female cases (23.07%) than male cases (13.5%). According to Kasem *et al.* (2018), various stress conditions in female cattle like pregnancy, parturition and feed supplied during the lactation period may be the reason for the high occurrence of disease in a female than in males.

Clinical symptoms and findings

The distinguishing character of the disease is the appearance of skin nodules in about 50% of susceptible animals, generally, of size less than 1cm to 8cm which are round in shape and emerge above the skin surface along with fever up to 40 to 41°C (50% of animals) and nasal discharge (in about 81.3% cases), swollen lymph nodes in 100% of cases, abortion (0.4%) in pregnant animals, decreased in milk production (on average 72.5% in buffalo and on an average 54.16% in cattle), lameness (6% of cases) (Awadalla and Hassan, 2011; Gibbs, 2021; KC *et al.*, 2020; Mathan, 2011; OIE, 2017; Spickler, 2008). The nodular lesion may be firm and hard to moist or necrotic or slough which is seen in the various region mainly in the abdomen, flank, and thigh. The nodular lesion may be seen in the upper part of the digestive tract (9.86%), rumen (2.82%), upper respiratory tracts (7.04%), and even in the lungs (4.23%) (Gharban *et al.*, 2019; Sanz-Bernardo *et al.*, 2020). Other symptoms may be mucopurulent nasal discharge, conjunctivitis, corneal opacity, and even blindness (Awadalla and Hassan, 2011; Coetzer *et al.*, 2018). In the histological examination of infected animals, the epidermis has degenerative and necrotic parts of the keratocyte, intracytoplasmic inclusion bodies, and vesicles, the dermis has edema, hemorrhage, and the influx of lymphocyte, disrupted wall of a muscular blood vessel (Sanz-Bernardo *et al.*, 2020).

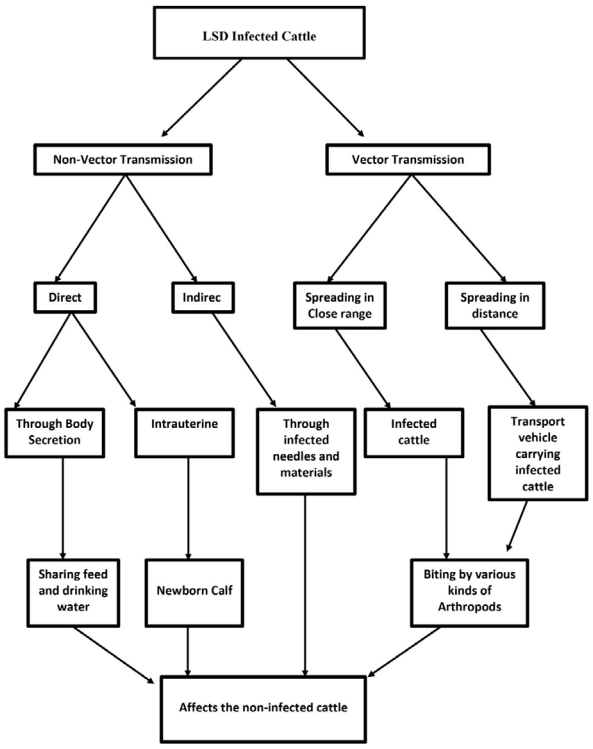

Figure 1: *Mode of transmission of Lumpy skin Disease, with both vectors borne and non-vector borne being explained in the paper of Das et al. (2021).*

Diagnosis

The diagnosis of Lumpy skin disease can be done based on clinical sigh and symptoms shown by the animals. The symptoms can be acute, mild, or chronic depending on the condition of the animal. In the lab condition, confirmatory diagnosis can be done by using various advanced techniques like Virus isolation and culture, serological test, Polymerase chain reaction (PCR), Dot blot Hybridization (DBH), agar-gel immunodiffusion test (AGID), indirect Enzyme-linked immunosorbent Assay (ELISA), direct fluorescent antibody test, west blotting, routine histopathology and immune histopathological staining (Awad *et al.*, 2010; OIE, 2021; Tuppurainen *et al.*, 2005). The disease's differential diagnosis should be done with pseudo cowpox, vaccinia virus, stomatitis, bovine herpes mammalities, dermatophilosis, insect bites, cutaneous tuberculosis ringworm (Das *et al.*, 2021; Gumbe, 2018).

Table 1: *Area wise case distribution in Nepal till August 2021.*

Area	Cases	Animal affected	Age group
Makawanpur	175	Jersey Cross-Breed	2 to 7 years old
Morang	500	Jersey cross breed, HF cross breed, Local cattle	4 months to 8years old
Kailali	6	Cross breed cattle	3 months to 7years old
Kavrepalanchowk	1	Murrah buffalo	3 years old
Kathmandu	1	Jersey cross breed	2 years old
Tanahu	1	Local cattle	4 years old
Rautahat	20	Jersey cross breed	4 to 6 years old
Chitwan	700	Jersey cross breed	various Age group
Kaski	16	Jersey, HF cross breed, Local cattle, Murrah buffalo	3.5 to 8 years old
Total	1420		

Source: *(OIE-WAHIS, 2021) https://wahis.oie.int/#/report-info?reportId=37253.*

Current scenario in Nepal

Lumpy Skin Disease (LSD) was first reported in 2020 June in the Morang district followed by several places (OIE-WAHIS, 2021). Among the Suspected cases of Diseases as of August 2021, about 99% of cases were seen in cattle (OIE-WAHIS, 2021). Total Cases reported for cattle are 1415 and for Buffaloes 6, and out of them 12 deaths were observed (OIE-WAHIS, 2021). The latest case distribution in Nepal compiled from (OIE-WAHIS, 2021), is shown in Table 1. Figure 2 shows the geographical distribution of the disease. From Table 1 and Figure 2, it can be seen that the disease is spread in the diverse geographical regions of Nepal. According to the report of (OIE-WAHIS, 2021), LSD was seen in the Morang district in June 2020, in July 2020 in Chitwan, Rautahat, Makawanpur, Kaski, Tanahu, Kathmandu, Kavrepalanchowk, and in Kailali district on August 2021. Nepal receives heavy monsoon from June to September (Nayava, 1974) and it can be noted that the disease is seen from June to August month which is coincidently the rainy season in Nepal, and a similar thing was reviewed by Mulatu and Feyisa (2018) as well. The molecular study by Koirala *et al.* (2022) found that the LSDVs isolated from the confirmed cases in Nepal are closely related to the virus from Kenya and similar to those found in neighboring countries like India and Bangladesh. Although the movement of animals is restricted by the quarantine system of the government of Nepal, the spread of disease is seen in several districts even during lockdown situations to control COVID-19 which may be due to the illegal movement of animals by animal traffickers from the neighboring countries (KC *et al.*, 2020). The information regarding risk, current situation, and distribution of vectors in Nepal are yet to be published to get a clear picture of the situation in Nepal (Poudel, 2020).

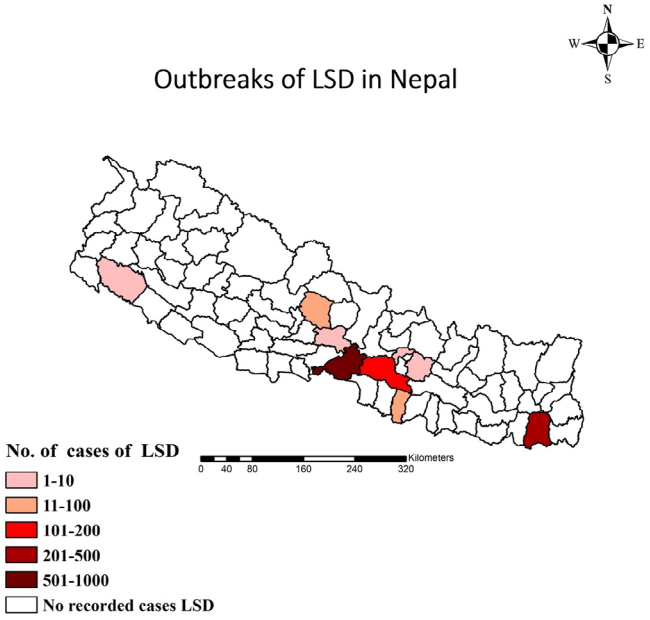

Figure 2: *Geographical Distribution of LSD Outbreaks in Nepal.*

Economic importance of LSD

There is the economic and social effect of lumpy skin disease on the society and economy of the country (Das *et al.*, 2021). It causes a reduction in milk production from 10% to 85% (Namazi and Tafti, 2021) and in the case of Nepal, the preliminary data shows the average reduction in milk production of 58.7% (Roche *et al.* 2020). The effects like abortion, infertility, and damaged animal causes loss. The infected animals either indigenous or exotic are replaced causing an economic burden to the framer (Alkhamis *et al.*, 2020). The disease is economically important even though the morbidity and mortality rate is low as the disease causes long-term loss in production (Abdulqa *et al.*, 2016). There may be indirect economic impacts like

restriction in trade of animals, cost of immunization, treatment and quarantine cost, and maintenance of biosecurity of the herd (Das *et al*., 2021). The viruses of the group Capripoxvirus like the LDV virus are regarded as the potential agent for agroterrorism by the government of the United States (Tuppurainen and Oura, 2012). The chance of LSDV being the source of agroterrorism is high in African countries as well (Mulatu and Feyisa, 2018). If it is used as the weapon of agroterrorism then it may lead to great economic loss in Nepal and the whole world as well. The disease is comparatively new in the context of Nepal (KC *et al*., 2020), so the exact scenario of farmers may not be figured out by the authority.

Public health/zoonotic importance

It was considered a non-zoonotic disease but, in the recent finding in Cairo, Egypt the human infection was also seen. In recent findings, the person to person transmission was also seen in the area with infected animals, with clinical findings like fatigue, weight loss, high fever, itching around nodules of skin, edema, and swollen lymph (Ahmed, 2019). The case of human infection is not reported from Nepal to date but there is scope for it.

Treatment and control

There are no specific antiviral drugs available but, supportive treatment can be given to the infected animals which include the treatment of the skin lesions and antibiotics against secondary skin infection and pneumonia, and some anti-inflammatory drugs (Babiuk, 2018; Thomas, 2002; Vinothraj *et al*., 2020). The use of diclofenac gel in the swelling region and the application of sulphonamide power on nodular lesions was found effective by Paul (2020). Feyisa (2018) found out the combination therapy of Dexamethasone for three days and broad-Spectrum antibiotics were effective in LSD virus infection. Dexamethasone has good anti-inflammatory action (Tsurufuji *et al*., 1984) and broad-spectrum antibiotics were found effective to check the secondary bacterial growth (Pandeya *et al*., 2021). The tropical application of antiseptic ointment with fly repellent properties can be a good choice (Islam *et al*., 2021; Vinothraj *et al*., 2020). Ethnoveterinary medicine has been reportedly used by various cow shelters (gaushalas) in Nepal with varying degrees of recovery. Vaccination plays a key role in the prevention of diseases and the vaccine used for LSD is a live vaccine Department for Environment, Food, and Rural Affairs (DEFRA, 2018) but is still not available in the context of Nepal (KC *et al*., 2020).

Prevention strategies for Nepal

The import of livestock and its product are already banned in Nepal by the government and control plans are being formulated at the government level (Poudel, 2020). The Department of Livestock Service (DLS) of Nepal closely monitoring the disease situation in Nepal and is adopting various control and prevention methods like epidemiological investigation of the disease, improving the animal quarantine system in high-risk border districts of Nepal, and controlling all possible vectors (Acharya and Subedi, 2020). The DLS is also actively educating the veterinarians and animal health workers and facilitating for tentative diagnosis and treatment at the field level.

Suggestion

The spread of the diseases can be controlled by restricting the movement of livestock, depopulating the infected and in-contact animals, quarantine system before introducing them to the herd, avoiding the mixing of the herd during grazing and watering (Gumbe, 2018), bulls used for breeding should be diagnosed for LSDV before use and annual vaccination program should be made (Mulatu and Feyisa, 2018), but slaughtering of cattle is prohibited in Nepal as the cow is considered sacred animals in a religious point of view (Acharya *et al*., 2019). Vector control and biosecurity can be key strategies to overcome the negative impact along with the quick introduction of a vaccination program in Nepal.

Conclusion and Recommendations

The disease is new in the context of Nepal, and is in spreading is the various geographical location of Nepal. Although much of the information is yet to be officially released and the death rate of animals is low in Nepal, there can be a great economic impact that should not be neglected. Cattle especially cross-breed should be taken care of and awareness at the farmers level should be made. The possible vector, biosecurity, and animal quarantine are key points to be watched out by the concerned authority in Nepal along with the vaccination program.

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Novelty Statement

This is a review paper describing about the Lumpy Skin disease (LSD) and the current scenario of LSD based on the database of OIE.

Author's Contribution

MG and KK Conceptualization of the study. PK and MG literature review. MG data collection. MG and PK writing the original paper. MG mapping. MG and KK review and editing. KK supervision. All authors have read and approved the manuscript.

Availability of data and materials

Data for the case outbreak of LSD in Nepal is based on OIE-WAHIS (2021) and can be accessed through the link: https://wahis.oie.int/#/report-info?reportId=37253

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

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Conflict of interest

The authors have declared no conflict of interest.

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