



Review Article

Lumpy Skin Disease Virus: An Emerging Challenge for Livestock in Pakistan

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Abstract | Lumpy virus causes the lumpy skin disease in live-stock animals like cattle and buffalo belong to Capri poxvirus genus and Poxviridae family, wide spread in across all country much damage the livestock sector in Pakistan reported in 2022. Cattle were more affected by lumpy virus than buffalo. In Pakistan transmission of lumpy virus mostly carry out via arthropods including as ticks and insects as well as toxic substances during blood feeding, has linear DNA in genome structure of 151 kb showed high stability against intense temperature. Lumpy virus affects badly to domestic animals including cattle and buffalo mainly. Symptoms of the lumpy skin disease such as high fever, respiratory and digestive tract mucous membrane, appearance of lesion on skin of affected animal. ELISAs, real-time PCR and Indirect fluorescent antibody test effectively use in diagnosis of lumpy virus. This disease leads to huge economic losses such as abortion, reduction of milk and decline in infertility. This review is also illustrating variety of vaccine recommended by authority to help full to minimize lumpy skin disease imposed by LSDV. There is no mostly effective treatment and vaccine available, only control and prevention encouragement in block and eradication of LSD.

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Introduction

Lumpy skin disease (LSD), a major threat to livestock breeding, can cause acute or subacute disease in cattle and water buffalo (Givens, 2018; Tuppurainen *et al.*, 2017). All ages and breeds of cattle are affected, but especially the young and cattle in the peak of lactation (Tuppurainen *et al.*, 2011). The reason why the World Organization for Animal Health (OIE) has placed this transboundary disease

on the notifiable disease list is due to its significant economic losses and the potential for rapid spread (Tuppurainen and Oura, 2012). The recent spread of the disease in disease-free countries indicates the importance of its transmission, as well as control and eradication (Sprygin *et al.*, 2019).

Lumpy skin disease is a contagious malady, caused by the Lumpy skin disease virus (LSDV), which belongs to genus Capripoxvirus subfamily Chordopoxvirinae

and family Poxviridae. “Neethling virus disease”, “exanthema nodularis bovis”, “Pseudo-urticaria”, and “knopvelsiekte” are some of the names given to this disease yet amongst these names, “LSD” is the one most commonly used (Carn, 1993; Capstick and Coackley *et al.*, 1961).

LSD is a vector borne pox viral disease of cattle and buffaloes that is characterized by appearance of skin nodules. The natural hosts for this virus are cattle and Asian water buffaloes (Elhaig *et al.*, 2017). Considering the potential for international spread and economic impacts the World Organization for Animal Health (OIE, 2020) classified the disease as a notifiable disease. LSD causes a huge economic impact on the livestock sector due to decreased milk production, loss of draught power, damage to skin, trade restrictions, loss of body condition, abortions, infertility and the cost of veterinary care. The disease was first identified in Zambia in 1929. LSD has spread from its origin in central Africa to the Middle east, Europe and Asia with rapid spread occurring since 2013. India reported first time in the year 2019 the State of Odisha. The surrounding countries of India-viz., Bangladesh, China, Nepal, Bhutan, Myanmar, Sri Lanka, Pakistan have also reported the LSD outbreaks (Gupta *et al.*, 2020). LSD has spread to several countries in Asia, since 2019. Recently, LSD has been detected in India, China, and Iran, all of which share Pakistan’s borders possibly indicating a transboundary transmission channel from Iran and India, both of which border southern Pakistan the outbreak started in October 2021. In November 2021, Sindh Livestock Department begin investigating an unknown skin disease in cattle which was spreading rapidly in different parts of Sindh province with significant mortality. Cows in Sindh and the southern areas of Punjab province are still infected with LSD. Insect control, Quarantines, depopulation, cleansing and disinfection is phrased as infected farms/herds are used to reduce disease burden, but vaccination remains the most effective prevention and control strategy. The GTPV and SPPV vaccination is effective against the LSD virus due to antigenic similarities (Imran *et al.*, 2022).

Materials and Methods

LSDV was first reported in the Zambia in 1929 (Morris, 1931) and insects were considered the main vectors of disease transmission. Later, the virus was

observed in Zimbabwe, Botswana and South Africa between 1943 and 1945 (Von Backstrom, 1945). In this outbreak approximately eight million cattle were affected and disease continued (Thomas and Mare, 1945; Diesel, 1949). In 1957 and 1972, LSD was reported in Kenya and Sudan, respectively (Ali and Obeid, 1977) while West Africa in 1974, Somalia in 1983 and Senegal, Mauritius and Mozambique in 2001. Now LSD has been widely spread and invaded majority countries especially African countries except Algeria, Libya, Tunisia and Morocco (Tuppurainen and Oura, 2012). It had reported in Oman, Kuwait, Egypt, Israel, and Bahrain in 2009, 1991, 2006, 2002–2003, respectively (Kumar, 2011; Tageldin *et al.*, 2014; Fayeze and Ahmed, 2011; Ali and Amina, 2013; Shimshony and Economides, 2006; Sherrylin *et al.*, 2013). This virus has then re-emerged in 2009 in a farm population of 3200 cattle in Oman (Tageldin *et al.*, 2014). At present, Pakistan is facing severe problems of LSDV almost in all districts. Global situation of lumpy skin disease showed in Figure 1.

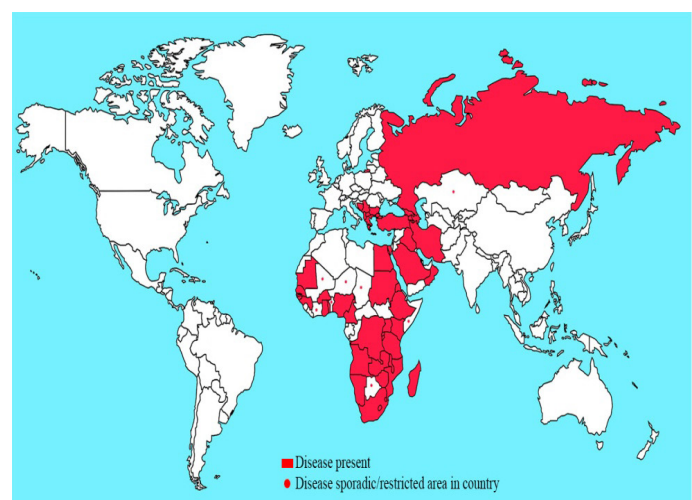


Figure 1: Global situation of lumpy skin disease.

Transmission

Lumpy skin disease can affect buffaloes, cattle, and many wild animals as reported by El-Nahas *et al.* (2011) and Lamien *et al.* (2011) while Baldacchino *et al.* (2013) observed LSD in sheep and goats. During the trade of various products such as contaminated meat, hides, fresh milk, carcasses, offal, susceptible hosts comes into contact with these poisonous or contaminated products. It has been reported that hematophagous arthropods like insects and ticks feed on the blood of infested animals and transmit virus to other animals during blood feeding (Annandale *et al.*, 2013; Lubinga *et al.*, 2015).

Genome structure

LSD is a contagious cattle disease caused by lumpy skin disease virus (LSDV; [Murphy et al., 2008](#)). The virus ([Figure 2](#)) is a large linear double-stranded DNA genome of 151 kb and belongs to one of the Capripoxvirus genus, subfamily Chordopoxvirinae, family Poxviridae ([Tulman et al., 2001](#); [Bhanuprakash et al., 2006](#); [Al-Salihi, 2014](#)). Viruses of the Poxviridae family are very similar in morphological characteristics ([Mcfadden, 2005](#)). Since the researchers have not yet resolved the particle pattern diagram of LSDV. The Capripoxvirus genus consists of SPPV, GTPV and LSDV ([Tulman et al., 2001](#); [Zare, 2010](#)). These three viruses can cause transboundary diseases with serious consequences among the ruminants, imposing a threat to the global animal husbandry ([Sprygin et al., 2018a](#)). They all have their own specific natural reservoir. The main hosts of the first two viruses are sheep and goat, while the LSDV mainly affects the cattle and water buffalo ([Afonso et al., 2012](#); [Fagbo et al., 2014](#); [Lefkowitz et al., 2018](#)).

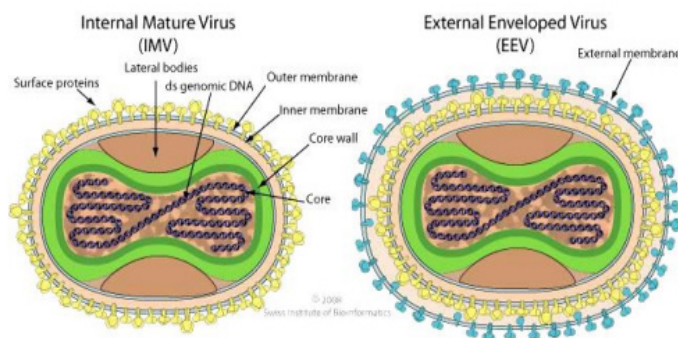


Figure 2: Structure of LSDV.

In recent years, researchers have observed the appearance of LSDV under the electron microscope, which is indeed similar to the appearance of other virus members in the Poxviridae that have been published ([Sanz-Bernardo et al., 2020](#)). The length of the virus genome is 151 kb, which consists of a central coding area and a 2.4 kb inverted terminal repeat sequence on both wings. According to the scientific prediction, LSDV has 156 putative genes. It has nine more genes than the other two viruses in the genus. Its morphological characteristics are similar to poxvirus, about 350 nanometers in length and 300 nanometers in width, with envelopes, without clotting. This virus can be proliferated in primary cells, such as lamb and calf kidney or testicular cells, sheep embryonic kidney and lung cells, and chicken embryo fibroblasts. It can also multiply in Madin-Darby bovine kidney cells

and baby hamster kidney cells (BHK-21), but the pathological changes are slower.

Stability

LSDV is resistant to high temperature and desiccation but viral particles are disinfected when exposed to direct sunlight. It has been reported that the virus becomes inactivated at 55 °C within 2 hours while takes 30 min at 65 °C temperature or direct contact with lipophilic detergents. Many disinfectants (iodine compounds, formalin, quaternary ammonium compounds, phenol, chloroform, sodium hypochlorite and ether are highly effective against LSDV ([Mulatu and Feyisa, 2018](#)).

Pathogenesis

There have been few studies conducted on the pathogenesis of LSD in cattle ([El-Kenawy and El-Tholoth, 2010](#)). In the generalized form there is viremia and fever, followed by localization in the skin and development of inflammatory nodules. Following subcutaneous or intradermal inoculation of cattle with LSDV, localized swelling at the site of inoculation developed 4 to 7 DPI which is varying in size from 1 to 3 cm and covering up to approximately 25% of the skin surface. Enlargement of the regional lymph nodes and generalized eruption of skin nodules usually follows 7 to 19 DPI. Viremia and low levels of viral shedding in oral and nasal secretions were detectable between 6 and 15, and 12 and 18 DPI, respectively following febrile reaction. LSDV is also demonstrated in saliva, semen and skin nodules for at least 11, 42 and 39 days after the development of fever, respectively. Viral replication in macrophages, fibroblasts, pericytes, endothelial cells and probably other cells in blood vessel and lymph vessel walls causes vasculitis and Lymphangitis in some vessels in affected areas, while thrombosis and infarction may result in severe cases ([Coetzer and Tuppurainen, 2004](#)). In natural infection, very young calves, lactating cows, and malnourished animals seem to develop more severe disease that may be due to an impaired humoral immunity. Antibodies were detectable 21 DPI using serum neutralization tests ([Babiuk et al., 2008](#)). Immunity after recovery from natural infection is life-long; calves of immune cows acquire maternal antibody and are resistant to clinical disease for about six months ([Al-Salihi, 2014](#); [Tuppuraine et al., 2005](#)). Eventually, affected animals clear the infection and there is no known carrier state for LSDV ([Tuppurainen et al., 2017](#)) [Figure 3](#).



Figure 3: Cattle affected by LSD.

Clinical signs

The distinguishing characteristic of the disease is the appearance of skin nodules in about 50% of susceptible animals, generally, size less than 1cm to 8cm 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 (Figure 4) (on average 72.5% in buffaloes and 54.16% in cattle), lameness (6% of cases) (Awadalla and Hassan, 2011; Gibbs, 2021; KC *et al.*, 2020; Mathan, 2011; OIE, 2017; Spickler, 2008). In the histological examination of infected animals, the epidermis has degenerative and necrotic parts of the keratinocyte, intracytoplasmic inclusion bodies, and vesicles the dermis has edema, hemorrhage, and the lymphocyte infiltration, disrupted wall of a muscular blood vessel (Sanz-Bernardo *et al.*, 2020).

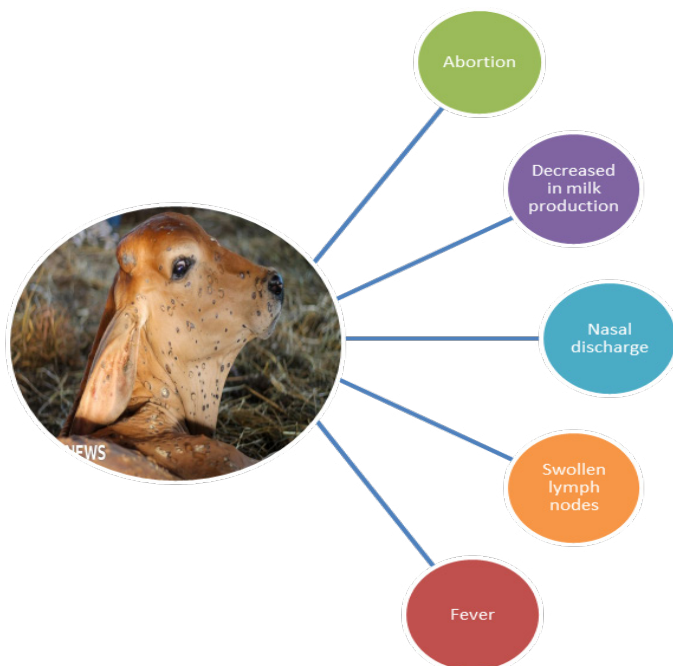


Figure 4: Clinical signs affected with LSDV.

Diagnosis

The diagnosis of exotic diseases is challenging due to lack of familiarity and logistics. In case of LSD, clinical signs can be confused with other diseases like foot and mouth disease (FMD), insect bite, demodicosis and hypersensitivity. Tentative diagnosis can be made on the basis of skin nodules on the face, eyelid, neck, muzzle, nostrils, udder, limbs. Skin biopsy sample can be collected for further confirmation of disease. Samples should be transported in transport medium with 20 to 50% glycerol in phosphate buffer saline. Skin samples can be checked by electron microscopy to identify virus (Davies *et al.*, 1971). Samples of skin also show characteristic histopathological changes, which include vasculitis and perivascular infiltration with white cells causing a thrombosis of the vessel in the dermis and subcutis. Epithelial “cells clave louses” cells, which are also reported in sheep pox, are invading the lesion. The agar gel precipitation test is not specific for LSD since other capripoxviruses and parapoxviruses share the LSDV antigen. In novel habitats, virus isolation can be employed for diagnosis. For viral isolation, pre pubertal lambs and bovine testes are the most sensitive primary and secondary cultures. The most effective test for disease diagnosis is molecular diagnostics using PCR. For quick diagnosis, conventional and real-time PCR have been developed (Bowden *et al.*, 2008; Heine *et al.*, 1999; Mangana-Vougiouka *et al.*, 1999; Orlova *et al.*, 2006; Tuppurainen *et al.*, 2005; Zheng *et al.*, 2007). It has been developed to distinguish LSDV from other Capripoxviruses using real-time PCR (Lamien *et al.*, 2011). Antibody ELISAs have been developed with limited success. Indirect fluorescent antibody test is labor intensive and requires longer time duration there by making it less cost effective than ELISA (Babiuk *et al.*, 2008). Institutes of Pakistan Government are fully equipped to test and report any outbreak in Pakistan. Some of these Labs might include ‘National Agriculture Research Council’ (NARC) Islamabad, Veterinary Research Institute (VRI), Lahore. VRI is a Punjab government institute that is dealing with infectious agents affecting animals and developing vaccines for local infectious agents like (Khan *et al.*, 2021).

Vaccination

A homologous live-attenuated LSD vaccine called Lumpi-ProVaCInd was created by the ICAR National Research Center on Equines (ICAR-NRCE), Hisar (Haryana), and the ICAR-Indian Veterinary Research

Institute (IVRI), Izzatnagar, Uttar Pradesh. There is a live attenuated vaccination for LSD. Businesses created various vaccines based on various LSD virus strains. It is either based on the SIS Neethling type or the Neethling strain used in products like the Lumpy Skin Disease Vaccine for Cattle (Onderstepoort Biological Products; OBP, South Africa) and Bovivax (MCI Sante Animale, Morocco) (Lumpyvax, MSD Animal Health-Intervet, South Africa). Since the virus that causes sheep pox and goat pox is closely related to LSD, the vaccination for those diseases can be used to treat LSD. According to OIE, many viral strains are employed as vaccine strains homologous virus causing lumpy skin disease. Three years of protection are provided by the South African Neethling strain, which is passed through 60 times in lamb kidney cells and 20 times on the chorioallantoic membrane of embryonated chicken eggs. Kenyan sheep pox virus passed 18 times in lamb testis (LT) cells or foetal calf muscle cells, Yugoslavian RM 65 sheep pox strain, and Romanian sheep pox strain are among the sheep pox strains utilized as vaccinations against LSD. Local adverse reactions are caused by the by the heterologous vaccines. As these vaccinations may act as a source of infection for a vulnerable population of sheep and goats, they are not recommended in locations where sheeppox and goat pox are prevalent. Live attenuated Gorgan goatpox strain offers effective side-effect-free protection for cattle. Since the LSD virus is stable and lasts a long time in the environment, long-term immunization with 100% coverage should be made mandatory for disease control and prevention. It is advisable to immunize fresh animals before bringing them to the impacted farm. At the age of 3 to 4 months, calves that have been nursed by moms who have received vaccinations or are infected naturally should be inoculated. Each year, pregnant cows and breeding bulls might receive vaccinations (Capstick, 1962; Capstick and Coackley, 1961; Brenner *et al.*, 2009).

Economic losses

Lumpy skin disease has led to serious economic losses in affected countries. The disease causes a considerable reduction in milk yield (from 10% to 85%) due to high fever and secondary mastitis. Other consequences of the disease include damaged hides, decline of the growth rate in beef cattle, temporary or permanent infertility, abortion, treatment and vaccination costs and death of infected animals (Alemayehu *et al.*, 2013; Babiuk *et al.*, 2008; Sajid *et al.*, 2012; Sevik and

Dogan, 2017). The total cost of the LSD outbreaks in 393 surveyed herds was 822 940.7 GBP in Turkey (Sevik and Dogan, 2017). In Ethiopia, the estimated financial loss was 6.43 USD and 58 USD per head for local zebu and Holstein Friesian, respectively (Gari *et al.*, 2010). Total production losses resulting from the disease have been estimated at 45%–65% in industrial cattle farming (Tuppurainen and Oura, 2012).

LSD is very dangerous and emerging disease, spreading very quickly in various countries like Pakistan. LSD has led to serious economic losses in many developed and developing countries. During high fever and mastitis disease caused abortion, 10–85% milk reduction, decline growth lumpy skin disease (Alemayehu *et al.*, 2013; Sajid *et al.*, 2012).

Impact

Emergence of LSD in the country like Pakistan having an agriculture-based economy and the 2nd largest livestock population in world would have devastating consequences. Livestock sector of Pakistan comprises a mighty population of 49.6 M cattle and 41.2 M buffaloes with increment of 3.1 M and 1.2 M annual, respectively. Livestock is the largest sub-sector of the country's agricultural production contributing Rs.1466 billion rupees as value addition which is 2.5% more than afore mentioned years. Livestock sector in Pakistan is contributing 60.6% in value addition in agriculture sector and have an 11.7% share in GDP with 3.1% share in total exports of the country serving as a crucial source of foreign exchange. About 8 M families are directly committed with livestock and earning 35–40% of their livelihood from this sector. The economic implications after the emergence of this devastating disease (LSD) on a country with already fragile and dwindling economy can be of grave nature and long lasting due to impositions of anticipated embargoes on livestock trade and significant decline in the rural livelihoods of eight million families (Khan *et al.*, 2021).

Prevention and control strategies

To this date, LSD does not have a viable treatment plan consequently, disease therapy is usually based only on the use of antibiotics and anti-inflammatory drugs. The only feasible solution to effectively control this disease is to develop a preventive plan. To minimize the possible transboundary spread of disease, animals from endemic regions should be restricted especially across the borders (Molla *et al.*, 2017).

Novelty Statement

This review offers an informative introduction to the lumpy skin disease virus (LSDV) as an increasing menace to the livestock sector in Pakistan. The review also concentrates general diagnostic methods used, economic implication of the disease as well as restrictions on the available methods of treatment, and the most up to date fight of the vaccine that should be essential in constriction of the disease-leaving an insightful commentary on the future management and according research on the disease in the region.

Author's Contribution

Rizwan Shaukat: data curation, writing – original draft. Hafsa Arshad: writing – review and editing. data curation. All authors read and approved the manuscript.

Competing interest statement

The authors have no relevant financial or non-financial interests to disclose.

Ethical approval

Not applicable. No human or animal studies were performed.

Informed consent

Not applicable.

Consent for publication

Not applicable.

Data availability statement

No datasets were generated or analyzed during the current study. The authors declare that the data supporting the findings of this study are available within the paper.

Conflict of interest

The authors have declared no conflict of interest.

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