



Lumpy skin disease virus: comprehensive insights into its pathogenesis, transmission dynamics, epidemiology, and control strategies

Muhammad Tayyab Sarwar¹, Shahida Younas^{1*}, Mudasser Habib², Muhammad Salahuddin Shah², Ayesha Jahangir¹

¹Department of Microbiology, FV&AS, The Islamia University of Bahawalpur-63100, Pakistan

²Animal Sciences Division, Nuclear Institute for Agriculture and Biology (NIAB), Faisalabad-38950, Pakistan

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Abstract

Lumpy skin disease is an acute, subacute, or asymptomatic viral infection in cattle, marked by fever and the abrupt emergence of hard, confined skin nodules that often undergo necrosis. The 151-kbp LSDV genome has a core coding region flanked by identical 2.4 kbp inverted terminal repeats and includes 156 putative genes. The dissemination of "lumpy skin disease virus" (LSDV) has incited rigorous research initiatives owing to the fast proliferation and significant consequences of the disease in recent years. Disease transmission primarily occurs by insects, sometimes through mechanical vectors, contaminated feed and water, infected saliva, and seldom through natural contact. LSD is prevalent in several African nations and primarily coexists with sheep pox and goat pox. Affected cattle had acute clinical manifestations including dermal nodules, pyrexia, lymphadenopathy, cachexia, and edema of the lower limbs. The disease has proliferated swiftly and extensively over the globe, predominantly in Asian nations and Pakistan. The disease has disseminated by the end of year 2021 in Sindh province Pakistan and then spread across all provinces of Pakistan, affecting large number of cattle and to some extent buffalo also. The purpose of this review is to strengthen and examine the previous as well as the most current research findings on lumpy skin disease virus transmission (vector and non-vector), clinical signs, geographical distribution, and vaccination against this virus.

Introduction

Lumpy skin disease is a contagious viral disease of cattle caused by the lumpy skin disease virus (LSDV), a member of the Capripoxvirus genus within the Chordopoxvirinae subfamily of the Poxviridae family. The Poxviridae family is a large and complex group of viruses that have a single linear double-stranded DNA (dsDNA) genome that encodes around 200 proteins (Abdulqa, Rahman, Dyary, & Othman,

2016b). This condition has multiple names, such as "Neethling viral illness," "exanthema nodularis Bovis," "pseudo-urticaria," and "knopvelsiekte." However, the most commonly used name for this condition is lumpy skin disease "LSD" (E Tuppurainen, 2017). LSD is responsible for causing high morbidity, but mortality rates are usually low (F. G. Davies, 1991). Some of the prominent symptoms of this disease include high fever, lymphadenitis, extreme weight loss, bilateral epiphora, reduced milk production,

Corresponding Author: *Shahida younas

Email: Shahidayounas5@gmail.com

sterility, skin erythema, and nodules (E. S. Tuppurainen, Venter, & Coetzer, 2005). Lumpy skin disease causes the aggregation of epidermal micro-vesicles, leading to the formation of large vesicles that ulcerate rapidly. In cattle experimentally infected with the disease, the lumpy skin disease virus (LSDV) was detected in their saliva eleven days after the onset of fever, followed by the presence of the virus in skin nodules 33 days later and in semen 22 days later (Jena et al., 2022). The first signs of the illness include despondency, immobility, lachrymation, inappetence, and a fever between 40°C to 41.5°C (Mafirakureva, Saidi, & Mbanga, 2017). The epidermis, dermis, surrounding abdominal layers, and possibly even the adjacent muscles can all be seen to have deep nodules. They are present in all skin layers (Milovanović et al., 2019).

There are three forms of LSD, including acute, sub-acute, and chronic, which can present with mild to severe symptoms. It is thought that this illness only affects big ruminants like water buffalo and cattle. Among the most prevalent vectors of this illness are mosquitoes, ticks, and biting flies (*Culicoides*) (S. Abutarbush et al., 2015; S. M. Abutarbush, 2017). This is because the arthropods transmitting the disease are the most active (F. Davies, 1991). LSD was first discovered in Zambia in 1929 and spread rapidly to other southern and northern African countries over the following three years (Sukoco et al., 2023). The disease later spread to Persian Gulf nations such as Yemen, Israel, Kuwait, and Oman (Dadakas, 2021). After several Egyptian states were reported to have suffered from severe cyclic outbreaks in 1989, 2006, and 2011, LSD cases were first detected in Iraq and Turkey in 2013, indicating that there is a chance the disease would spread to the European Union, the Caucasus, and the Asia (Abdulqa, Rahman, Dyary, & Othman, 2016a). Various ecological and climatic zones can be affected by lumpy skin diseases, which have the potential to spread throughout the world. Between 1981 and 1986, Tanzania, Kenya, and Zimbabwe were hit by LSD outbreaks (Mashamba, 2020). After this, LSDV outbreaks occurred in different region of Ethiopia such as Amhara and W/Oromiya in 2000/2001 (Gumbe, 2018). From 1929 to 1986, the deadly disease was closed to Sub-Saharan African nations (Al-Salihi, 2014). From 1989-2000, the disease disseminated to affect Egypt and Middle Eastern nations. From 2003-2009, this pandemic was spread in different countries like Asia, Europe, Turkey, and Iraq. By the end of 2013 to 2019, cases

were recorded in eastern Mediterranean, China, South Asia, Bangladesh and India (Abera, Degefu, Gari, & Ayana, 2015). The virus has spread across Pakistan after 2021. All Provinces of Pakistan were affected and are still facing this disease but to a lesser extent as compared to 2021 and 2022 (Imran, Hashmi, Khalique, & Iqbal, 2022).

The majority of LSD vaccines now available on the market are live attenuated vaccinations based on an LSDV strain, goat pox virus (GPPV), or sheep pox virus (STPV). The South African Neethling strain is used to protect cattle against LSD in countries where it is common (Stear, 2005). There have been instances of a local skin response at the injection site from the Neethling strain immunization. Israel, Egypt, and the Horn of Africa have all used the KSGP O-180 and O-240 LSD vaccines (E. S. Tuppurainen et al., 2014). LSDV vaccines include the KSGP O-180 and O-240 strains, as well as the well-known South African Neethling strain. A commercially available live attenuated vaccine is available for the eradication of LSD. KSGP O-180 and O-240 strains or the Neethling strain make up the attenuated vaccine. Egyptian veterinary authorities have approved the use of this vaccine for the vaccination of cattle and buffalo since 2019 (Authority et al., 2020). Vaccines based on the South African Neethling lumpy skin disease virus strain, the Yugoslavian RM 65 sheep pox strain, the Romanian sheep pox strain, and the Kenyan sheep and goat pox strain (KS-1) are now being utilized to fight the lumpy skin disease epidemic (Le Goff et al., 2009). Approximately 16,23,890 cattle and buffalo in Punjab, Pakistan, have received the Lumpyvac vaccination (Livestock Department, Government of Punjab, Pakistan) (Imran et al., 2022).

Lumpy Skin Disease Virus

The dsDNA virus known as LSDV causes lumpy skin condition. It belongs to the genus *Capripoxvirus* and family *Poxviridae*. *Capri poxviruses* (CaPV) are a subfamily of the *chordopoxviruses* and one of the eight genera (Alexander, Plowright, & Haig, 1957). The *Capripoxvirus* genus includes the LSDV virus as well as the goat pox and sheep pox viruses. Even though CaPV infections are serologically similar, they frequently have host-specific variations within certain geographic distributions (Fauquet, Mayo, Maniloff, Desselberger, & Ball, 2005). 156 putative genes were found to be encoded by the virus that causes lumpy skin disease (Rock et al.). Numerous genes found in lumpy skin disease are similar to those found in other poxviruses that have

undergone more extensive research (Ali & Obeid, 1977). There are 10 genera in the subfamily Chordopoxvirinae, with the Capripoxvirus genus being one of them. This genus includes three viral species: LSDV, SPPV, and GTPV. Goats are infected by the goat pox virus, sheep are infected by the SPPV, and cattle and buffalo are infected by the LSDV, which causes LSD in these animals (Kara et al., 2003). LSDV is a 320 x 260 nm sized enveloped virus. It possesses double-stranded DNA and a form akin to a brick. The 151kb genetic makeup of a virus includes a major coding region in the middle. The terminal ends of the viral genome for LSDV are composed of undetectable and reversed 2.4kb and have complicated symmetry around them.

There are thirty structural and non-structural genes in this virus. Infected cells' cytoplasm is where viral DNA is replicated. There are structural and non-structural similarities among the sheeppox viruses. Furthermore, about 97% of the nucleotide sequences of these genes are shared by both viral

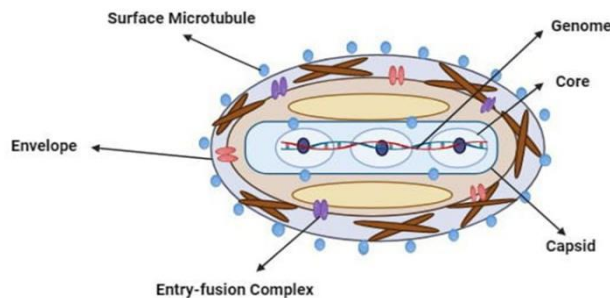


Figure 1. Genome of Lumpy Skin Disease Virus

species (Panel, 2015; Tulman et al., 2002). Unlike other members of the Chordopoxvirinae family, the LSD virus possesses 146 conserved genes that relate to transcription, nucleotide metabolism, DNA replication, virulence, mRNA synthesis, and host range. The LSD virus and the Leporipox, Suipox, and Yatapox viruses have core region genes that are 65% similar in terms of collinearity and amino acid composition (Tulman et al., 2002).

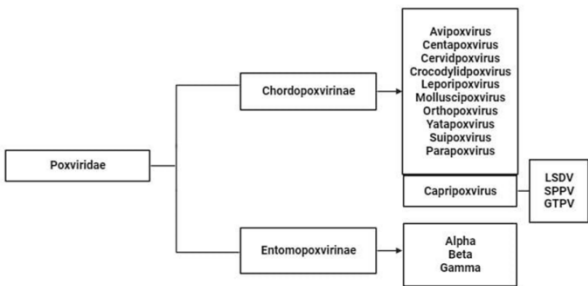


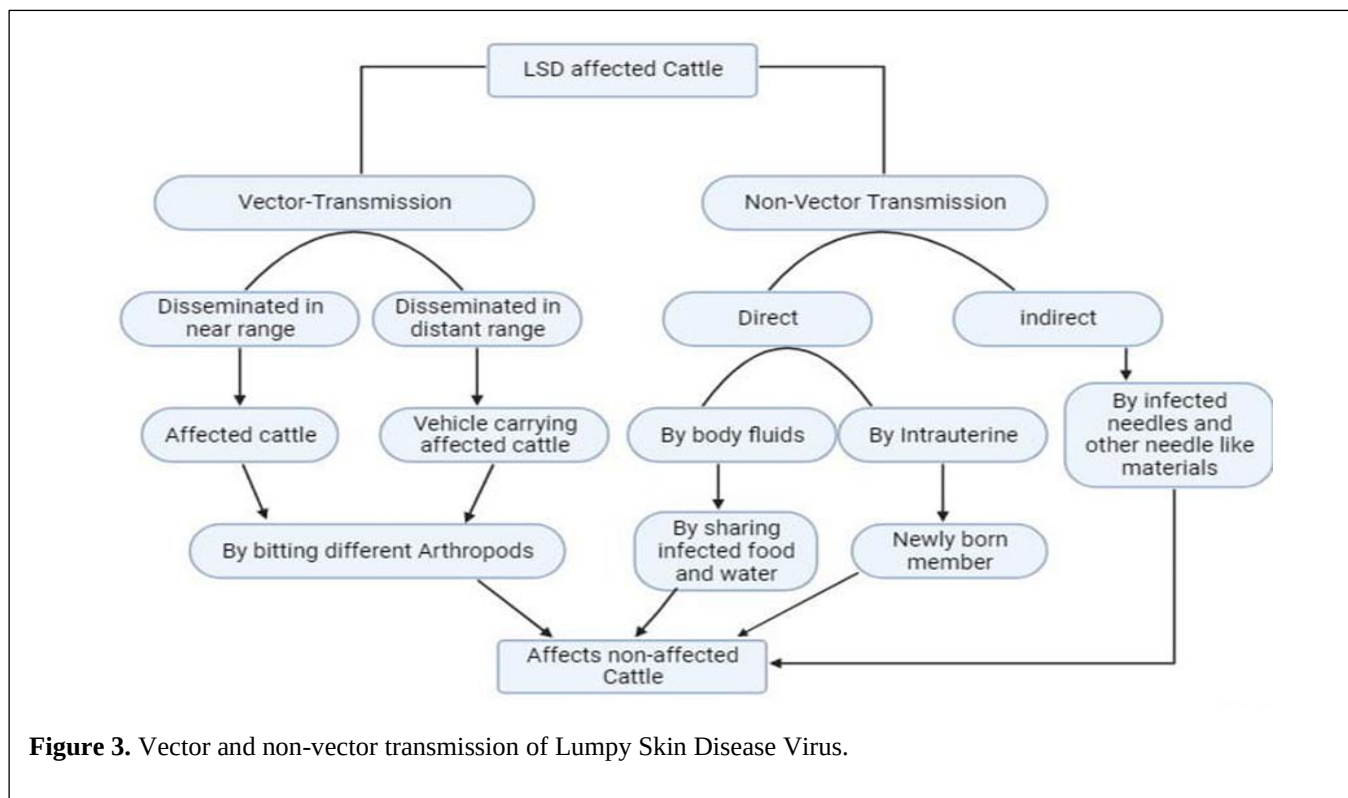
Figure 2. Detailed Classification of Lumpy Skin Disease Virus

Transmission of LSDV

It is thought that blood-feeding and biting arthropods, including several hard tick species and members of the Glossina, Muscidae, and Tabanidae families, are the primary vectors of the virus that causes lumpy skin disease (LSDV) (S. Kiplagat, 2019; S. K. Kiplagat, Kitale, Onono, Beard, & Lyons, 2020). Many flying and non-flying blood-feeding insects may mechanically transfer the LSDV virus, and they play a significant part in both intra- and inter-herd transmission (Roche et al., 2021). House flies (*Musca domestica*), which do not eat on blood, do consume both dead and living animals, but they have very little, if any, impact on the spread of LSDV to unknowing cattle (Roche et al., 2021). Different blood-feeding arthropods can transmit LSDV, although it is not known to reproduce in vectors (Sprygin, Pestova, Wallace, Tuppurainen, & Kononov, 2019). Sheep and goat pox and lumpy skin disease have different regional distributions, suggesting that cattle strains of the Capripoxvirus do not infect or transfer to sheep and goats (Gumbe, 2018). Additionally, communal grazing and watering have been linked to greater rates of LSD, most likely as a result of the enhanced potential for mechanical transmission of the virus by mosquitoes (*Aedes aegypti*) and *Stomoxys* spp (Gumbe, 2018; Selim, Manna, & Khater, 2021). The illness's morbidity and death rates vary greatly depending on the breed, immunological state, and insect vectors used for transmission of the disease in the herd of cattle (Dubey, Ghosh, Gupta, & Singh, 2023). Transmission

is thus mechanical and not biological in nature (Sanz-Bernardo et al., 2021). Arthropods that might act as vectors vary by location (Kayesh, Hussan, Hashem, Eliyas, & Anower, 2020). As LSD spreads into new climatic and geographic regions, where other vectors may become more common in transmigration, changes in seasonality should be anticipated (Datten et al., 2023). Animals that are moving or walking have a significant role in long-distance transmission, while flying vectors carry the virus at very sluggish rates (Collins, 2018). LSDV may be maintained by ticks during dry or cold seasons (Gammada, Morshed, Rabby, & Hossain, 2022). Although ticks don't travel very much, living animals aboard moving vehicles that are contaminated with ticks may spread LSDV across great distances (Zalcman & Cowled, 2022). In Africa, several birds could possibly serve as LSD transmission vectors (Gortázar, Barroso, Nova, & Cáceres, 2022). Each vector has a desired level of humidity, temperature, and vegetation (Nesterov et al., 2022). By using contaminated bull semen for artificial insemination, LSD might be passed on to heifers (Das et al., 2021). Some of the biting flies that contribute to the pathophysiology of this disease's vector are *Stomoxys calcitrans* and *Biomyia fasciata* (Y. R. Khan et al., 2021). Ticks like *Rhipicephalus*

decoloratus, *Rhipicephalus appendiculatus*, and *Amblyomma hebraeum* serve as LSDV reservoirs, whereas mosquitoes like *Aedes natrius* and *Culex mirificens* are mostly responsible for the disease's physical transmission (Moudgil, Chadha, Khullar, Chhibber, & Harjai, 2023). The possibility of LSDV being transferred directly is not very strong, and Weiss's 1968 clinical results and previous research confirmed the prior theory that there is very little chance of direct transmission (Sanz-Bernardo et al., 2021). These investigations, however, concentrated on indirect animal-to-animal transmission, in which the virus is expelled through milk or phlegm and mixes with the feed or water at the trough. It has also been shown that viruses may spread intrauterinally (Horigan et al., 2018). When a contaminated needle is used to administer a vaccine to a wide population, the virus may also spread (Sprygin et al., 2019). With the help of wind and storms, disease vectors may travel great distances and spread the illness. Therefore, to stop the transmission of illness, locations with a large vector population should implement vector control measures such as the use of vector traps and insecticides (Zalcman & Cowled, 2022). Because the active vector species that are present in



each region varies, there are variances in the attack rates in those regions (Authority et al., 2020).

Vectors of LSDV

Since arthropods do not allow the virus to multiply or circulate, it is hypothesized that LSDV is mechanically transmitted through them. The virus's remarkable stability allows it to persist in a wide variety of vectors (Ardestani & Mokhtari, 2020). The rate of mechanical viral transmission is negatively correlated with the virus survival time between vector blood feeds. Thus, true flies (Dipterans) that feed in a repeating or interrupted manner can be effective viral carriers (Machado et al., 2019). With this feeding pattern, the virus can survive. This is because even a single bite of blood is not sufficient. The host's reaction forces the vector to return to the same host or to a new one within a short time period (Macauley, Summers, & Engle, 1999). In order to qualify as LSDV vectors, arthropods need to demonstrate both their ability and competency. Vector competence is the ability of a vector to spread to a vulnerable animal after feeding on an infected animal, and it is often studied in controlled settings (Mercier et al., 2018). To put it quantitatively, "vector capability" refers to the vector's fundamental biological and ecological characteristics that are linked to viral transmission. These include traits including biting rate, preferred and regular feeding habits, and the size of the vector population (Kahana-Sutin, Klement, Lensky, & Gottlieb, 2017). There hasn't been a specific arthropod for which competence and aptitude haven't been proven yet. Several arthropods' vector competency was examined in a lab setting. Female *Aedes aegypti* mosquitoes were able to spread the virus to susceptible cattle for 2 to 6 days after consuming LSDV-infected cattle lesions. Even though the virus was identified in all the cattle, only five of them actually showed symptoms, which were typically mild. As a result, *Aedes aegypti* (*A. Aegypti*) is an effective LSDV vector (Sprygin et al., 2019). However, LSDV outbreaks have happened in several European and Middle Eastern nations, where this vector is not common (Swiswa, Masocha, Pfukenyi, Dhliwayo, & Chikerema, 2017). It is also known that *Aedes albopictus* (*A. albopictus*), a member of the same genus, is an efficient viral carrier. Despite being more prevalent than *A. aegypti*, there are only occasional reports of its appearance during LSD epidemics in different affected countries (Gubbins et al., 2020). As a result of their preference for human blood over that of other animals, these mosquitoes are less effective

LSDV carriers. Additionally, the abilities of the biting midges *Culicoides nubeculosus* and *Culex quinquefasciatus*, the stable fly *Stomoxys calcitrans*, and the mosquitoes *Anopheles stephensi* and *Culex quinquefasciatus* were evaluated. After eating blood contaminated with LSDV for 24 hours, none of these dipterans that feed on blood were capable of infecting sensitive cattle (Taylor, Berriman, Gale, Kelly, & Snary, 2019). Although *S. calcitrans* was unable to transmit LSDV in the research mentioned above, there are a number of indications that it has the ability to vector LSDV (Asghar et al., 2024). It has been shown that *S. calcitrans* may spread a number of animal diseases, including viruses, but most significantly, it can spread the Yemen Capri pox strain to a goat that is vulnerable. It may consume two to three blood meals per day and is an interrupted feeder that often resides close to the legs of horses and cattle (Taylor et al., 2019). The prevalence of LSDV outbreaks was strongly correlated with the relative abundance of *S. calcitrans* in affected dairy farms, which peaked in December, January, and April, according to research done to determine the seasonal pattern of potential dipteran vectors of LSDV in dairy farms. However, there was no significant correlation between the occurrence of the epidemics and the prevalence of other blood-feeding dipterans, such as mosquitoes and biting midges (Prozesky & Barnard, 1982). Summertime was when these epidemics mostly impacted grazing beef cattle. Thus, the idea that certain flies may act as vectors in herds that are grazing and those that are not was put up (Awad, Ibrahim, Mahran, Fararh, & Abdel Moniem, 2010). Due to accounts of its high abundance in beef cattle during the epidemics, the horn fly *Haematobia irritans* were suggested as a potential vector under these circumstances (Babiuk, 2018).

The fact that this data is circumstantial and that this fly has not successfully transmitted other viruses indicates that further research is required before the horn fly can be implicated as a potential LSDV vector (Issimov et al., 2020). Additionally, a number of studies have shown that ticks may spread LSDV. *Amblyomma hebraeum* and *Rhipicephalus appendiculatus* males demonstrated both mechanical and transstadial LSDV transfer (Allepuz, Casal, & Beltrán-Alcrudo, 2019). The virus was isolated from the saliva of adults that were fed or from adults who were given to infected cattle as nymphs, demonstrating this. Furthermore, the illness was transmitted by these ticks to susceptible animals (Gelaye & Lamien, 2019; J. Lubinga et al., 2015). In *R. decoloratus*

ticks, transovarial transmission of LSDV was observed. Susceptible calves were infected by adults that emerged from the eggs produced by infected ticks, which led to viremia and moderate clinical illness (J. C. Lubinga et al., 2014). These data point to ticks serving as critical LSDV reservoirs. Tick-borne transmission cannot account for the speed at which LSDV epidemics progress, therefore their function in the spread of the virus in big outbreaks of cattle must be determined by capacity studies. But although ticks are often rare in zero-grazing animals, significant outbreaks have frequently happened there (Abera, Degefu, Gari, & Kidane, 2015).

Clinical signs

Lumpy skin disease is a systemic illness that manifests as pronounced lymphadenopathy and cell-associated viremia prior to the development of lesions. Blood monocytes probably play a key role in the transmission of viruses to secondary infection sites (Young, Basson, & Weiss, 1970). The majority of the members of the Chordopoxviridae subfamily, including capripox viruses, have a specific affinity for keratinocytes. Skin lesions are characterized by stratum spinosum keratinocytes' proliferation and ballooning degeneration, the development of epidermal micro vesicles, and the influx of inflammatory cells into the dermis (Möller et al., 2019).

Epidermal micro vesicles combine to form huge vesicles that ulcerate fast in lumpy skin disease. (F. Davies, 1991). Severe vasculitis and lymphangitis are caused by viral replication in pericytes, endothelial cells, and maybe some cells in the blood vessel and lymph vascular wall in afflicted regions (Padilla, Dutton, Bauman, & Duncan, 2005). The initial sign of the illness is a temperature of 40°C to 41.5°C accompanied by inappetence, lachrymation, immobility, and sadness. After an experimental vaccination, a fever develops around day five and lasts for several days. After the fever starts, skin lesions and so-called nodules start to appear a few days later (Mafirakureva et al., 2017). These round, elevated, dense, well-circumscribed nodules have a size range of 5 to 50 mm. Fused nodules can form large irregularly shaped plaques. The dermis, epidermis, adjacent subcutaneous layers, and sometimes even the surrounding muscles exhibit deep nodules. They are present in every layer of the skin (Milovanović et al., 2019).

In cattle, the frequency and size of skin lesions can have a significant impact on how they show clinically. These nodules often develop around the mouth, nose, and eyes of the head initially, then on the neck, body, udder, genitalia, legs, and tail. They may be uncomfortable. An infected animal may have just one nodule or, in highly diseased animals, more than a thousand (Saegerman et al., 2018). Large skin ulcers are left behind when skin lesions develop into necrotic plugs, sometimes known as "sitfasts," that later peel off. These necrotic cores are appealing to flies and are very vulnerable to subsequent bacterial infections. Skin nodules that cure leave behind scars that are not removable. Blood creatinine phosphokinase, aspartate aminotransferase, and serum alanine aminotransferase levels can all be elevated in infected animals (Gubbins et al., 2020).

Rhinitis and nasal discharge begin as serious but gradually become mucopurulent. Ocular discharge, keratitis, and conjunctivitis are possible symptoms. Increased salivation, sadness, and a reduction in appetite that leads to weight loss are all potential (Gupta et al., 2020). Pox-like lesions may appear on the mouth's mucous membranes, such as the gingivae, inner lips and soft palate, epiglottis, dental pads, throat, tongue, and digestive tract. Primary and secondary pneumonia as well as respiratory discomfort can result from lung infections (Padilla et al., 2005). Scars lower the hide's value in the leather business. In lactating cattle, milk production is diminished, and mastitis can develop. Pregnant cows may experience abortions, and both aborted fetuses and newborn calves have been reported to have many skin lesions (Vidanović et al., 2016). In addition to swollen lymph nodes, the necropsy found nodules in the ruminal pillars, liver, and lungs (Bedecković, Šimić, Krešić, & Lojkić, 2018).

Geographic spread of virus

The virus that causes lumpy skin disease has expanded its geographic range in recent years, moving from endemic sub-Saharan countries to the Middle East and Asia, demonstrating transboundary spread. The cattle and dairy industries in many Asian countries, including Bangladesh, India, China, Nepal, Bhutan, Vietnam, Myanmar, Sri Lanka, Thailand, Malaysia, and Laos, are very concerned about the recent outbreaks of LSD (Azeem, Sharma, Shabir, Akbar, & Venter, 2022). Lumpy skin disease was originally described as a clinical ailment in Zambia in 1929 (Abera, Degefu, Gari, & Ayana, 2015; ESM Tuppurainen & Oura, 2012). Between

1943 and 1945, cases were documented in the Republic of South Africa, Botswana, and Zimbabwe (Salib & Osman, 2011). By 1970, LSD had spread north into Sudan; by 1974, it had spread west as far as Nigeria; and in 1977, it was found in Mauritania, Mali, Ghana, and Liberia (Abera, Degefu, Gari, & Ayana, 2015; A. Khan, Du, Hussain, & Kwon, 2022). Another LSD pandemic struck Tanzania, Kenya, and Zimbabwe between 1981 and 1986 (Salib & Osman, 2011). The fatal illness was exclusive to countries in Sub-Saharan Africa from 1929 and 1986 (F. G. Davies, 1991). In 1988, the Suez Governorate of Egypt officially recognized LSD. An LSD concentration was found in Israel in 1989 (Bickett-Weddle, Aquilino, & Roth, 2008; A. Khan et al., 2022).

Table 1. Percentage of LSDV (Study based on seroprevalence) in different regions (Azeem et al., 2022).

Region	Percentage (%)
Southern Ethiopia	6%
Southern Range land	11.6%
Wolli so town	27.9%
North Ethiopia	28%
Afar	51%
Tigray	37%

In the summer of 1989, it reappeared and, within five to six months, it had spread to 22 of Egypt's 26 governorates (Abera, Degefu, Gari, & Ayana, 2015; Davies, 1982). After the year 2000, Middle Eastern countries began to report an increasing number of outbreaks, and LSD is now regarded as a prevalent illness in the region (Liang et al., 2022). Several regions of Ethiopia saw a massive LSD pandemic breakout in various years, including Tigray, Amhara, and Benishangul in 2006/2007; Amhara and W/Oromiya in 2000/2001; and Oromiya and SNNP in 2003/2004 (Babiuk et al., 2009). The likelihood that LSDV may establish itself in the Middle East and spread to Asia and Europe is increased by recent LSD outbreaks in Egypt, Israel (2006 and 2007), Oman, and Bahrain (2009) (Brenner et al., 2009; El-Kholy, Soliman, & Abdelrahman, 2008). The illness has reached Iraq and Turkey by the end of 2013. In late 2014, the first LSDV infections were reported in the northern part of the eastern Mediterranean island of Cyprus. In 2015, the virus expanded to the Russian Federation (Byadovskaya et al., 2022). In

2019, the illness spread to Yi Li, Xinjiang Province, China; in July 2019, LSD was introduced for the first time in South Asia and Bangladesh; and in August 2019, it happened in India (Byadovskaya et al., 2022; Roche et al., 2021). The epidemic spread to South Asian countries including Nepal, Bhutan, Vietnam, Thailand, and Myanmar in the two years that followed, as well as to southern and eastern China. By 2022, the outbreak had moved from the east and north to Mongolia and Eastern Siberia (Mahfuza Akther et al., 2023; Liang et al., 2022).

Lumpy Skin Disease Virus in Pakistan

The virus has spread across numerous nations, including Pakistan. Pakistan is now dealing with serious LSDV concerns in practically all areas (Jamil et al., 2022). In late 2021, the first disease suspect was identified in Pakistan (Manzoor et al., 2023). The virus has spread to a great number of countries, including Pakistan. In certain of its areas, Pakistan is now grappling with dangerous LSDV problems. According to a recent research conducted in Pakistan, an LSD infection at the herd level often results in a USD 3 million overall economic loss (El-Neweshy, El-Shemey, & Youssef, 2013). In November 2021, the first occurrence of LSD was recorded in the district of Jamshoro, Sindh, Pakistan The Sindh livestock agency proclaimed an LSD epidemic after 36,000 cattle were affected by the end of April 2022, with a fatality rate of 0.8% (Shah & Khan, 2022). 10,826 cattle were infected with lumpy skin disorders in Southern and Northern Punjab. Southern Punjab's most impacted districts were Bahawalpur and Multan. Southern Punjab has a greater frequency of Lumpy skin disease than Northern Punjab (Imran et al., 2022). Pakistan was free from Lumpy skin disease until January, 2022. Then there was a rapid breakout of lumpy skin disease in many parts of Sindh province. Following Eid Al Adha, there was an influx of slaughtered animals from Sindh to Punjab, which was a main source of the epidemic in southern Punjab (Tageldin et al., 2014). LSD has reduced the market value of meat and milk products by much to 70% in Karachi, Pakistan (Javed et al., 2023). Pakistan has never had an LSD plague, but due to endemic LSDV in its neighbors, it now stands a significant risk of doing so (Naveed, 2023). Karachi had the most recorded occurrences; around 54 animals perished in the province, while 4751 were recovered. So far, 35,000 in Punjab, 53,668 in Sindh, 74,590 animals in Khyber

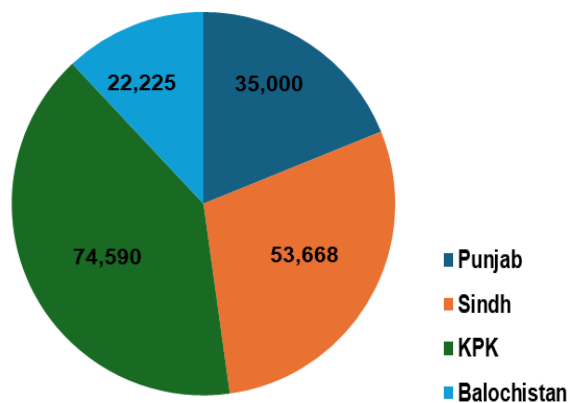


Figure 4. Photograph shows the number of animals affect by Lumpy Skin Disease Virus

Pakhtunkhwa, 22,225 in Baluchistan, and 6351 in Azad Jammu and Kashmir have been infected (Khatr et al., 2023).

Vaccination

The majority of LSD vaccines now on the market are live attenuated vaccines based on an LSDV strain, sheepox virus, or goatpox virus. A vaccination's capacity to prevent LSDV is influenced by the seed virus, the level of attenuation, the dose amount, and the titer of the attenuated vaccine virus in the finished products (Stear, 2005). The health of farmers and livestock depends on a vaccine product's effectiveness (Chapter, 2018). Molecular techniques must be used to identify the vaccine seed virus, and its origin and transmission history must be carefully recorded (E. S. Tuppurainen et al., 2014). All age groups, all sexes, breeds, and bovine species must be able to safely receive LSD vaccinations (Stear, 2005). The South African Neethling strain is the vaccine used to protect cattle against LSD in countries where the drug is prevalent. Despite its shown effectiveness, there may be some disadvantages. The Neethling strain vaccination may cause a local skin reaction at the injection site, according to studies. The KSGP O-180 and O-240 vaccinations against LSD have been used in Israel, Egypt, and the Horn of Africa. It has been said that these vaccines provide protection against adverse effects such as skin lesions and fever after immunization. Vaccinated dairy cattle with both the KSGP O-180 and KSGP O-240 strains showed a comparatively higher morbidity rate and insufficient protection. The Madagascan LSD strain is

another example of a virulent field strain that has been attenuated. According to reports, the original LSDV strain is also used to do this. Heterologous vaccinations against LSDV include the Gorgan goat pox strain (a vaccine based on the goatpox virus), Romanian SPPV strain (a vaccine based on the sheep pox virus), and the Yugoslavian SPPV RM65 strain (Ramyar). The Gorgan goat pox strain immunization was first used on LSD Ethiopian cattle and was shown to provide sufficient protection and seroconversion in cattle against the highly virulent LSDV (M. Akther et al., 2023). Homologous immunizations provide good protection for cattle against virulent field strains. LSDV vaccines include both the well-known South African Neethling strain and, despite their confusing names, the KSGP O-240 and O-180 strains. After 61 serial rounds in lamb kidney (LK) cells, 20 passages in the chorioallantoic membrane of embryonated chicken eggs, and three passages in LK cells, the vaccine strain was attenuated from the virulent strain. The Neethling strain was identified from South Africa's first LSD epidemics. Another instance of attenuation of a virulent field strain is the Madagascan LSD strain, which required 101 passes in rabbit kidney and five in deadly calf kidney cells. Even still, adverse reactions have been linked to homologous vaccinations when given to cattle for the first time. (Patel & Patani, 2022) In endemic locations, live attenuated vaccinations against LSD have been utilized successfully. Cross-protection of the immune system was advantageous since Capri poxviruses, including SPPV, GTPV, and LSDV, had antigenic similarity. There is a commercially available live attenuated vaccination for the elimination of LSD. Within 10 to 30 days after immunization, the immune system builds up. Unless there have previously been contemporaries displaying symptoms of illness, this vaccination is advised at any age (Jena et al., 2022). Currently available attenuated vaccines are either the well-known South African Neethling strain or the Kenyan sheep and goat pox O-180 and O-240 strains. Numerous studies have shown the presence of vaccine viruses in the milk, blood, and skin nodules of calves that have received Neethling immunizations. The KSGP O-180 and O-240 LSD vaccines have been used in Israel, Egypt, and the Horn of Africa. It has been said that these vaccines provide protection against adverse effects such as skin lesions and fever after immunization (ESM Tuppurainen et al., 2017). Kitching (2003) suggests using the cheaper and more effective sheep pox vaccine to curb LSD usage since it provides acceptable protection against the drug. It is important to note that Strain-

Table 2. Commonly used vaccines against Lumpy Skin Disease Virus (E. Tuppurainen & Dietze, 2021)

Vaccine	Target species	Titer/Dose/Administration
LSD Neethling strain	Cattle	Not known/2 ml SC
Lumpyvax™	Cattle	10 ^{4.0} TCID ₅₀ /dose/1 ml SC
Bovivax-LSD™	Cattle	10 ^{3.5} TCID ₅₀ /dose/2 ml SC
LumpyShield-N™	Cattle	10 ^{4.0} TCID ₅₀ /dose/1 ml SC
MEVAC LSD	Cattle	10 ^{3.5} TCID ₅₀ /dose/1 ml SC
Lumpivax™	Cattle	TCID ₅₀ not known/2 ml SC
Penpox-M™	Cattle	10 ^{2.5} TCID ₅₀ /dose/3 ml SC
Poxvac™	Sheep, Cattle	10 ^{2.5} TCID ₅₀ /dose/3ml SC
Poxdoll™	Cattle, Sheep, Goats	10 ^{2.5} TCID ₅₀ /dose/3ml SC
Sheep Pox Cultyril Dry™	Sheep, Cattle	Not known

A of the foot and mouth disease aphthovirus, which was initially brought to Egypt with African cattle in 2006, was previously exposed to Egyptian cattle (Salib & Osman, 2011). Vaccinations against attenuated goat and sheep pox. In nations where LSDV, SPPV, and GTPV are present, these vaccinations are utilized (E. S. Tuppurainen et al., 2014). Romanian and Yugoslavian RM65 sheep pox strains were used in Egypt to vaccinate vulnerable animals (Hamdi et al., 2020). Vaccines against sheep and goat pox did not provide Turkish animals with enough protection, especially when the dose was less than 10 times that administered to sheep. If there is complete vaccination coverage and movement control measures that limit freedom of movement, the partial protection against LSD provided by these vaccinations will be effective (S. M. Abutarbush & Tuppurainen, 2018). With a dose of ten times, the Romanian strain sheep pox vaccine (RM. 65 SPPV) is about four times less effective in preventing infection than the equivalent live attenuated LSDV vaccine (Neethling strain) (Hamdi et al., 2020). Since 2019, the Egyptian veterinary authorities have approved the use of this vaccine for the vaccination of cattle and buffaloes. The Sera and Vaccine Research Institute in Egypt presently

produces it, and it seems to provide cattle—including young calves and pregnant cows—complete protection against LSDV infection for around three years (Khafagi, Ghazy, & Mahmoud, 2022). The illness is controlled in endemic locations by annually immunizing animals older than 6 months. Currently, the South African neethling LSDV strain, the Romanian sheep pox strain, the Yugoslavian RM 65 sheep pox strain, and the Kenyan sheep and goat pox strain (KS-1) are used as vaccines to control the lumpy skin disease outbreak (Ahmed, Doley, Barlasakar, Nath, & Yadav, 2020). In Pakistan (Punjab), there are around 16,23,890 cattle and buffalo that have received vaccinations (Lumpyvac) (Livestock Department Government of Punjab) (Imran et al., 2022).

Conclusion

The disorder known as lumpy skin is caused by the double-stranded DNA virus, or LSDV. It is a member of the Poxviridae family and genus Capripoxvirus. One of eight genera, capripoxviruses (CaPV) are a subfamily of chordopoxviruses. There are different types of vectors by which LSDV can transmit as these vectors don't take part in dissemination or multiplication of virus. These vectors are *Aedes aegypti* (A. Aegypti), *Aedes albopictus* (A. albopictus), *Culicoides nubeculosus*, *Culex quinquefasciatus*, *Stomoxys calcitrans*, *Anopheles stephensi* and *Culex quinquefasciatus*. LSDV is a systemic disease that shows cell-associated viremia. Initial symptoms are high temperature leading to infertility and depression. Round, elevated, dense, well-circumscribed nodules could be seen in the skin of an animal. Nasal discharge and rhinitis are the secondary symptoms. From 1986-2022, this disease caused lethal outbreaks in different regions and countries in the world. It was first diagnosed in Zambia. In Pakistan, all provinces of Pakistan have highest percentage of LSDV with less mortality rate. In Punjab especially Southern Punjab is the most affected area. Only solution to eradicate this disease was vaccination. Different strains are used mainly Neethling strain. Either the well-known the Kenyan sheep and goat pox (KSGP) or South African Neethling strain O-180 and O-240 strains make up the attenuated vaccine that is now in the market. In Africa, Israel, and Egypt, the KSGP O-180 and O-240 vaccines against LSD have been used. In Pakistan Lumpyvac is most commonly used in different farms to protect the cattle/buffaloes.

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Conflict of Interest

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Authors' Contribution

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