REVIEW ON THE OUTBREAK OF LUMPY SKIN DISEASE IN INDIA

Pokale Prachi S., Lunawat Amruta D., Waghmare Mayuri S., Kalamkar Rajendra D., Satpute Jayshri B.
SAJVPM’s College of Pharmaceutical Science And Research Center Kada, Tal-Ashti, Dist-Beed, Maharashtra, India-414202.

Abstract

Lumpy skin Disease (LSD) is a viral infection of cattle. LSD is caused by Lumpy skin disease Virus (LSDV). LSD cause hug economic losses in the livestock industry. LSDV belongs to family Poxviridae, subfamily chordopox viridae and genus carpipox virus. This disease originated in Zambia in 1929, consequently extent to middle east, Europe and Asia. Starting from outbreaks in Gujarat and Rajasthan in three months cattle in states across India were affected LSD causes losses of milk, Beef production absorption in females and sterility in males. In this disease of cattle, the major symptoms are Fever, Nodules on skin, Mucous membrane and internal membranes enlarged lymph nodes, oedema of the skin. Complete recovery of LSDV takes 6-7 months. The disease is not zoonotic meaning it does not spread from animals to human and humans cannot get infected with it. This review article intends to discuss about the LSD virus in the light of recent situation raises concerns the spreading of the disease in LSD free country.

Keywords: LSD, LSDV, Zoonotic etc.

Introduction

In 1929 a new disease of cattle was reported from Zambia that manifested itself by the appearance of skin nodules. LSD is called as LSDV. LSDV belongs to family Poxviridae, subfamily chordopoxviridae and genus carpipox virus. This disease is known by various names such as LSDV, Pseudo-Urti Cavia, Neethling virus disease, exanthema noduloris bovis. It is vector born disease transmitted by different biting and biting blood feeding arthropods. All ages and breeds of cattle are affected but specially the young cattle’s (in the peak of lactation) are affected.

The World Health Organization for animal health (OIE) identified this vector born disease. LSD is non zoonotic disease and this disease is devastating because it causes a dramatic decline in milk yield; absorption-poor coat condition and sterility in bulls. The incubation period in the field is believed to 2-5 weeks and lesions first appears at the inoculation site in 4-20 days. Fever is the first stage is following within 2 days by the
development of nodules on the skin and mucous membrane. LSD can spread large disease even from one continent to another. If infected animals are moved from one place to another. In contrast, LSDV can experimentally infects sheep’s and goats but no natural infection of sheep’s and goats with LSDV has been reported. Consequently, it extended to middle east, Europe and Asia. In India starting from outbreaks in Gujrat and Rajasthan in 3 months cattle in 15 state across India were altered. The 2022 LSD Outbreaks in India resulted in the death of over 97,000 cattle in 3 months between July And 23 September over 50,000 deaths were reported from Rajasthan. In November 2019, LSD in the country was confirmed in a lab. It was mainly restricted to sporadic cases in lactation such as Odisha. The origin of disease in INDIA as well as the outbreak in 2022 remained unknown state such as Kerala reported 30-40 cases each between Dec-2019 to Jan-2021. In August-2020 cases were reported from Assam, cases were first reported in April-2022 from Gujarat. In late July 2022 Gujarat introduced bans on cattle movement in some districts. In Maharashtra’s first case was reported on Aug,04 in Jalgaon district. On 6th Aug Rajasthan imposed restriction on cattle fares, On 20th Aug Panchkula district banned interdistrict transport. On Aug,24 up stated restrictions. On 14th Sept, cattle transport in Mumbai was banned; health certification is needed for transport. In Aug-2022, Gujarat reported dip in milk collection amounting to approx. 1 Lac ltr per day in certain location. Collection of milk in Rajasthan failed by over 20% in Aug-2022; by Sept collection has decreased by 5-6 lacs liters per day. In some places Rajasthan collection has fallen to zero. The diagnosis of LSDV is building upon the basis of the typical clinical pattern (morbility and mortality). Indian laboratories have undertaken research on domestic vaccine in 2019. Lumpi-Provac Ind was launch in Aug-2022. The vaccine has not been cleared for emergency use. Goat pox vaccine been found effective And is belong administered. The present review is designed to provide exiting information on various aspects of the disease such as transmission, pathogenesis, pathology, economic importance, diagnosis and prevention.

**EPIDEMIOLOGY**

**Transmission**

The mechanism of LSDV transmission is useful in evaluating the epidemiology of the virus, thus contribute towards progressive control strategy and extinction of the disease. An epitome of possible modes of transmission of LSDV is shown in Figure 2.
Figure 2. Epitome of possible modes of transmission of LSDV. LSD infected cattle may affect non-infected cattle through vector or non-vector transmission.

Non-vector transmission

Although ineffective, non-vectored LSD transmission happens when clinically afflicted animals come into contact with contaminated materials, without the need of biological or mechanical vectors. Infectious LSDV is excreted in saliva, nasal and ocular discharges, contaminating communal eating and drinking areas and spreading the disease. Transmission Adv Biotechnol Exp Ther. 2021 through contaminated needles during vaccination, dispersion through infected semen during coitus, ingestion of milk, and intrauterine transmission may also act as a sources of infection.

Vector transmission

The role of arthropod vectors in the transmission of this virus was experimentally confirmed. Several blood-sucking hard ticks, for instance, Rhipicephalus appendiculatus (brown ear tick), Rhipicephalus decoloratus (blue tick), and Amblyomma hebraeum, mosquito Aedes aegypti and flies Stomoxys calcitrans, Haematobia irritans and Musca domestica have been implicated in the spreading of LSDV in sub-Saharan Africa. In the tick host, LSDV is trans-stadially and transovarially transmitted during cold temperatures. The virus may spread in short distances of a few kilometers, and even cover longer-distance due to unrestricted animal movements across international borders.

PATHOGENESIS

Intravenous, intradermal and subcutaneous routes are used in experimental infection. The intravenous route develops severe generalized infection, while the intraepidermal inoculation develops only 40% to 50% of animals may developed localized lesions or no apparent disease at all. A localized swelling at the site of inoculation after four to seven days and enlargement of the regional lymph nodes, develop after subcutaneous or intradermal inoculation of cattle with LSDV (Vorster and Mapham 2008). However, generalized eruption of skin nodules usually occurs seven to 19 days after inoculation. LSDV replicates inside the host cells such as macrophages, fibroblasts, pericytes and endothelial cell in the lymphatics and blood vessels walls lead to developing vasculitis and lymphangitis, while thrombosis and infarction may developed in severe cases.
Viraemia occurred after the initial febrile reaction and persisted for two weeks. 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. A lifelong cell-mediated immunity is developed in most animals that recover from clinical disease. Calves are born from the infected cow acquire maternal antibodies that may protect them from clinical diseases for approximately six months. LSDV was demonstrated in saliva at least for 11 days after the development of fever, in semen for 42 days and in skin nodules for 39 days, from experimentally infected cattle.

**Clinical Manifestations and Pathology**

**Clinical manifestations**

The time between inoculation and first observation of generalized clinical signs ranges from 7 to 14 days in experimentally infected cattle, irrespective of the route of infection and between 2 to 5 weeks in natural cases. LSD can be classified into mild and severe forms based on the number of lumps (nodules) and occurrence of complications, dose of the inoculum as well as the susceptibility of the host and the density of insect population. Accordingly appearance of one or two lumps or nodules within 2 days after onset of the fever (1 to 5 cm in diameter), depression, anorexia, excessive salivation, ocular and nasal discharge, agalactia and emaciation are clinical manifestation of mildly affected cattle. Also, nodular lesions which is painful and hyperemic may be observed on the animal body especially in the skin of the muzzle, nares, back, legs, scrotum, perineum, eyelids, lower ear, nasal and oral mucosa, and tail. In severe cases that may persist for 7-12 days, continuous high pyrexia (40-41.5°C), serious depression, anorexia and a characteristic several (more than hundreds) nodules and usually fairly uniform in size in the same animal, all over the animal body is observed.

![Figure 3](https://www.ijcrt.org/images/figure3.jpg)

**Figure 3.** Characteristic LSD nodular lesion indicating severity: Lesion covering the whole body in severe form (A) and LSD with few skin nodules in mild form (B)

The nodules are firm and slightly raised above the surrounding normal skin from which they are often separated by a narrow ring of haemorrhage (Figure 3A. they involve the epidermis, dermis, adjacent subcutis and musculature. Nodules may disappear, but they may persist as hard lumps or become moist, necrotic, and slough or ulcerated (Figure 3B). Lesions where skin is lost may remain visible for long periods. When lesions coalesce, large areas of raw tissue can be exposed, and these are susceptible to invasion with screwworm fly larvae. He
sloughed away lesion may create a hole of full skin thickness and characteristic lesion of “inverted conical zone” of necrosis, known as “sit fast”.

![Image of lesions](image)

**Figure 4.** Distinguishing lesions of LSD: Raised and separated narrow ring of hemorrhage” (A), skin lesions leaving ulcer (B) and “sit fast” like “inverted conical zone” of necrosis (C)

Severe cases of LSD are highly characteristic and easy to recognize, but early stages of infection and mild cases may be confusing with other diseases affecting the skin. For instance, Pseudo lumpy skin disease also known as Allerton virus caused by bovine herpes virus-2 (BHV) has related skin lesions with LSD and requires laboratory confirmation to distinguish. Pseudo lumpy skin disease has circular superficial lesions which may cover the entire body and up to 2 cm in diameter. It has distinctive intact central area (Figure 4B) and raised edges, accompanied by loss of hair. Urticaria, Streptotrichosis (Dermatophilus congolensis infection), ringworm, Hypoderma bovis infection, photosensitization, bovine popular stomatitis, foot and mouth disease, bovine viral diarrhea, and malignant catarrhal fever are all considered as differential diagnosis of LSD.

![Image of lesions](image)

**Figure 5.** Illustrative clinical feature of LSD (A) and BHV (B), with characteristic intact central area (blue arrow).

**Pathology**

**Gross pathological lesions:** Skin nodules are usually uniform in size, firm round and raised, but some may fuse into large irregular and circumscribed plaques, when incised the surface of the nodule is reddish-gray and edematous in the sub-cutis layer. A necrotic lesion which is circular in nature may be observed in different parts of alimentary, respiratory and urogenital tract. For instance, muzzle, nasal cavity, larynx, trachea, bronchi,
inside of lips, gingiva, dental pad, abomasum, uterus, vagina, teats, udder and testes may be involved. Regional lymph nodes become enlarged (up to 10 times their usual size), edematous, congested and having pyaemic foci, in addition to local cellulitis. Pleuritis and enlargement of mediastinal lymph nodes are also involved in severe cases. The LSD typical nodular lesions also encompass the musculature and the fascia over limb and appear grey-white surrounded by red inflammatory tissue. Furthermore, the lesions are separated from the necrotic epithelium far from the healthy tissue and leave an ulcer that slowly heals by granulation. Severely infected animals may show secondary bacterial pneumonia, tracheal stenosis, acute and chronic orchitis, mastitis with secondary bacterial infection, and similar lesions in the female reproductive tract.

**Histopathological findings:** Histopathological findings of the LSD are typical and provide a basis for diagnosis. The pathognomonic LSD lesion eosinophilic intracytoplasmic inclusion bodies may be detected microscopically in the keratinocytes, macrophages, endothelial cells and pericytes from skin nodules in addition to ballooning and degeneration of the cell layers. Inflammatory cells including macrophages, lymphocyte and eosinophils are infiltrated the affected area. In addition, widespread vasculitis which reflects the viral tropism for endothelial cells is seen histologically. If there is muscular damage during the course of LSD, histopathologically severe coagulative necrosis in subcutaneous muscle may be observed.

**HEALTH AND ECONOMIC IMPACT**

The socio-economic impact of LSD can be direct or indirect and has been registered by several major sectors and industries. The sharp drop in milk production is the fast and foremost visible effect directly associated with LSD in the South-Asian region which harbored 21% of the world’s dairy farm animals. According to a Turkish investigation, an impacted cow’s average milk yield fell by 159L each lactation. However, meat from LSD infected cattle is not prohibited from entering the food chain, despite the possibility of the meat having secondary bacterial infection. An estimated 1.2% and 6.2% reduction in beef production per annum among local breeds and Friesian cattle was reported in Ethiopia respectively, due to LSDV infection. Besides, any breaches, scars, or lesions in the raw cattle hides or skin may deteriorate the value of leather, as in the case of severely LSD affected animal hides. Bangladeshi leather is highly admired for its good quality and 56% of leather is generated from cattle, that contributed 3.5% of the country’s annual exports. Similarly, having the global exporting position of ninth, India earns annual revenue of US$ 8,500 million for its leather and leather products. Pyrexia and lameness hamper the use of animals for draught purposes.

LSD can be transmitted to breeding stock through artificial insemination with infected bull semen, resulting in a lower rate of pregnancy. What is more, several health complications including mastitis, orchitis, abortion, and infertility in bulls also cause huge economic losses for farm owners. The indirect economic impact of LSD is counted for trade restriction, immunization, quarantine and treatment costs, feed and labor costs, stamping out, maintenance of farm biosecurity, etc. Farm owners need to pay additional cost of feed supplement for sick animals during the period of recovery along with the prolonged duration for fattening. The expenses for LSD in Jordan that involved medication of the affected cattle with broad-spectrum antibiotic and anti-inflammatory drugs was estimated at US$ 35.04. Sometimes a large number of affected animals have to be stamped out, as
was done in Greece and Bulgaria where Bulgaria faced the highest economic disaster of around US$ 8000 per herd. As a transboundary infectious disease, the probability of rapid spread of LSD by means of production and marketing channel is high. A risk assessment study for LSD conducted on an Ethiopian bull market estimated the financial loss of US$ 6,67,785.6 considering the culling rates, and the sum of bulls at risk. In a peripheral farming scheme, it is not always rational to adopt quarantine cost-effectively. An estimation figure of quarantine budget in USA including manual labour, feedstuff, diagnostic testing, discarding test positives, and other apprehensive expenses accounted for $145,000 (2010 US$). Israel paid nearly US$ 750,000 for controlling the initial outbreak of LSD by discarding every suspected animal in the locality and executing the ring vaccination.

**DIAGNOSIS OF LSD**

The diagnosis of LSD is based on typical clinical signs combined with laboratory confirmation of the presence of the virus or antigen.

1. **A Field presumptive diagnosis of LSD can be based upon the:**
   
   A. Morbidity, mortality and clinical signs that reflect LSD such as:
   
   1. Contagious disease with generalised skin nodules.
   2. A characteristic inverted conical necrosis of skin nodules (stiffest), Enlargement of lymph nodes draining affected areas.
   3. Persistent fever, emaciation, and low mortality.
   4. Pox lesions of mucous membrane of the mouth, the pharynx, epiglottis, tongue and throughout the digestive tract, mucous membranes of the nasal cavity, trachea, and lungs
   5. Oedema and areas of focal lobular atelectasis in lungs
   6. Pleuritis with enlargement of the mediastinal lymph nodes in severe cases
   7. Synovitis and tendosynovitis with fibrin in the synovial fluid
   8. Pox lesions may be present in the testicles and urinary bladder

   B. Histopathological features Skin biopsies of early lesions are suitable for histopathology and should be preserved in 10 percent buffered formalin. The most diagnostic histopathological features are:

   1. Congestion, haemorrhage, oedema, vasculitis and necrosis are always associated with nodules that are involving all skin layers, subcutaneous tissue, and often adjacent musculature.
   2. Lymphoid proliferation, oedema, congestion and haemorrhage.
   3. Vasculitis, thrombosis, infarction, perivascular fibroplasia and cellular infiltrates
   4. Intracytoplasmic eosinophilic inclusions may be seen in different cells.
2. A confirmative diagnosis of LSD can be based upon the: • Laboratory investigations and identification of the agent based on (OIE Terrestrial Manual 2010; OIE 2013):

A. Isolation of the virus

Confirmation of lumpy skin disease in a new area requires virus isolation and identification. Samples for virus isolation should be collected within the first week of the occurrence of clinical signs, before the development of neutralising antibodies (Davies 1991; Davies et al 1971). Skin biopsies of early lesions (ones where necrosis has not occurred) provide samples that can be used for virus isolation and electron microscopy. In addition, LSD virus can be isolated fromuffy coat from the blood sample collected into EDTA or heparin during the viraemic stage of LSD. Samples should be taken from at least three animals. Samples aspirated from enlarged lymph nodes can be also used for virus isolation. LSD virus grows in tissue culture of bovine, ovine or caprine origin. Bovine dermis cells or lamb testis (LT) cells (Primary or secondary culture), are considered to be the most susceptible cells. LSD capripoxvirus have been also adapted to grow on the chorioallantoic membrane of embryonated chicken eggs and African green monkey kidney (Vero) cells, which is not recommended for primary isolation (OIE Terrestrial Manual 2010).

B. Electron microscopy

Transmission electron microscopic (TEM) diagnosis of LSD can be confirmed within a few hours of receipt of specimens. TEM demonstration of virus in negatively stained preparations of biopsy specimens taken from affected skin or mucous membranes. Mature capripox virions have an average size 320 x 260 nm and are a more oval profile and larger lateral bodies than orthopox virions (OIE Terrestrial Manual 2010).

C. Fluorescent antibody tests

Capri poxvirus antigen can also be identified on the infected cover-slips or tissue culture slides using fluorescent antibody tests.

D. Agar gel immunodiffusion

An agar gel immunodiffusion (AGID) test has been used for detecting the precipitating antigen of capri poxvirus, but has the disadvantage that this antigen is shared by parapoxviral.

E. Enzyme-linked immunosorbent assay

It is made by using expressed recombinant antigen to produce P32 monospecific polyclonal antiserum and the production of monoclonal antibodies (MAbs) (Carn, et al 1994).
F. Polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP) assay
   It have been used for detection of capri poxviruses with higher sensitivity.

3. Serology

Frozen sera from both acute and convalescent animals are used. Virus neutralisation (cross reacts with all capri poxviruses) and indirect fluorescent antibody test (cross reaction with parapoxviruses) are commonly used. Enzyme-linked immunosorbent assay for the detection of antibodies against capri pox virus has been developed using the expressed structural P32 protein (Carn et al., 1994; Heine et al 1999). Agar gel immunodiffusion tests (This test may give false-positive reactions due to cross reaction with bovine papular stomatitis virus and pseudocowpox virus). Western blot analysis provides a sensitive and specific system for the detection of antibody to capri pox virus structural proteins, although the test is expensive and difficult to carry out.

Differential diagnosis There are many diseases causing similar signs of LSD. It is important to obtain a definite diagnosis to ensure the best preventative and control measures for susceptible herds. LSD can be confused with the following diseases:

- Pseudo-lumpy-skin disease
- Bovine virus diarrhoea/mucosal disease
- Demodicosis (Demodex)
- Bovine malignant catarrhal fever (Snotsiekte)
- Rinderpest
- Besnoitiosis
- Oncocercariasis
- Insect bite allergies
Prevention and Control

Till date no effective treatment against LSD has been developed. Anti-inflammatory and antibiotics are used for symptomatic treatment. To control the disease, effective control and preventive measures need to be implemented, which include: a) Restrict movement: Movement of infected animals with LSD should be strictly prohibited to prevent the spread of transboundary disease. Within countries, if animal with such lesions are observed, they should be quarantined for inspection to prevent the rapid spread of disease. b) Restrict vector movements: Vectors movement due to prevailing winds may cause disease transmission. Vector control methods like use of vector traps, use of insecticides can also be used for preventing the disease. c) Vaccination: A live attenuated vaccine is available for LSD. Based on different strains of LSD virus, companies prepared vaccines. It is either based on Neethling strain like Lumpy Skin Disease Vaccine for Cattle (Ondersteapoort Biological Products; OBP, South Africa) or Bovivax (MCI Sante Animale, Morocco), or based on SIS Neethling type (Lumpyvax, MSD Animal Health-Intervet, South Africa). As LSD is closely related to sheeppox and goatpox virus, vaccine against sheeppox and goatpox can be used for LSD (Tuppurainen et al. 2015). Different strains of virus used as vaccine strain as per OIE. Homologous Lumpy skin disease virus Neethling strain from South Africa, passaged 60 times in lamb kidney cells and 20 times on the chorioallantoic membrane of embryonated chicken eggs provides immunity for 3 years. Sheeppox vaccines used against LSD includes Kenyan sheeppox virus passaged 18 times in lamb testis (LT) cells or fetal calf muscle cells, Yugoslavian RM 65 sheep pox strain, Romanian sheep pox strain. The heterologous vaccine strains cause some local reactions. These vaccines are not advised in sheeppox and goatpox affected areas as such vaccines may serve as source of infection for susceptible population of sheep and goat. Live attenuated Gorgan goatpox strain provide good protection in cattle with practically no side effect (Gari et al. 2015; Brenner et al. 2009; Capstick and Coakley 1961 1962; Carn et al. 1994). For effective control and prevention of disease, long term vaccination with 100% coverage should be made mandatory as LSD virus being stable survives in environment...
for long time. Before introducing new animals to the affected farm, they should be immunized. Calves should be immunized at the age of 3 to 4 months raised from mothers, who are vaccinated or naturally infected. Pregnant cows, breeding bulls can be vaccinated annually.

Conclusion

To recapitulate, this review summarizes eight virgin hotspots and their extent for the Lumpy Skin Disease (LSD) in South-East Asian cattle. The disease has become an extreme threat for marginal farmers. Until nineteenth century, the disease was endemic in greater Africa, which then outstretched into the Middle East, Eastern Europe, and the Russian Federation and recently in Asia. The recurrent assault by LSD in vulnerable areas has stricken the attention of the scientific community. Hence, it is needless to say, this is the high time to anticipate emergency preparedness to limit this trans-boundary disease from spreading enormously. Attention should be concentrated on vector control, movement restriction, harsh quarantine, improved vaccination programs, proper veterinary care, and overall farm sanitary management to avoid incursion and spread of the contagion. Thus, the study encourages future scholars to focus on identifying the source of infection, molecular detection and characterization of the causal agent, and finally, the epidemiology and ecology of LSDV in Southeast Asia.

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