



ISSN (E): 2277-7695  
ISSN (P): 2349-8242  
NAAS Rating: 5.23  
TPI 2022; SP-11(11): 1857-1861  
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Received: 27-09-2022

Accepted: 29-10-2022

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## Emergence of lumpy skin disease virus (LSDV) infection in cattle and buffaloes in India

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### Abstract

Lumpy skin disease (LSD) is viral, infectious disease, caused by lumpy skin disease virus (LSDV) characterized by nodules on the skin and spread to other parts of the body. It is major health problems affecting the livestock industry in India and other country. It is occasionally fatal disease. Major source of transmission is ulcerated skin lesion, although the virus is exiled via body secretions and excretions (including semen). Vector such as biting flies, mosquitoes and ticks (hematophagous arthropods) transmit infection mechanically. Under experimental conditions, the typical lumpy skin disease lesions may appear 7 to 14 days after infection, although in natural cases, it may take 2 to 5 weeks. Decreased milk production, abortions, temporary or permanent sterility, damage to the hide, and deaths will ensue, all of which causes significant economic loss to country. Therefore, the most efficient method of reducing the spread and financial burden of lumpy skin disease is mass vaccination along with other suitable control measures.

**Keywords:** Lumpy skin disease virus, cattle, buffaloes

### Introduction

LSD is viral disease of cattle and appears as firm, circumscribed skin nodules that may affect the mucous membranes of the respiratory system, urogenital system, and other internal organs. Secondary bacterial infection often aggravates the condition. Infectious viral agent LSDV of *Poxviridae* family causes LSD (Quinn *et al.*, 2016) [36]. It was first discovered in Africa and has since spread to the Middle East, Asia, and Eastern Europe. More recently, outbreaks of lumpy skin disease were reported in most of the states of country (India). International awareness has been raised by the lumpy skin disease's recent worldwide expansion (Mulatu and Feyisa, 2018) [32]. The principal method of transmission is mechanical by arthropod vectors. LSD symptoms in cattle are mild to severe including characteristic skin eruptions, fever, lacrimation, and hypersalivation. Multiple skin nodules over back, neck, tail, limb perineum, and internal & genital organs are important feature of LSDV infection. Animals also display lameness, emaciation and reduced milk production. Lymphadenitis and brisket edema are highly prominent and sometimes it may fatal and cause death. Pneumonia is a most common sequel in affected animals with lesions in the mouth and respiratory tract (trachea and lungs). Morbidity and mortality of LSD can vary considerably depending on the immunological status of the population including breeds of cattle and vectors involved in the spread of virus (Babiuk *et al.*, 2008) [10]. In addition, the incidence of LSD in Holstein Friesian and crossbred cattle was found to be significantly higher than in local zebu (Gari *et al.*, 2010) [18]. LSD can be diagnosed by histopathology, electron microscopy, virus isolation or molecular techniques including PCR. Mass vaccination and preventive measures such as control of vectors can be help to minimize outbreaks of LSD.

### Etiology

The Poxviridae family of viruses, which contains the two subfamilies Chordopoxvirinae and Entomopoxvirinae, infects both vertebrates and invertebrates, with the exception of dogs (Quinn *et al.*, 2016) [36]. The genus Capripoxvirus, which primarily affects ruminants, is one of the ten genera of the Chordopoxvirinae subfamily. This genus contains three species: the Sheep Pox Virus (SPPV), the Goat Pox Virus (GTPV), and the Lumpy Skin Disease Virus (LSDV), which is primarily responsible for LSD outbreaks in cattle and water buffalo (King *et al.*, 2012). The LSDV is a 320 260 nm enveloped ssDNA virus. The virus can remain infectious for up to 35 days in dry necrotic nodules and for up to 18 days in air-dried hides

long after the animal has been put to death since it is stable at room temperature (Khan *et al.*, 2021; Ali and Gumbe, 2018) [25, 6].

### Epidemiology

LSD was initially discovered in Zambia in 1929, but it went unnoticed (Ali and Gumbe, 2018) [6]. However, the degree of infectiousness was first documented when it struck Zimbabwe, Botswana, and the Republic of South Africa from 1943 to 1945 (Aber *et al.*, 2015) [2] and spread rapidly in the cattle population across African countries except some countries like Algeria, Libya, Tunisia and Morocco which have been spared from devastation and wrath of this disease (Tuppurainen and Oura, 2012) [16]. Until 1984, LSD was maintained within the countries of Sub-Saharan Africa (Tuppurainen and Oura, 2012) [16]. Egypt geographically being at the cusp of Saharan desert and Arabian Peninsula had the most proximity and probability of transboundary emergence for LSD. First outbreak of this disease in Egypt was reported in 1988 and then again it re-emerged in 2006 due to unrestricted movement of cattle from African countries (Ali *et al.*, 1990; Fayez and Ahmed, 2011) [7, 17].

The first confirmed transcontinental spread of LSD from the African to Middle-East Asian countries occurred when the disease was reported in Israel in 1989 (Yeruham *et al.*, 1995) [45]. Researchers have reported that LSD spread to Israel via *Stomoxys calcitrans* vector transmission that migrated from Egypt (Yeruham *et al.*, 1995) [45]. The disease hit the Middle Eastern countries since 1990 including Kuwait (1991), Lebanon (1993), Yemen (1995), United Arab Emirates (2000), Bahrain (2003), and Oman (2010) (Sudhakar *et al.*, 2020) [40]. Subsequently, outbreaks were reported in Jordan, Iraq, and Turkey in the year 2013, and Iran, Cyprus, and Azerbaijan in 2014 (Panel and Health, 2016) [34]. Then the virus made its way into the South East Asian country among which Bangladesh first reported an epidemic of LSD in July 2019 where sixty-six cases were reported (Moumita *et al.*, 2021). On the 3rd of August 2019, China became the second country in Southeast Asia to have an epidemic where 65 animals were infected in the Ili Kazak region, near the border of Kazakhstan which reported the last outbreak in 2016 (Calistri *et al.*, 2020) [13]. In India, first outbreak of the disease was reported in Odisha state in the month of August, 2019, in monsoon season with high humidity and vector density.

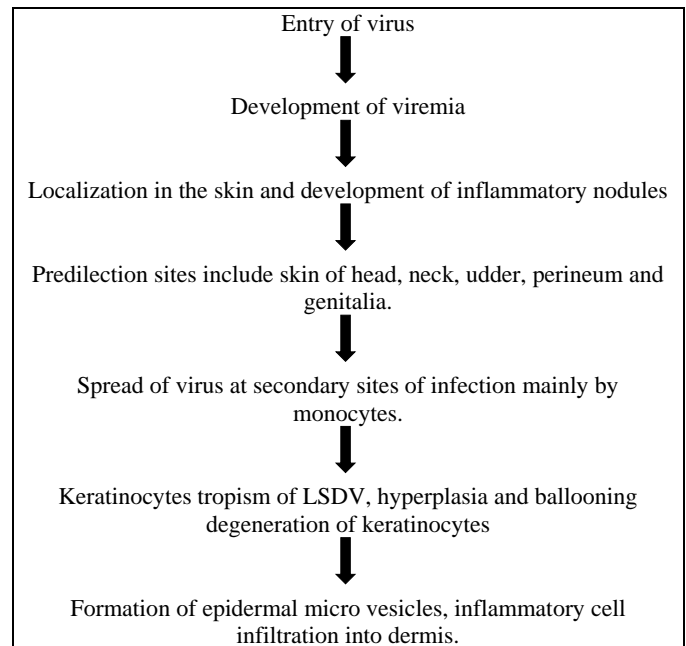
### Transmission

In general, there are two ways to categorise the LSDV transmission mode: non-vector and vector. There is very less evidence of direct transmission. Saliva, nasal, and ocular secretions include infectious LSDV that spreads disease by contaminating shared eating and drinking locations (Gubbins, 2019) [20]. Other potential sources of infection include consumption of contaminated milk, intrauterine transmission, dispersal through contaminated needles used for immunisation, and dispersion through contaminated semen used for coitus (Ali and Gumbe, 2018; Tuppurainen *et al.*, 2017) [43].

LSDV is primarily transmitted mechanically through arthropod vectors (Kasem *et al.*, 2018; Sprygin *et al.*, 2019) [24, 39]. The majority of sub-Saharan Africa is experiencing a sudden rise in disease incidence as a result of the warm, humid weather (Nawathe *et al.*, 1982; Kondela *et al.*, 1984) [15, 27]. *Aedes aegypti*, *Amblyomma hebraeum*, *Rhipicephalus appendiculatus* (Brown ear tick), *Rhipicephalus decoloratus*

(Blue tick), as well as the flies *Stomoxys calcitrans*, *Haematobia irritans* and *Musca domestica*, have all been linked to the transmission of LSDV in sub-Saharan Africa (Zeynalova *et al.*, 2016; Gubbins, 2019; Annandale *et al.*, 2014) [46, 20, 9]. LSDV is transmitted trans-stadially and transovarially during cold temperatures in the tick host (Kasem *et al.*, 2018; Sprygin *et al.*, 2019; Ali *et al.*, 2012; Rouby and Aboulsoud, 2016) [24, 39, 8, 37].

**Pathogenesis:** Incubation period of disease in natural condition is between 2 and 5 weeks (Lubinga *et al.*, 2015) [30]



### Coalescence of epidermal micro vesicles into large vesicles and ulceration development

- After formation of skin lesion, cells such as fibroblasts, pericytes, and endothelial cells of lymphatic and blood vessels, lesions are produced in those sites (Abdulqa *et al.*, 2016; Hailu *et al.*, 2014) [1, 22].
- Microscopic changes in acute skin wounds include edema, vasculitis, thrombosis, lymphangitis, infarction, and necrosis (Aber *et al.*, 2015) [2].
- Large nodules may become necrotic and eventually fibrotic and persist for several months (sitfasts); the scars may remain indefinitely. Small nodules may resolve spontaneously without consequences. (Ali and Gumbe, 2018; Lubinga *et al.*, 2014) [6, 29].

### Clinical signs

- The incubation period of disease in natural condition is between 2 and 5 weeks but in experimental condition, the duration ranges from 7 to 14 days (Gupta *et al.*, 2020) [21].
- There are three clinical manifestations of lumpy skin disease: acute, subacute, and chronic. The infection begins with biphasic fever.
- Clinical signs of a mild infection include one or two lumps of nodules that occur within two to three days of the initiation of fever, emaciation, ocular discharge, and agalactia.
- Later, it is possible to see nodular lesions on the animal's body that are painful and hyperemic, notably in the skin of the muzzle, nares, back, legs, scrotum, perineum, eyelids, lower ear, nasal and oral mucosa, and tail (Salib

and Osman, 2011) [38].

- In a severe situation, the skin on the body produced more than 100 nodules, and this stage lasted for 7 to 12 days. Over time, sores appear on the mucous membranes of the mouth, vulva, respiratory tract, and nose.
- The skin lesions harden and becoming necrotic after two to three weeks, making the animals uncomfortable and making them reluctant to move.
- The characteristic lesion "sitfast" may slough, leaving holes that could invite bacterial invasion and screwworm fly invasion, both of which could result in septicemia (Abutarbush *et al.*, 2013; Constable *et al.*, 2017) [4, 14].
- Hundreds of nodules appear all over the skin in large numbers in the severe condition, which lasts for approximately a week before they harden up and start to be encapsulated by narrow hemorrhagic rings.
- The lesions may extend to adjacent mucosae as they continue to scab over. The dermis and muscle are currently attached to these wart-like formations, which have an apparent ballooning degeneration pattern and the presence of eosinophilic intracytoplasmic inclusion bodies, according to the histopathology of these nodules (Tuppurainen and Oura, 2012) [16]. Within two to three weeks, these exposed components dry out and harden, causing pain upon movement of animals.
- The development of fistulas, also known as "sit fasts," is caused by the ongoing degradation of these sites and the inadequate re-epithelialization that results. It has been reported that fly maggots or screw worm fly larvae frequently infest these wounds.
- Additionally, suppuration and subsequent bacterial infections may cause fatal acute septicemia (Abutarbush, 2017; Constable *et al.*, 2017) [3, 14].

#### Post mortem changes

Pox lesions can be found throughout the entire digestive and respiratory tract and on surface of almost every internal organ.

- Ulcerative lesions in oral cavity
- Ulceration of skin lesion
- Lesions in trachea
- Lesions in gall bladder

#### Histopathological alterations

Microscopic examination of skin lesions and lymph nodes in lumpy skin disease virus affected cattle.

- Eosinophilic intracytoplasmic inclusion bodies
- Necrotic vasculitis in dermal arteriole with infiltration of neutrophils
- Zenker's necrosis in the dermal muscles and mononuclear cells aggregation
- Severe edema and infiltration of neutrophils

#### Diagnosis

The diagnosis of LSD can be established based on the typical clinical signs, enlarged superficial lymph nodes and generalized nodular skin lesions in animals combined with laboratory confirmation of the presence of the virus or antigen. Prior studies have established the comparative effectiveness of PCR and viral culturing whereby viremia was detected 4–11 days using PCR and 1–12 days using virus isolation (Heine *et al.*, 1999; Lamien *et al.*, 2011; Orlova *et al.*, 2006) [23, 28, 33]. Samples obtained from the skin lesions yield more positive results in PCR than the blood or those collected from septic viscera due to the greater load of viral

particles sheltered in the nodule [OIE (2021)]. Fluids like saliva, nasal swab, or whole blood can be collected from clinically infested animals for viral isolation and molecular testing (Peck and Bruce, 2017) [35]. Additionally, the disease can be detected using serological tests using Enzyme-linked Immunosorbent Assay (ELISA), Indirect Fluorescent Antibody test (IFAT), Indirect Immunofluorescence test, Virus Neutralization Test (VNT) and Serum Neutralization Test (SNT) (Molla *et al.*, 2017; Brenner *et al.*, 2006) [31, 12]. However, the ELISA has been confirmed experimentally showing higher sensitivity and specificity in comparison with IFTA or VNT (Alexander *et al.*, 2019) [5]. A fairly new assay called Immuno-peroxidase Monolayer Assay (IPMA) has been identified for potential use in LSD diagnosis. It is a cheap and convenient test, adapted to low biosafety levels, and has higher sensitivity and specificity than VNT and commercial ELISA (Bedekević *et al.*, 2018) [11].

#### Economic impact

Office International des Epizooties (OIE) has categorized Lumpy skin disease as notifiable outbreak considering its transboundary potential, high economic losses and threat as agro-terrorism (Abutarbush, 2017) [3]. The economic importance of the disease was mainly due to having high morbidity rate rather than mortality (Tuppurainen and Oura, 2011) [28]. Major consequences of the disease are retarded genetic improvement, limits the ability of the animal to work, draught power and traction loss, abortion in pregnant cows, marked reduction of milk yield during the active case of the disease, sterility and infertility in both sexes of cattle, permanent damage to hide and chronic debility in beef cattle etc. (Tuppurainen, 2005) [44]. The financial implication of these losses is greatly significant to the herd owners, consumers and the industrial sectors, which can process the livestock products and by products. Reports from Ethiopia indicated that the financial loss estimated based on milk, beef, draught power, mortality, treatment and vaccination costs in individual head of local zebu were lost 6.43 USD and for the Holstein Friesian 58 USD (Getachew *et al.*, 2010) [19]. If LSD became endemic, continuing economic loss and poor productivity would occur due to stock losses, reduced production in cattle industries and cost of preventative vaccination.

#### Control

No specific treatment has been recommended for LSD. However, vitamins, antibiotics, anti-inflammatory drugs are used to treat secondary bacterial infections or to deal with fever or inflammation and improvement of the animal's appetite. Biting flies and certain tick species are most probably the most important method of transmission of the disease so that control of Lumpy skin disease by quarantine and movement control is not very effective. Use of insecticides together with repellents can be an aid in the prevention of the spread of LSD. LSD outbreaks can be eradicated by quarantines, depopulation of infected and exposed animals, proper disposal of carcasses, cleaning and disinfection of the premises and insect control. LSD control can only be by vaccination or immunoprophylaxis. Homologous live attenuated virus vaccine (Neethling strain: immunity conferred lasts up to 3 years). Heterologous live attenuated virus vaccine (Sheep or goat pox vaccine, but may cause local, sometimes severe reactions). This vaccine is not advised in countries free from sheep and goat pox because the

live vaccines could otherwise provide a source of infection for the susceptible sheep and goat populations. There is no new generation recombinant capripox vaccines are commercially available.

### Conclusion

Bovines are important livestock species contributing considerably to the world economy. Previously, this disease was only found in some countries like Africa, but it has recently spread to Asia, a region that had previously been free of the disease, which is concerning for the livestock rearing industry because the economies of the majority of these nations are based on agriculture. The expansion of this disease to more extensive geographic areas of the Indian subcontinent will undoubtedly have a negative impact on all sectors of the economy, but the rural economy in particular LSD may also result in a decline in the export of cattle and livestock-related goods. To determine the true disease prevalence, the causes of LSD's introduction into India must be looked into, combined with epidemiological random screening in various areas. The only way to avoid the disease is through vaccination, in addition to efficient quarantine measures and vector control techniques.

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