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Lumpy Skin Disease – An Emerging Disease in India

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Abstract

Lumpy skin disease (LSD) is a vector – borne pox disease of domestic cattle and buffaloes caused by a single strain of Capri pox virus. The other members of the Capri pox genus are sheep pox and goat pox virus to which it is antigenically closely related. It leads to serious economic consequences and hence is categorized as a notifiable disease. The disease is characterized chiefly by generalized skin nodules all over the body and death can occur in complicated cases. LSD was first suspected and noticed in cattle in the month of August, 2019 in five coastal districts of Odisha. Till then cases have been reported from different parts of India causing devastating effects on cattle production and life. Occurrence of LSD outbreaks now in India has several implications with regard to its economic impact on dairy cattle population, laboratory diagnostic capacity, surveillance, prevention and control. The primary cause is usually associated with the introduction of new animal (s) into, or in close proximity to, a herd or village or region. Restricting the disease will need isolation of sick animals, restriction of movement of infected cattle, ban of cattle trade, closure of cattle markets, disinfection of infected premises and vector control. As per the OIE, vaccination is the only effective way to control LSD outbreaks in endemic countries. In India, for control of LSD a heterologous live attenuated GTPV (Uttarkashi strain) vaccine has been officially permitted for emergency use in cattle and buffaloes. This review aims to summarize the latest developments in the epidemiology of LSD with the focus on transboundary spread, prevention, control and economic implications on India.

Key words: Lumpy skin disease, Capripox virus, skin nodules, vector borne, vaccination.

Introduction

Lumpy skin disease (LSD) is a serious and economically important transboundary viral disease caused by a single strain of capripox virus affecting cattle mainly, but can also affect domestic water buffalo (*Bubalus bubalis*) and some wild ruminants. The virus is also called Neethling virus and thus, the diseases as "Neethling disease". It is known by various names such as Pseudo-urticaria", "Exanthema nodularis bovis", and "Knopvelsiekte" (Al-Salihi & Hassan, 2015; Tuppurainen *et. al.* 2017). After a sudden first appearance late in 1929 in Northern Rhodesia (Zambia), it spread throughout Africa over the following years and later spread to other countries. LSD has devastating effects on cattle production because of its serious economic consequences and hence is categorized as a notifiable disease by the World Organization for Animal Health (OIE, 2021). The economic losses occur both from direct losses due to decreased milk production, damage of animal skin, abortion, temporary or permanent sterility of bulls and death and indirect losses due to trade restrictions and costs for laboratory diagnosis, supportive treatment, disinfection of premises and vaccination.

Agent

LSD is caused by lumpy skin disease virus (LSDV), which along with sheep pox virus (SPPV) and goat pox virus (GTPV) belongs to the genus Capri pox virus (CaPV) subfamily *Chordopoxvirniae* in the family Poxviridae. The LSDV is enveloped and has a double stranded DNA genome of about 151 kbp coding for 156 putative genes. They can be propagated on a variety of cells of bovine and ovine origin, causing easily recognizable cytopathic effects (CPE). The replication of LSDV occurs in the cytoplasm of the host cell in intracytoplasmic eosinophilic inclusion bodies. Although LSDV, SPPV and GTPV have high antigenic similarity and genetic identity (>96%), nine genes are known to exist in LSDV, but disrupted in GTPV and SPPV and the host specificity is most likely genetically determined (Kumar et. al. 2021). Nonetheless, genome sequence analyses have shown that they are phylogenetically distinct. Based on phylogenetic analysis, LSDV strains can be classified into 3 subgroups, field virulent strains, vaccine strains and recently identified vaccine-like recombinant strains (Coetzer & Tuppurainen, 2004).

The virus is stable in normal environmental conditions for long period. It can persist in dried skin crusts for 35 days, in necrotic nodules for 33 days and in air-dried hides for at least 18 days. Virus gets inactivated at 55ºC temperature for 2 h and 65ºC for 30 min. It is susceptible to highly alkaline or acid pH but can sustain pH 6.6–8.6 for 5 days at 37 C without significant reduction in titres. The virus is susceptible to ether (20%), chloroform, formalin (1%), phenol (2% for 15 min), sodium hypochlorite (2–3%), iodine compounds (1:33 dilution) and quaternary ammonium compounds (0.5%) (OIE, 2017). LSDV is very stable and can be recovered even after 10 years from the skin nodules kept at -80ºC and after 6 months from the infected tissue culture fluid kept at 4ºC (Mulatu and Feyisa, 2018). The virus though very susceptible to sunlight and chemicals, it can persist for many months in dark environmental conditions, such as contaminated sheds.

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Clinical Manifestation

The clinical disease is characterized by malaise, anorexia, fever (up to 41˚C), enlarged superficial lymph nodes, watery/purulent nasal and ocular discharge and characteristic generalized skin nodules all over the body within 48 hrs. of infection The lumps are 1-3 cm in diameter and 1-2 cm deep. They are hard in consistency and affect the full thickness of skin and move easily with the skin when grasped between fingers and thumb. Nodules may appear in the mucosal linings which resemble skin nodule but with a "punched out" yellowish necrotic centre and irregular or circular outline. Within a few days, a circular dark line of necrosis appears around the surface of both skin and mucosal lesions to produce the "sit fast' that is typical of the disease. The central necrotic plug eventually sloughs to leave a raw granulating ulcer which heals subsequently over the weeks. Oedema of the legs and brisket may be seen. The purulent exudates from superficial lymph nodes and skin ulcers, in severe cases, may be seen tracking down the legs. However, the disease severity may vary from subclinical infection to death depending upon the LSD virus strain, vector prevalence, age and immune status of the host (Tuppurainen *et al*., 2017; OIE, 2018).

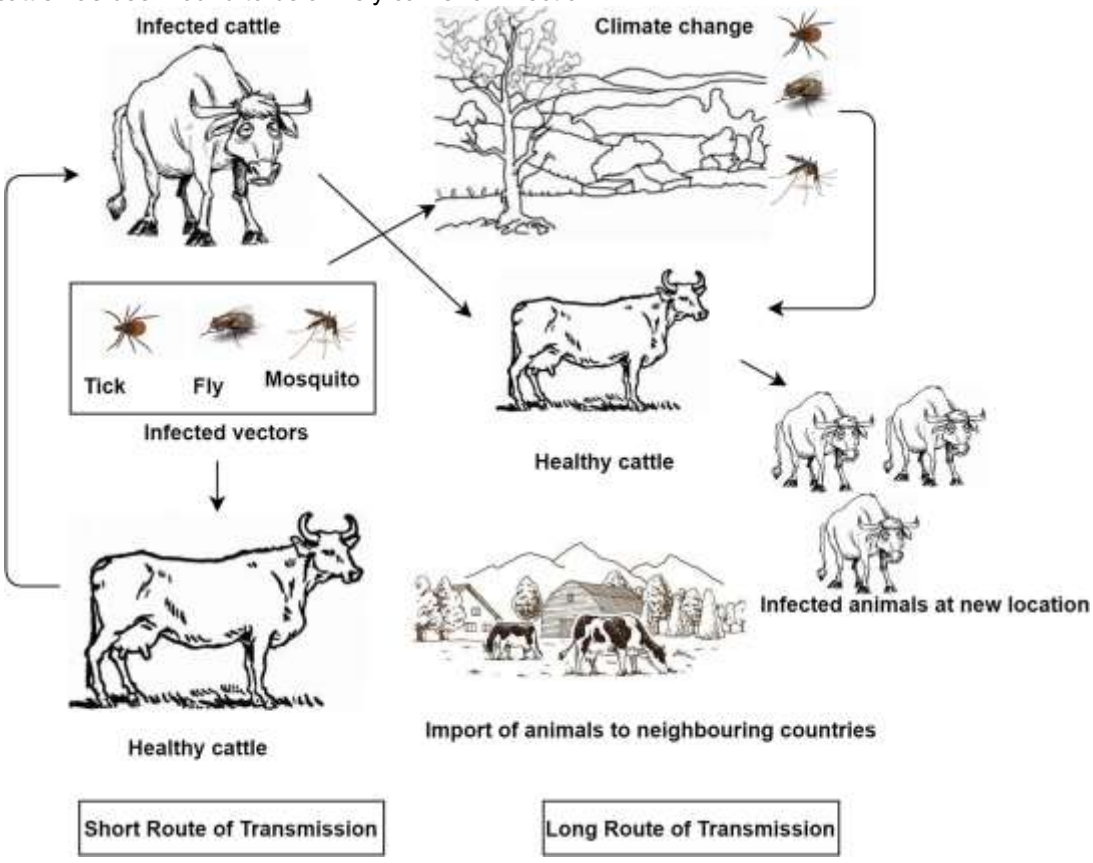
The morbidity rate can vary from 5 to almost 100% and mortality rate ranges most often between 1-3% but may reach up to 45%. A sharp drop (up to 90%) in milk yield occurs mainly during two weeks following appearance of nodular lesions. Secondary infections of the skin result in further debility and concurrent purulent mastitis. In cattle's occasional abortion, reduced sperm motility and increase in semen discard rate are observed.

Transmission and spread

LSD is transmitted predominantly by hematophagous arthropod vectors (dipterans and ticks) mechanically and the most important potential vector is stable fly *Stomoxys calcitrans*. *Lyperosia* fly*, Culex and Aedes* mosquitoes are also responsible for spread of diseases. It can also be transmitted by contact with saliva, nasal and ocular discharge. It is also vertically transmitted (Intrauterine) and through Semen (Annandale *et. al*., 2013).

The incidences of LSD are noticed mostly during the months of summer and the wet monsoon season coinciding with the most intense blood-biting insect activity period. Usually heavy rains have preceded epidemics and out breaks subside and disease tends to disappear at the end of rainy season.

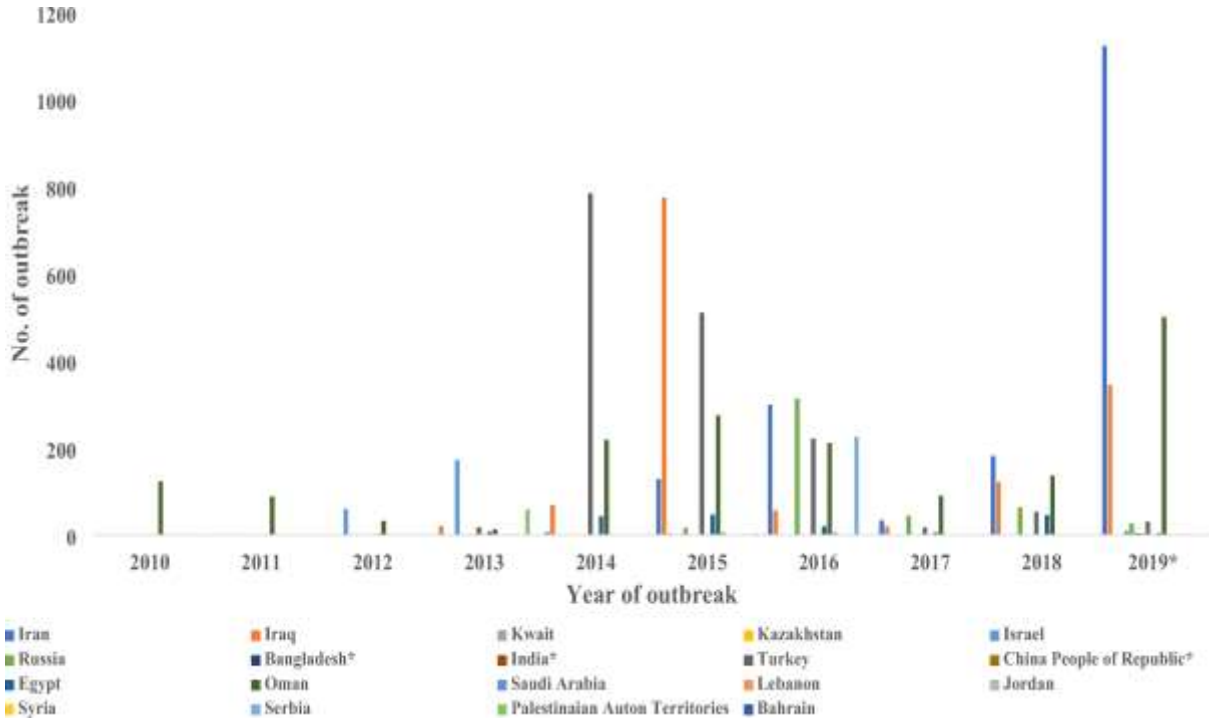
It is an important feature of the disease that epidemics recur after an interval of five to six year in an unvaccinated cattle population due to build-up of a fresh susceptible young population. No reservoir host apart from cattle has been found to be a likely carrier of infection.



Source: Gupta, T. *et al.* A review: Lumpy skin disease and its emergence in India. *Vet Res Commun* 44, 111–118 (2020).

Geographical spread

LSD was first recorded in Zambia in 1929, and historically restricted to Africa, before it spread into the Middle East and West Asia during 1988-2014 (Das et. al. 2021). In 2015, LSD further expanded its geographical range into Southern Europe and Central Asia including Russia and Kazakhstan (OIE, 2018; Hunter & Wallace, 2001). LSD was recently introduced into South, East and South-East Asia, with first reports of field outbreaks in China, Bangladesh and India in 2019, and subsequently in Nepal, Bhutan, Chinese Taipei, Myanmar, Hong Kong, Vietnam, Sri Lanka, Taiwan and Thailand (OIE, 2021; Al-Salihi & Hassa, 2015; Sameea *et. al*. 2017). The emergence of LSDV in 2019 in India and its rapid spread is a significant threat to cattle farming in India, which has the highest cattle population (192.49 million) in the world (Sudhakar *et. al*., 2020).



Temporal distribution of LSD virus in Asian countries from 2010 to 2019
(Data source: OIE disease record) * Mark shows the countries where disease appeared recently in 2019

Emergence of LSD in India

Of the several poxvirus infections affecting bovines, buffalo pox outbreaks in buffaloes and cattle have been reported in India but LSD was exotic until 2019. LSD was first suspected and noticed in cattle in the month of August 2019 in five coastal districts of Odisha. LSD outbreak investigations were carried out and laboratory testing of samples from LSD suspected animals were conducted at ICAR, NIHSAD, Bhopal. The results of virus isolation and identification and sequence analysis confirmed the involvement of field strains of LSDV in causing the LSD outbreaks in India (Sudhakar *e.t al*., 2020) and the first occurrence of LSD in India was notified by the OIE on 18th November 2019. LSD has since then spread across Eastern, Southern, Central, Western, Northern and North Eastern region of India (Gupta et. al. 2020). However, laboratory confirmed LSDV infection has not yet been reported in buffaloes in India, although recorded in neighbouring Nepal and Bangladesh.

A recent study on genetic and phylogenetic analyses of LSDV strains causing the first and subsequent field outbreaks in India confirmed that they are very similar (99.7-100% genetic identity) to the historical LSDV NI-2490/KSGP-like field strains from Kenya and LSDV (2019 outbreaks) from Bangladesh, but are different from contemporary field strains circulating in Africa, Middle East, Central Asia and Europe and vaccine-like recombinant strains circulating in Russia and China (Sudhakar *et. al*., 2020).

Diagnosis

The diagnosis can be made by observing characteristic skin lesions. Post mortem examinations reveal visceral lesions in the lungs, skeletal muscles, rumen, uterus and udder. Histopathological examinations reveal cellular infiltration in the dermis and sub cutis. Lymphocytes and macrophages with few plasma cells, neutrophils and fibroblasts can be seen in the inflamed zone. Cytopathic effect like rounding, shrinkage of cells and empty patches in the cell sheet in muscle cell culture provides additional confirmation, but confirmatory diagnosis requires OIE prescribed laboratory diagnostic tests (identification of LSDV by virus isolation, PCR or real-time PCR or serological tests). The molecular diagnostic tests such as Capri poxvirus generic gel based PCR and LSDV specific real time PCR are the most commonly used tests for laboratory diagnosis of LSDV,

while virus neutralisation test (VNT) and ELISA are recommended serological tests (OIE, 2018). PCR and real-time PCR are also used for differentiation between wild type LSDV and vaccine virus strains.

LSD in cattle need to be differentially diagnosed. For differential diagnosis from other closely related diseases of cattle, clinical samples need to be tested for pseudo lumpy skin disease caused by bovine herpes virus type 2 (BHV-2), buffalo pox caused by buffalo pox virus (BPXV), cowpox caused by cowpox virus (CPXV), pseudo-cowpox caused by pseudo cowpox virus (PCPV) and bovine pappular stomatitis caused by bovine papular stomatis virus (BPSV). The pseudo-LSD or Alleptron herpes virus infection is mild, the nodules are shallow with a depressed centre and the reaction being centred in the epidermis. A number of other conditions, parasitic, fungal, bacterial and allergic reactions can all produce lumps which are often difficult to differentiate, particularly in isolated cases.

LSDV field strains from India and Bangladesh possess 12-nt insertion in GPCR gene unlike other contemporary globally circulating LSDV field strains. But they have 27-nucleotide insertion in EEV gene similar to that found in other field strains. Moreover, emergence of vaccine-like recombinant LSDVs in causing typical LSD field outbreaks in Russia, China, Hong Kong and Vietnam has critical implications in LSD laboratory diagnosis including GPCR and EEV based DIVA tests (Tuppurainen *et. al*., 2020).

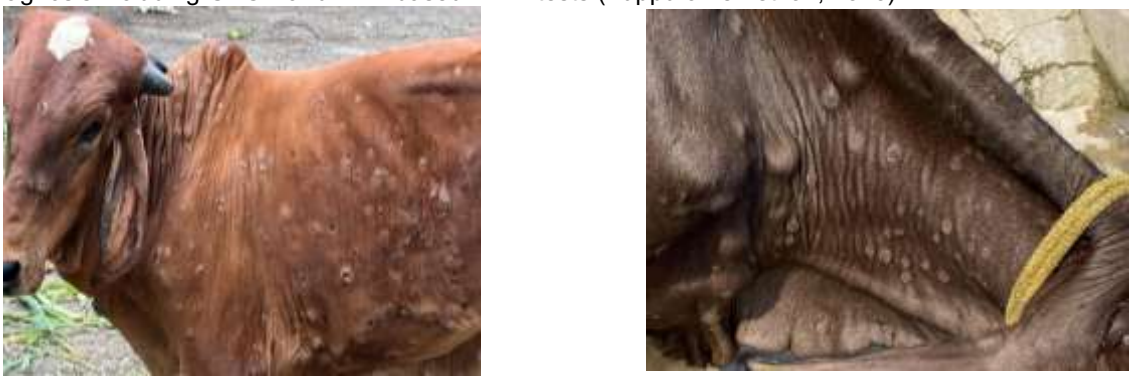


Fig: Showing characteristic generalized skin nodules all over the body.

Fig: Showing characteristic post mortem lesions in lungs and sub cutis.

Prevention and control

The three critical hallmarks of prevention and control of LSD are vaccination against LSD, restriction of cattle movement and farmer awareness. Restricting the disease will need isolation of sick animals, restriction of movement of infected cattle, ban of cattle trade, closure of cattle markets, disinfection of infected premises and vector control.

As per the OIE, vaccination is the only effective way to control LSD outbreaks in endemic countries (OIE, 2018). As Capri poxviruses are antigenically cross-reactive (strains like Kedong Valley, SP 143 and Isiolo), both homologous LSD live attenuated vaccine and heterologous goat pox or sheep pox live attenuated vaccines have been used in various countries with different success rates. Only mild allergic reactions were seen in some animals (Abutarbush, 2016). Successful vaccination with homologous live virus has been practised in Kenya, South Africa, Middle East and Eastern Europe and vaccinated animals have lifelong immunity. In India, for control of LSD a heterologous live attenuated GTPV (Uttarkashi strain) vaccine has been officially permitted for emergency use in cattle and buffaloes, only after the first documented LSD outbreak in 2019, while use of live attenuated LSD vaccine is prohibited (Sudhakar *et. al*., 2020).

Cattle once exposed to the disease appear to have a lifelong immunity whether or not they are clinically affected. Cell mediated immunity plays a pivotal role in this disease and humoral immunity is of less importance.

Conclusion

As the disease is expected to arise only after the onset of rains due to emergence of large number of vectors and the vector control is quite impracticable, herd immunity should be maintained by routine

vaccination during this critical period. If it is possible to diagnose early, ring vaccination and movement control of the affected animals have some value to halt its spread, but active immunization of all the susceptible population with a potent and effective vaccine is the only answer to prevent and control the disease.

In conclusion occurrence of LSD outbreaks now in India has several implications with regard to its economic impact on dairy cattle population, laboratory diagnostic capacity, surveillance, prevention and control.

Future perspectives

Although LSD occurrences have been reported in many States in India since 2019, the detail epidemiological studies at either State or National level has not yet been undertaken. Furthermore, there is no information regarding the mechanisms of LSDV transmission, arthropod vector species involved and transmission dynamics in India. Emergence of historical LSDV NI-2490/KSGP-like strains recently in India and Bangladesh and vaccine-like recombinant strains in China, highlights the importance of continuous monitoring and molecular characterization of LSDV in the region and development of multiple gene based DIVA diagnostic assays. Serious efforts should also be made to develop indigenous LSD vaccine and implement LSD prevention and control measures in the affected States with coordination of all stakeholders for immediate control of LSD to prevent losses in the Indian dairy sector.

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