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LUMPY SKIN DISEASE: A THREAT TO THE LIVESTOCK INDUSTRY - A REVIEW

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ABSTRACT

Lumpy skin disease (LSD) could cause huge economic losses to the farmers. It is a major obstacle to the international trade. Lumpy skin disease virus (LSDV) belongs to genus Capripoxvirus. The LSD causes substantial decrease in milk yield may be from 10% to 85% (no conjunction). In Karachi (Pakistan), milk and meat sales have been hampered by 60% to 70% because of LSD. All breeds and ages of cattle are involved, however, cows in peak lactation and young ones are more vulnerable. The LSD epidemics mostly occur in hot and humid environment at that time majority of the insects are active those acts as vector/insect species. Wildlife could promote the spread of LSD. The clinical picture of the LSD includes nasal discharge, inappetence, fever, lachrymation along with salivation and inflamed lymph nodes, body weight loss, and occasionally death. The LSD is described by slightly elevated, firm, demarcated skin nodules (2-7cm in diameter) that are typically spread all over the body. Morbidity varies from 0.75% to 100% whereas mortality is mostly low (0 to 7%). Tissues of digestive, respiratory, and reproductive tract show lesions. Secondary complications of serious LSD could be mastitis, pneumonia, keratitis, lameness, dysentery, and myiasis. Under a microscope, in skin nodules eosinophilic intracytoplasmic inclusion bodies in the keratinocytes are considered as pathognomonic. The LSD doesn't belong to the zoonotic diseases. Milk and meat from infected animal are reliable and safe for human consumption. It is urgent to opt strategies for the control and prevention of the disease. Restricted movement of infected animals is a major factor in the transmission of the LSD in the non-endemic area. Curtailment of vectors/insects is also proposed for the control of the disease. Additionally, vaccination/immunization with the homologous strain of the LSDV could be the best strategy for the control of the disease. Diagnosis has also prime importance that should be prompt and precise especially in the endemic areas has prime importance so that control measures could be opted well in time for the curtailment of the LSD.

***Keywords*:** Lumpy skin disease, Pathology, Prevention and control

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1. INTRODUCTION

Lumpy skin disease (LSD), acute or subacute systemic viral disease of cattle and water buffalo, is a major threat to livestock (Tuppurainen et al. 2017b; Givens 2018; Selim et al. 2021; Tran et al. 2021). All breeds and ages of cattle are involved, however, cows in full swing of lactation and young ones are more vulnerable (Tuppurainen et al. 2011; Khan et al. 2021). Due to its substantial economic losses and quick propagation, the World Organisation for Animal Health (OIE) has declared as notifiable this transboundary disease (Tuppurainen and Oura 2012; Sajid et al. 2012; Sevik and Dogan 2017; Tran et al. 2021; Lu et al. 2021). LSD has potential of rapid spread and substantial economic importance (Badhy et al. 2021). Domestic ruminants, like sheep, goats, cattle and water buffaloes are important animals affected by the LSDV. It causes huge economic losses to the farmers.

2. DISEASE DESCRIPTION

2.1. Etiology of LSD

Lumpy skin disease virus (LSDV) is within the genus Capripoxvirus, family Poxviridae. The genus Capripoxvirus also consist of goatpox virus and sheeppox virus. Thus, LSDV is linked to the sheeppox and goatpox viruses genetically (Namazi and Tafti 2021). LSDV is a double-stranded DNA virus, and the genome size is about

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150kbp with comparatively larger size about 290nm×270nm (Lu 2021), and around it there is lipid wall (Haftu et al. 2012; Elkady, 2016; Givens 2018; Gumbe 2018; Fig. 1). Zhang et al. (2020) and Cao et al. (2021) has shown negatively stained LSDV by electron microscope (EM) and transmission EM, respectively (Fig. 2).

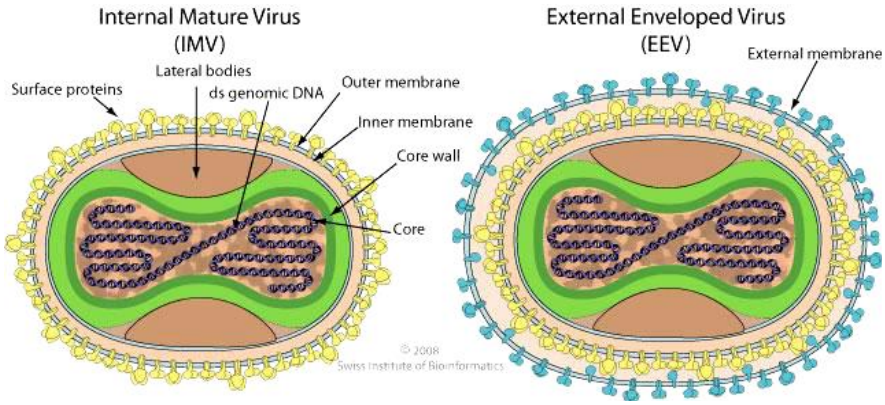

Fig. 1: Morphological structure of LSDV (Haftu 2012; Elkady, 2016; Gumbe 2018).

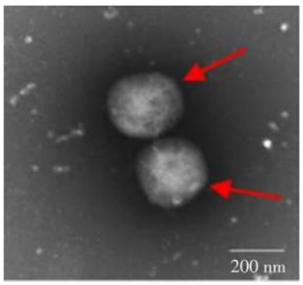

Fig. 2a: Visualization of negatively stained LSDV by Electron microscopy (Zhang et al. 2020).

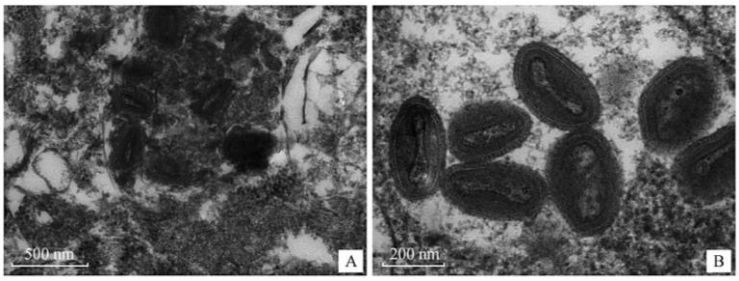

Fig. 2b: Transmission Electron microscope observation of LSDV (Cao et al. 2021).

For many years, the LSDV genome seemed to be stable. In fact, following its first explanation in Zambia in 1929 (Tuppurainen et al. 2011), LSDV field isolates retrieved for years in Africa showed only minor genomic variation (Kara et al. 2003; Le Goff et al. 2009; Badhy et al. 2021). As LSD spread into the Middle East from 2012 (Alkhamis and VanderWaal 2016) and Europe in 2015 (Tuppurainen et al. 2017), the recaptured LSDV field isolates showed little change to contemporary African LSDV field isolates (Stram et al. 2008; Abutarbush et al. 2016). This genetic constancy has been utilized for the variation of LSDV live attenuated vaccines from contemporary field isolates (Menasherow et al. 2014; Gelaye et al. 2015; Menasherow et al. 2016; Agianniotaki et al. 2017; Pestova et al. 2018; Badhy et al. 2021). Serologic cross-reaction and cross-protection amongst members occur as a result of massive DNA cross-hybridization among species (Namazi and Tafti 2021). Though Capri poxviruses are believed to be host specific, sheeppox and goatpox viruses can cross-infect naturally or experimentally by trigger off disease in both the host species.

2.2. Transmission of LSD

The LSD has infected water buffalo, cattle, and wild ruminants (Givens 2018; Namazi and Tafti 2021). Though sheep and goats are vulnerable to the LSDV, however, seems little or not infected (El-Nahas et al. 2011; Lamien et al. 2011a; Khan et al. 2021). At ambient temperatures, LSDV can survive for long periods in the atmosphere, particularly in dried up crusts/scabs. The LSDV endures upto 33 days or more as the skin necrotic nodules persist and virus remains in scorched scabs for 35 days and minimum for 18 days in dried skins (Namazi and Tafti 2021). The virus can be deactivated at 55°C and 65°C for 2hr and 30min, respectively (Mulatu and Feyisa 2018).

Major resources of virus remain skin lesions as LSDV stays in the lesions or scabs for long time (Namazi and Tafti 2021). The LSDV is also emitted via saliva, lachrymal and nasal excretions, blood, milk, and semen. Suckling calves get infection via milk. It was proved that blood-sucking arthropods/insects (Fig. 3) spread LSDV (Chihota et al. 2003; Sprygin et al. 2019), infected water and feed spread through direct contact (Fig. 3) in the advanced phases of the LSD through lachrymal and nasal excretions, saliva, and even by semen (Irons et al. 2005; Annandale et al. 2014; Tuppurainen et al. 2017b; Namazi and Tafti 2021). At early stage of LSD, cattle population and LSD morbidity percentage has no positive correlation, suggesting low significance of direct LSDV transmission of LSD (Carn and Kitching 1995; Magori-Cohen et al. 2012). Intrauterine transmission of LSDV is also reported (Rouby and Aboulsoud 2016; Das et al. 2021).

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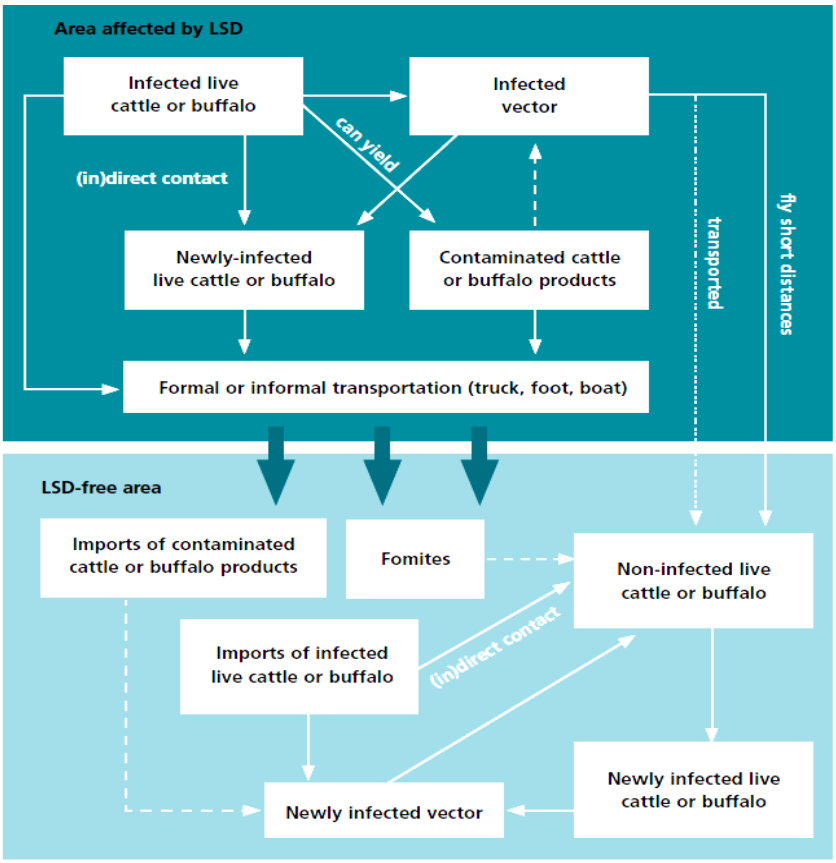

Fig. 3: This figure illustrates most important risk routes for LSD introduction from an affected to an unaffected area. The long-dashes lines indicate probable, but likely minor pathways of LSD spread. The short-dashes lines show the transportation of infected vectors. Vectors include all blood-sucking arthropods for LSD spread which vary from region to region (Roche et al. 2020).

The LSD epidemics mostly occur in the hot and humid conditions when majority of the insects are active, indicating the participation of vector/insect species (Fig. 4) in the LSDV spread (Gumbe 2018; Sprygin et al. 2019; Das et al. 2021). Most likely vectors for LSDV spread arthropods such as mosquitoes (*Aedes aegypti*), hard ticks (Rhipicephalus and Amblyomma species) and stable flies (*Stomoxys calcitrans*). In published literature, it is indicated that the house fly (*Musca domestica*) may play a role in the spread of LSDV, but not yet proved clinically (Tuppurainen et al. 2011, 2013; Lubinga et al. 2015; Sprygin et al. 2019).

The LSDV and viral antigen have also been reported to be present in tick's various organs, including the salivary glands, hemocytes, and midgut and saliva (Lubinga et al. 2014, 2015). The ticks could take part in the spread of the LSD as reservoirs for the LSDV (Kahana-Sutin et al. 2017). The mechanical spread by ticks has been proved by molecular techniques (Tuppurainen and Oura 2012). *Aedes aegypti* is fully able to transmit the LSDV to susceptible cattle (Chihota et al. 2001; Sprygin et al. 2019). *Culicoides punctatus* has also been confirmed to be the carrier of LSDV, thus could play an active part in the spread of LSDV (Sevik and Dogan 2017). The LSDV in bovine semen has been proved by PCR and virus isolation (Irons et al. 2005; Annandale et al. 2010; Givens 2018). LSDV has also been found in semen inseminated to heifers (Annandale et al. 2014).

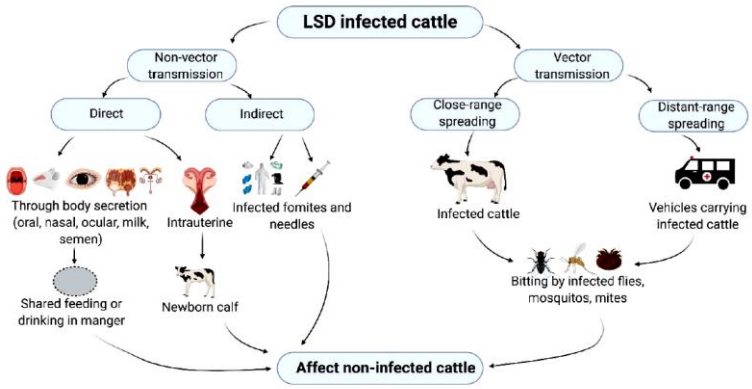

Fig. 4: Possible modes of transmission of LSDV. LSD infected cattle may affect non-infected cattle through vector or non-vector transmission (Das et al. 2021).

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2.3. Pathogenesis of LSD

Coetzer (2004) and Sanz-Bernardo et al. (2020) have explained the pathogenesis of LSDV in detail (Table 1). Following LSDV infection, virus replication in epidermal tissue takes place which leads to viremia and resultantly fever. LSDV localizes in the cutaneous tissue and then cause the nodules to develop (Constable et al. 2017).

The LSDV replicates intracellularly in macrophages, fibroblasts, endothelial cells and pericytes. This replication causes vasculitis and lymphangitis (Coetzer 2004). Lactating cows, young ones, and weak cows/buffaloes are more vulnerable to LSD, probably due to impaired humoral immunity (Babiuk et al. 2008b; Gaber et al. 2022). Calves born to infected dam's are resilient to frank illness at least for six months as they acquire maternal antibodies through colostrum (Tuppurainen et al. 2005; Mulatu and Feyisa 2018; Gupta et al. 2020). Infection in sick cattle is cleared and further in life no carrier condition/state has recognized for LSDV yet (Tuppurainen et al. 2017a). Immunity after recovery from natural LSD is throughout the life (Mulatu and Feyisa 2018).

Table 1: Events observed post intradermal inoculation of the LSDV

Day Post Inoculation	Lesions development
4 to 7	Localized hard well delineated swelling; 1–4cm raised cutaneous lumps (nodule) at injection site
After 7 DPI	1) Nodules reduced in size (2 calves) 2) In other 2 calves, nodule increased to 8cm. 3) In one calf nodules first appeared at 7 DPI and remained to emerge during the entire study till euthanasia at 19 or 20 DPI
7-9	1) In non-clinical animal, peak temperature (39°C to 40.6°C). 2) Clinically affected animal: High temperature persisted for the remaining period of the study
6 to 18	Viremia; LSDV excretion via nasal and oral secretion
7-19	Local lymphadenopathy develops along with of widespread skin lumps
42 days post fever	In male animals LSDV seen in semen

DPI: Day post inoculation. Source: Coetzer (2004) and Sanz-Bernardo et al. (2020).

2.4. Clinico-Pathology

2.4.1. Clinical Picture: There is a significant variation of clinical signs with LSDV infections ranging from subclinical infection to death (Badhy et al. 2021). The clinical picture of the LSD includes nasal discharge, inappetence, fever, lachrymation along with salivation and inflamed lymph nodes, body weight loss, huge drop in milk production, and occasionally death (Babiuk et al. 2008a; Khan et al. 2021; Selim et al. 2021). There is an initial incubation period of 6 to 9 days during acute cases followed by a fever that may exceed 41°C (USDA 2016). The LSD is described as slightly elevated, firm, demarcated skin nodules (2–7cm in diameter; Fig. 5 and 6) that are typically spread over the face, nasal and oral mucosa, ears, neck, legs, tail, udder, back, scrotum, perineum, those start soon after the fever (Sevik and Dogan 2017; Pandey et al. 2022). Only 40-50% animals develop skin lesions (USDA 2016). The ulcerative and necrotic nodules increase the probability of myiasis (Beard 2016). Edema of the limbs along with lameness have also been reported (Tuppurainen and Oura 2012). Moreover, enlargement and edema of limbs, generalized skin nodules (Fig. 5) in the whole body and necrotic skin nodule (Fig. 5) can be seen (Selim et al. 2021). LSDV is also reported to cause abortion (Radostitis et al. 2006). Aborted fetuses could be free from nodules (Sevik and Dogan 2017). Recovery is slow and often scars are left on the hides of animals (USDA 2016).

2.4.2. Gross Pathology: At postmortem, edematous, and congested lungs along with nodules in the respiratory tract especially lungs and GI tract were present (Coetzer 2004; Zeynalova et al. 2016; Rouby et al. 2021). Tissues of digestive, respiratory, and reproductive tract such as the muzzle, lips (inner side), gingiva, dental pad, nasal cavity, trachea, larynx, abomasum, teats, udder, and reproductive tract in male and female could show lesions of the LSD. The impediments of serious LSD could be mastitis, pneumonia, keratitis, lameness, dysentery, and myiasis (Awadin et al. 2011; Al-Salihi and Hassan 2015; Tuppurainen et al. 2017a; Namazi and Tafti 2021; Pandey et al. 2022).

2.4.3. Histopathology: The skin nodules under microscope (Fig. 7 and Fig. 8) reveal eosinophilic intracytoplasmic inclusion bodies in the keratinocytes (Fig. 7C; Fig. 8A) those are considered as pathognomonic. There could be infiltration of macrophages and proliferation of endothelial cells lead to ballooning degeneration of spinosum cells (Salib and Osman 2011; El-Neweshy et al. 2013; Abdallah et al. 2018). Infiltration of macrophages, lymphocytes and eosinophils in the superficial skin tissue of affected parts have been reported (El-Neweshy et al. 2013). In subcutaneous muscles severe coagulative necrosis and pervasive vasculitis may develop in some cases (Radostitis et al. 2006; Sevik et al. 2016; Abdallah et al. 2018). Zenker's necrosis in the dermal muscles with infiltration of mononuclear cells was noted (Abdallah et al. 2018).

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Experimental production of LSD has shown various histopathological lesions (Sanz-Bernardo et al. 2020). On 15 DPI (Fig. 7B, 7C), degeneration and necrosis of keratinocytes (Fig. 7B), intracytoplasmic inclusion bodies (Fig. 7C), and vesicles were present in the superficial layer of skin, i.e., epidermis. In the dermis, hemorrhages, edema, and infiltration of macrophages and lymphocytes have been reported. There was a well-delineated wedge-shaped area of dead tissue, necrosis (infarct; Fig. 7D). In the center of this necrosed tissue (infarct), the wall of a bigger blood vessel was interrupted by mononuclear cells along with fibrin in the form of fibrinonecrotic vasculitis (Sanz-Bernardo et al. 2020).

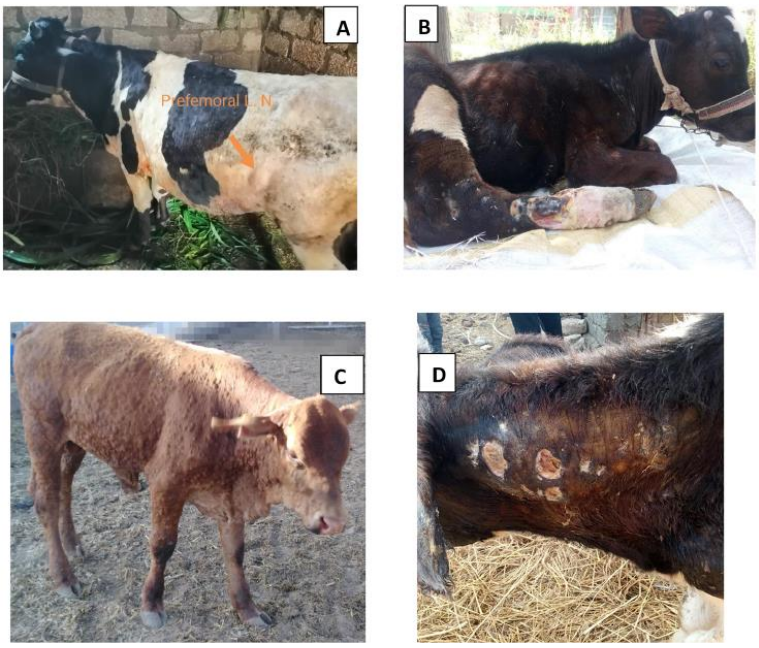

Fig. 5: Lesions of LSD in cattle. A) nodule (arrow), B) enlargement and edema of hind limb, C) generalized skin nodules on whole body and D) severe necrotic skin nodule (Selim et al. 2021).

Fig. 6a: A buffalo infected by lumpy skin disease in Karachi **(**Khan 2022).

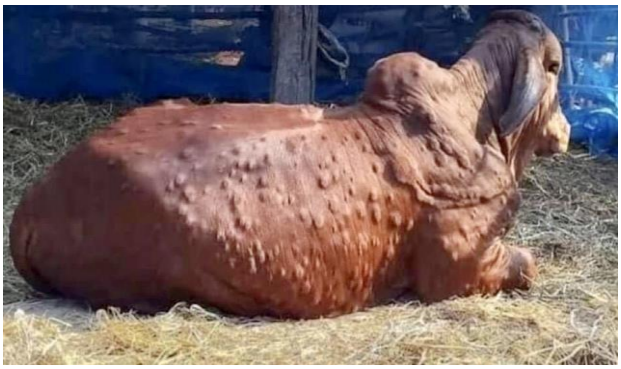

Fig. 6b: A Sahiwal bull calf infected with lumpy skin disease

2.5. Epidemiology of LSD

2.5.1. Topographical Distribution: The LSD was first diagnosed in 1929 in Zambia, and afterward it has been reported from various regions of Africa (Tuppurainen and Oura 2012; Wainwright et al. 2013; Selim et al. 2021) as well as other countries (Sameea Yousefi et al. 2017; Ali et al. 2019; Gupta et al. 2020; Tran et al. 2021; Lu et al. 2021; Koirala et al. 2022). After that, the disease spread throughout Africa, including countries such as Botswana, Zimbabwe, South Africa (Davies et al. 1991), Sudan, Egypt (Salem 1989), and Kenya (Ali and Obeid 1977; Davies 1982). Over the years, the disease has extended to many Middle East countries, including Iran, Israel, Syria, Jordan, Lebanon, Kuwait, Saudi Arabia (Tuppurainen and Oura 2012; Abutarbush et al. 2013; Al-Salihi and Hassan 2015; Ben-Gera et al. 2015; Alkhamis and VanderWaal 2016; Sameea Yousefi et al. 2017), Nepal (Koirala et al. 2022), Pakistan (Ali et al. 2019; Khan et al. 2021), Vietnam (Tran et al. 2021), India (Gupta et al. 2020; Pandey et al. 2022), China (Lu et al. 2021), Balkans includes six countries i.e., Bulgaria, Serbia, Albania, Greece, FYROM and Montenegro (Klement et al. 2020), Russia (Krotova et al. 2022), Thailand (Sariya et al. 2022), and Turkey (Ince et al. 2016; Mat et al. 2021). Ever since 2015, LSD has spread to Armenia, Russia, Albania, Azerbaijan, Bulgaria,

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Greece, Kosovo, Montenegro and Serbia (OIE 2015; Ripani and Pacholek 2015; Beard 2016; Tasioudi et al. 2016; Zeynalova et al. 2016; EFSA 2017). Tran et al. (2021) had claimed that the LSDV isolated from first outbreaks in Vietnam was 100% identical to LSDV isolated in China (2019). Reports of LSD outbreaks from diverse countries were registered from some Middle Eastern countries like Turkey, Iran, Iraq, Russia, Azerbaijan, Kazakhstan, and Armenia during 2014 to 2016. Since 2019, several outbreaks of LSD have been reported by members countries in Asia (Bangladesh, India, China, Chinese Taipei, Vietnam, Bhutan, Hong Kong (SAR-RPC), Nepal, Sri Lanka, Myanmar, and Thailand- as of 02/6/2021 (Asia-WOAH 2022).

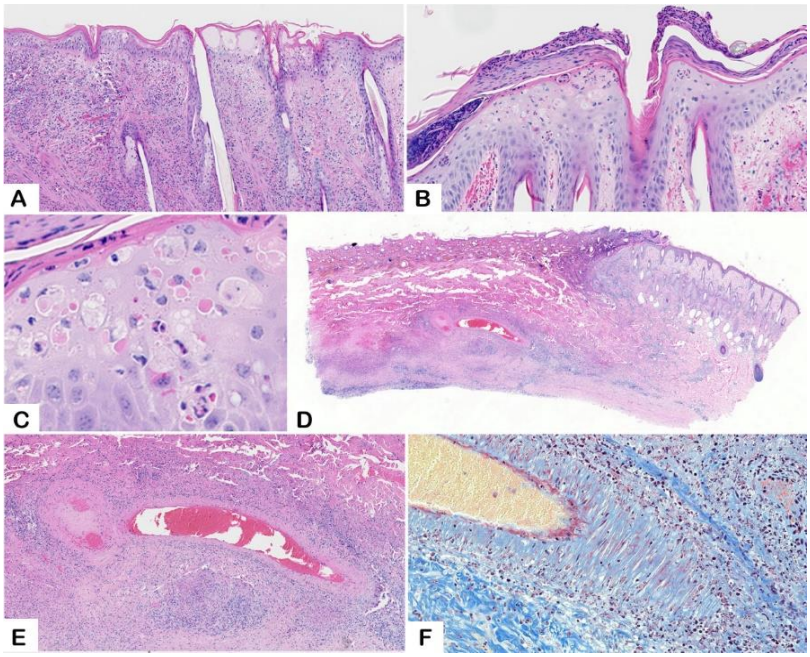

Fig. 7A-7C: Acute LSD, skin of a calf (9 DPI; Fig. A) and 15 DPI (Fig. B, C). Typically, degenerative and necrotic changes in keratinocytes along with intracytoplasmic inclusion bodies, and vesicles in the epidermis are obvious (Fig. C). Hemorrhage, edema, and infiltration of macrophages and lymphocytes are seen in the dermis (Fig. 7D-7F). A well-demarcated area of dead tissue (necrosis; infarct; Fig. D) while in the middle of the infarct, mononuclear inflammatory cells are infiltrating the wall of a bigger blood vessel and also fibrin formation (fibrino-necrotic vasculitis; Fig. E) and red staining (Fig. F) (Sanz-Bernardo et al. 2020).

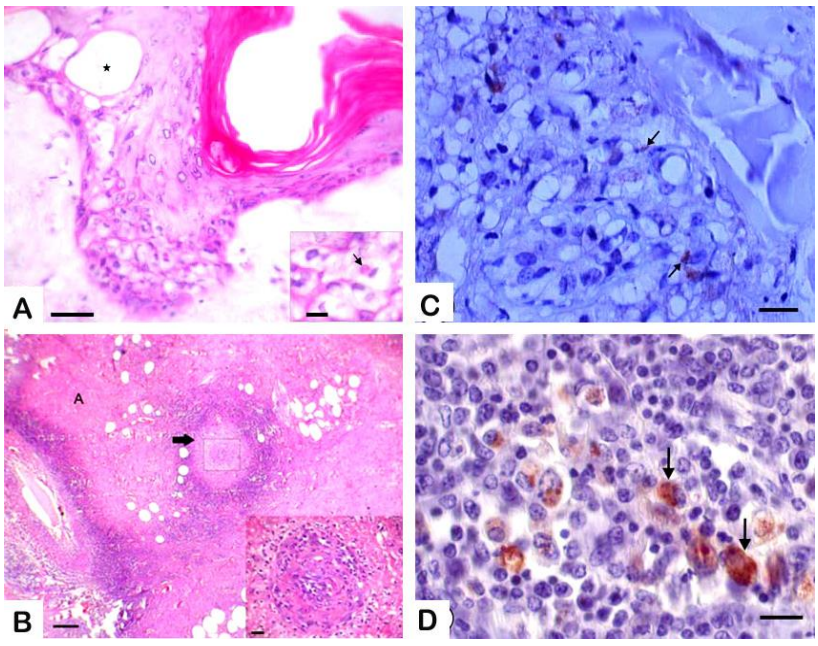

Fig. 8: Photomicrograph of skin of cow showing A) severe ballooning degeneration of the epidermis with formation of microvesicles (asterisk) in dairy cow (H&E; Bar=20µm). Inset, degenerated epidermal cell with an intracytoplasmic inclusion (arrow) (H&E; Bar=5µm); B) pannicular infarction in dairy cow (A) and severe vasculitis (arrow; inset) (HE. Bar=100µm, inset Bar=20µm); C) skin of beef calf showing positive intracytoplasmic immunoreactivity for LSDV within the degenerated follicular epithelium. labeling for LSDV (Bar=20µm) and D) Prescapular lymph node of beef calf showing positive intracytoplasmic intrahistiocytic immunoreactivity for LSDV (Bar=20µm) (El-Neweshy et al. 2013). A & B: HE; C & D: Immunoperoxidase labeling.

2.5.2. Morbidity, mortality and risk factors: Morbidity varies from 0.75% to 100% whereas mortality is mostly low, i.e., from 0 to 7% (could be up to 40%) (Table 2). Morbidity, mortality, and case fatality is usually affected by the breed, immune status, age and lactation stage (Tuppurainen et al. 2017b). LSDV did not discriminate between sexes, thus both sexes of cattle are vulnerable to the virus (Das et al. 2021). Local breeds of cattle are mostly resistant to LSD whereas imported breeds are more vulnerable to clinical disease (Ali and Gumbe 2018; Sudhakar et al. 2021) whereas Tuppurainen et al. (2011) reported that all breeds of cattle are vulnerable to the disease.

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Table 2: Morbidity and mortality of lumpy skin disease in various countries and areas

Country	Morbidity (%)	Mortality (%)	References
Bangladesh	23	0.002	Badhy et al (2021)
Greece	8.7	0.4	Tasioudi et al. (2016)
China	19.5	0.9	Lu et al. (2021)
Egypt	100	1.8	Salib and Osman (2011)
Hong Kong	91-94	0.07-0.10	OIE (2021)
India	7.1	0.0	Gupta et al. (2020)
India	0.75-38.34	0	Sudhakar et al (2021)
Myanmar	3-6	0	OIE (2021)
Nepal	100	0	Acharya and Subedi (2020)
Turkey	12.3	6.4	Sevik and Dogan (2017)
Vietnam	93	7	OIE (2021)

There are controversial reports about the vulnerable age for LSD. Tuppurainen et al. (2011) and Das et al. (2021) reported that regardless of the age, all cattle are susceptible to the LSD, however, there are published reports that young animals demonstrated higher vulnerability and harshness of the disease than the aged cattle (Babiuk et al. 2008b; Ali and Gumbe, 2018; Tuppurainen et al. 2011; Khan et al. 2021; Gaber et al. 2022). The degree of the LSD severity is controlled by the hosts' vulnerability and immunological condition (Brenner et al. 2009; Tuppurainen et al. 2017b; OEI 2021; Das et al. 2021; Gaber et al. 2022). Ochwo et al. (2019) were of the view that LSDV could be associated with sex, age, management type, common water source and mean annual rainfall.

Other threat elements linked with the transmission of LSD comprised of hot and humid climate, such conditions are supporting proliferation of mechanical vectors, and other factor could be entry of new animals in a herd (Ince et al. 2016; Sevik and Dogan 2017; Gumbe 2018). The herd size, migration of herd, common pasture, vector populations, movement of sick cattle into non-infected areas, and common water sources those can increase the prevalence of LSD (Gari et al. 2010; Sevik and Dogan 2017).

2.5.3. Vaccinated vs non-vaccinated cattle: Klement et al. (2020) reported that overall average vaccine efficiency across all countries in the prevention of LSD was 79.8% (Fig. 9). Vaccine used in this study was LUMPYVAX® MSD (live attenuated Neethling LSD vaccine). The highest vaccine efficiency was seen in Bulgaria, reaching 97.3%, followed by Serbia (97.1%), FYROM (94.0%), Montenegro (80.4%), Greece (78.4%) and Albania (62.5%). Klement et al. (2020) study revealed the significance of immunization/vaccination for limiting LSD. These results are applicable only for the Neethling attenuated vaccination.

2.5.4. The Role of Wildlife in LSD Spread: According to Azeem et al. (2022), the role of wildlife in the spread of the LSD is not yet clear, however, various studies proposed that wild animals may play an active part in the spread of LSD (Dao et al. 2022). Seropositivity in wild animals shows the possibility in spreading the LSD (Namazi and Tafti 2021). Cases of LSD at initial stage in wildlife can simply overlooked as it is too hard to observe lesions on the skin (Barnard 1997). The vulnerability of impala, giraffe and springbok to the LSDV has been confirmed (Young et al. 1970; Lamien et al. 2011a). Dao et al. (2022) identified and characterized the LSDV from a giraffe *(Giraffa camelopardalis)* in Vietnam. Specific antibodies to LSDV have previously been reported in wildlife, such as African buffalo (*Syncerus caffer*), Arabian oryx (*Oryx leucoryx*), blue wildebeest (*Connochaetes taurinus*), giraffe, eland (*Taurotragus oryx*), greater kudu and impala (Davies 1982; Hedger and Hamblin 1983; Greth et al. 1992; Barnard 1997; Fagbo et al. 2014; Molini et al. 2021). Molini et al. (2021) collected 40 swab samples from Namibian wildlife such as black wildebeest (*Connochaetes gnou*), blesbok (*Damaliscus pygargus phillipsi*), blue wildebeest (*Connochaetes taurinus*), duiker (*Sylvicapra grimmia*), eland (*Taurotragus oryx*), greater kudu (*Tragelaphus strepsiceros*), hartebeest (*Alcelaphus buselaphus*), impala (*Aepyceros melampus*), lechwe (*Kobus leche*), oryx (*Oryx gazelle*), sable antelope (*Hippotragus niger*), and springbok (*Antidorcas marsupialis*) and only one sample tested positive by conventional PCR from an eland (*Taurotragus oryx*). In the epidemiology of LSD, what is the exact role of wildlife is not yet fully assessed (Tuppurainen et al. 2017b; Namazi and Tafti 2021).

2.6. Diagnosis of LSD

Clinically, gross lesions in the live animal are very clear for its diagnosis, if multiple nodules are present on the body (Fig. 5 and 6). Researchers have applied various tests in the diagnosis of LSDV, however, molecular techniques proved to be the best. Molecular diagnostic techniques are more quick, accurate, and trustworthy than other techniques (Stubbs et al. 2012). Traditional PCR can confirm LSDV (Tuppurainen et al. 2005), moreover, real-time PCR technique is also useful (Şevik et al. 2016; Alexander et al. 2019; Agianniotaki et al. 2021). Real-time PCR is used to test the differentiation among sheep and goat poxviruses and LSDV (Lamien et al. 2011b). Restriction Fragment Length Polymorphism is used to differentiate among vaccinal strain and virulent LSDV

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(Menasherow et al. 2014; Erster et al. 2019). Additionally, various detection methods like serological techniques, virus isolation, virus neutralization and electron microscopy are also in use for the detection of LSDV (OIE 2018). The virus neutralization test is slow and costly but has a high specificity and low sensitivity, however, it is the only validated/valid test (Beard 2016). In an experimental study, Babiuk et al. (2008b) recognized immunohistochemical for the recognition of LSDV antigen. Regardless of the specificity and sensitivity of the western blot test, it is costly as well as tricky to execute (OIE 2018).

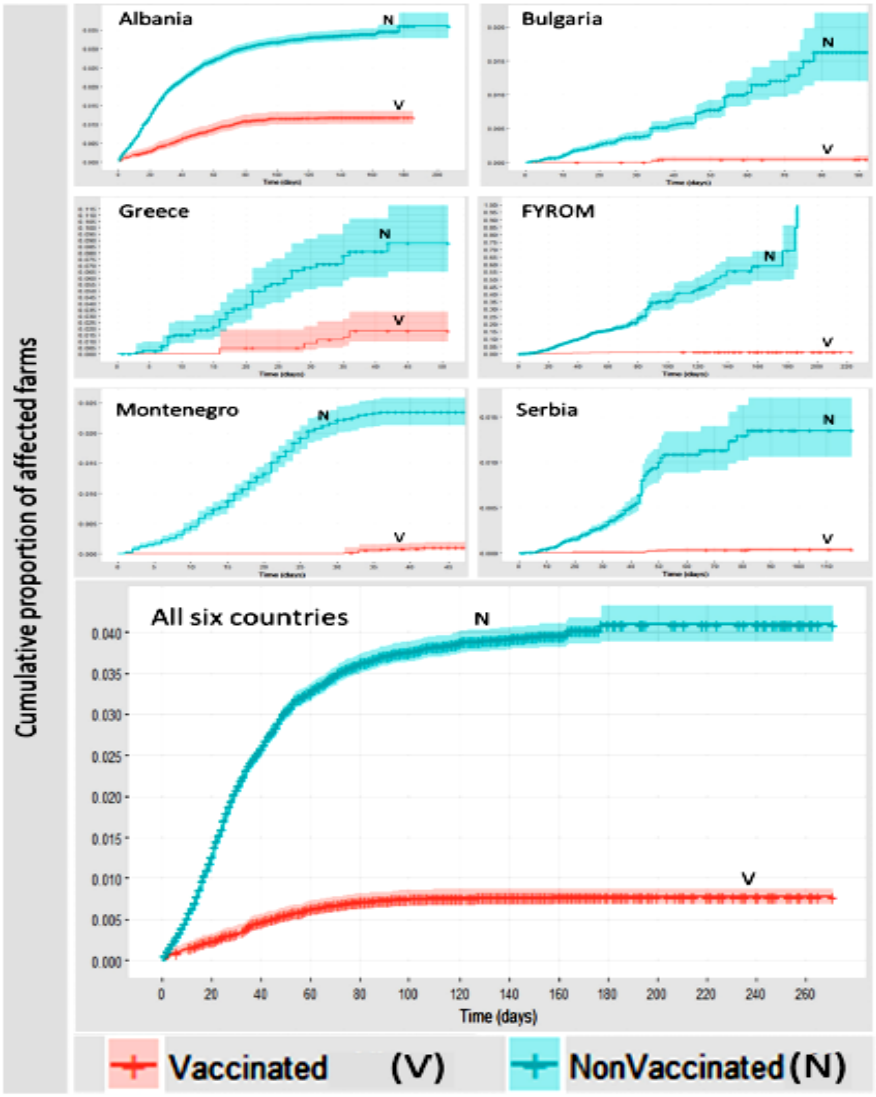

Fig. 9: LSD affected farms during 2016 among LSD vaccinated (red) and non-vaccinated (blue) farms in Greece, Bulgaria, Albania, FYROM, Serbia and Montenegro. The shaded area stands for the 95% confidence intervals (Klement et al. 2020).

2.7. Prevention and Control of LSD

Till now, there is no effective antiviral drug available against LSDV. For the prevention and control of LSD, various methods are applied in LSD outbreaks. Only depending on a single approach, it is hard to control and inhibit LSDV infection successfully (Kayesh et al. 2020). Thus, numerous approaches are required for the prevention and control of LSDV infection. These approaches could be inhibited movements of sick animals, regular testing, quarantine, and decontamination of the infected animals, vectors control, vaccination/immunization, and treatment of morbid animals to avoid secondary bacterial infections (Tuppurainen et al. 2017a; Sevik and Dogan 2017). Till today, immunization/vaccination is the only successful approach to control the LSD in disease prevalent areas and decreased/stopped movement sick animals and removal/quarantined of sick animals (Sevik and Dogan 2017; Klement et al. 2020; Lu et al. 2021). Various countries have proved the achievement in limiting LSD outbreak by immunization/vaccination campaign. In this context, it is stated that cattle vaccination campaign in

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Balkan countries with LSD homologous vaccine strain decreased the outbreaks from 7483 to 385 and zero cases respectively in 2016, 2017 and 2018, validating the efficacy of LSD homologous vaccine strain (EFSA 2019).

The treatment of LSD is only symptomatic with anti-inflammatory, supportive therapy, antimicrobials, and anti-septic solutions with the objectives to prevent secondary bacterial infection (Salib and Osman 2011). The culling/slaughtering and restricted/no movement of affected animals has been partially effective in limiting LSD along with mandatory and steady vaccination have been suggested as control approaches (Beard 2016; OIE WAHIS 2016; Tuppurainen et al. 2017b). Without control of vectors, eradication of LSD is too tough (Tuppurainen et al. 2017b; Sevik and Dogan 2017). Training of Veterinary Doctors and livestock farmers/laborers will empower them to diagnose clinical cases timely that will help to slow down the spread of LSD (Beard 2016).

Capripoxvirus genera members are able for cross-protection. Therefore, homologous (Neethling LSDV strain) and heterologous (sheeppox or goatpox virus) live attenuated vaccines are safe for cattle against LSDV infection (OIE 2013). In those countries free of LSD, it is suggested to use the sheep pox vaccine to safeguard sheep. Further it was recommended to use the same vaccine during LSD outbreaks for the reason of possible protection issues related with the live attenuated LSDV vaccine (Tuppurainen and Oura 2012).

It is further reported that live vaccines yield a robust and long-lasting immune reaction and are competent in controlling LSD transmission (Tuppurainen et al. 2020). At the site of injection, local inflammatory and/or mild skin lesions can be produced by live vaccines (Bedekovic et al. 2017). Inactivated vaccines are safe but expensive and require several injections for attaining immunity. Additionally, inactivated vaccines can be used in the terminal stage of LSD as extermination approach that utilizes live vaccines first (Hamdi et al. 2020). Wild field strain and the live vaccine can be combined to cover the risk of coinfection. Vaccinating infected animals in natural infection probably make the condition worse (Sprygin et al. 2019).

Additionally, the quick recognition of a clinical diagnosis is vital so that extermination actions, such as slaughter-out of morbid animals, quarantine, deep dumping of carcasses, scrubbing and cleansing of the barns (Tuppurainen et al. 2005; Constable et al. 2017). Moreover, thorough import limiting livestock, hides, carcasses, and also semen from prevalent areas in disease-free areas will help to limit the LSD in defined area (Sevik and Dogan 2017).

It is well-known that sheep pox vaccines don't provide full immunity against LSD (Brenner et al. 2009). However, these are used in African countries, Turkey, Iran and Iraq with overlap between sheeppox and goatpox and LSD (Sameea Yousefi et al. 2017). Vaccines commercially available for LSD protection are live attenuated. Though skin lesions have been observed in some vaccinated animals, however, there were more clinical cases in unvaccinated cattle herd than vaccinated herd (Brenner et al. 2009; Stram et al. 2008). These low-cost vaccines can provide satisfactory protection by annual vaccination programs (Tuppurainen et al. 2017b). Hamdi et al. (2020) developed an inactivated oily adjuvanted vaccine based on Neethling strain and tested it on cattle in Bulgaria. The vaccine was safe, no adverse reaction, high level of specific antibodies and protection against virulent challenge strain. It is general opinion that on the prophylaxis basis, inactivated vaccine could be of excellent in endemic countries or countries in risk regions.

2.8. Economic Losses Caused by LSD

The LSD has caused huge economic losses. The disease renders substantial decrease in milk yield may be from 10% to 85%, could be as a result of elevated fever and development of secondary mastitis. Additional effects of LSD could comprise of decreased growth rate, hurtled hides, infertility (permanent or temporary), abortion, medication cost and vaccination cost and death of morbid cattle (Sajid et al. 2012; Alemayehu et al. 2013; Sevik and Dogan 2017). Post LSD production losses have been assessed at 45-65% in private commercial cattle farming (Tuppurainen and Oura 2012). In this context, Kiplagat et al. (2020) stated that LSD caused great economic losses at the farm level in Nakuru County, Kenya. In Ethiopia approximate economic losses due to LSD outbreak at herd level have been reported to be USD 1,176 with huge mortality followed by significant decreased in milk output (Molla et al. 2017).

Capripoxvirus, an etiological agent can produce sheep and goat pox, and these poxes have significant monetary importance as these are a major impediment to international trade (Gumbe, 2018; Klement et al. 2020). These viruses could be misused as an economic bioterrorism tool (Hikmet et al. 2019; Namazi and Tafti 2021). Klement et al. (2020) have emphasized on the significance of vaccination for limiting the LSD.

Livestock in Pakistan have a problem with LSD. LSD has reportedly emerged first in Pakistan's Sindh province, where it has killed more than 570 cows, and has spread in animals all over Punjab (Singla 2022). It is estimated that five million dairy farmers and meat sellers are suffering from the economic fallout of the LSD outbreak (Khan 2022). According to Ilyas (2022), cattle farmers have been badly affected by the propaganda about the LSD, and sales of milk and meat in Karachi (Pakistan) have gone 60% to 70% down despite veterinary experts' repeated explanation that the disease cannot be transmitted to humans from meat or milk. Overall, milk, meat sales fall as lumpy skin disease spreads to 22 districts in Sindh (Ilyas 2022).

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2.9. Public Health Concern of LSD

The LSD is not a zoonotic disease (Kumar 2011; Anonymous 2017; Gelaye and Lamien 2019; Kayesh et al. 2020; Das et al. 2021; Khan et al. 2021). According to Khan et al. (2021), the LSD has been predominantly reported in large ruminants e.g., water buffalo and cattle, therefore, its host range is believed to be quite limited. Infected/diseased cattle are not a source of any infection for humans. Their milk is reliable and safe for human consumption (Anonymous 2022b; Ilyas 2022). It is not appropriate to eat the flesh of infected cattle, due to possible carcass contamination by secondary bacterial infections, though, no harm has been reported by its consumption. Hence, there is no proof and narrative that the virus can affect humans (Rich and Perry, 2011; Gumbe 2018; Limon et al. 2020). The virus is highly host specific and does not cause disease in humans. There is no risk from consuming beef or dairy products (Anonymous 2022). Though in published literatures, there is strong evidence that LSDV doesn't affect humans, still there is one report (Kamal 2019) that pleads that LSDV has infected humans with co-infection of herpes virus.

3. CONCLUSION

Lumpy skin disease is spreading in many countries and is source of huge economic losses. It is urgent to opt strategies for the control and prevention of the disease. Restricted movement of infected animals is a major factor in the transmission of the LSD in the non-endemic area. Curtailment of vectors/insects is also proposed for the control of the disease. Additionally, vaccination/immunization with the homologous strain of the LSDV could be the best strategy for the control of the disease. Diagnosis has also prime importance that should be prompt and precise especially in the endemic areas has prime importance so that control measures could be opted well in time for the curtailment of the LSD.

Conflict of Interest: None

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