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Lumpy skin disease an emerging outbreak in cattle and its impact on human life

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Abstract

A viral disease known as lumpy skin disease (LSD) that infects cattle has recently become a danger to the global livestock industry. Capripoxvirus, which causes LSD, can contract through insect bites or through direct contact with infected animals. Cattle with the disease develop nodules on their skin, which reduce their ability to produce milk, cause them to lose weight, and eventually kill them. LSD significantly reduces milk production, which may decrease from 10% to 85%. Milk and meat sales have decreased by 60% to 70% in Karachi (Pakistan), as a result of LSD. Calves of all strains and ages are affected, although lactating cows and young cattle are more at risk. The bulk of LSD outbreaks occur in hot, humid environments when a large percentage of insects that serve as vectors are active. LSD may be transmitted more quickly by wildlife. Nasal secretions, inappetence, fever, lachrymation with salivation, swollen lymph nodules, body weight loss, and sometimes death are all symptoms of LSD. Farmers and the cattle industry have suffered enormous financial losses because of the increase in LSD. Concerns regarding the disease's effects on human health have also been raised due to its zoonotic potential. Although there is no evidence that LSD may be transmitted to others, the risk still exists, especially for those with compromised immune systems. This article discusses the current knowledge of LSD, its clinical manifestations, transmission, and preventive measures. It also draws attention to the effects of LSD breakouts, including financial, social, and medical fallouts, on people's lives. The paper highlights the necessity of continuing research and surveillance to comprehend the illness better and create efficient controls to stop its spread.

Introduction

Lumpy Skin Disease Viruses (LSDV), Sheep Pox Viruses (SPPV), and Goat Pox Viruses are all members of the Capripoxvirus (CaPVs) family, one of the eight genera that comprise the Chordopoxvirinae family of Poxviridae (GTPV). The majority of domestic ruminant illnesses in Africa and Asia that are economically relevant are caused by these viruses [1]. The geographical distribution of CaPV infections can also be determined. Most African nations, the Mideast, Central Asia, and the Indian subcontinent have endemic SPPV and GTPV infections [2, 3]. LSDV, on the other hand, is mostly found in southern, central, eastern, and western Africa [4]. According to Morris (1931), the LSDV virus originated in Zambia in 1929, and insects were thought to be the primary disease vectors [5]. Later, between 1943 and 1945, the virus was seen in South Africa, Zimbabwe, and Botswana. Eight million cattle were infected by this epidemic, and the illness persisted until 1949 [6]. According to Ali and Obeid (1977), LSD was first documented in Kenya and Sudan in 1957 and 1972, respectively. Currently, LSD has grown rapidly and entered most nations, notably African ones, except for Algeria, Libya, Tunisia, and Morocco [7]. From 2002–2009, Bahrain, Kuwait, Egypt, Israel, and Bahrain, reported its presence [8]. This virus re-emerged in 2009 from a farm population of 3200 cattle in Oman [9]. Currently, Pakistan is one of the numerous nations where this virus has spread. Pakistan is now dealing with hazardous LSDV in all its districts.

LSD incidents have been documented in the Middle East, Europe, and West Asia [10]. South-east Europe, the Balkans, and the Caucasus all experienced illness outbreaks in 2015 and 2016 [1]. Arthropod vectors are the main mechanical means of transmission [8, 11]. According to Gari et al., LSD has been shown to aggregate overtime during the hot, humid periods of the year, which is directly related to vector abundance [12]. These authors also made clear the part that animal husbandry methods, such as mixing herds at community watering and grazing areas, play in the spread of LSDV. The host range of LSDV is limited, and non-ruminant hosts do not support the completion of the replication cycle [13]. Bos taurus is much more prone to clinical illness in cattle than Bos indicus, and Asian buffalo has also been shown to be prone [1, 14]. All cattle breeds, regardless of age or sex, are vulnerable to Lumpy Skin Disease Virus.[15]. The signs of LSD include fever and many skin lumps covering the mucous membranes, legs, limbs, and reproductive organs, as well as subcutaneous tissues, muscles, and even internal organs. Additionally, pneumonia is a frequent complication in animals with oral and respiratory tract lesions [9].

The prevalence and morbidity of LSD may vary depending on the species of cow, the population's immune condition, insect vectors used for transmission, and the viral isolates. Mortality in endemic regions often varies from 1% to 3%, while morbidity is typically about 10% [16, 17]. It was discovered that Holstein Friesian as well as cross-pollinated cattle had a substantially greater prevalence of LSD than indigenous zebu [18]. It is recently reported that adult cattle have a greater incidence of LSD [19]. Additionally, Lumpy skin disease (LSD) resulted in a drastic reduction in milk production, prolonged debilitation weight loss, conception failure, and abortions. It is also regarded as a sickness that must be reported, and in nations where it is prevalent, commerce is severely restricted [20].

Disease description

The Origin of LSD

Lumpy skin disease viruses (LSDV) belong to the family Poxviridae and genus Capripoxvirus. Goatpox and sheeppox viruses are also members of the genus Capripoxvirus. Thus, LSDV is genetically related to the sheep pox and goatpox viruses. LSDV is a double-stranded DNA virus with a genomic size of around 150 kbp and a comparably bigger size of approximately 270-290nm [21]. It also has a lipid membrane surrounding. It is observed using electron microscope (EM) and the genome appeared to remain stable for a long time. LSDV field isolates collected for years in Africa revealed fairly minimal genetic change after its first introduction in Zambia in 1929 [7]. The recovered LSDV field isolates revealed minimal difference from modern African LSDV field isolates as LSD expanded throughout the Mideast in 2012 and Europe in 2015 [20, 22]. From recent field isolates, LSDV live attenuated vaccines have been developed using this genetic consistency [23]. Massive DNA cross-species hybridization results in antigen detection cross-reaction and cross-protection between individuals [24]. Capri poxviruses are thought to be host-specific, however, sheeppox and goatpox viruses may infect each other spontaneously or artificially by inducing sickness in both host species.

Transmission of LSD

Cattle, wild ruminants, and water buffalo have all contracted LSD. Although susceptible to LSDV, sheep, and goats seem to be little or not affected [19, 25]. When temperatures are normal, LSDV may persist for a very long time in the atmosphere, especially in crusts and scabs that have dried up. LSDV may last for up to 33 days or more due to the persistence of skin necrotic nodules, the virus's persistence in burnt scabs for 35 days, and its minimum duration of 18 days in dry skins. At 55°C for two hours and at 65°C for thirty minutes, the virus may be rendered inactive[26]. Skin lesions continue to be a major source of the virus since LSDV persists in lesions or scabs for a long period [24]. Additionally, the LSDV is released through blood, milk, semen, lachrymal and nasal excretions. Dairy products infect nursing calves. Blood-sucking arthropods/insects disseminate LSDV by direct contact with contaminated water and feed, lachrymal and nasal excretions, saliva, and even semen in the latter stages of the disease [27]. Cattle population and LSD morbidity % do not positively correlate during the early stages of LSD, indicating a low likelihood that LSD was directly transmitted via the LSDV [28]. There are additional reports of LSDV intrauterine transmission [2] (**Fig. 2**).

Clinical signs and symptoms

Regardless of the manner of infection, the time between infection and the first detection of widespread clinical symptoms in clinically infected cattle ranges from 7 to 14 days; in natural situations, it is between 2 and 5 weeks. [14, 29]. Based on the number of lumps (nodules), the prevalence of problems, the dosage of the inoculum, the host's vulnerability, and the number of insect populations, LSD may be divided into moderate and severe variants. Accordingly, the clinical signs of slightly infected cattle include the formation of one or two lumps or nodules within two days after the commencement of the fever (1–5 centimeters in diameter), lethargy, anorexia, lacrimation, ocular and nasal secretion, agalactia, and emaciation. The skin of the animal's body may also develop nodular lesions, which are painful and hyperemic, particularly in the snout, nares, back, legs, genitalia, perineum, eyelids, bottom ear, nasal and buccal mucosa, and tails [30, 31]. The lumps are hard and raised above the surrounding normal skin, often with a thin ring of blood separating them. They involve the muscles, surrounding subcutis, epidermis, and dermis. Nodules may go away, but they can have the potential to stay as hard lumps. Lesions of skin could be apparent for a very long time. Large regions of undeveloped tissue may be exposed when lesions merge, making them vulnerable to insects and flies larvae [32].

The sloughed-off lesion may leave an opening with a complete thickness of skin and the "sit fast" necrosis lesion, which is an "inverted conical zone" of necrosis [33]. Affected animals also exhibit increased salivation, lacrimation, nasal discharge, and emaciation due to necrotic plaques and distinctive LSD ulcers in the oral cavity, conjunctiva, and nasal passages, respectively. Other characteristics of LSD include lymphadenopathy and the enlargement of the superficial lymph nodes. Additionally, breastfeeding cows' milk supply may decrease, mastitis develops, and some pregnant cows may have miscarriages; calves born with severe skin lesions, brought on by intrauterine infection, are also possible.

Infected bulls additionally experience orchitis and swollen testicles. Bulls and cows may become temporarily or permanently sterile after lesions in the reproductive system [32]. Some of the infected cows have severe ulcerative skin lesions, skin infections (unilateral or bilateral), edema, and proinflammatory swellings of belly, face, and one or more limbs that may be visible and might significantly impede mobility. The throat, larynx, trachea, lungs, and whole digestive system may also have varicella lesions. Pneumonia often develops after respiratory tract lesions [17, 34].

Confirmative diagnosis of LSD

The virus's isolation

It is necessary to isolate and identify the virus to confirm lumpy skin disorder in a new location. Before the generation of neutralizing antibodies, samples for viral isolation should be obtained during the first week after the emergence of clinical symptoms [16]. Early lesions (those without necrosis) on the skin may be biopsied to obtain samples for viral isolation via electron microscopy. Additionally, during the viremic phase of LSD, blood samples taken in EDTA, or heparin may be used to isolate the LSD virus from buffy coat. At least three different animals should used for the samples. For viral isolation, samples aspirated from swollen lymph nodes may also be employed. In tissue cultures of bovine, ovine, or caprine origin, the LSD virus multiplies. The most vulnerable cells are

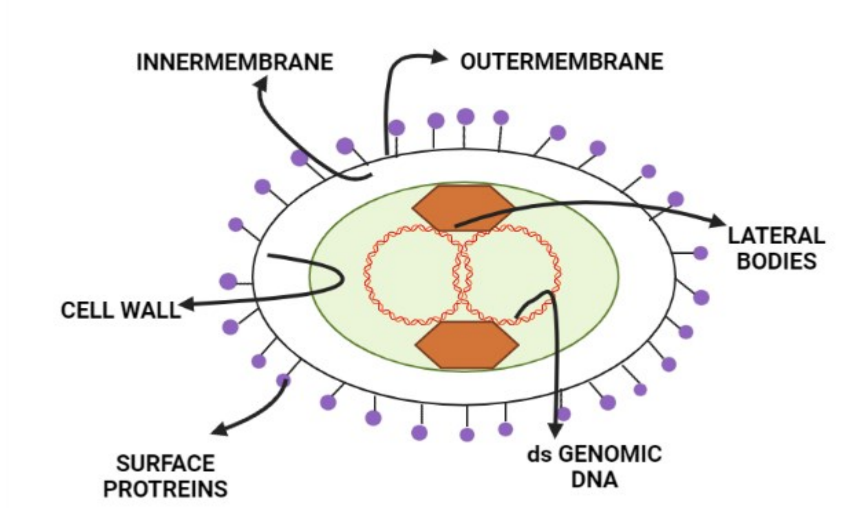

Fig. 1: Morphology of mature Lumpy skin disease virus

thought to be lamb testis (LT) cells or ovine dermis tissues (primary or secondary culture). The African green monkey kidneys (Vero) cells and the chorioallantoic membranes of embryonated chicken eggs have both been modified to promote the development of LSD Capripoxvirus, which is not advised for isolation and identification [8].

Atomic/electron microscopy

Within a few hours after receiving the samples, a transmission electron microscopy (TEM) diagnosis of LSD may be verified. In preparation for biopsy specimens collected from afflicted mucous membranes or skin that were negatively stained, TEM demonstrated the virus. 320 × 260 nm is the average size of mature Capri pox virions, which have a more oval shape and bigger lateral lobes than orthopox viral particles [8] (**Fig. 1**).

Testing for fluorescent antibodies

Fluorescent antibody assays may also be used to detect the Capripoxvirus antigen on contaminated tissue culture slides or coverslips [35].

Immunodiffusion using agar gel

The precipitating antigens of Capripoxvirus have been detected using an agar gel immunodiffusion (AGID) assay, although the same antigen is also present in parapoxvirus, which is a drawback [36].

Multiple diagnoses

Other illnesses, such as vaccine virus, bovine papular stomatitis, cowpox virus, and pseudo cowpox virus, may emerge due to confusion in diagnosis. These diseases include bovine herpesvirus (pseudo lumpy skin disease), vaccine virus, bovine papular stomatitis, cowpox virus, and pseudo cowpox virus [37]. Dermatophilosis (wide blowout skin disease) is also contagious among cattle, and the lesion might be mistaken for infection with the LSD virus. The only way to differentiate between dermatophilosis and any other condition is to examine the surface (soggy and appear as coats of keratinized significant) scabs, which range in size from (0.5-2) cm [38]. Along with bug or tick stings, rinderpest, photosensitization, rashes, onchocerciasis, and cutaneous TB, the mild infection might also clash with other conditions [16].

Histopathological findings

LSD has characteristic histopathological features that may be used to make a diagnosis. In addition to ballooning and cell layer degeneration, the common pathological LSD lesions' eosinophilic intracytoplasmic inclusion bodies may be seen under a microscope in keratinocytes, macrophages, endothelial cells, and pericytes from skin nodules. The affected region has been invaded by inflammatory cells such as eosinophils, lymphocytes, and macrophages. Histologically, extensive vasculitis that exhibits viral endothelial cell tropism is also seen [32, 39]. Histopathologically severe coagulative necrosis

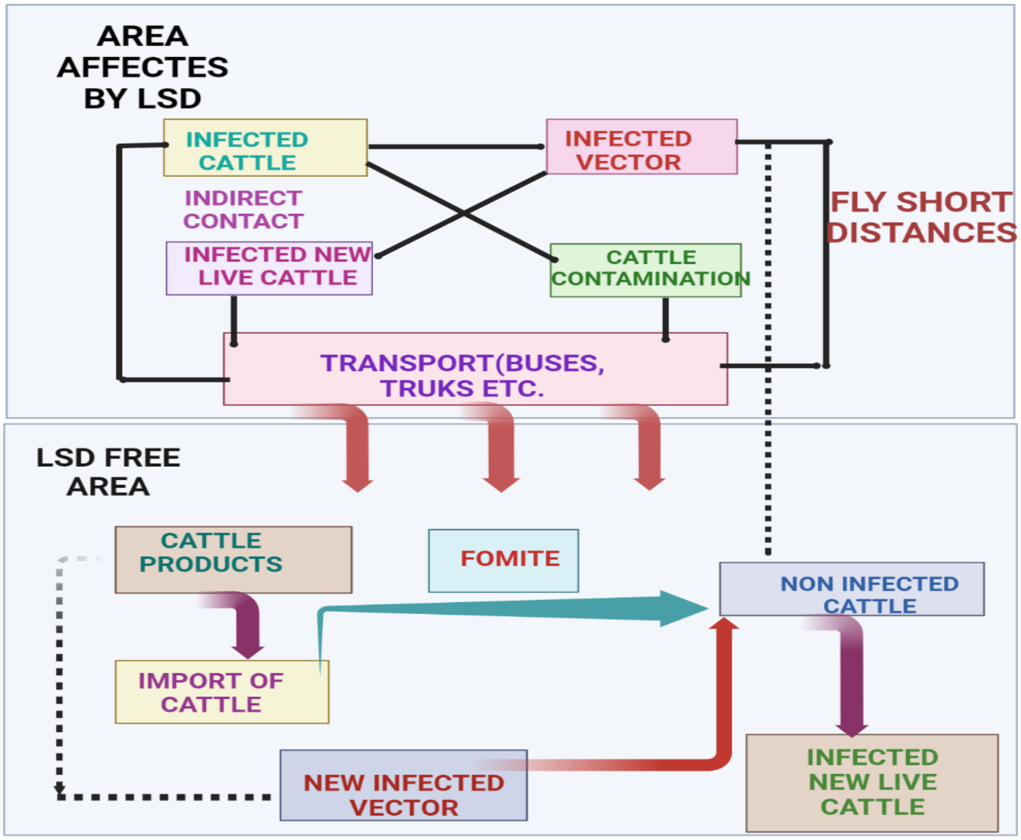

Fig. 2: Shows common routes of transmission of Lumpy skin disease Virus by vector and infected cattle

in cutaneous muscle may be seen if there is muscular injury throughout the course of LSD [40].

Hematologic and serum biochemical analyses

Hematologic and serum biochemical analyses of animals that had been infected with LSDV spontaneously or in an experiment were recently researched and reported [40-42]. The Neamat-Allah study's findings showed macrocytic hypochromic anemia in experimentally infected animals, which is indicated by a significant reduction in red blood cells, hemoglobin, packed cell volume, and corpuscular volume (MCV hemoglobin concentration with a considerable increase in average corpuscular volume [41]. On the other hand, the findings of the leucogram revealed leucopenia, lymphopenia, and granulocytic leukocytosis, which may be caused by viral infections and subsequent acute bacterial infections, particularly pyogenic bacterial infections. In naturally infected cattle, LSD has also been linked to inflammation-related thrombocytopenia, hyperfibrinogenemia, reduced creatinine concentration, hyperchloremia, and hyperkalemia [42]. Studies by Neamat-Allah and Abu Tarbush revealed that total protein and albumin levels in serum had significantly decreased, but globulin levels, particularly gamma globulins, had significantly increased in LSD-infected cows [41, 42]. Along with an increase in globulin protein and creatinine concentrations, Sevik et al findings' from their blood biochemical examination of LSD-infected calves also revealed an increase in aspartate aminotransferase and alkaline phosphatase [40]. The investigations concluded that the change in serum biochemical examination may be caused by liver and renal failure, a severe inflammatory process, and illness consequences such as anorexia and decreased muscle mass after LSDV infection.

Risk factors

Host-related factors

Asian water buffaloes (Bubalus bubalis) and cattle are both affected by LSD, a disease that is peculiar to the host [43]. Compared to cattle, buffalo have a much lower risk of morbidity[11]. Cattle of both sexes may be infected with the virus. The vulnerability and immunological state of the hosts influence the severity of the illness [43]. Native breeds (Bos indicus) are less susceptible to clinical illness than the Bos Taurus [38, 44]. Additionally, young animals showed greater vulnerability and severity than older cattle [38]. Clarification is required about the potential significance of animals as virus reservoirs [43]. In experimental inoculations, giraffes (Giraffa camelopardalis) and impalas (Aepyceros melampus) showed vulnerability to LSDV [11].

Agent-related elements

Under a variety of environmental circumstances, LSDV is very stable. It can live in dried scabs, is resilient to dryness and inactivation, and can sustain freezing and thawing[45]. According to reports, the virus may also be found in saliva, plasma, milk, and semen as well as in the nasal, lachrymal, and esophageal secretions of sick animals. Within about 8.8 days, the virus was isolated from infected cow blood, and viral DNA was discovered in 16.3 days [43]. In a favorable environment, it may persist for up to 22 days in semen and 11 days in saliva [44, 46]. There is evidence of longer-lasting existence in fabrics, clothes, and equipment, but no sign of longer-lasting existence in insects has been discovered [38].

Management and environmental factors

When given the right conditions, LSDV may infect, survive, and grow inside a vulnerable host. Environmental risk factors include warm, humid weather that encourages a bigger population of ticks, flies, and mosquitoes [11]. When there are a lot of blood-sucking insects around, such as during rainy seasons, the illness is more prevalent [43, 44]. Few studies revealed that intensive big farms had higher morbidity rates than backyard small farms [44]. Through the spread of vectors, common grazing and watering areas may promote the spread of viruses. A further risk factor for LSD was observed to be the introduction of additional animals into herds without following the appropriate quarantine periods [38, 43, 46].

Acceptability to eat infected cattle

It has been shown that the LSD virus may infect humans, causing zoonotic illness and skin conditions similar to those in cattle. Direct contact with sick animals, contaminated utensils, aerosol, laboratory-acquired illnesses, and person-to-person transmission are the modes of transmission. In humans, it seems that these diseases are very infectious. Those who come into touch with sick animals may very readily get infected with LSDV. Therefore, Infected livestock should be put down since their flesh is unfit for human consumption. By using a standard PCR, samples from humans tested positive for the LSD virus, which was then genetically identified as the isolate of the LSDV by a partial sequence with 99% identity. The ORF103 partial sequencing demonstrated that a person had contracted the same strain of infection that was prevalent during that outbreak [47].

Another study concluded that there are no zoonotic issues with LSD. Humans cannot get any diseases from infected animals, and milk may safely be consumed by humans. While it is not advisable to consume the meat of diseased animals because the carcass may get contaminated with subsequent bacterial diseases, there has never been any reported damage from doing so. As a result, there is no proof and no information on how the virus may damage people [38, 48].

Social and economic effects

According to the OIE (2017), LSDV often results in 10–20% morbidity and 1% fatality in cattle. However, some studies have shown 100% morbidity [49]. In central Ethiopia, the death of 108 cattle resulted in a total loss of 51,590 USD [50]. The death rate varies depending on the virus strain, its virulence, and the sensitivity of the host; it is typically between 1 and 5 percent; 50 percent in young animals, and 5 percent in adults [51]. LSD's economic effect and epidemiological implications have been researched by [52]. Due to the protracted debilitating effects of LSD in severely affected animals, such as reduced weight gain, a temporary or permanent cessation of milk output that may be accompanied by mastitis, a permanent or temporary infertility or even infertility in bulls as a result of orchitis, along with permanent skin damage, LSD is important economically. In 10% of pregnant cows, infection may be followed by abortion [53]. Due to afflicted cattle's persistent debility, decreased milk output, poor development, infertility, abortions, and even death, LSD results in significant economic losses. According to breed-specific LSD infection risk data, male local Zebu cattle were more likely to get LSD infection than females [18].

Prevention, treatment, and management

LSD is only treated symptomatically, and antibiotics are needed to prevent further bacterial infections. [33]. In a study, Salib and Osman (2011) effectively employed a combination of antimicrobials, anti-inflammatory medications, supportive care, and anti-septic therapies in treatment studies to decrease LSD effects and preserve lives. [30]. The treatment of LSD is considered costly and complete recovery is not usually achieved. Therefore, prevention should be followed to avoid substantial financial losses from milk loss, and animal product destruction. A study by Gari et al. demonstrates the value of immunization on the epidemiological aspects and economic effects of lumpy skin disorders in Ethiopia in treating lumpy skin disorders (LSD) in areas where they are prevalent[18]. The authors also provide information on how vaccination might reduce LSD-related costs by 17% per head for local zebu herds and 31% per head for Holstein Friesian/cross-bred herds. As a consequence, in endemic areas, limiting movement and eliminating sick animals are often insufficient to manage the disease. (There are LSD vaccines that work, and the sooner they are given, the less severe the projected economic impact of an epidemic will be. [46]. The Capripoxvirus family is considered to offer cross-protection. Therefore, using both identical (Neethling LSDV strains) and different (sheep pox/goat pox viruses), in live-attenuated vaccines cattle may be safeguarded against LSD infection. [54].

The LSDV Neethling strain, the Kenyan sheep and goat pox viruses (KSGPV) O-240 and O-180 strains, the Yugoslavian RM65 sheep pox (SPP) strain, the Romanian SPP strain, and the Gorgan goat pox (GTP) strain are among the Capripoxvirus (CaPV) vaccine strains that are commercially available [55]. A recent study on the efficacy of 3 CaPV isolates against LSD in Ethiopia by Gari et al. demonstrated that now the Gorgan GTP vaccine could fully protect cows against LSDV and the Neethling, as well as KSGP O-180 vaccine, seemed to be incompetent, suggesting the need for additional molecular identification for those inefficient vaccines [56]. In countries that have traditionally been immune to LSD and that protect sheep from sheep pox, it is advisable to employ the same immunization due to potential safety issues with the use of the low virulence LSDV vaccine. [11]. A clinical diagnosis must also be quickly confirmed to conduct eradication measures such as quarantine, slaughtering of infected and exposed animals, correct corpse disposal, cleaning and disinfecting of the area, and pest control as promptly as possible during the outbreak [29, 32]. Furthermore, strong import regulations must follow in disease-free regions for cattle, corpses, skins, and semen coming from endemic areas.

Conclusion

Recently, LSDV has been quietly invading other regions, including Europe. The lesions, chronic debility, decreased milk output, weight loss, infertility, miscarriage, and death, cause enormous economic losses. Additionally, they could have a significant effect on rural communities that depend heavily on cattle, resulting in significant production losses. The sickness has resulted in severe trade restrictions, which have had devastating implications at the national level. Therefore, it is critical to put into place efficient controls and prevention of disease spread, such as immunization programs, enhanced biosecurity measures, and quick diagnosis and response systems. Additionally, more research should be conducted to learn more about the illness, its dynamics of transmission, and its propensity to infect humans. Recent developments in bioinformatics have the potential to support the management and avoidance of lumpy skin disease (LSD) in cattle. To further understand the disease's molecular underpinnings and find genetic markers for resistance, one strategy is to employ genomics. Additionally, by analyzing massive databases and forecasting disease outbreaks, bioinformatics methods like machine learning and artificial intelligence can support prompt and efficient interventions. By following these steps, we can lessen the effects of lumpy skin disease on both animal and human health as well as protect individuals whose livelihoods depend on cattle.

Conflict of interest

The authors declare no conflict of interest.

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