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Review Article

Overview on Diagnostic Techniques and Economic Importance of Lumpy Skin Disease

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Abstract

Lumpy skin disease (LSD) is among the most economically significant viral diseases of cattle caused by Neethling virus prototype strain classified in the genus *Capripoxvirus* of family *Poxviridae*. Lumpy skin disease is currently endemic in most Sub-Saharan African countries and subsequently spread to Middle East, Asia and to Europe countries. Lumpy skin disease is a pox disease of cattle characterized by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, oedema of the skin, and sometimes death. The disease is of economic importance as it can cause a temporary reduction in milk and beef production, loss of draft performance in draft animals, abortion, infertility, loss of body condition, temporary or permanent sterility in bulls, damage to hides and death due to secondary bacterial infections. All breeds and age group, both sex are susceptible however, *Bos Taurus* are particularly more susceptible to clinical disease than *Bos indicus*. LSD is transmitted by mechanical vector insects and also wildlife plays a potential role in its maintenance. The herd-level LSD prevalence is significantly higher in the midland agro climate than in lowland and highland agro climate zones due to abundance of speculated mechanical vector insects. Laboratory diagnosis involves polymerase chain reaction (PCR) and different serological test methods. Currently Effective control measures of this disease is achieved through mass vaccination, import restrictions on livestock and their products, control of vectors and quarantine station. Furthermore, culling of infected animals is also optional method. Therefore, large-scale vaccination combined with other appropriate control measures are the most effective way of limiting the spread and economic impact due to lumpy skin disease. This review is designed with the aim of providing, latest information on the diagnostic techniques and economic importance of lumpy skin disease virus.

INTRODUCTION

Livestock production constitutes one of the principals means of achieving improved living standards in many regions of the developing world (1). The livestock sector globally is highly dynamic, contributes 40% of the global value of agricultural output and support the livelihoods and food security of almost a billion people (2). In many developing countries (In Sub-Saharan African countries), livestock keeping is a multifunctional activity and plays a crucial role both in national economies and the livelihood of rural communities (3). Ethiopia basically comprises an agrarian society; the socio-economic activities of about 85% of the population are based on farming and animal husbandry (4). Ethiopia has the most abundant livestock population in Africa with the estimated domestic animal number of 57.83 million and cattle population is estimated to be 28.89 million (5). Consequently, Ethiopia livestock production is an integral part of the agricultural system. The livestock sub sector accounts for 40% of the agricultural gross domestic product (GDP) and 20% of the total GDP without considering other contribution like traction power, fertilizing and mean of transport (6). Diseases are an important cause of reduced productivity of meat and milk as well as draft, hides and dung fuel.

Lumpy skin disease (LSD) is one of the most economically significant transboundary, emerging viral diseases. It is currently endemic in most Africa countries and expanded to Middle East region (7). It is a disease with a high morbidity and low mortality rate and affects cattle of all ages and breeds. It causes significant economic problems as a result of reduced milk production, beef loss and draft animals, abortion, infertility, loss of condition and damage to the hide (8). It becomes an important threat to livestock and dairy industry in the Middle East and Africa (9).

LSD is an acute infectious disease characterized by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, edema of the skin, and sometimes death (10). It is caused by the LSD virus that is classified in *Capripoxvirus* genus and family *Poxviridae.* Various strains of capripoxvirus are responsible for the disease and these are antigenically and serologically indistinguishable from strains causing sheep pox and goat pox but distinct at the genetic level (11). LSD has partially different geographic distribution from sheep and goat pox, suggesting that cattle strains of capripoxvirus do not infect and transmit between sheep and goats (12). The disease occurs in different ecological and climatic zones and extends its boundaries to different areas (13).

The LSD virus in combination with sheep and goat pox viruses severely affects ruminants. Consequently, it brought high economic pressure on subsistence of the poor farmers particularly pastoralists because their central economy relay on the production of livestock and in some areas in mixed farming system (14). As a transboundary disease, it causes international

ban on the trade of livestock and their products. LSD was spread to East Africa in 1957 in Kenya and disease was extensively expanded to rest of the countries in subsequent years (13). Determination of seroprevalence of LSD has a time limitation for the presence of detectable antibodies in the serum for more than seven months of post infection.

Serological tests such as virus neutralization are less sensitive and time consuming to detect the low-level antibody titers following the infection of the animals (15; 12). In Ethiopia limited works has been done on this disease so far and few works have been reported on risk factors assessments, epidemiological aspects, seroprevalence and financial impacts in selected areas of the country (16-17). Recently, a report on seroprevalence of disease using virus neutralization and indirect fluorescents antibody test indicated that the disease is widely distributed across the country and increases its impacts (18). Therefore, the objective of this paper is to review economic impact and available diagnostic methods that are used for screening, isolation and confirmatory of Lumpy Skin Disease.

EPIDEMIOLOGY

History of LSD

For the first time in 1929, skin disease with new clinical symptoms was occurred in Zambia. At that time, it was considered as it was caused by either plant poisoning or an allergic response of insect bite (19, 20). After fourteen years, in October 1943, another outbreak of the disease was occurred in Botswana and named it provisionally as "Ngamiland cattle disease" as the case was occurred for the first time in Ngamiland. After two years, 1945 the disease spreads to Zimbabwe and South Africa where the disease named as the lumpy skin disease and demonstration of transmission of the infectious agent by inoculation of cattle with suspension of the skin nodules was determined (13).

The disease was diagnosed in Kenya in 1957; Sudan in 1971; Chad and Niger in 1973; Nigeria in 1974 and Somalia in 1983 (21). In 1988, the first outbreak was occurred in Egypt in Ismailia and although control and eradication measures had been taken place the disease remains endemic in these areas (22). It was also observed clinically in Israel in herds of dairy farms in 1989 which was suggested as it was spread from Egyptian outbreaks by insect vectors carried by wind (23). The disease was primarily considered as an endemic disease to Africa and Middle East and other areas. According to annual livestock disease information released by OIE, outbreak cases were reported from Bahrain in 1993, 1994, 2002, Iran in 1996 and 2001, and other similar cases has been reported in United Arab Emerate, Kuwait and Oman (12).

Etiology

LSD is caused by Lumpy Skin Disease virus (LSDV) within the genus Capripoxvirus and the prototype strain is Neethling Virus. It is an enveloped DNA virus, ovoid in shape with a molecular size of 350*300nm and a molecular weight that ranges from 73 to 91 kilodalton (KDa). LSDV genome sequences were assembled into a contiguous sequence of 150.8 kilobase pair (kbp) which is in accordance with previous size estimates of 145 to 152 kbp (24-25). These genes encode several poxviral proteins known to be structural or involved in virion morphogenesis and assembly. The terminal genomic sequences contain a unique complement of at least 34 genes which are responsible in virulence, host range and/or immune evasion (24-25). Comparison of LSDV genome with published restriction fragment analysis of the SPPV and GTPV genome indicates that there may be additional terminal sequences of less than 200 bp present (24).

LSDV is susceptible to sun light and detergents containing lipid solvents. The virus could be inactivated after heating for 1 hour at 55°C (26). However, it withstands drying, pH changes if not an extreme pH and can remain viable for months in dark room such as infected animal shade off its host. LSDV can persist in skin plugs for about 42 days (27-26). It is likely that the viral A type inclusion body protein in infected cells may protect the virion after the scab has disintegrated, although this has not yet been proven (28). The members of this family are among the largest of all viruses. It is an envelope, Linear ovoid shape with a molecular brick shaped or ovoid virions measuring 220-450 nanometer (nm) by 140-266nm (Figure 1). LSDV has ds DNA genome of about 151kb (29).

Viral genome

Eight genera are found within the Chordopoxvirinae subfamily of the Poxviridae (Table 1) and other viruses affecting different animals and humans are indicated in table 2 below. The members of this family are among the largest of all viruses, brick shaped or ovoid virions measuring 220-450 nanometer (nm) by 140-266nm. The virions have an external coat containing lipid and an irregular arrangement of tubules on the outer membrane in most genera except the Parapox viruses that have regular spiral arrangement of "tubules" on the outer membrane (Sharma and Adlakha, 1995). The virions contain about 30 structural proteins and several enzymes. The nucleic acid is a double stranded deoxyribo nucleic acid (DNA) of molecular weight in the range between 150 and 240*106 daltons. The evolutionary biology of the poxviruses, phylogeny, with particular emphasis on transfer of poxviruses across host species boundaries (Tables 1 and 2); (30-31). The multiplication takes place in the cytoplasm and the cytoplasmic accumulations produce A type inclusion bodies (32). The members of some genera are ether resistant while other genera are ether sensitive. The pox viruses withstand drying for months and even storage at room temperature. They are destroyed by moist heat at 60°C within 10 minutes. They are also resistant to many common disinfectants (33). The spread of infection occurs by the respiratory route or through the skin. Some members are also mechanically transmitted by arthropods (32).

Viral replication

Replication of poxvirus occurs in the cytoplasm. After fusion of the virion with the plasma membrane or via endocytosis, the viral core is released into the cytoplasm. Transcription is initiated by viral transcriptase and functional capped and polyadenylated messenger Ribonucleic Acid (mRNAs) are produced within minutes after infection. The polypeptides produced by translation of these mRNAs complete the uncoating of the core and about half of the viral genome is transcribed prior to replication, comprising genes encoding proteins involved in host interactions, viral DNA

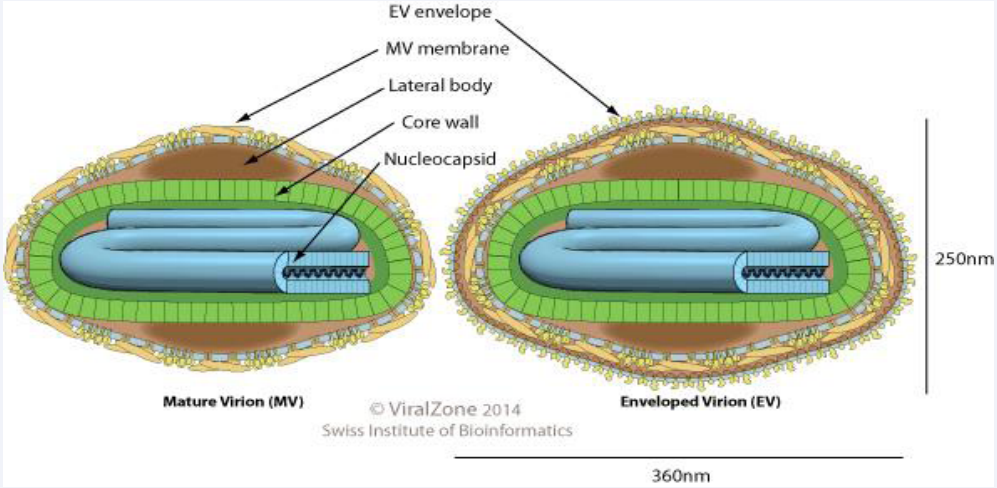

Figure 1 Morphological structure LSDV.

Table 1: Classification of Poxviruses of vertebrates: Subfamily Chordopoxvirinae.

No Genera	**Prototype virus**
1. Orthopox virus	Vaccinia
2. Parapox virus	Orf virus
3. Capripox virus	Sheep pox virus
4. Suipox virus	Swine pox virus
5. Leporipox virus	Myxoma virus
6. Avipox virus	Fowl pox virus
7. Yatapoxvirus	Yaba monkey tumor virus
8. Molluscipoxvirus	Molluscum contagiosum virus

synthesis, and intermediate gene expression. With the onset of DNA replication 1.5 to 6 hours after infection, there is a dramatic shift in the gene expression and almost the entire genome is transcribed, but transcripts from the early genes (i.e., those transcribed before DNA replication begins) are not translated. Two forms of virions are released from the infected cells (virions with one membrane, and virions with two membranes) and both types are infectious (32).

Mode of transmission and host range

The virus of LSD does not spread readily among animals held in insect-proof pens. While infection by contact can occur, it is not considered a major component of transmission during epizootics (34). Most infection is thought to be due to

Table 2: Poxviruses of veterinary importance that affect domestic and laboratory animals.

Genus	**Virus**	**Animals naturally affected**	**Host range**	**Geographical Distribution**
Parapoxvirus	Pseudocowpox virus	Cattle, human	Narrow	Worldwide
	Bov.Papular stomatitis virus	Cattle, human	Narrow	Worldwide
	Orf virus	Sheep, goat, human	Narrow	Worldwide
Capripoxvirus	Sheeppox virus	Sheep, goat	Narrow	Africa, Asia
	Goatpox virus	Goat, Sheep	Narrow	Africa, Asia
	LSD virus	Cattle, buffalo	Narrow	Africa
Suipoxvirus	Swine pox virus	Swine	Narrow	Worldwide
Leporipoxvirus	Myxoma virus, Hare	Rabbit	Narrow	Americas
	fibroma virus, Rabbit	Hare		Europe
	fibroma virus, Squirrel fibroma virus	Squirrel		Australia
Avipoxvirus	Fowlcholera virus,Canary pox virus, Pigeon pox virus,Turkey pox virus,Quailpox virus	Chickens, turkey, other birds	Narrow	Worldwide
Orthopoxviruses	Vaccinia virus	Human, cow, buffalo, pig, rabbit	Broad	Worldwide
	Cowpox virus, Buffalo pox virus	Cow, human, numerous spp.	Broad	Europe Asia
	Ectromelia virus, Rabbit pox virus	Mice, Rabbit	Narrow	Europe
	Monkeypox virus	Monkeys, Squirrel, many others	Broad	West and Central Africa
	Uasin Gishu virus	Horse	Broad	East Africa

mechanical transmission by blood sucking arthropods (35). The multiplication of LSDV in the vector insects has not been demonstrated. In the infected animal virus is present in blood, nasal and lachrymal secretions, semen and saliva, which may be sources for transmission (36). LSD is transmissible to suckling calves through infected milk. Direct transmission can occur when the animals share the same drinking trough due to contamination by nasal and salivary discharges from infected animals (26). The virus enters the host either through the skin or the digestive tract mucosa.

Particular types of insects incriminated in the transmission of LSDV are not all elucidated. Virus has been isolated from Stomoxys (S) species and *Biomyia fasciata* species commonly associated with cattle and found in large numbers during LSD epizootics (19). *S. calcitrans* has been thought as the most likely insect to have a role in the epidemiology of LSD based on the detection and isolation of virus from flies that had fed on infected cattle during an outbreak (37). Stomoxys spp have been shown to transmit SGPV successfully (38). In 1989 the LSD outbreak in Israel was attributed to infected *S. calcitrans* carried over by wind from Ismailiya in Egypt (39). The introduction of LSD to La Réunion in 1991 was also exclusively attributed to stomoxys insects despite implementation of all the official quarantine and prohibition of cattle movement measures (26). However, there are still doubtful issues on this assumption which could raise some questions on the very nature of mechanical transmission that requires short time period to transmit the pathogens, and the distance that these flies could be blown by wind, if any because of the large size of Stomoxys flies which might unlikely be able to blow by wind like mosquitoes to far distances.

In an experimental transmission attempt, *Aedes aegyti* (Diptera: Culicidae) was reported to transmit LSDV in cattle (35) whereas the transmission by Stomoxys spp. was not successful (40). Other biting flies like Tabanids, Glossina spp, Culicoides spp have been suspected to be involved. The potential of Ixodid ticks to transmit LSDV was also reported (41). An embarrassing gap in our knowledge requires defining the transmission mechanisms of LSD and research efforts are required to understand the prevalence of the different biting flies potential association with LSDV transmission in the various biotypes of countries.

Some wild species like Giraffe (*Giraffa camelopardalis*), Impala (Aepyceros melampus), and Thomson's gazelle have been infected experimentally by parenteral inoculation with LSDV and have developed characteristic lesions. However, under natural conditions, lesions of LSD have not been seen on these animals when they have been present during epizootics of the disease (42). Sheep and goats do not become infected during outbreaks of LSD even when held in close contact with infected cattle. African buffaloes (*Syncerus caffer*) and Asian water buffaloes (*Bubalus bubalis*) do not show lesions in the field during epizootics of LSD but both buffalo types may suffer an unapparent infection and seroconvert (13). In anenzootic area of LSD in Kenya, many African buffaloes had high titers of antibodies to Capripox virus whereas in another area, no antibody was found (13). Infection has been reported in Arabian Oryx in Saudi Arabia (43). In general, the role of wildlife in the transmission and maintenance of LSDV was found almost negligible (44). The absence of reservoir host for LSD virus might lead us to the assumption that infection might persist in the endemic areas at a low level as unapparent or mild form in the cattle population (26).

Morbidity and Mortality rate

LSD can occur as sporadic cases or in epizootics. The incidence of disease is highest in wet, warm weather, and decreases during the dry season. New foci of disease can appear at distant sites; in these cases, the virus is thought to be carried by insects. The morbidity rate varies widely, depending on the presence of insect vectors and host susceptibility, and ranges from 3% to 85%. Calves and lactating cows tend to be most susceptible to disease. In addition, the disease signs can vary widely among the cattle in a group, with some animals having inapparent infections and others developing severe disease. The mortality rate is low in most cases (1-3%), but has been as high as 20% in some outbreaks. Unusually high mortality rates of 75-85% have been reported Kenya but remain unexplained (13). The current study in lowland of Ethiopia showed that 18% morbidity, 1.34% mortality, and 7.44 case fatality rates was observed in single outbreak investigation (45).

Geographical distribution

LSD distribution has extended from sub-Saharan countries to Egypt and Western Africa. Outside the African continent, Israel has reported LSD outbreaks and sporadically. Some Middle East countries showed that there is a real potential risk of the disease to establish endemically there (46). Epidemiological trend of LSD suggests that there could also be a considerable potential risk of the disease spreading further into North Africa (Figure 2), into the Middle East countries and to Mediterranean regions because of global climatic changes and trade movement in animals and animal products (13).

In Ethiopia, LSD was first observed in 1983 in the western part of the country (southwest of Lake Tana) (47). After its first appearance, an explosive sudden epidemic spread from the north through the central to the southern part of the country. In the subsequent three to five years, it had covered the vast area of the highland and midland parts of the country. LSD is one of reported diseases in Ethiopia which deserves outbreak notification to the National veterinary services. However, a variable degree of under-reporting of the outbreak cases could exist from different parts of the country. Data investigations from the national disease outbreak report database during the period 2000-2009 showed that major epidemic outbreaks of LSD occurred in 2000/2001 in the northern parts of the country in Amhara and West Oromia regions. Then it had extended to the central and the southern parts of the country in 2003/04 covering large parts of Oromia and Southern Nation, Nationalities and Peoples (SNNP) regions.

In 2006/07 another extensive outbreak reappeared in Tigray, Amhara and Benishangul regions in the northern and north-western parts of the country. From 2007 up to 2009 the outbreak number progressively increased in Oromia Region situated in the central part of the country while it seemed to be gradually decreasing in the northern part of the country including Tigray, Amhara and Benishangul regions. This showed that an epidemic reoccurs after an interval of 5-6 years cycle in unvaccinated cattle

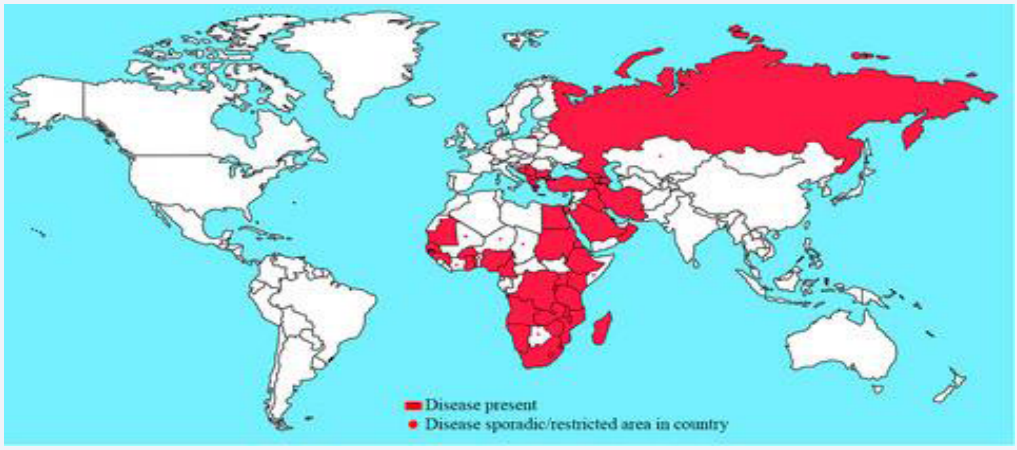

Figure 2 Global situation of lumpy skin disease (FAO, 2016).

population. Studies based on clinical disease observation done around Nekemt town, Wolliso town and in Southern rangeland in Ethiopia have reported different animal level prevalence of LSD ranging from 7 to 28% (48-50). A mortality of 1-3% was observed in the same study and was similar to a previous report by (13).

CLINICAL SIGNS AND PATHOGENESIS

The characteristic clinical signs of LSD are a fever of 40-41.5°C that may last 6-72 hours and occasionally up to 10 days which is accompanied by watering eyes (table 3), increased nasal and pharyngeal secretions, loss of appetite, reduction in milk production, some depression and reluctance to move (17). Within 1–2 days onset of the clinical signs there is a cutaneous eruption of nodules or lumps, which may cover the whole body of affected cattle. The most common sites are the head and neck, perineum, genitalia and udder, and the limbs. The nodules are 0.5-5 cm in diameter, appearing as round circumscribed areas of erect hair, firm and slightly raised from the surrounding skin. The lesions are full skin thickness involving the epidermis, dermis and subcutis, which may be oedematous. Regional lymph nodes are enlarged and oedematous (17).

Lesions develop on the muzzle, in the nostrils, and in the mouth and pharynx. They show a ring-like margin where there has been separation from the surrounding healthy epithelium. Lesions in the larynx and trachea, and throughout the alimentary tract, especially the abomasum, become ulcerated and necrotic. Mucopurulent nasal discharges, persistent dribbling of infected saliva, coughing and stertorous (snoring) and often distressed breathing are manifested. Inflammation and hyperemia of the conjunctiva and cornea of the eyes is common (13, 51).

Inflammatory and oedematous swellings of the limbs, brisket and genitalia may develop. Skin lesions become necrotic. Some remain in situ and others slough leaving a full skin thickness hole, known as a ''sitfast", which becomes infected by pus-forming bacteria and can also be infested by fly strike. Large areas of skin may slough causing substantial down grade of the hide quality (52). Lesions in the skin, subcutaneous tissue, and muscles of the limbs, together with the severe skin inflammation caused by secondary infection of lesions, greatly reduce mobility. Rapid deterioration in body condition results and animals that recover may remain in poor condition for 1-3 months and in extreme cases for up to 6 months. Pneumonia is a common and often fatal complication. Absence of oestrus cycles during the severe debility and abortion is frequent in the early stages due to prolonged fever (53). Painful genitalia in bulls can prevent from serving for long periods. Foetus born to infected cows may show skin lesions at birth presumably acquired through intra-uterine infection (13). (Figure 3)

DIAGNOSIS

LSD can be clinically diagnosed by its pathognomic nodular lesions on the skin, mucous membranes, swelling of the superficial lymph nodes and systemic involved symptoms by experienced practitioners. However, mild and inapparent disease

Figure 3 An inflammation and whiteness of the eyes of cattle infected with LSD.

may be difficult to diagnose and rapid laboratory methods are needed to confirm the diagnosis. Confirmation of the diagnosis through laboratory techniques can be done using various methods discussed below (28).

Virus isolation and identification

Rapid confirmation can be made by demonstration of the typical capripox virion in biopsy material or desiccated crusts using the transmission electro-microscope in combination with the clinical history of a generalized nodular skin disease and enlarged superficial lymph nodes in cattle. Capripox is morphologically distinct from Parapox virus which causes bovine pustular stomatitis and pseudocow pox, but cannot be differentiated from Cowpox and Vaccinia viruses in Orthopox virus. But neither of these causes a generalized infection and both are uncommon in cattle (28, 12). LSDV causes a characteristic cytopathic effect and intracytoplasmic inclusion bodies, and is distinct from the virus of pseudo-LSD (Allotron- Herpes mammilitis), which is a herpesvirus producing syncytia and intranuclear inclusion bodies (28).

Virus isolation could be attempted and is best carried out in primary lamb kidney cell or lamb testis cell cultures. Secondary lamb testis cell line (OA3.Ts) has been proved to replace the primary cell cultures for better efficiency and easily managed to grow Capripoxvirus (54). LSDV can be grown on a variety of sheep, goat and cattle cells (55). The LSDV isolation can be confirmed by immunostaining technique using anti- Capripoxvirus serum which allows the visualization of the LSDV plaques in the cell culture (54). Antigen detection can be demonstrated in tissue culture using immunoperoxidase or immunofluorescent staining (12). A Polymerase Chain Reaction (PCR) technique to detect capripoxvirus antigen from cell culture and biopsy specimens has been developed and the reagents are available commercially (21, 51). An immunocapture enzyme-linked immunosorbent assay (ELISA) for the detection of Capripoxvirus antigen is also reported (56).

Serodiagnosis

Neutralizing antibody appears 3-4 days after the onset of the clinical signs and reaches the peak titre level in 2-3 weeks. Both complement fixing and precipitating antibodies are present in the serum of infected and recovered animals. Immunological defense against capripoxvirus relies mainly on cell-mediated immune response and humoral immunity would remain in the circulation for a short period within the time range of mostly seven to eight months (26, 12).

Virus Neutralization Test (VNT)

VNT is the most widely used serological test for capripox antibody detection (12). It has high specificity to rule-out false positives due to cross- reaction with cowpox and Parapoxvirus antibodies but its sensitivity is lower to trace small antibody titration (57).

Indirect fluorescence antibody test (IFAT)

An indirect fluorescence antibody test using the capripoxvirus antigen fixed in the tissue culture plate can be used to detect antibodies against LSD in the serum. The test was reported to have good sensitivity but cross reacting Parapox and Orthopox viruses might affect its specificity at lower serum dilution rates (12).

Agar gel immunodiffusion test (AGID)

It has been used for detecting the precipitating antigen of capripoxvirus, but has the disadvantage that this antigen is shared with Parapoxvirus and has also less sensitivity (12). So far, a diagnostic assay that can be easily run for an epidemiological study of LSD is not yet validated and commercially not available. Moreover, the accuracy of the conventional diagnostic techniques which are currently being used for diagnosis purposes have not been evaluated in particular in the context of the target population in Ethiopia (17).

Enzyme-linked immunosorbent assay (ELISA)

Following the cloning of the highly antigenic capripoxvirus structural protein P32, it is possible to use expressed recombinant antigen for the production of diagnostic reagents, including the raising of P32 monospecific polyclonal antiserum and the production of monoclonal antibodies (MAbs) (34). Using hyperimmune rabbit antiserum, raised by inoculation of rabbits with purified capripoxvirus, capripox antigen from biopsy suspensions or tissue culture supernatant can be trapped on an ELISA plate. The presence of the antigen can then be indicated using guinea-pig serum, raised against the group-specific structural protein P32, commercial horseradish-peroxidase-conjugated rabbit anti-guinea-pig immunoglobulin and a chromogen/substrate solution.

Polymerase chain reaction (PCR)

The conventional gel-based PCR method described below is a simple, fast and sensitive method for the detection of capripoxvirus genome in EDTA blood, biopsy, semen or tissue culture samples. However, it does not allow differentiation between LSD and sheep and goat pox viruses. Primers for the viral attachment protein gene and the viral fusion protein gene (58) are specific for all the strains within the genus Capripoxvirus. By the use of sequence and phylogenetic analysis; strains of virus can be identified (59). Additional to skin biopsy, whole blood and semen the virus was isolated from nasal swabs (45). Virus isolates can also be characterized by comparing the genome fragments generated by HindIII digestion of their purified DNA (38). This technique has identified differences between isolates from the different species, but these are not consistent and there is evidence of the movement of strains between species and recombination between strains in the field (60). More recently, quantitative real-time PCR methods has been described that are reported to be faster and have higher sensitivity (51, 61). The LSD virus genome contains 156 putative genes (62).

Status of the lumpy skin disease in Ethiopia

As Ethiopia has the largest number of livestock population in Africa. The Ethiopian economy is highly dependent on agriculture, which contributed about 48% of the GDP, followed by 39% from the service sector and 13% from the industrial sector. As a result of the country has much gain from the growing global market for livestock products. However, the livestock disease is

one of the major livestock production constraints including LSD. LSD is one of the newly emerging diseases of cattle in Ethiopia (63). The current status and occurrence of LSD is associate with the different agro-climatic conditions and the associated risk factors. There are three variables expected to influence the distribution and occurrence of LSD in Ethiopia: the effect of agro climate, communal grazing/watering management and introduction of new animals. Moreover, Ethiopia has two major seasons of rainfall: a shorter rainy season that usually begins in mid-February and continues up to end of April and the long rainy season (75%) starting mid-June and ending mid-September (64). Hence this association might be attributed to the availability and abundance of effective mechanical vector insects. Thus, the temporal involvement between LSD occurrence and increase in the biting-fly population was positively correlated and significant increase to the occurrence of the disease. Consequently, both biting-flies activity and disease outbreak frequencies begin to increase from April reaching a maximum in September which suggested that mechanical vector insects might play a major role in the disease outbreak of LSD. As mention environmental factor of sharing common watering points and grazing plots would allow contact and intermingling of different herds that would probably increase the risk of exposure and enhance the virus transmission through contamination and/or the speculated mechanical vectors such as Stomoxys spp. and mosquitoes (16). Subsequently the potential risk of agro-climate variations to LSD occurrence showed that herds in midland and lowland agro-climates were more likely infected by LSD than in the highland agro-climate. Seeing that the herd level sero-prevalence was higher in the midland (64 %) as compared to the lowland (50 %) and the highland (26 %), (65). because Agro-climate variation is the basis for the type and abundance of considered mechanical vector insects. Therefore, the warm and humid climate in midland agro-climates might be a more favorable environment for the occurrence of large populations of biting flies than the remaining two agro-climates (66).

Economic Importance of the Lsd

Capri pox viruses are becoming an emerging worldwide threat to sheep, goats and cattle (11). LSD is one of the economically significant diseases in Africa and the Middle East countries that cause severe production loss in cattle. The world organization for animal health (OIE) categorizes the disease as notifiable diseases because of its severe economic losses. The economic importance of the disease was mainly due to having high morbidity rate rather than mortality (67). 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.

In intensive farming of cattle, the direct and indirect production losses caused by LSD were estimated to be as high as 45-60% (67). It was reflected that the severity of the disease was much more in developing countries where the poorest small-scale farmers was found. 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 6.43 USD and for the Holstein Friesian 58 USD (16).

The disease mainly affects cattle with subsequent effects on production through the morbidity and reduced productivity (68). 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 (21, 12).

The morbidity and mortality rates for LSD vary greatly in different endemic areas depending on the severity of strain, prevalence of insect vectors and susceptibility of the host (16). An outbreak in a previously free country could be expected to result in a high morbidity rate. 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. Permanent loss of some markets would also be expected, with associated downturn in rural economy and increased rural unemployment (7).

High susceptibility of high producing breeds imported from Europe or Australia could also pose a considerable hindrance for the development of small scale and intensive dairy production in Africa and in particular in Ethiopia. Being one of the transboundary diseases, Capripox viruses have impediments to livestock and livestock product trades. This could affect particularly the economic well-being of the farmers and that of pastoral communities but also more globally the country's economy (69).

Overall, LSD is considered as a disease of high economic pressure because of its ability to compromise food security through protein loss, loss in draft power, reduced output of animal production, increase production costs due to increased costs of disease control, disrupt livestock and their product trade, result of reduced milk yield, weight loss, abortion, infertility in cows, mastitis and infertility in lactating cows, infertility in bulls (9). In addition, as the disease affects hide, it can cause permanent damage to the skin and hide that greatly affect leather industry. It also causes ban on international trade of livestock and causes prolonged economic loss as it became endemic and brought serious stock loss (70, 16).

CONTROL AND PREVENTION

Vaccination in endemic areas

Control and prevention of LSD in endemic countries like Ethiopia relies mainly on vaccination. The experience in the major parts of the country showed that the vaccination approach is commonly chosen and is often that of ring vaccination around a local foci outbreak when it occurs. Animals that recover from virulent LSD infection generate lifelong immunity consisting both a humoral and cell mediated protective immunity (71).

Immunity acquired from natural infection of the disease might be lifelong and vaccination has been successfully used. LSD could be kept under control by vaccination of cattle every year (72). All strains of capripoxvirus examined so far, whether of bovine, ovine or caprine origin, share a major neutralizing site, so that animals that have recovered from infection with one of the strains are resistant to infection with any other strain.

Consequently, it is possible to protect cattle against LSD using strains of capripoxvirus derived from either of the sheep or goats as used in Egypt by Romanian sheep pox strain (12). Live, attenuated vaccines against LSD are commercially available. These have antigenic homology and there is cross protection among them. Local strain of Kenyan sheep and goat pox virus has been shown to effectively immunize sheep, goats and cattle against infection with capripoxvirus with a remarkable success. The next one is attenuated South African LSD virus (Neethling strain) vaccine derived from cattle, freeze dried product is also available (10). In countries where LSD is endemic, vaccination against this infection was successfully used by vaccinating animals every year.

Vaccination in new areas

Maternal immunity provides protection from LSD in calves at least for 6 months. Risks of introduction of the disease in to the new areas are by the introduction of infected animals and contaminated materials. If the occurrence of LSD is reported or confirmed in new areas, before the spread of the disease to other areas extensively, quarantine of the area, and slaughtering of the diseased and in contact animals are used to control the disease. When equipment's contacted it must be cleaned and disinfected (13). Ring vaccination of cattle within the foci of infection with a radius of 25-50 km, quarantine and restriction of animal movement should be applied to eradicate the disease from infected area, but if the area coverage of the disease is large, the most convenient techniques for the control of the disease is mass vaccination.

Other control techniques

For countries free of the disease, the introduction of the disease can be prevented by restriction of the importation of the animals and their products. In those nations which experience the infection, the spread of the LSD can be limited by restriction of the animal movement from one place to another, quarantine or keeping of sick animals well apart from the rest of the herd and such animals must not share drinking or feeding troughs and also by awareness creation of the farmers' (72).

Animals older than six months must be vaccinated against LSD during spring. It is safe to vaccinate pregnant cows. All animals must be vaccinated once a year. When vaccinating the animals during a disease outbreak, it is important to use one needle per animal so that the virus is not spread from sick to healthy animals but the practicality and economic feasibility of use of one needle per cattle need to be carefully considered. Professional help and recommendation on vaccines must be carefully followed and practiced. Broad spectrum antibiotics are also given to prevent the secondary bacterial complication as the defense mechanism of the body weakened which can prolong the complete recovery of the diseased animals (68).

CONCLUSIONS AND RECOMMENDATIONS

LSD is an acute infectious disease characterized by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, edema of the skin, and sometimes death. The disease is usually associated with high morbidity and low mortality, causes economic losses because of decreased weight gain, permanent damage to hides, decreased milk production and infertility. Clinical diagnosis is based usually by the presence of fever, nodules on the skin, mucous membranes, enlarged superficial lymph nodes and edema of the skin in livestock, but it is a presumptive diagnosis that must be confirmed by laboratory methods. Direct diagnosis of LSDV involves polymerase chain reaction (PCR), tissue culture and ELISA methods. Molecular techniques are important tools for diagnosis and epidemiologic studies, providing relevant information for isolation and identification of LSDV strain circulating in the area.

Serological methods are among the well-established indirect laboratory diagnosis of LSDV like virus neutralization test is the most specific serological test, but because immunity to LSD infection is predominantly cell mediated, the test is not sufficiently sensitive to identify animals that have had contact with LSD virus and developed only low levels of neutralizing antibody. The agar gel immunodiffusion test and indirect immunofluorescent antibody test are less specific due to cross-reactions with antibody to other poxviruses. Western blotting using the reaction between P32 antigen of LSD virus with test sera is both sensitive and specific, but is difficult and expensive to carry out. The use of this or another appropriate antigen, expressed by a suitable vector, in an ELISA offers the prospect of an acceptable and standardized serological test. Based on the above conclusion the following recommendations are forwarded.

- The government should establish strategic policies for effective control and eradication of the disease, i.e., restriction of livestock movement, strategic vaccination program and depopulation of infected and in contact animals.
- Regular community awareness creation to the herd owners should avoid herd mixing and contacts by using private grazing plots and watering sources.
- To develop the main method to control LSD is through Ring and mass vaccination of susceptible stock using matching live vaccine. Fenner

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