An Overview On: Lympy Skin Disease Virus

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***Abstract*- Lumpy skin disease (LSD) is a viral trans boundary disease endemic throughout Africa and of high economic importance that affects cattle and domestic waterbuffaloes. Since 2012, the disease has spread rapidly and widely throughout the Middle Eastern and Balkan regions, southern Caucasus and parts of the Russian Federation. Before vaccination campaigns took their full effect, the disease continued spreading from region to region, mainly showing seasonal patterns despite implementing control and eradication measures. The disease is capable of appearing several hundred kilometers away from initial (focal) outbreak sites within a shorttime period. These incursions have triggered a long-awaited renewed scientificinterest in LSD resulting in the initiation of novel research into broad aspects of thedisease, including epidemiology, modes of transmission and associated risk factors. Long-distance dispersal of LSDV seems to occur via the movement of infected animals, but distinct seasonal patterns indicate that arthropod-borne transmission is most likely responsible for the swift and aggressive short-distance spread of thedisease. Elucidating the mechanisms of transmission of LSDV will enable thedevelopment of more targeted and effective actions for containment and eradication of the virus. The mode of vector-borne transmission of the disease is most likely mechanical, but there is no clear-cut evidence to confirm or disprove this assumption.**

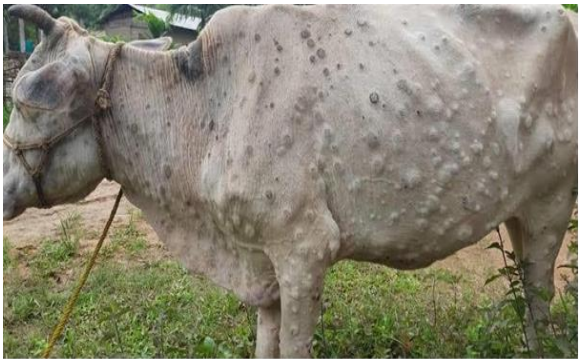
***Keywords* - Lympy virus, LSDV, transmission, skin**

INTRODUCTION

Capri pox virus (CaPVs) is one of the eight genera within the Chordopoxvirinae subfamily of the Poxviridae and is comprised of Lumpy Skin Disease Virus (LSDV), Sheep Pox Virus (SPPV), and Goat Pox Virus (GTPV).These viruses are responsible for most economically significant diseases of domestic ruminants in Africa and Asia[1]. CaPV infections have specific geographic distributions [2,3]. SPPV and GTPV isendemic in most African countries, the Middle East,Central Asia and the Indian subcontinent. In contrast, LSDV occurs largely in southern, central, eastern andwestern Africa [4-7]; its occurrence in north Sahara Desert and outside the Africancontinent was confirmed for the first time in Egypt and Israel between 1988 and1989, and was reported again in 2006, 2011 and 2014 in Egypt [8-10]. LSDoccurrences have also been reported in the Middle Eastern, European and west Asianregions [11-13]. In 2015 and 2016 the disease spread to south-east Europe, theBalkans and the Caucasus [14].Lumpy skin disease is caused by lumpy skin disease virus(LSDV)for which Neethling strain is the prototype.

The principal method of transmission is mechanical by arthropod vectors [15,16].Temporally LSD is shown to be aggregated during the warm and humid months of the year Gari et al. which is directly associated with vector abundance [17]. This author also revealed the role of husbandry practices such as of animals at communal grazing and watering points in the transmission of LSDV. LSDV has alimited host range and does not complete its replication cycle in non-ruminant hosts [18]. Besides, LSD has not been reported in sheep and goats even when kept in a close contact with infected cattle although typical skin lesions, without systemic disease, have been produced experimentally in sheep, goats, giraffes , impalas, and Grant's gazelles [2]. Natural cases of lumpy skin disease were recorded in waterbuffalo (Bubalis bubalis) during an outbreak in Egypt in 1988, but morbidity wasmuch lower than for cattle (1.6% vs. 30.8%) [16,19,20]. Among cattle Bos taurus is more susceptible to clinical disease than Bos indicus; the

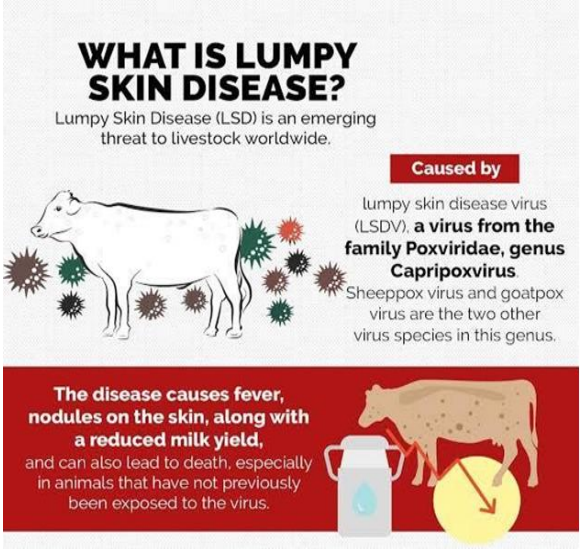
Asian buffalo has also been reported to be susceptible [14,21]. Cattle breeds of both sexes and all ages aresusceptible to LSDV, but there is some evidence to support that young animal may bemore susceptible to the severe form of the disease [22,23]. LSD symptoms in cattleare mild to severe; characterized by fever, multiple skin nodules covering the neck,back, perineum, tail, limbs and genital organs, the mucous membranes; the lesionmay also involve subcutaneous tissues and sometimes musculature and internalorgans. Affected animals also exhibit lameness, emaciation and cessation of milk production. Edema of limbs and brisket, and lymph adenitis are highly prominent and sometimes affected animals may die. In addition, pneumonia is a commons equel in animals with lesions in the mouth and respiratory tract[11,24].



Morbidity and mortality of LSD can vary considerably depending on the breed of cattle, the immunological status of the population, insect vectors involved in thetransmission and isolates of the virus. In endemic areas morbidity is usually around10% and mortality ranges between 1% and 3% [2,5]. In addition the incidence of LSDin Holstein Friesian and crossbred cattle was found to be significantly higher than in local zebu [25]. Recently, Abera and Elhaig showed that the prevalence of LSD is higher in adult cattle but, they observed no statistically significant association between the age groups in which they are equally exposed to risk [10,26].Furthermore, LSD results in overwhelming economic losses due to severe reductionin milk yield, reduced hide quality, chronic debility, weight loss, infertility, abortionand death. It also considered as notifiable disease, and in endemic countries, itresults in serious restrictions to international trade [2,7,27]. The financial cost ofclinical LSD has been computed by Gari et al. in Ethiopia and, the average financialcost in infected herds was estimated to be 6.43 USD per head for local zebu and 58 USD per head for Holstein Friesian or crossbred cattle [25]. Therefore, this review isaimed to highlight the biology of LSDV, mechanism of spread, clinical and pathological features of lumpy skin disease in cattle

CLINICAL HISTORY AND SAMPLE COLLECTION

In April 2009, a severe disease of cattle resembling LSD was reported from Nezwa(Interior), Alqabel (Eastern), Sohar, Saham (Batinah) and Burimi regions. The outbreaks involved seven herds (64 North Oman, Jersey and cross-bred cattle) andone herd (3,300 Holstein–Friesian dairy cows) at Nezwa and Sohar, respectively. Samples were collected from 22 and 38 cows from Nezwa and Sohar, respectively. Skin biopsies were collected for virus isolation, polymerase chain reaction (PCR),negative staining for transmission electron microscopy and histopathology. Serawere collected for serum neutralization testing (Beard et al. 2010) and necropsies were performed on two dead Holstein–Friesian animals. Biopsies and tissuescollected at necropsy were fixed in 10 % buffered formalin, processed, sectioned and stained with either haematoxylin and eosin or phloxine–tartrazine stain (BancroftandGamble2008).



SAMPLE PREPARATION FOR ELECTRON MICROSCOPIC EXAMINATION

Small tissue sections were excised from visible lesions on the affected tissue and homogenised using a mortar

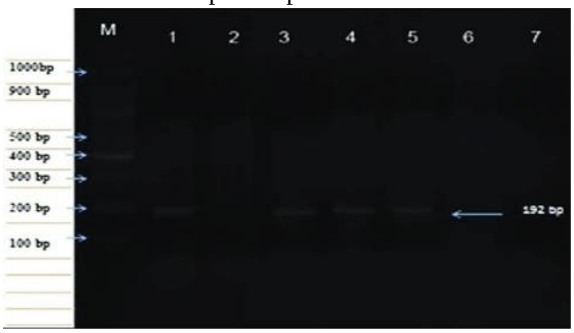
and pestle in sterile double-distilled water (ddH_2O).The suspension was centrifuged at low speed (1,000 × *g*) for 5 min to remove coarse debris. The supernatant was further centrifuged at 10,000 × *g* for 20 min and the supernatant fraction discarded. The pellet was gently washed twice with ddH_2O and suspended in phosphotungstic acid (pH 6.4). This suspension was then applieddropwise to a Formvar-coated copper grid, allowed to dry and viewed at 80 kV using a JeolJEM-1200 transmission electron microscope (Japan).

SAMPLE PREPARATION FOR POLYMERASE CHAIN REACTION ANALYSIS

A thin tissue section removed from each sample using sterile technique was chopped into 5 mm^3 cubes and transferred to a separate mortar. Sterile phosphate-bufferedsaline (PBS) (2 ml) was added and the pieces were ground with a pestle incarborundum powder. The mixtures were then transferred to Eppendorf tubes andallowed to stand for 3 min to precipitate large detritus. The supernatants were transferred to new Eppendorf tubes and sonicated using a Sonorex TK52 water bath sonicator (Bandelin, Germany) at 35 kHz for10 min. The mixtures were subsequently vortexed and centrifuged at 2,000 rpm (358 × *g*) for 2 min in an Avanti30 Beckman benchtop centrifuge (Beckman, USA). The supernatants were transferred to new Eppendorf tubes and centrifuged at 16,000 rpm (22,897 × *g*) for 15 min to pellet the viral particles. The supernatants were discarded, and the virus-containing pellets resuspended in 200 µl PBS for DNA extraction using a MagNAPure LC Total Nucleic Acid Isolation Kit (Roche, Germany) on a MagNA Pure LCInstrument (Roche, Germany) according to the manufacturer's instructions.

PCR CONDITIONS

The primers were designed from sequence data derived from the South African vaccine strain and Warm baths field isolate of LSDV (Genbanka ccession numbers AF409138 and AF409137, respectively) (Kara et al. 2003). Primer pair 1, consisting of primer DW-TK (5′- GCC GAT AAC ATA TAT AGA CCC −3′) and primer OP49 (5′- GTG CTA TCT AGT GCA GCT AT −3′), is used to amplify a 434-bpLSDV genomic fragment between positions 56698–57132, and primer pair2, consisting of primer L132F (5′- CAC TTC CCT TTT AAG C −3′) and primer L132R (5′- CAT TCT ACA ATC TCC ATG CG −3′), amplifies a 492-bp fragment between genomic positions 119801–120292. The PCRs were performed using an Eppendorf Master Cycler® gradient thermo cycler (Merck, Germany) and 25 µl reaction volumes consisting of 2.5 µl 10× PCR buffer (containing 20 mM $MgCl_2$) (TakaraBiomedical, Japan), 2 µl 2.5 mM dNTPs (Takara Biomedical, Japan), 0.25 U Taq DNA polymerase (TaKaRa Ex Taq™, Takara Biomedical, Japan), 20 nmoles of each primer (Gibco-Brl, Scotland), template DNA (~0.1 ng) and sterile ddH_2O. Template DNA was denatured initially for 90 s at 95 °C, followed by 35 cycles of denaturation(45 s at 95 °C), primer annealing (45 s at 56 °C) and strand extension (60 s at 72 °C), ending with a final strand extension step for 7 min at 72 °C. These conditions were used for both primer pairs.



TRANSMISSION

In most of Sub-Saharan Africa, LSD has been seen to occur after seasonal rains, when the number of certain arthropod species increases[21].The study that looked at the risk variables involved with the development of LSD in Ethiopia discoveredthat a warm and humid agro-climate, which supports an abundance of vectorpopulation, was linked to a higher incidence of LSD [22]. LSDV can be mechanicallytransmitted by a number of hematophagous arthropod vectors, according to evidencefrom several sources. The disease is high, with 50- 60% attack rates where

mosquitopopulations are abundant and low, 5-15% morbidity in arid areas where there arefewer potential mechanical vectors [2,23]. Mechanical transmission of some poxvirusspecies by insect vectors such as Stomoxyscal citrans may occur due to high viral load sin skin lesions[24].Invasive blood-feeding arthropods, such as mosquitoes and sand flies, are suspected to be associated with LSD outbreaks characterized bygeneralized lesions [25]. Stomoxys calcitrans and Biomyiafasciata were caught afterbeing fed on sick cows, and the LSD virus was isolated from them [26]. Chihota et al found that Aedes aegypti female mosquitos can mechanically transmit LSDV frominfected cattle to susceptible cattle [27]. Such a vector feeding regularly and changinghosts between feedings is likely to transmit LSDV mechanically [26]. Chihota et alidentifi ed the LSDV genome in mosquitoes (Anopheles stephensis and Culexquinquefasciatus) and biting midges (Culicoidesnubeculosus) feeding on LSD-positive animals but did not observe LSDV transmission by these insects.

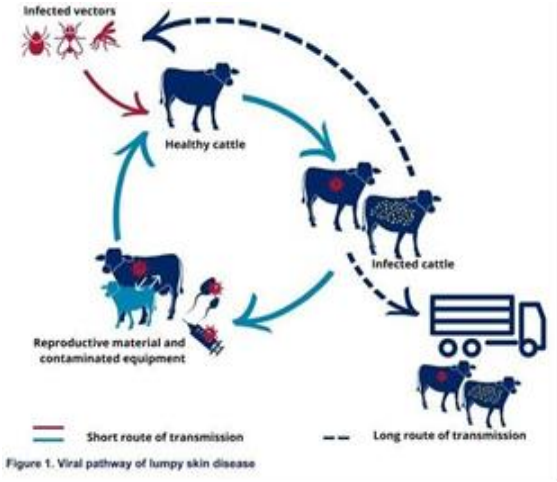
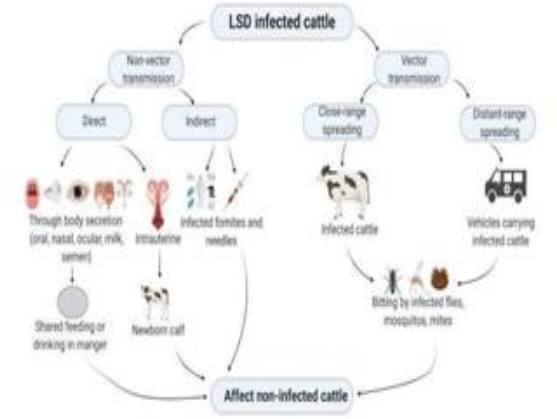


Figure 1. Viral pathway of lumpy skin disease



PREVENTION AND TREATMENT OF LYMPY SKIN DISEASES IN CATTLE

Attenuated virus vaccine may help control spread the spread of lumpy skin disease in recent years beyond its ancestral home of Africa is alarming. Quarantine restriction shave proved to be of limited use. Vaccination with attenuated virus offers the most promising method of control and was effective inhalting the spread of the disease in the Balkans

Administration of antibiotics to control secondary infection and good nursing care are recommended, but the large number of affected animals within aherd may ProzeskyL, BarnardBJ.A study of the treatment Overall, the majority of suspected infected cattle recovered, although it is unclear which, if any, treatmentregimens contributed to recovery. All affected farms were instructed to restrictanimal movement off the farm for 30 days from the time the last case was identified. Ectoparasiticides were applied to healthy ruminants on the infected farms and onsurrounding farms where outbreaks occurred. One of three locally available ectoparasiticides was used to spray animals, including Ektosan (Brovafarma Ltd,Ukraine), Blotic 7% Emulsion (Topkim, Turkey) or Butox (MSD Animal Health,India). Dilutions were made according to manufacturer's recommendations andfarmers were asked to apply the ectoparasiticide twice weekly. After the outbreak, two million doses of live sheep and goat pox vaccine(Poxvac, Vetal Company, Turkey)were purchased.

In 2015, a targeted 5-year vaccination campaign was initiated to control the spreadof this disease in Azerbaijan. A total of 1.6 million cattle in the affected rayons,neighboring rayons, and rayons on the southern Azerbaijan border were vaccinated in 2015 with some vaccine held in reserve in the event of additional

outbreaks.Cattle3 months of age and over were included in the campaign with a focus on animals that migrate to summer pastures. For 2016–2019, approximately 15 million cattle are planned to be vaccinated throughout the country annually with 9 million cattle in high-risk areas being vaccinated twice a year

CONCLUSION

Lumpy skin disease is one of the most economically significant transboundary, viral diseasesof domestic cattle. It is economically significant in animals because of chronic debility,decreased milk production and weight, damaged skins, abortion, and mortality [2]. LSD iscurrently present in the majority of African and Middle Eastern countries. LSD is oftendiagnosed based on specific clinical signs and differential diagnoses. Milder and subclinicalforms, on the other hand, require quick and accurate laboratory testing to prove the diagnosis[31]. The disease's economic impact was mostly due to its high morbidity rate rather than its mortality rate [38]. Based upon the above conclusion, the following recommendations are forwarded:

1. The disease's global expansion requires special attention
2. Action plans for effective control and prevention should be developed to reduce the disease's economic losses.
3. If LSD is introduced into a disease-free country, rapid identification and culling of infected herds, as well as ring vaccination, should be undertaken.
4. Additional research into control strategies is required.

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