



A High Light on Lumpy Skin Disease in Iraq and The Middle East: A Review Article

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ABSTRACT

Lumpy skin disease is an infectious, eruptive disease that affected the different animal species, especially cattle . The causing virus is a member of the poxviridae family with Neethling strain. Transmission of the disease occurs by insect vectors and the most effective mean of control is by vaccination. The disease characterized by viremia, nodules on the skin, sit-fast formation, weight loss, emaciation, and reduction in milk and meat production. During the past five years, lumpy skin disease has spread through the Middle East into the southeast, Europe, Russia, western Asia, and the Caucasus, nowadays LSD causing high morbidity and mortality rate in different epizootic sides; the morbidity and mortality of LSD range between 3-85 and 1-40 % this is due to genetic differences in lives stock resulting in varying susceptibility to the disease.

Keywords: Iraq, Lumpy Skin Disease, LSD, Neethling strain.

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INTRODUCTION

LSD is a skin virus that belongs to the family of poxviridae and genus of Capripoxvirus (Greth, et al.,1992; OIE, 2014), it has nucleotide sequence, and it also encoded by (30) homologs of proteins of poxviral (Tulman, et al., 2001). It closely concerns antigenically to sheeppox and goat pox virus, but not complete its life cycle of replication in the non-ruminant host (Shen, et al., 2011), it is a vector –born disease which Transmitted by arthropods, blood-feeding insect including (stable flies and mosquitoes)(Carn and Kitching, 1995), the disease severity depended on the breed of cattle as well as capripoxvirus strain involved, dry season affects the spread of the virus and may cause an increase in the prevalence of disease (Gari et al., 2011).The skin lesion is experimentally produced in different types of animals like goats, sheep, impalas (Davies, 1991).In water buffaloes, there was a natural cause for this virus.

Lumpy skin disease leads to reduced milk production and sometimes death due to secondary bacterial infections, it also causes considerable economic losses owing to damage to hides, loss of milk

production, mastitis, emaciation, mortality of up to 20% and disruption in the trade of cattle and their products. Infected cows may be suffering from temporary or permanent infertility (Irons et al., 2005; Tuppurainen and Oura, 2011). LSD was limited to countries in sub-Saharan Africa; from 1984 to 1988, the disease has distributed to the surrounding states, during 1988 in Egypt there was an outbreak, but the percent of morbidity was low than that for cattle (El-Nahas, et al., 2011; World Organisation for Animal Health,2017).

Cows are more severely affected with LSD virus (Sameea, et al., 2017)also, Jersey and Holstein Friesian are considered the high contagiousness and the virus causes significant economic losses of trading (Barnard et al., 1994 ; Tuppurainen, et al ., 2011), the disease has first detected during 1929 in Rhodesia then spread to a different area of the middle east (Tuppurainen and Oura,2012); during 2015 there was spread of the disease to Caucasus, Balkans and also to southeast Europe (Jameel, 2016). Iraq in 2014 has joined the ranks of LSD-affected countries (Al-Salihi, 2014; OIE, 2015).

History of LSD.

LSD, as an epidemic disease, was recorded in Zambia in 1929. It was considered as a score of insect bites hypersensitivity or even poisoning (Brenner,2006). Other cases have occurred between 1943 and 1945 in Zimbabwe, Botswana, and South Africa. LSD was first identified in east Africa during 1957 and in Sudan in 1972 and west of Africa during 1974 and then spreading to Somalia during 1983; where about 8 Million of cattle is becoming ill and affected in 1989, the disease is still spread to different parts of the world until 1983 (Davies, 1991).

Nowadays the disease occurs in the most countries of Africa (Tuppurainen and Oura, 2012) between 1984 and 2009, the highest number of outbreaks of LSD were reported in middle east area (Oman) (House et al., 1990; Kumar, 2011; Tageldin et al., 2014), where the morbidity was about (4.97%) and (13.6%) (Ayelet et al., 2014). Also during this year the disease is reported In Iraq in August 2013 in Nineveh (Mosul), and Baghdad government then spread through all over the country (Table1) (Al-salihi and Hassan,2015); also in Iran and Turkey during October 2013 (Sherrilyn et al., 2013; Calistri et al.,2019).

Etiology of LSD

The causative agent of LSD is a member of the Poxviridae family, genus Capripoxvirus; it concerns antigenically to goat pox virus (GTPV) and sheep pox virus (SPPV) (Greth ,1992; Buller et al.,2005). The Capripoxvirus have oval profile shape that is a larger size than Orthopoxvirus so that this virus can grow on the different type of tissue, like chicken embryo fibroblasts, thyroid gland, rabbit kidney, skin and equine lungs, through primary isolation of virus the cytopathic effect may take up to eleven days accompanied to various kinds of serotype, except one types that are closely related serologically to poxvirus of goats and sheep and not easy to distinguish by routine technique (Tulman, et al., 2002; Katsoulos et al., 2018). The virus has many properties that make it resistant to physical and chemical factors, and it can stay inside the necrotic skin for more than one month (Bhanuprakash et al., 2006).

Animal susceptibility

The cattle and buffalo are the most species that become infected with LSD (Ali et al., 1990). A celibate clinical condition of Capri pox infection perhaps was described in Arabian Oryx(Greth , et al., 1992; Boshra et al.,2015). The clinical sign of the disease is starting within one week after entering the virus to the animal body (Ben-Gera et al.,2015). Many studies show that LSD is more severe in Friesian and crossbreed than native cow and more

intense in young animals than the adult. It results in edema in the brisket and skin cellulite and grows of nodules, which facilitate the infestation of screwworm (Jameel,2016; Kate et al.,2003).

Epidemiology and Transmission of LSD

LSD virus does not spread easily among animals held in insect-proof pens, while contagion by contact can occur. The virus is still for an extended period as a skin lesion or inside the scabs so that it has a strong tropism for skin and dermis, and nodules appear on a different part of the animal body (nose, eye, rectum, genitalia) (Babiuk et al., 2008b). The virus is also excreted via lachrymal and nasal secretions, blood, saliva, milk, and semen of the infected animals may be sources of infection to other susceptible animals. Nodules that appear on the mucous membranes of the eyes, mouth, nose, udder, rectum, and genitalia also ulcerate and shed viruses, which serve as sources of infections (Babiuk et al. 2008b).

In cattle, direct contact and ingestion of food are not considered as a common route of transmission even when viruses existing in lacrimal, nasal discharge and semen of infected animals. Although the transmission of the virus through semen has not been expounded experimentally, the virus can be transmitted through the semen of infected bulls and also by the milk of the lactating cow (Irons, et al., 2005; Osuagwuh et al., 2007) with a peak of lactation as well as in young animal that shows the more rate of clinical signs (Coetzer and Tuppurainen, 2004). Mechanical transmission of LSD mainly related to flying insects, the scourge of LSD occurs during the peak period of the effectiveness of the mosquitoes so that the warm and humid weather play essential roles in increasing morbidities (Ali et al., 2012; AU-IBAR, 2013).

The recent study shows that the virus of LSD has the ability to persist as transracial and transovarial in *Rhipicephalus appendiculatus* and *Rhipicephalus decoloratus* and as a mechanical transmission in *Amblyomma hebraeum*(Lubinga et al., 2013; Lubinga et al., 2014). The virus also has the ability to recover from *Musca Glossina*, *Biomyia* and other species that a potentially transmitted virus of LSD, the virus is detected in *stomoxy calcitrans* and *Anopheles stephensi*(Chihota et al., 2003), in Turkey, there was an outbreak due to the role of *Culicoides* species (biting midges) in the transmission of virus of LSD (Sevik and Dogan, 2017).

The clinical sign of LSD

LSD is considered as an acute infectious disease, The incubation period ranged 7-14 days that

starting by fever then nodules (2–5 cm in diameter), enlargement of superficial lymph nodes (Elhaige *et al.*, 2017), the lesion may resolve rapidly, or they stay indurate and persisting as a hard lump (Wainwright *et al.*,2013), location of this nodule is usually on the udder, muzzle, as well as in hairless area and perineum (Babiuk *et al.*, 2008a). The lesion in the respiratory system leading to pneumonia, the presence of the typical skin nodules is strongly suggestive of LSD (Babiuk, *et al.*, 2008b); it may appear in lung, larynx, trachea and also throughout the digestive tract, in the reproductive system the lesions may cause temporary or permanent sterility in cow and bulls (Constable *et al.*, 2017).

Infected cattle also may develop edematous swelling in their limbs and exhibit lameness(Abdulqa *et al.*,2016; Sprygin *et al.*, 2018). Skin lesion, keratitis it may be bilateral or unilateral are also seen in the infected cow (Salib and Osman, 2011; Al-Salihi, 2014), the cutaneous lesion have the ability to persist as hard lumps, or it sequestered so that it will be lead to a deep ulcer that filled with granulation tissue (Wainwright *et al.*, 2013). liver and kidney failures occur during LSDV infection, very young calves, lactating cows, and malnourished animals seem to develop more severe clinical signs that may be due to an impaired humoral immunity (Sevik *et al.*, 2016). Other clinical signs include general malaise, fever, ocular and nasal discharge,inflammatory nodules (Constable *et al.*, 2017), and a sudden decrease in milk production.

Morbidity and mortality in the recent Eurasian epidemic have been approximately 10% and 1%, respectively(Body *et al.*,2011). The severity of disease in the 10% of affected cattle in the herd can vary from mild to fatal, and some animals develop minimal numbers of nodules, which can be difficult to spot. In contrast, others develop innumerable nodules up to 3cm in diameter. The factors determining which cattle develop mild and which developed a severe disease are unknown(El-Neweshy *et al.*,2013; Limon *et al.* ,2020).

Economic losses caused by LSD

LSD is categorized as a notifiable disease(OIE). Capri pox virus considers as worldwide impendence affected animals in Asia and Africa (king, *et al.*, 2012; Babiuk *et al.*, 2008a). LSD is regarded as a severe disease that is affecting on the product and leading to economic losses (Gezahegn *et al.*, 2013), the disease has subsequent effects on cattle production including a decrease in feed intake, weight losses, abortion, infertility and decreases milk production (Hailu, 2015; Pritchett *et al.*, 2006), and effect on

international trade (Babiuk *et al.*, 2008a; Abutarbush *et al.*, 2013; EFSA, 2015).

The monetary implication of these casualties is significant to the flock owners, consumers and manufacturing sector which can process cattle products, losses of animals product is predestined when LSD is high between 40-60% (Tuppurainen and Oura,2012; Gumbe, (2018).The disease disrupts the trade of cattle in endemic countries (Babiuk *et al.*, 2008a), during 2009 in Oman there were a high morbidity and mortality rates that occur in a farm population in Holstein cattle (Sherrylin *et al.*, 2013). The disease can be transmitted from Africa to outside (Gari *et al.*, 2011; Alemayehu *et al.*,2013).

Pathogenesis and clinical observation of LSD

Investigations on the pathogenesis of this disease are few (kenawy and Holoth, 2010). In general pathogenic mechanism includes implantation of the virus at the portal of entry, replication in the cells, spread to target organs, and diffuse into the surrounding environment. (Baron, *et al.*,1996; MaGavin and Zachry,2017). There have been few studies confirmed on the pathogenesis of LSD; in general, there is fever and viremia, followed by localization in the skin and development of nodules. Following Subcutaneous inoculation with LSDV, swelling at the site of inoculation developed 4 to 7day, which is varying in size from 1 to 3 cm (Constable *et al.*, 2017). The regional lymph nodes are enlarged, then an eruption of these nodules usually follows 7 to 19 days.

LSDV is also demonstrated in saliva, semen, and skin nodules for several days after infection and development of fever. Viral replication occurs in fibroblasts, microphages, endothelial cells, and other cells in blood and lymph vessel walls cause vasculitis and lymphangitis in the affected areas. At the same time, infarction and thrombosis may result in severe cases(Al-salihi *et al.* ,2015).there is vasculitis and lymphangitis also can be observed in diseased animals (Lindsay and Thomes, 2013), respiratory system involvement and manifestation are mainly due to stenosis of the trachea, with the formation of nodules that persist for a few weeks even to one month (Cfsph,2008).

Gross and histopathological finding

Grossly there is a nodule with different size, that become firm and raised but in some cases, they persist to fused into irregular plaques; photomicrograph(1) Mulatu and Feyisa,2018, also there are necrotic lesions in different parts of the animal body (Tuppurainen *et al.*, 2017), the regional lymph nodes are also enlarged they become congested and give a pyaemic focus in addition to cellulitis

(Salib and Osman, 2011). The infected animal may show other clinical signs like tracheal stenosis, mastitis, as well as chronic orchitis (El-Neweshy et al., 2013).

Histopathological changes of nodular skin lesions include hyperemia, edema severe hydropic degeneration, acanthosis and hyperkeratosis in the epidermis, granuloma, infiltration of the mononuclear cell, inclusion bodies and vacuolation. Hyperplasia also can be noticed, with the characteristic intracytoplasmic inclusion bodies could be seen in photomicrograph(2) (Ahmed and Dessouki,2013; Hasanain et al.,2019and Vaskovic et al.,2019), with eosinophilic cell and macrophage, lymphocytes, vasculitis due to tropism of the virus (Body et al., 2011). Coagulative necrosis and muscular damage can be seen during LSD infection (Sevik et al., 2016).

Diagnosis

Diagnosis of LSD is depended on morbidity, mortality rates also on histopathological features, laboratory investigations including biopsy material or crust through routine diagnostic techniques by using the electron microscope (Gari et al., 2008; El-kenway and Holoth, 2011), the detection of virus by using an electron microscope (OIE,2010); enzyme-linked immune sorbent assay (Carn et al., 1994); polymerase chain reaction (Balinsky et al., 2008; Bowden et al., 2009; OIE, 2011), or virus neutralization test and ELISA methods (Heine et al., 1999). At present, there are no test kits for LSD (Tuppurainen and Ourea,2012). The virus is not distinguished morphologically from cowpox (OIE,2010), the virus has the ability to propagate in caprine, ovine and bovine cell culture, especially lamb testis cell (Yacob et al., 2008).

Differential diagnosis

LSD can be confused with a group of diseases, including Bovine papular stomatitis (Parapoxvirus), Pseudo lumpy skin disease (caused by Bovine Herpesvirus 2), cutaneous tuberculosis, Pseudocowpox (Parapoxvirus), urticarial, Demodicosis (Demodex), insect or tick bites, Cowpox, Rinderpest, photosensitization, Dermatophilosis, Hypoderma bovis infection Besnoitiosis, Papillomatosis (Fibropapillomas, "warts") and Oncocercosis (Tuppurainen et al.,2005; Abutarbush, 2017).

Treatment, control, and prevention

There are no specific drugs used for the treatment of LDS. The only treatment available is supportive care of animals, including the use of

antibiotics to prevent secondary bacterial skin infections and pneumonia, Intravenous fluid administration to avoid dehydration and treatment of skin lesions using wound care sprays. Also use Anti-inflammatory drugs to keep up the appetite of animals. (Allen, et al.,2010; Neamat-Allah,2015 ; Babiuk ,2018b).

Control of LSD

One of the difficult but essential steps for LSD control is the vector control (Ticks & Biting flies), where using repellents with insecticides can aid in the prevention of the disease. Also, the most effective means of control by using live homologous vaccines containing a Neethling-like strain of LSDV are recommended (Kate, et al., 2003; Ayelet et al., 2014; Gumbe, 2018), as well as the immune prophylaxis using immune stimulants (Brenner et al., 2006). Restricted animal movement and quarantine make a big difference in the disease prevalence. The calves of unvaccinated cow should be vaccinated before their age reach to 6 months (Lindsay and Thomas, 2013) the disposal of carcasses, insect control disinfection of premises and clearing slaughter out of affected animal of this can help in control measure (Irons, 2005; Gonstable et al., 2017).

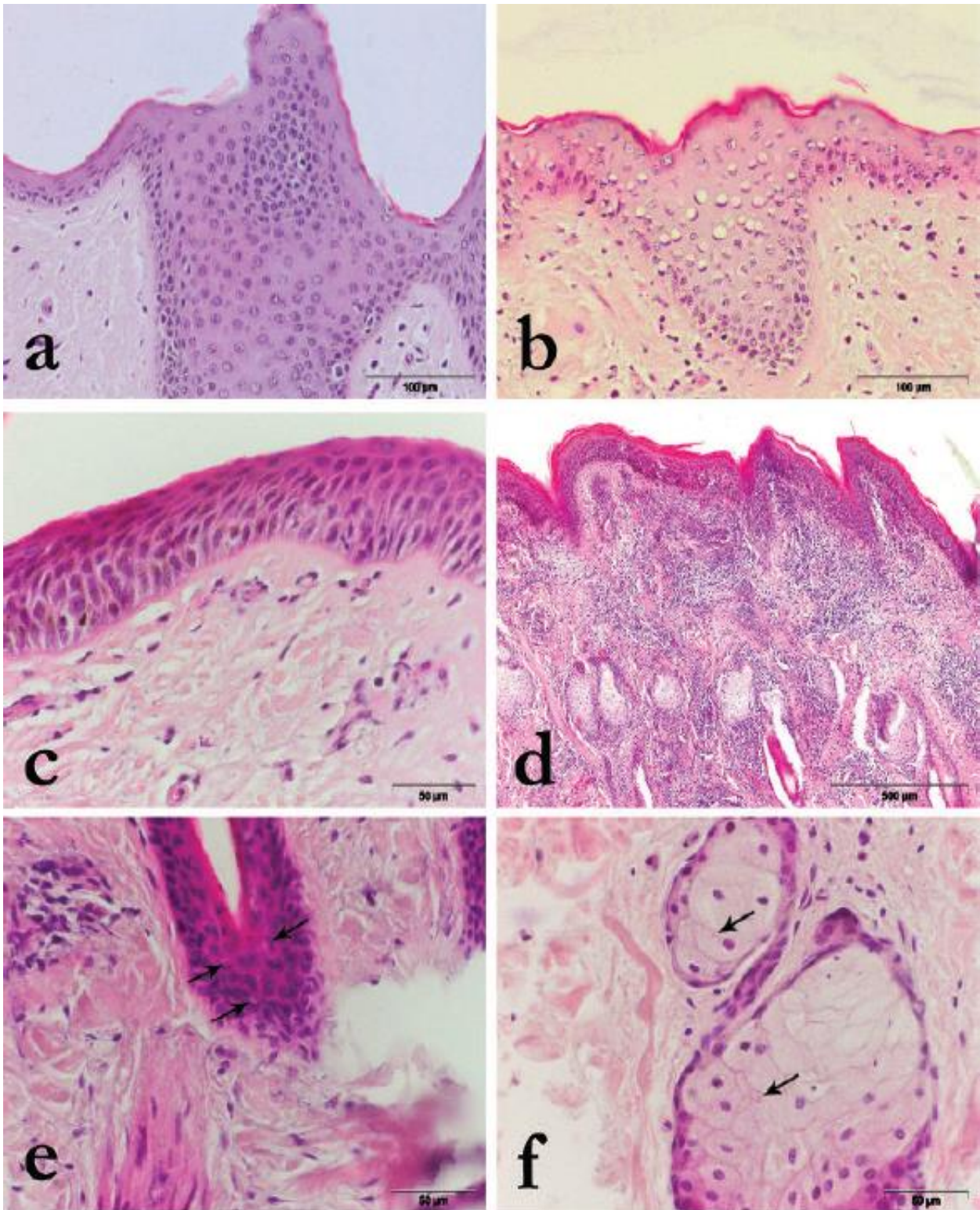


Photomicrograph 1: Shows Raised and separated narrow ring of hemorrhage (A) , ulcerated nodules(B) and sit fast like inverted conical necrosis zone (C) (Mulatu and Feyisa,2018).

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Tables1: The number of the outbreak of affected animals with lumpy skin disease in Iraq(Al-Salihi and Hassan,2015).

No. of Outbreak	Date of outbreak and name of governorate	Species of animals	No. of animal in the herd	No. of affected animals	Summary of status of infected animals
1	End of August 2013(Nineveh)	Cattle	20	1 calf	Skin nodules, sever deterioration
2	End of August 2013 (Nineveh)	Cattle	20	4 calf	Skin nodules, weakness, nasal discharge, reduce milk Production
3	End of August Baghdad	Cattle	70	15 cow	Skin nodules, reduce milk Production, mastitis
4	End of August Baghdad	Cattle	200	1 calf	weakness, Skin nodules nasal discharge
5	Early of Sept. 2013 Baghdad	Cattle	16	1 calf	Skin lesion with severe deterioration
6	Early of Sept. 2013 Nineveh	Cattle	3	1 cow	Skin nodules, mastitis, mouth lesion with severe respiratory sign
7	End of Sept. 2013 Baghdad	Cattle	8	1 cow	Skin nodules, reduce milk production, mastitis, mouth lesion with severe respiratory sign
8	Early of October 2013 Nineveh	Cattle	12	4 cow	Skin lesion, mouth lesion, reduces milk production, severe respiratory mouth sign
9	Mid of October 2013 Baghdad	Cattle	9	4 cow	Skin lesion and nodules, reduce milk production, severe mouth and respiratory lesion



Photomicrograph 2: Skin lesion of cattle affected with LSDV show (a) acanthosis in the epidermis, (b) presence of vacuoles in the epidermis, (c) degenerative changes and spongiosis in the epidermis, (d) infiltration of inflammatory cell and hyperkeratosis in the epidermis, (e) intracytoplasmic inclusion bodies (arrow), (f) degenerative changes and intracytoplasmic inclusion bodies in the sebaceous gland cell (arrow) H & E (Vaskovic *et al* .,2019).

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