

## Review On: Sheep and Goat Pox Disease; Current Updates on Epidemiological, Diagnosis, Prevention, and Control Measures in Ethiopia

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### ABSTRACT

The livestock sector plays a vital role in economy of many developing countries like Ethiopia. The country has the largest livestock population in Africa. Among this sector, Small ruminants are important components of the livestock subsector and are sources of cash income, meat, milk and wool for smallholder keepers and foreign currency. Due to different constraints, however, small ruminant production in Ethiopia did not deliver the expected benefit to the national economy. Infectious diseases such as Sheep pox (SPP) and Goatpox (GTP) are some of the main challenges faced by this sector. SPP and GTP are highly infectious disease of sheep and goats caused by a virus belonging to the Capripoxvirus genus of the family Poxviridae. SPP and GTP are currently endemic in African, Middle Eastern and Asian countries. These diseases pose challenges to food production, distribution, and kill and impair animals, affect rural livelihood in most African countries including Ethiopia. Transmission of SPPV and GTPV occurs by direct and indirect contact to aerosols, respiratory droplets or contact with secretions of acutely infected animals. SPP and GTP virus cause systemic disease in sheep and goats that is often associated with high morbidity and high mortality. Diagnosis is mainly based on clinical signs, electron microscopy, and isolation of the virus, identification of the agent using real-time PCR methods, serological tests and Histopathological lesions. Even though there is reports of insufficient protection of the Kenyan sheep and goat pox virus (KSGPV) vaccine strains against LSDV, live attenuated vaccine derived from KSGP strains available in Ethiopia is safe and effective for the control of SPPV and GTPV throughout the country if and only if all vaccines are stored and handled correctly and consistent vaccination strategies has been implemented.

**Keywords:** GTPV; outbreak; sheep and goat pox disease; SPPV; vaccine

### INTRODUCTION

In Ethiopia, livestock sector has enormous potential to achieve several of its national and international commitments on poverty alleviation, food security, and improved nutrition. The sector accounts for about 45% to the total value of agricultural production and supporting the livelihoods of a large share of the population [1]. The country has the largest livestock population in Africa and estimated 31.3 million sheep, 32.74 million goat and 60.39 million cattle. Thus, small ruminant (Sheep and goats) production has been supporting the national economy of the country by generating hard currency from meat exports [2].

Despite the huge cattle population, the current productivity and commercialization of sheep and Goat remains very low. Hence,

infectious diseases are the major constraint that hinders the development of the sector by decreasing production and hamper trade in animal and animal products. In addition, Sheep pox (SPP) and Goatpox (GTP) are posing a significant economic threat globally in general and particularly in developing countries like Ethiopia [3] [4].

SPP and GTP are caused by the members of the Capripoxvirus (CaPVs) genus, in the family Poxviridae. These viruses are intimately linked to the lumpy skin disease virus (LSDV). Sheep pox virus (SPPV) and Goatpox (GTPV) causes disease in sheep and goat respectively and LSDV causes disease in cattle [5][6]. SPPV and GTPV are prevalent and found across north and central Africa, parts of Asia, the Middle East and the Indian subcontinent [6][7].

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Sheep and goat pox are highly contagious and economically devastating viral diseases of small ruminants (sheep and goats) in many parts of the world and characterized by generalized pox lesions throughout the skin and mucous membranes, persistent fever, lymphadenitis, pyrexia, generalized nodules on non-wool skin, generalized pocks and often a focal viral pneumonia [8] [9]. Therefore, the current review aims to discuss effective control of SPPV and GTPV and to highlight the current status of SPP and GTP, its epidemiology, diagnosis, and treatment.

## LITERATURE REVIEW

### Epidemiology

#### Characteristics of the Causative Agent

SPP and GTP are probably the most significant pox diseases of small ruminants which are caused by SPPV and GTPV respectively. These viruses are members of the Poxviridae family, the sub-family Chordopoxvirinae and genus Capripoxvirus [6]. SPPV is mainly thought to affect sheep and GTPV primarily to affect goats, but some isolates can cause mild to serious disease in both species [10]. CaPVs are very resistant in the environment and can remain viable for long periods on or off the animal host. They are susceptible to sunlight, but survive well at cold temperatures [11].

#### Poxvirus Genome

The genome size of the different poxvirus species is very variable [12]. The genome of CaPVs are large (170–260 nm by 300–450 nm), brick-shaped. GTPV and SPPV genome are complex viruses approximately 150 kbp, double-stranded DNA and enveloped viruses. GTPV and SPPV share at least 147 putative genes, including conserved genes involved in virulence and host ranges [13]. A false lipid envelope surrounds the genome of CaPVs and susceptible to many disinfectants, lipid solvents, and acids [13], [14].

The genomes of CaPVs have similarity in their nucleotide identity (LSDV is >98% identical to GTPV and SPPV) [13]. While SPPV is >97% identical to GTPV [15]. Thus, conventional serological test cannot distinguish SPPV, GTPV and LSDV [16]. However, genetic sequencing of the host-specific G-protein-coupled chemokine receptor (GPCR), or RNA polymerase subunit (RPO30) genes, species-specific molecular assays have been developed for differentiation of CaPVs [14] [17] [18].

#### Viral Replication

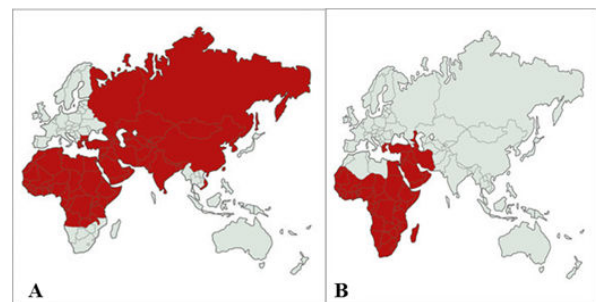
The replication of SPPV and GTPV occurs in the cytoplasm of the host cell in intra-cytoplasmic eosinophilic inclusion bodies [19]. This can be detected by using microscopic examination of a haematoxylin and eosin-stained sheep and goat poxvirus-infected monolayer of cells [20].

#### Geographic Distribution

SPPV and GTPV have worldwide distribution and are wider than LSD (Figure 1A). The distribution of SPP and GTP are relatively stable, and currently the disease occurs in north and central Africa, the Middle East, Eastern Europe and Asia, including the Indian subcontinent and China [7]. In contrast,

LSDV occurs largely in central and southern Africa and is absent in Asia (Figure 1B) [21]. Frequent outbreaks in Greece and occasional outbreaks in Bulgaria are thought to be caused by viruses that enter these countries during outbreaks in Turkey [10].

Sporadic outbreaks of SPP and GTP were reported in southern Europe and other parts in the world [8]. The most recent outbreaks of SPP and GTP were recorded in Bulgaria and Greece in 2013, Israel in 2014, and Russia and Mongolia in 2015 [7]. In Ethiopia, the diseases have wide spread distribution in all regional states of the country. Thus SPP and GTP are affecting the production and productivity of sheep and goat in the country [4].



**Figure 1:** (A) Geographical distribution of SPPV and GTPV in Africa, Middle East countries and Europe; (B) Geographical distribution of Lumpy skin disease virus; Source [22].

#### Susceptible Hosts

SPP and GTP are viral diseases of sheep and goats. These diseases are caused by strains of Capripoxvirus, all of which can infect sheep and goats. Most of the strains examined cause severe clinical disease in either sheep or goats, but some strains have equal pathogenic effects in both species [23]. In contrast, LSDV affects cattle and domestic Asian water buffaloes [24], but it does not naturally infect sheep and goats [11] [25].

Although, some strains of LSDV replicate in sheep and goats, there is no epidemiological evidence that revealed the role of small ruminants acts as reservoir for LSDV [24]. In the past, CaPVs were considered to be host-specific, but GTPV has been entirely responsible for all outbreaks of sheep and goats in Ethiopia [26].

#### Host-specificity

Majority of CaPVs are highly host specific, with only some exceptions. Very few data are available on the susceptibility of wild ruminants to LSD [27]. SPPV isolates cause disease primarily in sheep and GTPV isolates cause disease primarily in goats. However, single strain of the virus can cause disease in both sheep and goats. Some sheep strains cause mild disease in goats and severe disease in sheep, whereas sheep can be infected with virulent goat strains [6] [28]. SPPV and GTPV are able to make cross-infection either naturally or experimentally and cause disease in sheep and goats [29]. However, no evidence has been reported that LSDV can cause disease in sheep and goats [30].

#### Transmission

SPP and GTP are highly contagious viral disease of small ruminants. Thus, the main mode of SPP and GTP transmission is considered by direct contact with respiratory droplets [31]. However, these viruses are viable for prolonged periods in the environment, making transmission possible on fomites such as human movement. Thus, movement of infected animals acts as the main cause of transmission of the viruses [8] [32] [33] whereas the main mode of transmission of LSDV is by blood-feeding arthropods [34] [35].

Experimentally, sheep and goats were infected with intra-dermal inoculation and intranasal administration of SPPV and GTPV [16], [36]. Additionally, Stable flies (*Stomoxys calcitrans*) were demonstrated to transmit SPPV and GTPV mechanically [10] [15].

Viral shedding occurs in oral, nasal, and conjunctival secretions starting from the appearance of papules, with the quantity and duration of shedding dependent on the virus isolate and host species. Viral DNA and infectious virion can be detected in some secretions for up to a month following resolution of acute disease [36]. Hence, viruses can be isolated from infected animal secretions, feces, skin lesions and their scabs [37]. SPPV and GTPV remain viable for up to 6 months in the environment (in shaded, un cleaned sheep pens), making transmission possible on fomites [10].

#### Morbidity and Mortality Rates

SPP and GTP have major economic impacts on small ruminant production due to high morbidity and mortality in susceptible animals [15] [38]. Thus, in endemic areas morbidity between 75-100%, similarly, case fatality is between 10-85% in outbreak areas and mortality is up to 100% in stressed and naïve animals have been reported [39] [40].

Different strains of the virus have different degrees of virulence in different species. Moreover, severity of the clinical diseases are depends on the species, stress, concurrent infection, breed, age, immune status and stage of production of the host [41].

Indigenous breeds are more resistant to CaPVs than European breeds. Kids and lambs are generally more susceptible than adults due to the extensive interstitial viral pneumonia with obstruction of the airways and most likely high body temperature [16]. However, animals of all ages were affected in the outbreak [41].

#### Public Health Significance

Currently there is no conclusive evidence that SPPV and GTPV can infect humans [10] [23]. Furthermore, LSDV has not been reported to humans [42] [43]. However, from the CaPVs genus, LSDV can infect humans without the need for insect vector [44]. Though more studies are required to confirm this contradicting report.

### Economic Impacts of SPP and GTP in Endemic Areas

Livestock production has an important contribution for food supply of rural and urban areas and contributes to the family nutrition, supplying animal protein. Among the livestock sector,

small ruminant productions are a major part and play a crucial role by contributing to the world's economy [8].

However, different infectious diseases affect the productivity; among which SPP and GTP are more important as the disease limit international trade and beside other economic losses [45]. Hence, the World Organization for Animal Health (OIE) categorizes CaPVs as a modifiable disease due to their rapid trans boundary spread and substantial economic impacts on the livestock industry [36]. Similarly, SPP and GTP are economically devastating viral disease of sheep and goat respectively. Globally, the disease causes a serious risk for small ruminant production and food security and jeopardizes international trade [46], [47].

Furthermore, the damage and loss caused by CaPVs on small ruminants and cattle causes substantial economic loss due to the disruption to trade in livestock and livestock products, and the costs associated with disease control and eradication [48]. The Economic losses of SPP and GTP have been reflected by reduced milk and mutton, decreased weight gain, increased abortion rates, significant damage to wool and hides and increased susceptibility to pneumonia and fly strike direct cause of morbidity and mortality in susceptible sheep and goats [6], [15].

In India, an average morbidity and mortality rates of 63.5 and 49.5% have been reported respectively from small ruminant production [9]. Moreover, significant production losses because of reduced milk yield (up to 30 %), high mortality in lambs (95 %), and decreased average conception rate (32 %) have been reported following outbreak in Israel [41].

#### Current scenario in Ethiopia

In Ethiopia, sheep and Goats contribute substantially to the livelihoods of smallholder households as a source of income, food, and high potential for foreign exchange earnings. They also serve as a means of risk mitigation during crop failures, savings and investments in addition to other socioeconomic and cultural functions. For instance, in 2010/11, the export value from sheep and goats meat and live animal were about 63 million and 148 million USD, respectively [49].

Likewise, the current utilization of hides and skins is estimated to be 75% for goat's kin and 97% for sheep skin with the expected annual off-take rate of sheep and goats is 33% and 35%, respectively. The country supplies a wide range of both processed and semi-processed sheep and goat skins to the world market and account for about 12-16% of the total value exports [50][51].

However, a number of factors such as SPP and GTP hindered the development of the sector in the country [52]. Similarly thorough information is currently unavailable or inadequate at best on the prevalence and trends of SPP and GTP in Ethiopia. But, 893 pox outbreaks were reported in 2007/08. From these outbreaks, a total of 57,638 sheep and goat became sick. Out of the 57,638 sick animals, 6,401(11.1%) animals were died as a result of the disease [53].

Moreover, from 2010 to 2014, a total of 366 outbreaks were reported. From these outbreaks 12,822 sick and 1480 deaths were reported due to sheep pox and 182 outbreaks, 10,066 cases



and 997 deaths were reported due to goat pox in Amhara National Regional State [54]. Furthermore, the Annual economic losses due to mortality ranges from 12 to 14% for sheep and 11 to 13% for goats have been reported [55].

Hence, these diseases are the major constraints to trade and prevent the importation of improved breeds of small ruminants into endemic regions and are responsible for significant economic impact in animal industry in Ethiopia. Furthermore, SPP and GTP comparably more serious in lowland arid areas than in midland and highland agro ecologies of the country [54].

## DIAGNOSIS OF SHEEP AND GOAT POX DISEASE

### Clinical diagnosis

Diagnosis of SPP and GTP can be done clinically on the basis of signs and lesions, host species affected and post-mortem lesions [8]. In the field however, a wide range of clinical and pathological manifestations are recognized due to differences in the host response and virulence strains[56]. The incubation period varies from 4 to 21 days [57]. But it is usually 21 days [43]. In general, CaPVs have similar clinical manifestations [8] [58].

At the start, the lesions appear as papules, further progress to nodules, vesicles, pustules (raised lesions), and finally scab formations have detected on the skin [15]. Most affected animals become weak and loss of appetite, high fever (40-42°C), labored breathing due to blisters inside the respiratory tract and lungs [36].

The lesions may cover the entire body but easily detected on the hairless parts of the skin and mammary glands. Lesions in the mouth, nose and eyelids can cause nasal discharge and excessive salivation (figure 2). Affected mucous membranes may become necrotic and ulcerate. Nodules in the intestines can cause diarrhea. Depression and emaciation may be seen in some animals[8],[42].



**Figure2:** Thick discharges from the nose, and nostrils and eyes; Source: [59].

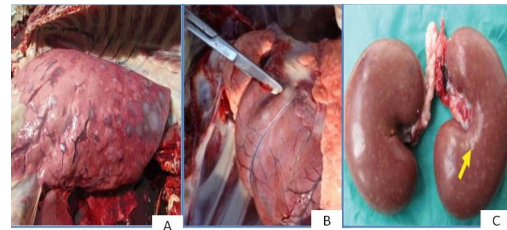
### Differential diagnosis

Mild forms of SPP and GTP may be confused with contagious ecthyma (orf), dermatophilosis, sheep scab, mange, photosensitization/urticaria, peste des petits ruminants, parasitic pneumonia, mange, and insect bites. Whereas in severe case, clinical signs are highly characteristic [10].

### Pathology and post-mortem diagnosis

#### Gross lesions

At postmortem examination, Pox lesions have been distributed throughout lung, kidney, heart (figure 3) and digestive and respiratory tracts.



**Figure3:** Pox lesions in, (A); Lung, (B); kidney and (C) heart muscles; Source (Courtesy: photograph Colin Scrivener).

Popular lesions have also been appreciated over the animal body especially hairless areas such as the tail (figure 4A), face and ear (figure 4B). Moreover, the development of lesions were detected in infected animals all over the body starting from the tip of the tail including the two face, lips, nose muzzle, eyelids, ear, flank, abdomen, vagina, udder and all limbs [57].



**Figure4:** Papular lesions under the tail (A); source [60] and Pox lesions on the face and ears (B); source[61].

#### Histopathological lesions

In histopathological study, the affected parts of the skin layers (epidermal and dermal changes) are characterized by hyperkeratosis, acanthosis, hyper-keratinization, degenerative changes, micro abscesses, oedema and proliferative changes in sebaceous glands and hair follicles [62]. Besides, the pulmonary lesion and proliferative alveolitis with occasional cytoplasmic inclusions in alveolar cell and macrophage was reported [62] [63].

Laboratory diagnosis is necessary for confirmation of the disease and the following methods are used. Laboratory procedure for the diagnosis of CaPVs includes Serological test such as serum neutralization tests, indirect fluorescent antibody test. (IFAT), Enzyme-linked immuno-sorbent assay (ELISA), and Agar Gel Immunodiffusion Assay (AGID) [64]. Serum/virus neutralization tests are the gold standard test for serology [65]. However, these are very specific but not sufficiently sensitive for detection of low antibody titers [66] [67].

Virus isolation is needed to confirm the infectivity of the virus. Thus SPPV from GTPV can be isolated in lamb testis, sheep or goat kidney cell cultures and sheep, goat, or bovine cell lines [68]. Antigen detection, Polymerase Chain Reaction (PCR), easy and convenient method to detect CaPVs genomes in tissue samples [69] But cannot differentiate SPPV from GTPV[8].

However, digestion of p32 gene with Hinf I and sequence alignment of GpCR gene were developed to differentiate GTPV

and SPPV [56] [70]. Moreover, specific and sensitive duplex PCR method has been developed for differential diagnosis of GTPV and SPPV especially in countries that lack the resources needed for molecular diagnostic techniques in endemic areas [71]. Electron microscopy can differentiate characteristic morphology of the Capripoxvirus [72]. CaPVs are readily distinguishable in the laboratory from other poxviruses that cause similar clinical signs in ruminants. However, strains of SPPV, GTPV and LSDV cannot be differentiated serologically due to antigenic and biochemical similarities of causative agents [20] [40].

SPP and GTPs were earlier thought to be caused by a single species of virus. The genetic sequence analysis revealed that these viruses are distinct and related to LSD, but the recent finding states that GTPV and LSDV are more closely related than SPPV is to LSDV [14].

## TREATMENT, CONTROL AND PREVENTION

Treatment is directed at preventing or controlling secondary bacterial infection. Administration of antibiotics to control secondary infection and good nursing care are recommended. Tetracycline ointment and powder may be applied topically on scab or ulcerated lesions [73]. Beside, better understanding of disease prevalence and its distribution would lead to improve its control measures [54].

If SPP and GTP viruses occur in a previously free country, eradication is usually by slaughter of all infected and in-contact animals [74]. Because the use of live virus vaccines in non-endemic countries may not be desirable [36], but effective live attenuated SPPV and GTPV derived vaccine strains are widely used in many endemic countries to control the disease since a replicating agent generates more broad protective immunity than a non-replicating one [75] [76]. Furthermore, the use of live attenuated vaccines are safe and effective for control of disease in sheep and goats [7]. While killed vaccines do not provide long lasting immunity [40].

In CaPV infection, both antibody and cellular immunity provides lifelong immunity [15]. However, cell-mediated immunity elicits long-term protection [77]. The close antigenic relation (share 98% sequence similarity) between SPP, GTP, and LSD tend to use a single vaccine to protect against all members [78]. In Ethiopia, annual mass vaccination with the Kenyan sheep and goat pox virus (KSGPV) O-240 and O-180 strains (KSGP) is the best feasible, economic and viable method for the control of sheep and goat pox [54]. However, the absence of adequate infrastructure could hinder the implementation of sufficient herd immunity [79].

In Ethiopia, the National Veterinary Institute (NVI) has been producing more than 20 different types of vaccines for domestic use and for export to African and Middle East countries. Hence, live attenuated (KSGPV) O-180 vaccine strains has been manufactured using primary cells, locally by NVI, and is a freeze-dried vaccine with stabilizer and can be stored at -20 degrees for 2 years and these vaccines can give immunity up to 2 years. In Ethiopia, the current KSGP vaccine strain is safe and effective

for the control of SPPV and GTPV if and only if storage, transportation and handling of the vaccines are properly implemented as the NVI's vaccine management and handling methods. These vaccines are inexpensive (currently 0.004 ETB per dose) and provide good protection if sufficient herd immunity is maintained by carrying out consistent vaccination strategies.

## CONCLUSIONS

Even though small ruminants are important components of Ethiopian farming system, their contribution are far below the expected potential. This is because small ruminant production in Ethiopia is constrained by different infectious diseases such as sheep and goat pox. SPP and GTP are infectious disease of sheep and goats, and distributed to different part of the world including Ethiopia. Transmission is considered by direct contact with respiratory droplets or contact with secretions of acutely infected animals. SPP and GTP have a great economic significance to farmers in regions in which they are endemic and are a major constraint to international trade in livestock and their products. Economic losses are also reflected by reduced meat and milk production, abortion, depreciation of wool and skin quality, and as a result of trade restrictions. In Ethiopia, livestock movements are uncontrolled, therefore, in order to alleviate the trouble, consistent vaccinations with live attenuated safe and effective KSGP vaccine strains are the best feasible, economic and practical method for the control of sheep and goat pox. Furthermore, in enzootic areas strict bio-security measures should also be considered.

### Ethical statements

This article did not include animal experiments

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### Competing interests

The authors declare that there is no conflict of interest regarding the publication of this article.

### Additional information

No additional information is available for this article.

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