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REVIEW ARTICLE

A Review on Sheeppox and Goatpox: Insight of Epidemiology, Diagnosis, Treatment and Control Measures in Ethiopia

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Abstract

Sheeppox and goatpox are caused by a genus of Capripox virus causing a severe problem and great economic loss in Ethiopia and also in sheep and goat rearing countries in many parts of the world. The objective of this review is to give insight on epidemiology, diagnosis, treatment and control measures of sheeppox and goatpox disease. Generally, the disease is less commonly seen in indigenous breeds in area where it is endemic as compared to exotic breeds. Mostly the disease is transmitted by direct contact. After it enters, goatpox virus replicates locally in the tissues. In endemic areas the morbidity rate reaches 70-90% whereas the mortality rate is up to 5-10% and approaches 100% in newly imported animals. In Ethiopia, the disease is distributed in all parts of the country and in endemic areas it is economically important due to lose of production, loss of weight, decreased milk yield, damage to hide and skin, cause abortion and expose to other diseases, while also being a direct cause of death. Diagnosis of SGP depends on clinical signs, laboratory confirmation and post mortem examinations. Sheeppox and goatpox require an urgent and precise laboratory confirmation as the diseases are severe and contagious. Samples for test must be collected during the first week of illness. Sheeppox and goatpox (SGP) disease can affect trade, import export and intensive production of animals. Since the disease has no effective treatment, control measure is targeted by effective vaccination and limitation of animal movement and their products between different nations. Even though live attenuated vaccine has been produced at National veterinary institute in Ethiopia, there is low coverage of vaccination throughout the country.

Keywords

Epidemiology, Ethiopia, Pox virus, Sheep and goat, Vaccination

Introduction

Sheeppox and Goatpox (SGP) is a disease that results in substantial loss in the production and productivity of sheep and goats in Ethiopia. The disease is a major constraint to the introduction of exotic breeds of sheep and goats and to the development of intensive livestock production. The economic losses from Sheeppox and Goatpox result from decreased milk production, damage to the quality of skins and other production losses. Moreover, existence of the disease severely affects trade of animals and products resulting in loss of export earnings.

Generally, SGP is less commonly seen in indigenous breeds in area where it's endemic as compared with exotic breeds. Indigenous animals are more likely infected from the disease in areas where it has been not found or dormant for a period of time and when intensive husbandry methods are introduced. The virus that causes sheeppox and goatpox disease is Sheeppox and goatpox virus of family poxviridae, genus *Capripoxvirus*, one of the largest (170-260 nm by 300-450 nm), enveloped double stranded DNA viruses [1]. Mostly the disease is transmitted by direct contact, but indirect contact with infected object and mechanical insect can also transmit. Aerosol and nasal secretions can also spread sheeppox and goatpox virus [2]. Sheeppox and goatpox (SGP) is a highly devastating viral systemic disease of sheep and goats characterized by widespread skin eruption, fever, generalized papules or nodules, vesicles (rarely) on non-wool skin (Figure 1), internal lesions in the lungs (Figure 2), respiratory and gastrointestinal mucosa and cause death [3].

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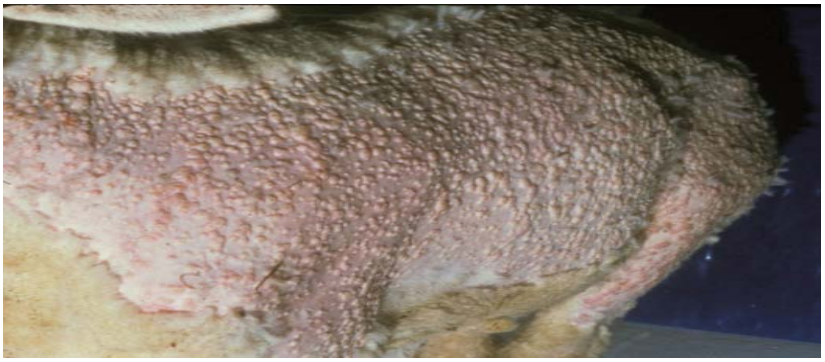

Figure 1: Clinical sign of Malignant type of sheep and goat pox.

Figure 2: Benign type of sheep and goat pox. (Source: slideplayer.com).

Sporadic outbreaks of sheeppox and goatpox occur in Middle East, Africa, the Indian subcontinent, and much of central Asia, Turkey, Iraq, Iran, Afghanistan, Africa north of the equator, and in South-Eastern Europe [3]. Recently outbreaks have been recorded in Kazakhstan, Mongolia, Azerbaijan, Turkey, Greece and Bulgaria. Although the gene sequence of Mongolian goat pox (GP) virus in 2008 P32 was distinct as compared to sequences of several other GP viruses originated from China, it has not been identified the source of Mongolian outbreak [4].

Ethiopia is believed to have the largest livestock population in Africa with sheep and goat populations exceeding 49 million, which is one of the largest populations of small ruminants in Africa [5]. Small ruminants (sheep and goats) have a unique role in smallholder agriculture as they require small investments; faster growth rates, have shorter production cycles, and greater environmental adaptability as compared to large ruminants. They are important protein sources in the diets of the poor and help to provide extra income and support survival for many farmers in the tropics and sub-tropics [6,7].

In Ethiopia, sheep are the second most important livestock species next to cattle [8]. Sheep and goat play an important economic role and make a significant contribution to both domestic and export markets through provision of food (meat and milk) and non-food (manure, skin and wool) products [9,10]. Although sheep and goat plays a significant role in national economy of the country to date the benefit obtained from these livestock are held back by different constrains. Livestock diseases are among the important technical constraints that have hindered the development of the sector by decreasing production and hampering trade in animal and animal products [11,12]. Sheeppox and goatpox is among the major and widely distributed livestock diseases in all region of the country [13].

According to Nesradin Yune and Nejash Abdela review, in recent study around Gonder of Ethiopia, a total of 1296 ruminants were studied for skin disease, the total prevalence of sheeppox and goatpox is 77(48.12%) and 64(40%), 13(8.12%) respectively [14].

Sheeppox and goatpox (SGP) is a highly infectious systemic viral disease of sheep and goats that cause high economic losses. Despite the huge economic losses, in endemic area of the country, there is lack of information.

Therefore, the objective of this article is to review on epidemiology, diagnosis, treatment and control measures of sheep and goat pox.

Literature Review

Epidemiology

Distribution: According to the study conducted by

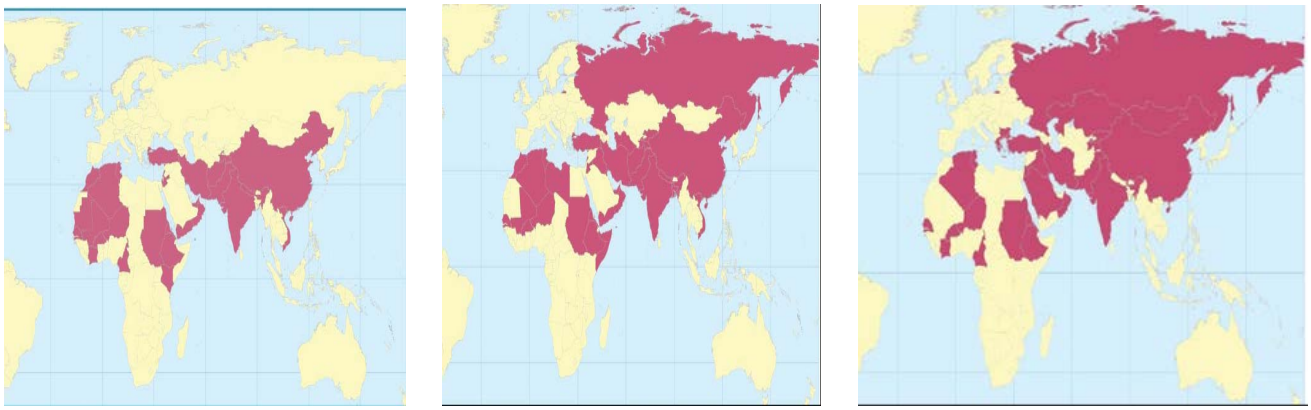

Figure 3: Global occurrence of SPP and GTP as reported to OIE in 2010, 2013 and 2015 respectively, Countries reporting SPP and GTP are highlighted in red color as revealed on the figures, the disease is propagating in Africa, Middle East and Asia. (Source: OIE).

Bhanuprakash, et al. Outbreaks were recorded during all months of the year, but mostly occur between November and May, and the peak outbreaks occurred in March. During cold seasons, sheep are exposed to low temperature exerting stress which could suppress the immune system, and ultimately the sheep become vulnerable to infection. The seasonality of SGP observed could be explained either by the capability of the viruses to survive for many months in wet and cold weather, by association with the lambing season, or by the poor physiological condition of flocks in the autumn [15-17].

Geographical distribution of the SGP has been relatively stable. SGP have seen in North and Central Africa, Middle Eastern countries, Asia and the former Soviet Union (Figure 3). These diseases are endemic in Nepal, China, Bangladesh, Equator, Iran, Turkey, Pakistan Iraq, Afghanistan, Indian subcontinent and Africa. Sporadic outbreaks occur in southern Europe and other parts in the world [18-20]. Recent outbreaks have been occurred in Mongolia, Kazakhstan and Azerbaijan in 2008 and 2009 and in Bulgaria, Greece and Turkey in 2013. It has not been identified the source of Mongolian outbreaks, although the gene sequence of Mongolian goatpox (GP) virus 2008 P32 was distinct as compared to sequences of several other GP viruses originated from China [4]. The geographical position of Greece between Europe and Asia makes the rapid and accurate diagnosis and control of SGP and other exotic diseases. Sheeppox and Goatpox are considered exotic to the EU and is classified in the notifiable diseases list of the OIE. SGP have been absent from the countries of Central and Western Europe for many years [21].

Transmission: The virus enters via the respiratory tract and transmission commonly is by aerosol infection associated with close contact with infected animals. Spread can also occur from contact with contaminated materials and through skin abrasions produced iatrogenic ally or by insects. But there is no evidence about importance of this route of transmission in the field. Viruses are shed in secretions and excretions of infected animals, but it is believed that they are not important sources of transmission during outbreaks, because it is difficult to recover live virus on tissue culture from scabs materials. Movement of infected animals acts as the main cause of spreading SGP viruses [19,22,23]. Highest level of shedding of infectious virus and viral DNA in secretions of infected animals occurred between about 1-2 weeks post inoculation, and this secretion continued for up to an additional 3-6 weeks [24,25]. Stomoxys calcitrans is considered as one of the important vectors for SGP viruses. The flies that were previously infected may transmit pox virus to susceptible sheep and goats [26]. The presence of antibody in animal species against a virus indicates its susceptibility to the virus. However, animal having antibody against a virus may not produce the infection, and the animal may not transmit the virus [27].

Morbidity and mortality: All breeds of domestic as well as wild sheep and goats are affected by sheep and goat pox virus infection. Although most strains cause more severe clinical disease in only one species. In endemic areas the morbidity rate reaches 70-90% whereas the mortality rate is up to 5-10% and approaches 100% in newly imported animals. Native breeds in endemic areas are far less susceptible than introduced breeds of European or Australian origin [28].

Etiology: The disease is result from infection caused by sheeppox virus (SPV) or goatpox virus (GPV), of family poxviridae, Subfamily *Chordopoxvirinae*, genus *Capripoxvirus*. It is DNA virus. Poxviruses of sheep and goats (Capripoxviruses) are closely related, both antigenic ally and physicochemically. According to Authors', it is unable to distinguish poxvirus from each other with serological techniques (including serum neutralization), and were once thought to be strains of a single virus. SGP viruses are usually species specific; however, strains do exist that can infect both sheep and goats. Genetic sequencing has now confirmed that these viruses are

distinct, but recombination can occur between them, however some *Capripoxvirus* are not host specific. Kenya sheeppox and goatpox virus and Yeman and Oman infect both sheep and goat [2].

Capripoxvirus is highly stable in normal environment condition and can survive for prolonged time with or without susceptible animal. They are inactivated by sun light and heat but can survive in cool dark environment for up to 6 months [29]. The sheeppox and goatpox viruses are generally considered host specific, but some strains affect both species [30].

Pathogenesis: Incubation period of sheeppox is 4-8 days and of that of goatpox is 4-15 days. After it enters, goatpox virus replicates locally in the tissues. Since the virus is epitheliotropic, it will infest the epithelium tissues of the organism. Based on a trial conducted, on the 7th day post-inoculation, the virus titer reached to its peak. The virus spread to the regional lymph nodes, after 3-4 days of primary viremia. The viremia spread in the body and affected spleen, lungs and liver. The virus inhaled may also cause lungs lesions. In skin nodules from 7 to 14 days after inoculation, the virus titers persisted and decreased with the development of serum antibodies. Within 24 hours of the appearance of generalized papules, affected animals develop conjunctivitis, rhinitis and enlargement of all the superficial lymph nodes, in particular the prescapular lymph nodes. Excessive salivation can also occur after infection [31].

There are five stages in the development of poxvirus infection. Roseola stage is stage in which Skin lesions typically begin with small red spots within three days of infection which is followed by papules. The affected animals are febrile at this stage. The second stage of pox lesion is Papules which develops after 3 days of roseola stage. Nodular skin lesions that are developed from roseola stage (red spots) those are hard during palpation. Papules within 5-6 days are changed to vesicles and known as vesicular stage. Pustular stage develops after 3 days of vesicular stage. As stated by researchers, the last stage of pox lesion is scab. Study has shown that, Quantitative analysis using real-time PCR and isolation of the pathogenesis of Sheeppox virus and Goatpox virus in their respective hosts' revealed high viral loads in skin [25].

Diagnosis

Clinical sign and finding

Both sheeppox and goatpox have similar clinical signs [30]. The incubation period of SGP is between 4-15 days in field condition [32]. The clinical signs of sheeppox and goatpox can be either malignant or benign. The malignant form of sheeppox and Goatpox is mostly common in lamb. Affected lambs may die without observable pox lesion. Fevers which peak at 40-42 °C, dyspnea and oculonasal discharge and pox lesion on unwooled skin are manifested in malignant form of sheeppox and Goatpox (Figure 3). The diseases are more severe in young animals than adults. In benign form of sheeppox and Goatpox only skin lesions occur particularly under the tail (Figure 1). This form of sheeppox and Goatpox is common in adults. There is no systemic reaction and the animal recovers in 3-4 weeks. Abortion and secondary pneumonia are complications. Lesions may be seen on the vulva, prenium, nostril and mucous membranes of the mouth. If lesion is present in the lung acute respiratory distress occurs [33].

Post mortem lesions

Post mortem Lesions of sheeppox and goatpox can develop in lung (Figure 4A) kidney (Figure 4B), spleen, lymph node and other internal organs. Lesion may also present in the mouth, nares, eye or eyelid. Affected mucous membranes may become ulcerate or slough and necrotic. Nodules occur in digestive, respiratory and urogenital system. Animals with lung lesions may have respiratory signs including coughing, nasal dis-

Figure 4: Malignant form of SGP on lung (A) and kidney (B) from left to right (Source: [54]).

charge and dyspnea. Nodules in the digestive system can cause diarrhea. Depression and emaciation may be seen in some animals. Abortions can occur but are not common. In acute disease some breeds of sheep can die before the characteristic skin lesions develop [2]. At necropsy, skin lesions have congestion, hemorrhage, edema, vasculitis and necrosis and will be seen to involve all layers of the epidermis, dermis, and, in severe cases, extend into the adjacent musculature. Histologically, pox lesions have extensive inflammatory, necrotic and proliferative changes. The presence of Borrel cells and intracytoplasmic inclusion bodies similar to the inclusions found with all poxviruses, are characteristic of Sheeppox and goatpox. Poxvirus of sheep and goat can be seen under electron microscope and can be readily differentiated from the virus particles of contagious pustular dermatitis but, indistinguishable from orthopoxviruses [33].

Differential diagnosis

The clinical signs of severe sheeppox and goatpox are highly characteristic. However, in their mild form they can be confused with parapoxvirus causing orf or urticaria from multiple insect bites, Contagious ecthyma (contagious pustular dermatitis), insect bites, Bluetongue, Peste des petits ruminants, Photosensitization, Dermatophilosis, Parasitic pneumonia, Caseous lymphadenitis and mange [28,34].

Laboratory Diagnosis

Samples

Samples for Capripox virus isolation must be sent to the laboratory as soon as possible. They should be kept cold and shipped on gel packs. If these samples must be shipped long distances without refrigeration, glycerol (10%) can be added; tissue samples must be large enough that glycerol does not penetrate into the center of the tissue and destroy the virus. Neutralizing antibodies can interfere with virus isolation and some antigen-detection tests; samples for these tests must be collected during the first week of illness. Samples for PCR can be taken after neutralizing antibodies have developed. Paired serum samples should be collected for serology in live animals; Full skin thickness biopsies, vesicular fluid if available, scabs, skin scrapings, lymph node aspirates, whole blood collected into heparin or EDTA. For necropsy; skin lesions, lymph nodes, lung lesions and for histology; full set of tissues, especially those with lesions should be collected [28].

Serological and molecular tests

Virus neutralization is the most specific serological test but not sufficiently sensitive since immunity to Capripox infection is predominantly cell mediated, infected animals may only produce undetectable low levels of neutralizing antibody. The demerit of Indirect fluorescent antibody test and Agar gel immunodiffusion (AGID) is cross reactivity with other poxviruses, Western blotting using P32 antigen of *Capripoxvirus* is sensitive and more specific for reaction with test sera but it is expensive and difficult to carry out. ELISA using P32 antigen or another appropriate antigen expressed by a suitable vector could be used to develop an acceptable and standardized serological test. Initially agar gel precipitation test was the principal test for identifying these viruses. With the advancement of time, use of soluble antigen fractions from the viruses has been incorporated and several test and their modifications have been developed [18].

Histopathology, electron microscopy and virus detection are the essential laboratory diagnosis tests for these diseases. Using electron microscopy, large numbers of characteristic 'Sheeppox cells' containing inclusion bodies and typical Capripox virions can be seen in biopsies of the skin. Virus detection can be done before the development of neutralizing antibodies. The virus can be cultured in tissue culture but virus isolation as a method of rapid diagnosis is limited and it takes time for virus to develop cytopathic effects and needs with some strains for several blind passages. Direct fluorescent antibody test is used to detect the presence of pox virus in the edema fluid and the antigen can be detected in biopsies of lymph glands by ACID using specific immune sera. An antigen detection ELISA is also available [19,23]. For the detection of antibodies specific for CaPVs in sheep, goats and cattle sera, an indirect ELISA has also been developed [35]. Sheeppox and Goatpox require an urgent and precise laboratory confirmation as the diseases are severe contagious. Molecular diagnosis via amplification of genetic material (DNA or RNA) by PCR has become a “gold standard” for rapid diagnosis of viral diseases, including CaPVs. Several PCR-based assays have been reported for rapid diagnosis of CaPVs, including conventional and real-time PCR or qPCR [25,36-39]. Some of the advantages of qPCR include speed, sensitivity and detection of results in real time; however, it requires expensive high-precision instruments and specialized training for operation and data analysis. Virus isolation is also considered a gold standard for the diagnosis of viral diseases, but its application to the detection of CaPVs is limited due to the long incubation time (10 to 14 days) typically needed to obtain results [25]. The duplex PCR assay described by Zheng, et al. can be completed in less than 5 hrs, provides significant savings in cost, materials and time. This is an advantageous as compared to individual PCR assays or virus neutralization test that is practiced for the identification of SGP viruses. Furthermore, sensitivity of this test is similar to that of virus isolation in cell cultures [40].

Comparison between conventional gel-based PCR and real-time PCR techniques revealed that the later one is more sensitive allowing detection of even low viral titers of SP virus [41].

Economic importance of sheep and goat pox

Sheeppox and goatpox is highly devastating systemic viral disease of sheep and goat and the most common cause of economic loss in Ethiopia. Moreover, limiting international trade of animals and animal products [3]. The disease is fatal in newly introduced animal, but may be mild in indigenous breeds from endemic region. The outbreak of sheeppox and goatpox may cause serious problem and economic loss in sheep and goat industries [42]. In endemic areas the disease are economically important due to losses of production, decreased weight gain and milk yield, damage to hide and skin, cause abortion and increase susceptibility to other disease while also being a direct cause of death. In young animal's mortality and Morbidity rates can be very high, approaching 100% [26].

Sheeppox and goatpox (SGP) disease can affect trade, import, export and intensive production of animals. Flock size, number of adult animals and number of days of illness play significantly in influencing the economic losses due to SheepPox [43,44].

Management as treatment

There is no effective treatment for sheeppox and goatpox infection. Management strategies should be directed to control secondary bacterial infection. As per indicated by studies, Parenteral administration of abroad spectrum antibiotic is important to control secondary bacterial infection. Clean, well ventilated enclosure and balanced diet should be provided. If Animals are unable to feed 100% glucose saline should be given parentally. To limit secondary bacterial complication, all diseased animals should be treated with antibiotics. Wash and clean the nostril with weak solution of potassium permanganate (1:10000) to relieve respiratory related sign. Topically applying antibiotic ointment is important for skin lesion [43]. Heating at 56 °C (133 °F) for 2 hours, or to 65 °C (149 °F) for 30 minutes are reported to destroy Capripoxviruses. Although some strains are resistant to ether, *Capripoxvirus* are generally inactivated by chloroform, formalin and ether 20% [2].

Control

The countries that are considered as Capri pox virus free control the importation of sheep and goats and their products from enzootic areas. Control of the disease once it has entered is usually by early detection and notification, prompt movement restriction of animals, culling affected and in contact animals and ring vaccination with an inactivated vaccine. Sentinel animals could be used prior to re-stocking culled herds [19,45,46]. Routine control measures include the cleaning and disinfection of depopulated premises and establishment of protection and surveillance zones, with a radius of 3 and 10 km, respectively, around the outbreak, as recommended by EU Council Directive [47].

As stated before, uncontrolled movement of infected animals in SGP endemic areas possess serious difficulties in efficient control of the disease. Therefore, it is essential to vaccinate sheep and goat flocks regularly on an annual basis with a safe and efficient vaccine for the control of this serious and economically important disease in endemic regions [16].

In most countries in which Capri pox is enzootic, a slaughter policy would be impracticable and movement controls impossible to enforce. In these countries vaccination and implementation of biosecurity measures are considered the only suitable control measure. The best feasible, economic and viable method is considered as implementation of mass vaccination program. For control and eradication of SGP, it can be adopted the same strategy as followed in case of rinderpest as per the guidelines of OIE. This may include an initial mass vaccination followed by serological surveillance for a period of 2 years, and then cessation of vaccination program. After that, some serological surveys are necessary to be conducted. In general, about ten years is required officially to declare a country free from SGP [45,48,49]. In endemic areas, mass vaccination against SGP to total susceptible population may cause to dying out the circulating virus [23]. In hyper endemic areas, ring vaccination should be undertaken for about 3 years to try to eradicate the [15].

National programs for control and finally eradication of SGP need fortifying of the veterinary infrastructure, reporting system, technology and financial resources, whereas developing nations like Africa lack some of these elements and thus suffer economic losses from endemic diseases [50].

International trade in animal and their products will compensate costs of control and eradication of SGP. The other factors that favor to initiate the control programs includes easy detection of diseases/agents, economic impact of the diseases, absence of reservoir hosts other than domestic small ruminants, induction of solid immunity after vaccination, nonexistence of a carrier state, relatively low annual turnover rate of animals in flocks and easy diagnosis of infected or exposed animals. In contrary, the factors which may hinder the control program are prolonged stability of the virus on wool, hair of recovered animals, long incubation period of the diseases, unregulated introduction of livestock through importation or by illegal means of infected sheep and goats into the country [49].

Vaccination

Immunity induced by pox viruses or vaccines is strong enough and may persist long time as compared to some other pathogens. Pox viruses cause to produce both cellular and humoral immune responses. Maternal immunity provides protection from SGP virus for up to 3 months. The animals that are recovered from SGP infection con-

tained lifelong immunity. So, the virus can only survive by constant transmission from infected to susceptible animals, and therefore requires a certain minimum size of susceptible population. The size of this population depends on the strain of the virus, the susceptibility of the host population, and on the basic reproductive number (R0), *i.e*., the number of susceptible animals infected, on average, by a single diseased animal [22,49,51,52]. Active mass vaccination to SGP may induce strong herd immunity that can effectively control the disease. Single vaccination is considered as enough for providing lifelong strong immunity [49]. Even though live attenuated vaccine has been producing at national veterinary institute in Ethiopia, there is low coverage of vaccination throughout the country [53].

Conclusion

Sheeppox and goatpox (SGP) is highly infectious disease in sheep and goats, which is distributed to different part of the world including Ethiopia. It seriously affects exotic breeds. Mortality and morbidity rate get to 100%. The virus enters via the respiratory tract and transmission commonly is by aerosol and infection is usually associated with close contact with infected animals. After the virus get in to the body of shoats (sheep and Goat) it has five developmental stages. This disease is more severe in young animals than adults; the affected lambs die without showing clinical signs. Moreover, sheeppox and Goatpox is highly divastitating and cause limitation of international trade, alongside affects the economy of a nation. Sheeppox and Goatpox require an urgent and precise laboratory confirmation as the diseases are severe contagious. Management strategies like clean water, well enclosure housing, balanced diet and minimizing stress during cold season and lambing stage should be provided. Since this disease has no effective treatment, it is essential to vaccinate sheep and goat flocks regularly on an annual basis with a safe and efficient vaccine for the control of this serious and economically important disease in endemic regions. In enzootic areas biosecurity measures should also be considered.

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