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REVIEW ARTICLE

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A review of sheep pox and goat pox: perspective of their control and eradication in Iran

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ABSTRACT

Sheep pox and goat pox (SGP) of small ruminants are most severing pox diseases of domestic animals, and they have a very important role in agricultural economy. Thereby, SGP are included in the notifiable diseases of Office International des Epizooties (OIE). Time and place distributions of these diseases are relatively stable worldwide. Transportation of infected animals could spread these viruses to the new areas. In most countries in which capripox are enzootic, vaccination and bio-security are the only two main control measures. SGP control programs have been commenced about 50 years ago in Iran, and there is a good situation for eradication of it. In this review, readers can find latest information in some essential aspects of etiology, distribution, transmission, and control of the diseases. Besides, current situation of the disease in Iran has been described, which perhaps are similar to the other endemic areas in the world.

Keywords

Capripox, Control, Endemic areas, Iran

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INTRODUCTION

Sheep pox and goat pox (SGP) viruses are belonging to Poxviridae family, Chordopaxvirinae sub-family, and Capripox viruse genus (Buller et al., 2005). These are large (170–260 nm by 300-450 nm), double stranded, DNA, and enveloped viruses (Tulman et al., 2002). The length of genome of SGP viruses is about 150-kbp, and are very similar to each other but by sequencing, researchers have categorized the viruses in Capripox virus genus. The genomes of SGP and lumpy skin disease (LSD) viruses have 97% similarity in their nucleotide identity (Bhanuprakash et al., 2006). On the other hand, genomes of SGP viruses include some nucleotide differences, revealing that they are phylogenetically distinct, and probably both of them have derived from an LSDV-like virus. One of the most important differences between SGP viruses is about to aspartic acid at position 55 of P32 in SP virus; because it is not present at such position in the rest viruses of the genus. Capripox viruses (CaPVs) conained lipid, and are susceptible to many disinfectants, lipid solvents, and acids (Tulman et al., 2002; Hosamani et al., 2004; AHA, 2011).

CaPVs are not easily distinguishable morphologically from Orthopoxviruses. Serologically, these viruses share antigens with parapox viruses that are used in precipitation (Roy et al., 2008; Babiuk et al., 2008a). In general, SGP viruses will be inactivated at 56°C within 2 h, or at 65°C within half an hour. They can survive at a pH between 6.6 and 8.6. These viruses are susceptible to highly acidic or alkaline pH; for example, 2% HCl or H_2SO_4 can completely destroy these viruses within 15 min (OIE, 2014). CaPVs are considered as stable in the environment. They are susceptible to sunlight; however, they may survive in a dark and cool environment for up to 6 months. The SGP are included in the OIE list as one of the notifiable diseases; it should be notified within 24 h of confirming the disease. Animals are susceptible during all age groups, and it has a very important role in agricultural economy (AHA, 2011). Capripox viruse infections of small ruminants are most severing pox diseases of domestic animals. In susceptible herds, morbidity is 75-100% and case fatality, depending on the virulence of the virus, is between 10-85% in the outbreaks (**Figure 1**). Mortality in older animals can reach up to 90% when capripox is superimposed on another viral condition such as peste des petits ruminants (PPR). Breeds of sheep and goats originated from Europe are very susceptible to capripox, and mortality may reach up to 100% (Kitching, 1986; Radostits et al., 2006; AHA, 2011). Mondal et al. (2004) reported that Sheep of the Rambouillet breed was highly susceptible to infection as compared to Australian cross and American Merino breeds (Mondal et al., 2004).

Figure 1: High mortality rate due to SP outbreak, Qom, Iran.

DISTRIBUTION

Outbreaks are recorded during all months of the year, but mostly occur between November and May, and the peak outbreaks occurred during 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 (Bhanuprakash et al., 2005; Yeruham et al., 2007; Zangana et al., 2013).

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. 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 (Rao et al., 2000; Kitching, 2002; Radostits et al., 2006; OIE, 2010). 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 goat pox (GP) virus 2008 P32 was distinct as compared to sequences of several other GP viruses originated from China (Beard et al., 2010).

The geographical position of Greece between Europe and Asia makes the rapid and accurate diagnosis and control of SGP and other exotic diseases very important. SGP 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. But considering the recent outbreaks of SGP in southeastern Europe, there is potential for further spread of these CaPVs to the Europe (AHA, 2011), (Mangana, 2008).

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 iatrogenically 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 (Kitching, 2004; Radostits et al., 2006; AHA, 2011). 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 (Kitching et al., 1989; Bowden et al., 2008). Stomoxys calcitrans is considered as one of the important vectors for SGP viruses. The files that were previously infected may transmit pox virus to susceptible goats (Bhanuprakash et al., 2006). 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 (Tuppurainen et al., 2012).

ECONOMIC IMPACTS

There is little information on the epidemiology and economic losses caused by SP in dairy sheep flocks. It causes considerable economic loss due to morbidity, mortality, reduced meat and milk production, abortion, depreciation of wool and skin quality (**Figure 2**), and as a result of trade restrictions (Yeruham et al., 2007). While sheep and goat producers which have been under investigation in India have ranked SGP below some other infectious diseases, when SGP occurs, it usually has a major impact. Economic investigations have indicated that some variables such as number of adult animals affected, number of days of illness, and flock size are significantly influencing the economic losses due to SP (Garner et al., 2000; Senthilkumar et al., 2010).

There is a large amount of trade of hides, skin and wool from the countries where SGP is persistently present to other countries around the world, particularly European Union (EU). The hides and skins that are processed by salting treatments or drying only may pose a risk for introduction of SGP viruses to other coutnries particularly to the EU (EFSA Panel on Animal Health and Welfare, 2014). The risk posed by untreated skins, hides and wool imported from endemic countries has recently been evaluated by the UK Department for Environment Food & Rural Affairs (DEFRA). In this qualitative assessment it is concluded that the risk of release of CaPVs into the UK, via the importation of one untreated animal skin/hide/wool bale from the EU, is low. However, this estimate is highly dependent on the probability that a herd/flock is infected within the EU; should this increase, the overall risk of release will increase (Gale et al., 2014). These diseases are endemic in Iran, giving rise to economic losses such as abortion, decreasing milk production and damage to wool and hides (Davari et al., 2013).

CLINICAL SIGNS AND PATHOLOGY

The incubation period of SGP ranged from 4-14 days; however, OIE recorded a maximum incubation period of 21 days (OIE, 2010). Usually, the first manifestation of the disease is swelling of nostrils, followed thick discharges from the nose and watery discharges from the eyes (**Figure 3**). High body temperature (41 to 42°C) is found in infected animals, and keratitis may develop (Daoud, 1997).

In lambs, malignant form of SP has been recorded as the most common type. There is prostration, high fever, marked depression, and discharges from the eyes and nose. Lesions occur on un-wooled skin and on the buccal, respiratory, digestive, and uro-genital tract mucosa. They commence as papules, then become nodular, occasionally become vesicular, pustular and finally scab. Pox lesions have seen in the heart muscles in this form of the disease, most rarely (**Figure 4** and **Figure 5**). In the benign form, more common in adults, only skin lesions occur, particularly under the tail, and there is no systemic reaction and animals recover in 3-4 weeks. Abortion and secondary pneumonia are complications (Radostits et al., 2006), (Iran Veterinary Organization, 2014).

IMMUNITY AND VACCINATION

Immunity induced by pox viruses or vaccines is strong enough and may persist long time as compared to some other pathogens. Pox viruses causes 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, contained 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 (R_0), *i.e.*, the number of susceptible animals infected, on average, by a single diseased animal (Kitching, 2004; Panchanathan, 2008; Sadri et al., 2010; Bhanuprakash, 2011). Active mass vaccination to SGP may induce strong herd immunity that can effectively control the disease. Single vaccination is considered as enough for providing life-long strong immunity (Bhanuprakash et al., 2011).

In previous, SGP viruses were believed to be same virus. However, genetic sequencing proved that these are separate viruses. Most strains of SGP are host-specific, and cause severe clinical disease in either goats or sheep; however, some strains have equal virulence in both species. Indeed, isolates from most regions are host-specific but isolates from Kenya, Yemen and

Figure 2: Depreciation of wool and skin quality, Qom, Iran.

Figure 3: Swelling of nostrils and thick discharges from the nose and eyes (left), Pox lesions on the face and ears (right), Qom, Iran.

Oman naturally infect both goats and sheep. Therefore, in most countries, at least two different vaccines containing the isolates of either GP or SP virus, are necessary to protect small ruminants against both virses (Carn, 1993; Rao et al., 2000; Abu-Elzein et al., 2003; Radostits et al., 2006; OIE, 2013; Iran Veterinary Organization, 2014). However, recent studies have confirmed that the identity of Kenyan SGP vaccine (commonly used vaccine) virus O-240 is not SP virus, and this vaccine may cause clinical disease (Tuppurainen et al., 2014). Furthermore, researchers have recently reported some SP outbreaks occurred in both sheep and goat flocks at roughly the same geographical location in India. The report published by Bhanuprakash et al. (2010) provides evidence of SP virus infection in goats.

New introductions of SGP are generally only identified in one of the two animal species concerned (i.e. goats or sheep) depending on the strain introduced, so that GP was introduced into Bangladesh in 1984 from India, and SP has caused occasional outbreaks in Italy (1983), Greece (1988, 1995, 1996, 1997, 1998 and 2000) and Bulgaria (1995 and 1996) having spread from Turkey, probably in illegally imported animals (Sadri et al., 2010).

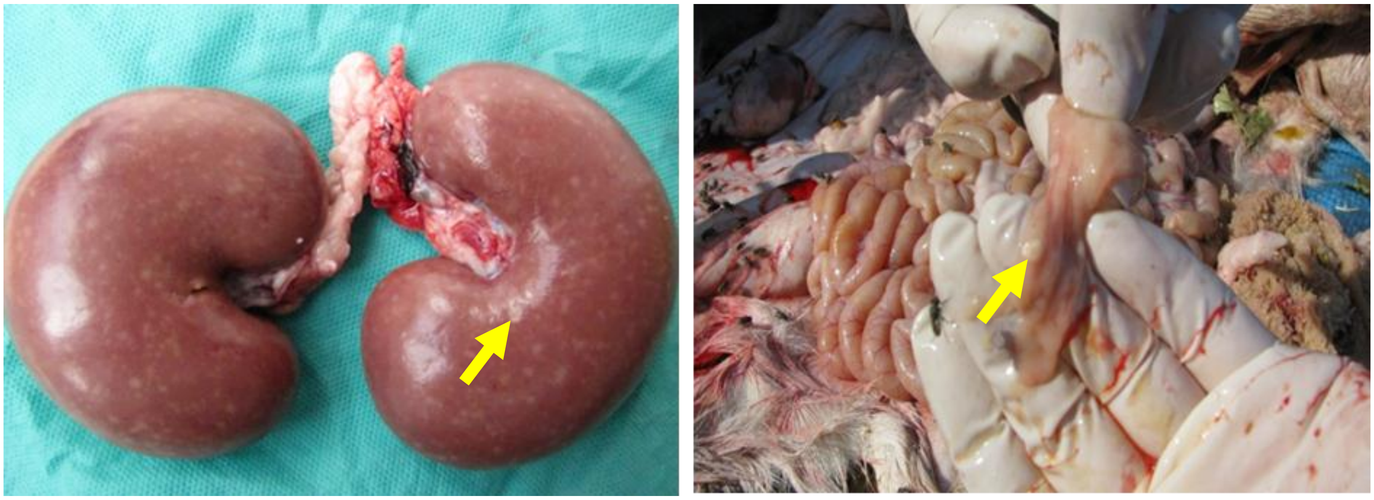

Figure 4: Malignant form of SGP: Pox lesions on the kidney (left), and small intestine (right), Qom, Iran.

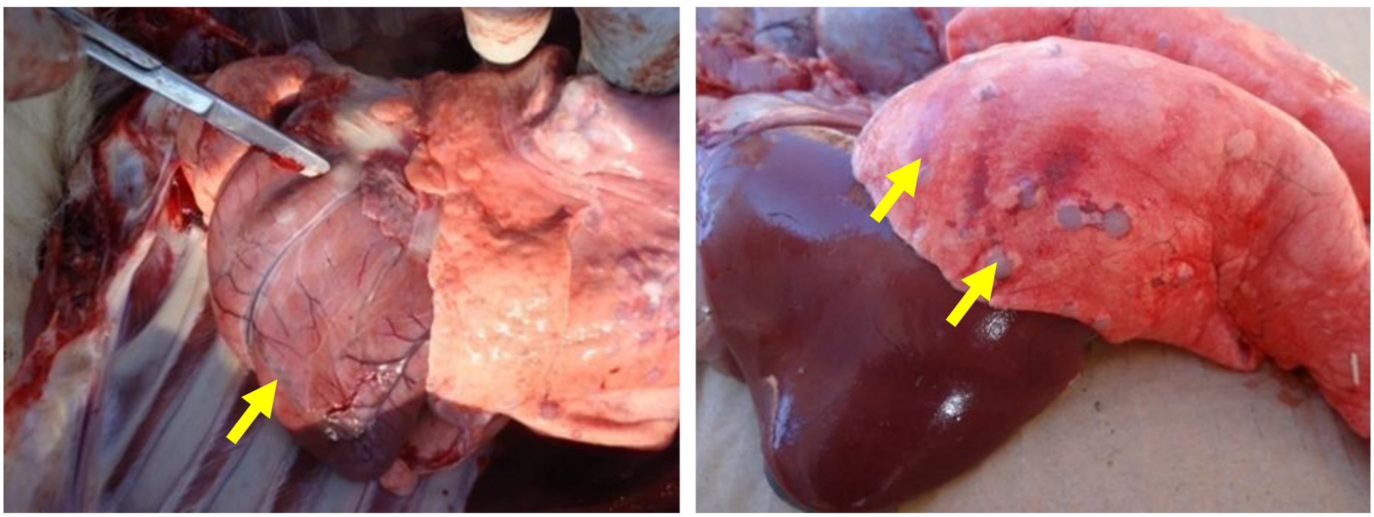

Figure 5: Malignant form of SGP: Pox lesions on the heart muscles (left), and lungs (right), Qom, Iran.

CLINICAL PATHOLOGY AND DIAGNOSIS

Diagnosis of SGP is depended on clinical signs and laboratory confirmation. Initially, agar gel precipitation test was the pricipal test for identifying these viruses. With the advancement of time, use of soluble antigen fractions from the viruses have been incorporated, and several test and their modifications have been developed (Rao et al., 2000).

Histopathology, electron microscopy and virus detection are the essential laboratory diagnosis tests for these diseases. Using electron microscopy, large numbers of characteristic 'SP 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 by the time it takes for virus cytopathic effects to develop and the need, with some strains, for several blind passages before this develops. 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 (Radostitset al., 2006; AHA, 2011).

SGP require an urgent and precise laboratory confirmation as the diseases are severe contagious. The duplex PCR assay described by Zheng et al. (2007), can be completed in less than 5 h, provides significant savings in cost, materials and time. This is an advantagious as compared to individual PCR assays or virus neutralization test that are practiced for the identification of SGP viruses. Furthermore, sensitivity of this test is similar to that of virus isolation in cell cultures (Zheng et al., 2007).

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 (Tian et al., 2012). For the detection of antibodies specific for CaPVs in sheep, goats and cattle sera, an indirect ELISA has also been developed (Babiuk et al., 2009).

CONTROL

The countries that are considered as capripox 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 a dead vaccine. Sentinel animals could be used prior to re-stocking culled herds (Kitching, 1986; Radostits etal., 2006; EFSA Panel on Animal Health and Welfare, 2014). 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 (Mangana et al., 2008).

As stated before, uncontrolled movement of infected animals in SGP-endemic areas poses serious difficulties in efficient control of the disease. Therefore, it is essential to vaccinate sheep 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 (Yeruham et al., 2007).

In most countries in which capripox is enzootic, a slaughter policy would be impracticable and movement controls impossible to enforce. In these countries vaccination and implementation of bio-security 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 progam. 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 (Kitching, 1986; Rweyemamu et al., 2006; Bhanuprakash et al., 2011). In endemic areas, mass vaccination against SGP to total susceptible population may cause to dying out the circulating virus (Animal Health Australis, 2011). In hyper-endemic areas, ring vaccination should be undertaken for about 3 years, to try to eradicate the disease (Bhanuprakashet al., 2005). However, vaccine efficiency is not always perfect. For example, Israel Veterinary Service (IVS) has been using the RM65strain (Ramyar strain) of SP virus to control SP and LSD for more than 20 years, but using this vaccine did not completely eliminate further outbreaks (Brenner et al., 2009). Vaccine efficacy should be experimentally studied, and because SGP viruses do not replicate in small rodents, there are no small animal models available to evaluate the efficacy of the vaccine. Vaccine challenge using a virulent field strain is then only method available to measure the protection provided by the vaccine (Abbas et al., 2010).

National programs for control and finally eradication of SGP, need fortifying of the veterinary infrastructure, reporting system, technology and financial resources, whereas developing nations lack some of these elements and thus suffer economic losses from endemic diseases (Breeze, 2006).

International trade in animal and their products will compensate costs of control and eradication of SGP. The other factors that favor the initiate the control programs included 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 impede 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 (Bhanuprakash et al., 2011).

It is possible that, in the same way that smallpox was controlled and eradicated, Capripox could be eliminated. However, the African experience with rinderpest would suggest that the production of a suitable vaccine is not all that is required (Kitching, 1986).

CAPRIPOX INFECTIONS STATUS IN IRAN

Vaccination and minimizing transportation stress are some of the major control measures to reduce losses due to sheep and goat pox. In Iran, SGP vaccines are free and part of governmental plans. These attenuated live vaccines along with anthrax vaccine are impregnated simultaneously on goats and lambs which are older than 3 months once a year. Nevertheless, prevention of the disease would be difficult because Capripox virus remains viable on the wool or hair of previously infected animals for several months. Moreover, the infectivity is resistant to the environmental conditions (Davari et al., 2013; Iran Veterinary Organization, 2014).

SGP control and eradicating programs in Iran have been commenced about 50 years ago. Nonetheless, sometimes we observe sever outbreaks in the country with high morbidity and mortality rates every year, yet (Baraniet al., 1999; Bokaie et al., 2003; Barani et al. 2010). Analysis of Iran Veterinary Organization (IVO) data from 1996 to 2001, and Razi Vaccine & Serum Research Institute (RVSRI) data from 1995 to 2001, revealed that vaccination coverage in only 6 provinces were above 90% in susceptible animals during these years, while clinical signs of the disease became absent only in one province; other provinces despite high coverage of vaccination in susceptible animals, had reported to have some outbreaks during these years. SGP occurs during all months of the year, but highest and lowest outbreaks have been reported in December and September, respectively; which it might be due to overcrowding of animals in their sheds, parturition stress, and migration to find new meadows. In another study, Sadri (2012) has reported that GP is significantly higher in older female goats, and also in rainy seasons in Iran. In abovementioned analyses, expected significant and reverse correlation between vaccination and incidence of the disease, have not been detected. This is might be related to quality and handling of vaccines, vaccination operation, etc. (Namdari, 2000; Bokaie et al., 2003; Sadri, 2012; Iran Veterinary Organization, 2014).

SGP have different distributions in Iran; SP outbreaks are mostly reported in northeastern, northwestern, and central provinces, while GP is more prevalent in southern provinces. According to the analyses performed on data during recent years, authors believe that timely vaccination of hot points of disease distribution has been important to reducing outbreaks in recent years (Iran Veterinary Organization, 2014).

CONCLUSIONS AND PERSPECTIVES

Effective live attenuated vaccines and improved diagnostic tests may facilitate in initiating effective control measures. Control programs should be monitored by active surveillance especially for the detecting viruses, because serologic tests cannot differentiate between infection and vaccination. On the other hand, in vaccinated animals with mild clinical disease the rise of the antibody titers may take up to two weeks (on 21 days post infection of experimentally infected animals) and these animals may show only low levels of antibodies, not detectable using neutralization assay.

Socioeconomic and political stability, availability of veterinary services, and adequate infrastructure and logistic supports are essential for implementing effective control programs. Inadequate infrastructure in most of developing countries is one of the major elements that conflict with effective implementation of building herd immunity.

May be similar to most endemic areas, implementation of vaccination in significant number of doses of SGP vaccines throughout our country every year has an immense economic burden on government due to vaccine production and distribution, vaccination operation and supervising all stages of that, control programs assessments, etc. Therefore there is a need to assess the value of this vaccination campaign and current control strategies in endemic countries. For this reason, it is essential to proposing to conduct studies to estimate the actual prevalence and to explore potential risk factors that can contribute to the spread and maintenance of these viruses among small ruminants in endemic areas. Authors believe that results of such studies will help modeling patterns of the diseases and determining high risk geographical areas which may need more attentions than other areas to implementing control measures.

COMPETING INTERESTS

The authors declare that they have no conflict of interests.

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