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RESEARCH ARTICLE

Epizootiological serosurvey on small ruminant lentiviruses: Prevalence, age and breed effects

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ABSTRACT

In this study, the prevalence of small ruminant lentivirus, i.e. Maedi-Visna and caprine arthritis encephalitis virus infections in sheep and goat populations were investigated through epizootiological serosurveillance in the Aegean region located in western Türkiye in 2018. A total of 1,840 serum samples (595 goats, 1,245 sheep) were collected from 92 villages in the region and examined by indirect ELISA. Thirty-nine goat and 304 sheep sera were found positive for small ruminant lentivirus antibodies. The prevalence was 24.42% in sheep and 6.55% in goats. An average of 18.64% was found in small ruminants in the Aegean region. The prevalence of small ruminant lentiviruses was found to be higher in Pirlak and Pirlak hybrid sheep and in Saanen and Saanen hybrid goats ($P < 0.05$). The prevalence was found to increase with age, as it was higher in animals older than 48 months than in the age groups of 0–24 or 25–48 months ($P < 0.05$). Moreover, the small ruminant lentivirus prevalence was higher in sheep than in goats ($P < 0.0001$). With the epizootiological approach, this study is expected to contribute to the control and prevention of small ruminant lentivirus infections.

KEYWORDS

caprine arthritis encephalitis, maedi-visna, goat, sheep, ELISA

INTRODUCTION

Maedi-Visna (MV) and caprine arthritis encephalitis (CAE), also known as small ruminant lentivirus (SRLV) infections, are important and persistent viral infections with economic importance in sheep and goats (Minguijón et al., 2015). Maedi, also known as ovine progressive pneumonia, affects the respiratory system and visna the central nervous system. Maedi causes loss of condition, slowing of gait, increased respiration, pneumonia, cough and nasal discharge as clinical signs, whereas visna is accompanied by muscle tremors, ataxia, partial or complete paralysis and blindness with death as a frequent outcome. MV may also cause mastitis and arthritis. CAE virus causes arthritis, encephalitis and pneumonia. CAE clinically presents as progressive arthritis and/or chronic mastitis in adults and as progressive paresis in the young. There have been various reports on experimental and natural infections causing CAE in sheep and VM in goats (CFSPH, 2015; Blacklaws et al., 2004; Michiels et al., 2010; Molaee et al., 2020; Norman et al., 1983; OIE, 2015; Shah et al., 2004; Timoney et al., 1988).

Both MV virus (MVV) and caprine arthritis encephalitis virus (CAEV) belong to the *Lentivirus* genus in the *Orthoreovirinae* subfamily of the *Retroviridae* family (Coffin et al., 2021). SRLVs are spherical, 100-nm-sized, positive-sense RNA viruses. Epizootiological and phylogenetic studies have shown that MV and CAE viruses are different despite transmission between species being possible (Agnarsdottir et al., 2000; Andresson et al., 1993; CFSPH, 2015; OIE, 2015). SRLVs are classified into five sequence groups, namely

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A, B, C, D and E, according to phylogenetic analyses. Group A has 22, group B has 5 and group E has 2 serotypes (Michiels et al., 2010; Molaee et al., 2020; Shah et al., 2004). MV/CAE infections are chronic, progressive and difficult to diagnose (Norouzi et al., 2015). Horizontal transmission, especially through ingestion of contaminated colostrum or milk and inhalation of secretions, plays a major role in spreading the infection, thus herd management and screening the livestock are crucial tasks (Blacklaws et al., 2004). There are no treatment or vaccination possibilities, and therefore, the diseases cause great economic losses. More epizootiological studies are necessary for the control and prevention of the disease (Norouzi et al., 2015). An increase in the quality and efficiency of molecular and serological identification methods can give a greater chance of MV/CAE eradication (Shuaib et al., 2010).

MV has been detected in many countries with sheep herds except New Zealand and Australia. Conversely, CAE distribution is higher in industrialised countries, and this situation is considered to be due to the international movement of dairy breeds. The high economic loss of SRLV infections has led to the development and adoption of control programs in many countries (OIE, 2015; Andress et al., 2005; Peterhans et al., 2004).

Although there are many publications reporting the occurrence of MVV/CAEV in Türkiye, there is a lack of epizootiology-based studies showing the prevalence of the viruses on a statistical basis. The aim of our study was to reveal the prevalence of MVV/CAEV infections according to the age, breed and location in the Aegean region, where the small ruminant population is significant.

MATERIALS AND METHODS

Field material

Sampling for determination of the seroprevalence of SRLV was carried out according to a multi-stage sampling method with a 95% confidence interval (CI), 50% estimated prevalence and (+/−5) tolerance rate from a population of 5,761,158 sheep and 2,063,451 goats from 3,757 villages in the Aegean region in 2018. In the first stage, each province was considered to be a cluster, with villages chosen according to population size (92 villages). In the second stage, in order to find at least one positive from the village when 15% of sheep/goats are accepted to be positive with 95% probability, from each village, 20 serum samples were collected using simple random sampling technique. The information regarding the population and animal sample size is summarised in Table 1. The geographical location of the sampled area is shown in Fig. 1. The numbers of goat and sheep samples according the provinces, towns and villages are listed in Table 2.

Blood samples were aseptically taken into tubes without anticoagulant and transported to the laboratory under cold chain conditions. The samples were then centrifuged at 2,000×*g* for 10 min. The sera were collected in Eppendorf tubes and stored at −20°C until use.

Serological studies

A commercial ELISA kit (IDEXX MVV/CAEV p28 Ab Screening Test, IDEXX, Montpellier, France) was applied to detect antibodies to SRLVs. This test is an indirect ELISA that uses an immunogenic peptide of a transmembrane protein and a recombinant p28 protein. According to the

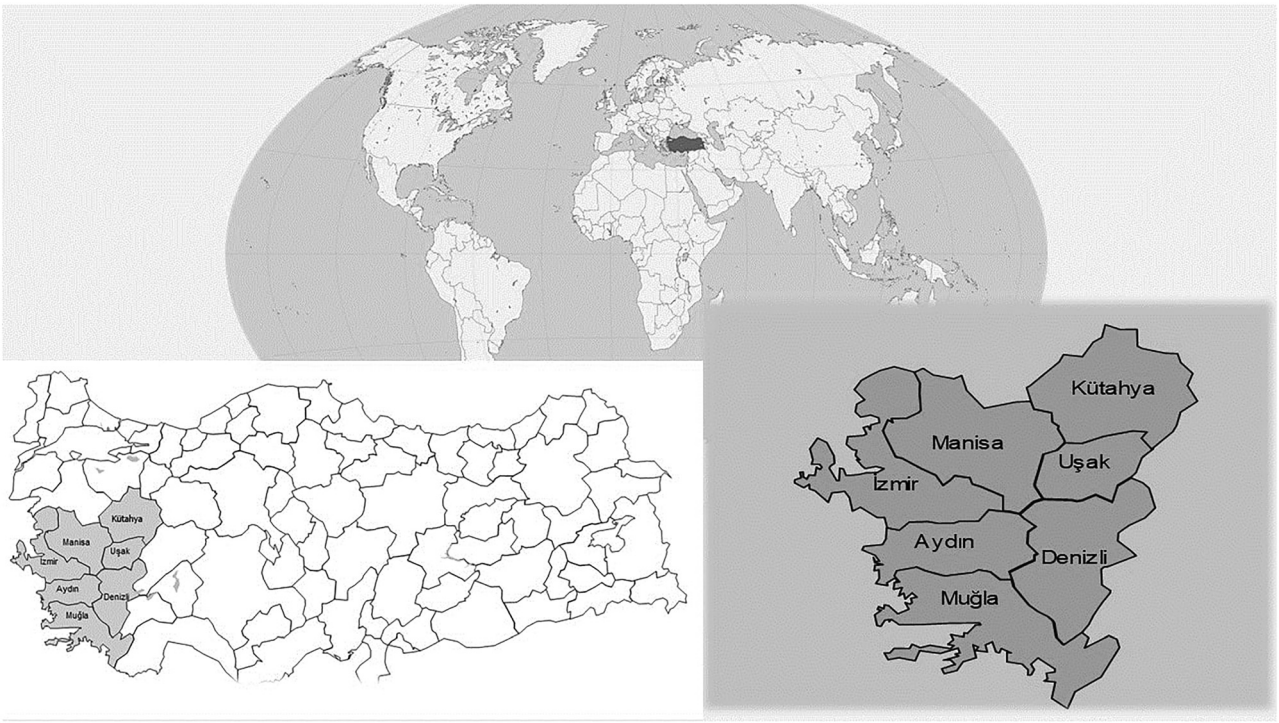

Fig. 1. Geographical location of collected samples

Table 1. Population and sample size

	Epizootiologic Unit (Village)	Sheep	Goats	Total
Population	3,757	5,761,158	2,063,451	7,824,609
Number of samples	92	1,245	595	1,840
Sample (%)	2.45	0.02	0.03	0.02

Table 2. Sample size of goat and sheep populations in province and district level

Provinces	Number of Sampled District	Number of Sampled Village	Number of Sampled Goat	Number of Sampled Sheep	Total
Aydın	9	13	121	139	260
Denizli	9	16	67	253	320
İzmir	13	15	93	207	300
Kütahya	7	14	43	237	280
Manisa	5	7	20	120	140
Muğla	9	16	251	69	320
Uşak	4	11	—	220	220
Total	**56**	**92**	**595**	**1,245**	**1,840**

manufacturer's declaration, the sensitivity and the specificity of the test is 97.9% (95% CI: 95.6%–99.0%) and 100% (95% CI: 99.6%–100.1%), respectively. The ELISA test was performed according to the protocol supplied by the manufacturer. The plates were evaluated with an ELISA reader (Biotek ELx800, USA) under 450 nm wavelength.

Statistical analysis

Prevalence, 95%CI, standard deviation, design effect, homogeneity and average sample size were evaluated with the WINPEPI/DESCRIBE version 3.02 program. A chi-square test was applied to evaluate the importance of the differences in prevalence according to species, breed and age groups.

RESULTS

Prevalence

Among the 1,840 sera samples tested in this study, 343 (18.64%) were found to be positive for MVV/CAEV antibodies and 1,497 (81.36%) were negative. In goats, 39 (6.55%) of the 595 sera samples were found to be positive, and 556 (93.45%) were negative. In sheep, 1,245 sera samples were studied, and among them, 304 (24.42%) were positive and 941 (75.28%) were negative. The results are summarised in Table 3. In this study, the prevalence of MVV/CAEV was 6.55% for goats and 24.42% for sheep, with a general total for both species of 18.64% (Table 4). Chi-square testing was conducted to evaluate whether MVV/CAEV positivity was important when breeds were compared with each other. According to the data obtained by this study, MVV/CAEV prevalence was found to be significantly higher in sheep than in goats ($P < 0.0001$).

Breed-related prevalence

Breed results are shown in Table 5. According to the data, MVV/CAEV susceptibility was more marked in the Pirlak and Pirlak hybrids, in which the prevalence was higher, followed by the Chios and Chios hybrid sheep. Awassi, Kivircik and Pirit breeds and hybrids were not found to be different. Apart from the breeds and their hybrids mentioned above, data were not sufficient to perform a chi-square test, and thus the differences could not be evaluated. Nevertheless, when these breeds were calculated collectively as other breeds, their susceptibility was found to be lower than the chi-square test ($P < 0.005$) (Table 6). The Tahirova breed sheep (75% Eastern Frisian+25% Kivircik) were not found to be positive for antibodies. In goats, the Saanen and Saanen hybrids were found to be more

Table 4. Epizootiological parameters of the study

Epizootiological Parameters	Goats	Sheep	Sheep and Goats*
Prevalence (%)	6.55	24.42	18.64
Prevalence (%) at 95%CI	1.59–11.52	17.94–30.90	13.64–23.64
Standard Deviation (%)	2.44	3.25	2.52
Design Effect	5.79	7.11	7.68
Homogeniety	0.287	0.326	0.350

*Significant differences were found in goat and sheep populations by Chi-Square test ($P < 0.0001$)

Table 3. MVV/CAEV prevalence according to provinces

Provinces	Goats				Sheep				General Total	General (%)
	Negative	Positive	Total	Positive (%)	Negative	Positive	Total	Positive(%)		
Aydın	111	10	121	8.26	134	5	139	3.60	260	5.77
Denizli	57	10	67	14.93	178	75	253	29.64	320	26.56
İzmir	79	14	93	15.05	188	19	207	9.18	300	11.00
Kütahya	42	1	43	2.33	126	111	237	46.84	280	40.00
Manisa	20	0	20	0.00	110	10	120	8.33	140	7.14
Muğla	247	4	251	1.59	60	9	69	13.04	320	4.06
Uşak	0	0	0	0.00	145	75	220	34.09	220	34.09
Total	**556**	**39**	**595**	**6.55**	**941**	**304**	**1,245**	**24.42**	**1,840**	**18.64**

Table 5. Prevalence of seropositivity to MVV/CAEV according to breeds

Species	Breed	Negative	Positive	Number of sampled animal	Positivity (%)
Sheep	Cine capari	4	1	5	20.00
	Daglic	18	2	20	10.00
	Esme hybrid	1	2	3	66.67
	Awassi	22	1	23	4.35
	Awassi hybrid	5	9	14	64.29
	Karya	32	3	35	8.57
	Kivircik	152	13	165	7.88
	Kivircik hybrid	199	60	259	23.17
	Merino hybrid	21	3	24	12.50
	Pirit	7	7	14	50.00
	Pirit hybrid	18	3	21	14.29
	Pirlak	250	122	372	32.80
	Pirlak hybrid	31	26	57	45.61
	Chios	74	24	98	24.49
	Chios hybrid	70	28	98	28.57
	Tahirova	13	0	13	0.00
	Tahirova hybrid	24	0	24	0.00
	Total	**941**	**304**	**1,245**	**24.42**
Goat	Kilis	2	0	2	0.00
	Malta	8	0	8	0.00
	Malta hybrid	7	0	7	0.00
	Kil	408	15	423	3.55
	Saanen	102	24	126	19.05
	Saanen hybrid	29	0	29	0.00
	Total	**556**	**39**	**595**	**6.55**

Table 6. Prevalence of seropositivity to MVV/CAEV according to sheep breeds*

Breed	Negative	Positive
Pirlak and pirlak hybrids	281	148
Kivircik and kivircik hybrids	351	73
Other breeds	309	83
Total	**941**	**304**

*Significant differences were found in breed by Chi-Square test ($P < 0.005$)

susceptible than the Kil, Kilis and Malta breeds at a 95% CI. The Kilis, Malta and hybrids were negative for MVV/CAEV antibodies.

Age-related prevalence

When the MVV/CAEV positivity in sheep and goat species were evaluated, animals older than 49 months were found to be high positive than the other age groups, with the chi-square test at a 95% CI ($P < 0.05$). However, no statistically significant difference was found between the age groups of 0–24 and 25–48 months (Table 7).

Table 7. Prevalence of seropositivity to MVV/CAEV according to age groups*

Age groups (months)	Negative	Positive	Total	Positivity within the same age group (%)	Positivity in total (%)
0–24	327	54	381	14.17	2.93
25–48	603	93	696	13.36	5.05
49–108	567	196	763	25.69	10.65
Total	**1,497**	**343**	**1,840**		

*Significant differences were found in age groups by Chi-Square test ($P < 0.05$)

DISCUSSION

Prevalence

Serological and molecular studies on SRLVs have been carried out in Türkiye and around the world, and thus different prevalence values have been reported several times. MVV prevalence in sheep was found to be varying from 9 to 40.7% in different countries (Bouljihad and Leipold, 1994; Cuttlip et al., 1992; Honger et al., 1990; Hüttner, 2010; Kita et al., 1990; Lago et al., 2012; Lujan et al., 1993; Olech et al., 2017; Schaller et al., 2000; Simard and Morley, 1991). MVV prevalence in Türkiye's neighbouring countries including Syria, Iran, Irak, Greece and Bulgaria has been found to range between 2.5 and 65% (Bizaki et al., 1993; Giangaspero et al., 1993; Hamza and Özkan, 2017; Masalski et al., 1999; Minas et al., 1994; Norouzi et al., 2015). Many serological studies on MVV have reported seropositivity rates of 0–51% (Albayrak et al., 2012; Alkan and Tan, 1998; Ameen and Karapınar, 2018; Arık et al., 2015; Aslantaş et al., 2002; Azkur et al., 2011; Burgu et al., 1990; Çimtay et al., 2004; Karaoğlu et al., 2003; Muz et al., 2013; Tan and Alkan, 2002; Preziuso et al., 2010; Ün et al., 2018; Yaman et al., 2019; Yıldırım et al., 2011; Yilmaz et al., 1998, 2002; Yavru et al., 2012). Burgu et al. (1990) and Tan and Alkan (2002) have found high prevalence in certain farms and have emphasised that importing sheep from enzootic countries could be an important risk factor. In the present study, the mean seroprevalence of SRLVs in sheep was found to be 24.42%. Seropositivity was obtained at a rate of 3.6% in Aydın, 8.33% in Manisa, 9.18% in İzmir, 13.04% in Muğla, 29.64% in Denizli, 34.09% in Uşak and 46.84% in Kütahya. Different results were obtained in different regions, according to the different animal breeds and breeding conditions. Therefore, it is difficult to compare our results with those from previous studies. CAEV infects goats to a great extent and shows a broad geographical variation in prevalence. CAEV prevalence has been determined to be varying from 0.4 to 82% in different countries (Al-Qudah et al., 2006; Cutlip et al., 1992; Dawson and Wilesmith, 1985; Garcia et al., 1992; Grewal et al., 1986; Krieg and Peterhans, 1990; Nord et al., 1998; Tariba et al., 2017; Torres-Acosta et al., 2003). CAEV prevalence in countries neighbouring Türkiye, including Syria, Iran, Greece and Bulgaria has been found to vary from

2.7 to 65% (Karanikolaou et al., 2005; Giangaspero et al., 1993; Masalski, 2000; Moazed et al., 2018; Sakhaee et al., 2011). In Türkiye, prevalence of CAEV has been reported to be from 1 to 13% (Aslantaş et al., 2005; Azkur et al., 2011; Burgu et al., 1994; Çimtay et al., 2004; Duman et al., 2014; Yapıcı et al., 2013; Yavru et al., 2002). In our study, seroprevalence to CAEV in goats was found to be 6.56%. CAEV prevalence on a province-by-province basis was 1.59% in Muğla, 2.3% in Kütahya, 8.26% in Aydın, 14.93% in Denizli and 15.05% in İzmir. No seropositivity was detected in Manisa. With regard to the findings, prevalence increases in provinces where intensive livestock breeding is practiced.

Breed-related prevalence

Many studies have discussed the prevalence of SRLVs of varying ages and breeds. Serological studies have revealed that some sheep breeds show different susceptibilities to MV infection (Cutlip et al., 1986; Houwers et al., 1989). Previous serological studies in Türkiye have shown that Awassi, Chios, Daglic, Kivircik and Merino breeds have higher prevalence varying from 32.5% to 64.7 (Aslantaş et al., 2002; Burgu et al., 1990; Çimtay et al., 2004; Karaoğlu et al., 2003; Muz et al., 2013; Preziuso et al., 2010; Tan and Alkan, 2002; Yaman et al., 2019; Yavru et al., 2012; Yilmaz et al., 2002). In the present study, MVV susceptibility was higher ($P < 0.05$) in Pirlak sheep, and its crossbreeds had a higher prevalence (34.49%). The next susceptible breed was Chios sheep and its crossbreeds (26.53%). However, no difference was found between Awasi, Kivircik and Pirit and their crossbreeds in terms of susceptibility. Türkiye consists of seven geographical region and different breeds of sheep are reared in each. For example, Morkaraman breed is reared in east, while Kivircik and Merino breeds are reared in west of Türkiye. For this reason, comparisons regarding previous studies could have been made only for the breeds localised in the Aegean region. Researchers have obtained different CAEV prevalence varying from 0.98 to 4.94 in different breeds (Çimtay et al., 2004; Duman et al., 2014; Gümüşova and Memiş, 2016; Yapıcı et al., 2013). In the present study, Saanen and its crossbreeds were more susceptible than the Kil + Kilis + Malta breeds ($P < 0.05$). However, no MVV/CAEV antibodies were detected in Kilis and Malta and their crossbreeds. On the other hand, the seropositivity of Saanen breeds was found at least 7 times higher than in previous studies. This situation could be explained by the differences of sampling frames.

Age-related prevalence

A significant positive relationship was found between lentivirus infections and age. Perrin and Polack (1987) have calculated the CAEV prevalence to be 45% in goats of one year of age and 83% in goats of five years of age in France. Palfi and Forgach (1991) have reported the MVV seroprevalence to be 6% in sheep younger than two years of age, 15% in sheep three years of age and 80% in sheep eight years of age in Hungary. Kita et al. (1990) have found an MVV seroprevalence of 7% in sheep younger than one year of age and 52% in sheep older than five years in Poland. In the Sanilurfa region of Türkiye, Çimtay et al. (2004) have found no seropositivity in sheep and goats younger than one year of age and determined that both CAE and MV infections showed an increase depending on age. They have reported MVV seropositivity of 7.7%, 9.2% and 13.8% in sheep, and 5.6%, 6.4% and 7.9% in goats, for age groups of 2–3, 4–5 and 6–7 years, respectively. Preziuso et al. (2010) have found that sheep older than one year of age are five-fold more susceptible than those younger than one year. Muz et al. (2013) have also reported that MVV prevalence increased by age in sheep. In the present study, MVV antibody was found in one sheep aged 0–12 months, and no CAEV antibody was found in goats aged 0–12 months. When the data were assessed, consistent with previous studies, sheep and goats older than 48 months were found to show higher seroprevalence of SRLVs than the other age groups ($P < 0.05$). This might be associated with age-related positivity due to persistent infection. However, no statistically significant difference was found in animals between 0–24 and 25–48 months of age.

Here we report our results on the study of seropositivity of lentiviruses in sheep and goats by comparing the prevalence on the basis of age and breed. Obviously, other factors including host (stress, coinfections and mutations in genes playing role in immune responses) and pathogen (virulence genes, strain differences) that also significantly influence susceptibility should not be ignored.

In conclusion, MV/CAE infections continuously circulate within herds because of their lifelong persistent characteristics. Infected animals that do not show clinical signs are the major source in the spread of the infection across herds, regions and countries. Most of the previous studies aiming to determine MVV/CAEV prevalence in Türkiye, have been limited to a smaller region or population, and epizootiological approaches were not used in the sampling strategy. Moreover, the age and breed of the sampled animals have not been reported in these studies. The fact that our study represents all the provinces in one region in terms of sampling design, that the number of villages to be sampled was determined by a multi-stage cluster sampling method, and that the number of animals to be sampled in each village was determined in consideration of the estimated prevalence/population size, make it an original approach. Additionally, the calculation of prevalence based on province, breed and age allows identification of risk groups and facilitates the control and eventual eradication of SRLVs.

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