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Serological evidence of Maedi-Visna and Caprine Arthritis Encephalitis in sheep and goats in the Korça region in Albania

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Abstract

Lentiviruses infect small ruminants and cause similar but different two significant diseases: Maedi-Visna in sheep and Caprine Arthritis Encephalitis in goats. In the current study, 91 of 413 adult sheep and goats from the Korça region tested positive for small ruminant lentiviruses. Furthermore, 11 of the 25 small ruminant herds have at least one positive animal for small ruminant lentiviruses. The overall observed herd prevalence was 44.0% (95% Confidence Interval (CI): 29–59) for both diseases, 38.6% (95% CI: 18.6-55.1) for Maedi-Visna in sheep, and 66.7% (95% CI: 43.1-90.2) for Caprine Arthritis Encephalitis in goats. The average observed prevalence rate ranges from 20% to 82.9% (95% CI: 12–89.2) within positive goat's herds, while within sheep-positive herds, it varies from 23.1% to 57.1% (95% CI: 11.7–70.4). There was a positive correlation between seroprevalence rate and animal species; goats seem to have an odd 2.36 (Odds Ratio (OR) 95% CI: 1.48-3.76) higher than sheep to test positive in ELISA. Other risk factors, such as farm size, indoor versus outdoor rearing, and close farm biosecurity, may play a role in disease transmission between and within small ruminant animals' herds. This is the first study on the prevalence of Maedi-Visna infection in sheep and one of the few published Caprine Arthritis Encephalitis studies in Albania. These findings support the presence of Small Ruminant Lentiviruses (SRLV) in the Korça district and emphasize the need for monitoring and controlling SRLV infection in sheep and goats. According to the study's conclusions, a yearly monitoring program is essential and must be developed in the future to keep the disease under control. This initiative aims to help owners understand SRLV and the need to raise seronegative animals.

Keywords: Lentiviruses, Maedi–Visna, Caprine Arthritis Encephalitis, Small ruminant, Seroprevalence, Risk factors

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Introduction

Small Ruminant Lentiviruses (SRLV) are a group of RNA viruses associated with the occurrence of two economically important diseases, Maedi-Visna (MV) in sheep and Caprine Arthritis Encephalitis (CAE) in goats (Peterhans et al., 2004; de Miguel et al., 2021). The main target cells for the SRLV are monocyte/macrophage lineage (Narayan et al., 1983), and the infected animals develop a lifelong persistent infection. Gross pathological lesions are usually located on the mammary gland, lungs, joints, and the neurological system, resulting in a variety of clinical symptoms, including a decrease in milk production, weight loss, indurative mastitis, progressive interstitial pneumonia, arthritis, and hind-limb paralysis (Minguijón et al., 2015; de Miguel et al., 2021). However, only a small percentage of affected animals developed clinical symptoms, and most infected animals go undetected in the flock (de Andrés et al., 2005; Herrmann-Hoesing, 2010; de Andrés et al., 2013).

Horizontal transmission from animal to animal nearby is reported to be the most important mode of transmission; however, colostrum and milk are the second most important routes of transmission, while in utero, iatrogenic and semen may also play a role in disease transmission (Alvarez et al., 2005; Lacerenza et al., 2006). Several risk factors have contributed to disease transmission, including demographic characteristics (flock size, animal age, and rate of replacement) and breeding management system (intense versus semi-intensive or extensive management, management of newly born animals) (Kaba et al., 2013; Junkuszew et al., 2016; Thomann et al., 2017; Michiels et al., 2018; Pavlak et al., 2022). SRLV are classified into five main genotypes (A-E), each containing multiple subgroups. This evolutionary diversity indicates a high genetic and antigenic variation, challenging serological and molecular diagnosis (Ramírez et al., 2013; Minguijón et al., 2015).

Serological assays such as the agar gel immunodiffusion test (AGID) and the western blot have been used historically to detect specific antibodies against SRLV. However, nowadays, enzyme-linked immunosorbent assay (ELISA) is the most widely used serological assay. Throughout the last two decades, molecular diagnostic assays, such as the polymerase chain reaction (PCR) and sequencing, have been employed to detect the virus and to study its genetic characteristics and variabilities (Pavlak et al., 2022; Lacerenza et al., 2006). There are no effective vaccines or therapies against SRLV infections; thus, culling seropositive animals remains the main method for disease control in affected flocks. However, other measures, such as separation of the lambs/kids from the infected ewes/does, may also be effective in preventing the virus spread (Lacerenza et al., 2006; Ghanem et al., 2009; Kalogianni et al., 2020; de Miguel et al., 2021; Pavlak et al., 2022).

Small ruminants are of essential importance for the livestock sector in Albania, contributing significantly to overall general domestic production, farmer income, and family employment. Based on the author's experience and expert opinions, SRLV circulates throughout small ruminant animals. However, no published data are available. This study aims to detect the presence of SRLV in the sheep and goat population on the territory of the Korça region in Albania. In addition, we assessed the between-herd and within-herd seroprevalence and the seroprevalence on a species level and evaluated the role of limited potential risk factors.

Material and methods

The study area and sample collection

Korça County is one of Albania's 12 counties and covers an area of 3,711 km^2. Devolli, Kolonja, Korça, and Pogradec are all part of the Korça district. Macedonia borders Korça County from the northeast and east, while Greece is located to the south. It is the fifth most populous district in the country, with a population of 258,100 individuals. The region is known for its significant role in small ruminant farming and ranks second in the country in terms of the number of sheep and goats combined, with around 334,000 heads (16% of the national herd of small animals). Of this total, 244,000 are woolly sheep, while 90,000 are goats (INSTAT, 2023).

Twenty-five flocks (19 sheep and six goat flocks) located on the territory of the Korça region (http://www.maplandia.com/albania/korce/korce/) were randomly selected for this study. 413 blood samples from randomly selected adult sheep and goats (age > two years) were collected in 9 mL plane test tubes. The sera were harvested after centrifugation at 3000 rpm for 5 minutes and kept at -20°C until the analysis.

Enzyme-linked Immunosorbent Assay (ELISA)

To detect specific SRLV antibodies, a commercially available Indirect ELISA (iELISA) kit, ID Screen® MVV/CAEV (ID.VET, France), was used per the manufacturer's instructions. The optical density (OD) was read at 450 nm on a "TECAN" ELISA plate reader (Tecan Austria GmbH ("Tecan") 5082 Grödig, Austria). The S/P value was determined using the formula: S/P% = (OD sample- ODNC) / (ODPC - ODNC)*100%, and the S/P value <110% was judged positive, the S/P value at range 110-120% doubtful, while the S/P > 120, negative. A flock was considered positive if antibodies against SRLV had been determined in at least one animal. The observed and true prevalence was calculated based on test sensitivity and specificity.

Statistical analysis

Statulator and Epitools, online statistical applications, and Excel Tool Data analysis were used to analyze the results. A Chi-square test was conducted to investigate the association between animal species and the possibility of being seropositive to SRLV (Agresti, 2012). The odds ratio and its 95% confidence limits were calculated to measure the magnitude of the association. A 5% significance level was used to evaluate the significance of the association (the p-value was considered significant if it was less than 0.05). Analysis was performed using the "Statulator", an online statistical program (Dhand and Khatkar, 2014). The chi-squared test for contingency was used to estimate the significance of the within-herds prevalence. p-value < 0.05 was considered significant. Analysis was performed using Epitools, a free online statistical tool (https://epitools.ausvet.com.au/).

Results

Serum samples from 413 animals collected from 25 sheep and goat flocks in the Korça region were tested for the presence of specific antibodies against SRLV using the iELISA method. Of 413 tested animals, 91 were found positive, corresponding to an overall seroprevalence of 22%. Seropositive animals were found in 11 out of 25 flocks included in the study, giving an overall between-herd prevalence of 44%. Seven out of 19 sheep flocks (36.8%) were positive for specific antibodies against SRLV, while four out of six goat flocks (66.7%) tested positive (Tables 1-2). Sero-prevalence in sheep was lower than in goats, between and within herds (Figures 1-2).

In sheep, 35 of the 246 tested animals were positive, resulting in a 14.2% frequency. At least one seropositive animal was found in 7 of the 19 sheep flocks, resulting in a 36.8% between-herd frequency. Within-herd prevalence varied significantly (p-value <0.0001) in the positive sheep flocks, ranging from 23.1% to 57.1% (Table 1). In goats, 56 of the 167 animals tested were found positive for SRLV antibodies, corresponding to a prevalence of 33.5% (Table 2).

Table 1: The serological results in the tested 19 sheep herds based on iELISA test results.

Sheep	Herd size	No. of tested animals	No. of positive	Prevalence%
Herd 1	500	14	8	57.1
Herd 2	280	13	5	38.5
Herd 3	250	13	0	0.0
Herd 4	180	13	0	0.0
Herd 5	210	13	0	0.0
Herd 6	230	13	3	23.1
Herd 7	17	12	0	0.0
Herd 8	110	13	0	0.0
Herd 9	200	13	6	46.2
Herd 10	120	13	4	30.8
Herd 11	110	13	0	0.0
Herd 12	120	13	0	0.0
Herd 13	100	13	0	0.0
Herd 14	140	13	4	30.8
Herd 15	125	13	0	0.0
Herd 16	110	13	0	0.0
Herd 17	60	12	0	0.0
Herd 18	120	13	0	0.0
Herd 19	170	13	5	38.5
Total		**246**	**35**	**14.2**

Table 2: The serological results in the tested six goat herds based on iELISA test results .

Sheep	Herd size	No. of tested animals	No. of positive	Prevalence%
Herd 1	56	20	0	0.0
Herd 2	91	35	29	82.9
Herd 3	205	37	15	40.5
Herd 4	77	25	7	28.0
Herd 5	87	25	0	0.0
Herd 6	114	25	5	20.0
Total		**167**	**56**	**33.5**

Table 3: Observed and true herd seroprevalence of Small Ruminant Lentiviruses and 95% confidence interval limits.

Animal species	Observed prevalence	Lower 95% CI	Upper 95% CI	True prevalence
Sheep herds	36.8	18.6	55.1	40.6
Goat herds	66.7	43.1	90.2	72.5
Total	**44.0**	**29.0**	**59.0**	**48.6**

Table 4: Observed and true herd seroprevalence of Caprine Arthritis Encephalitis in goats and 95% confidence interval limits.

Positive goat herds	Observed herd prevalence	Lower 95% CI	Upper 95% CI	True prevalence
Herd 2	82.9	76.5	89.2	91.5
Herd 3	40.5	32.5	48.6	44.6
Herd 4	28.0	19.0	37.0	29.8
Herd 6	20.0	12.0	28.0	21.0

Table 5: Observed and true herd seroprevalence of Maedi-Visna in sheep and 95% confidence interval limits.

Positive sheep herds	Observed herd prevalence	Lower 95% CI	Upper 95% CI	True prevalence
Herd 1	57.1	13.2	70.4	63.0
Herd 2	38.5	13.5	52.0	42.4
Herd 6	23.1	11.7	34.8	24.4
Herd 9	46.2	13.8	60.0	49.9
Herd 10	30.8	12.8	43.6	32.9
Herd 14	30.8	12.8	43.6	32.9
Herd 19	38.5	13.5	52.0	41.4

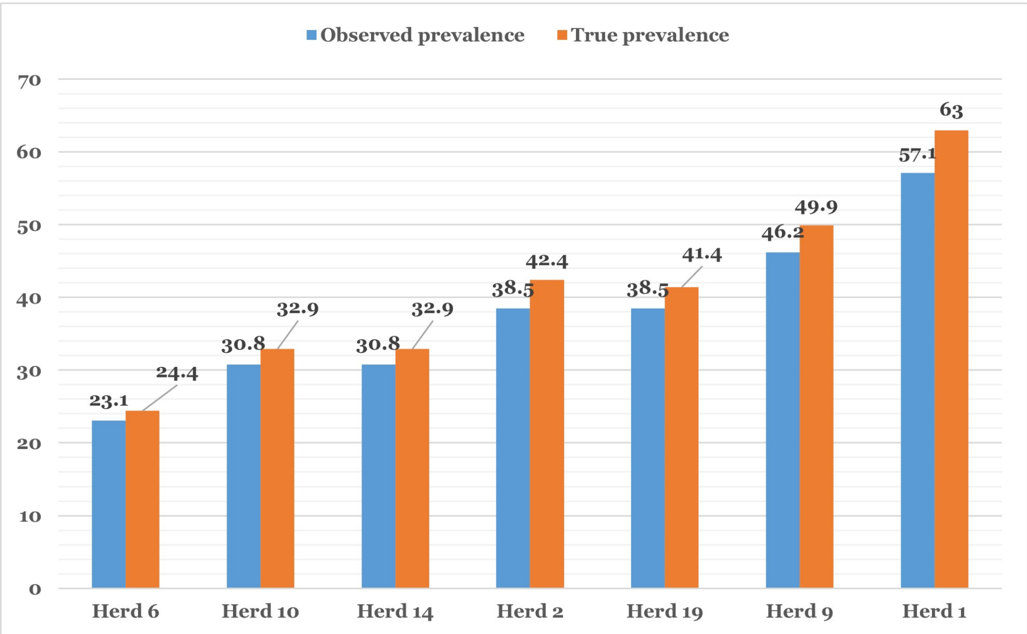

Figure 1: Prevalence of Maedi–Visna (MV) within sheep herds based on iELISA test results.

A chi-square test of independence showed a significant association between the species and the prevalence of SRLV, with goats having 3.04 (Cl 95%: 1.88-4.92) times the odds of a positive result than sheep, X^2 (1, N = 413) = 20.47, p <0.0001. A higher between-herd prevalence of 66.7% (4 out of 6) was observed in goats compared to sheep. Like sheep herds, the within-herd prevalence in seropositive goat flocks showed significant variations (p-value < 0.0001), ranging from 20% to 82.9%. The observed and true herd seroprevalence of SRL in sheep and goats is shown in Table 3.

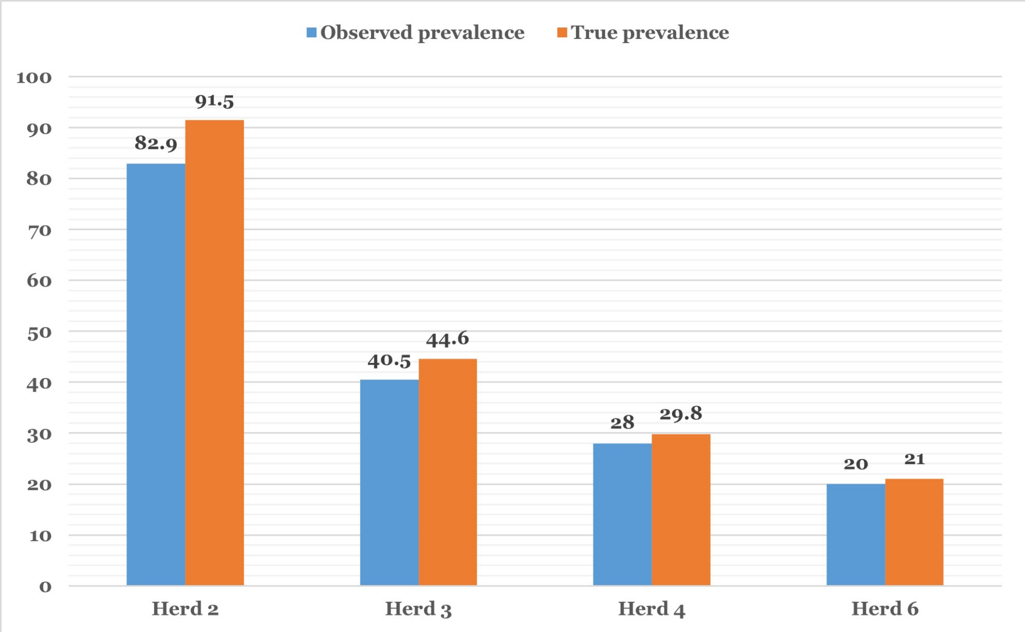

Figure 2: Prevalence of Caprine Arthritis Encephalitis (CAE) within goat herds based on iELISA test results.

The within-herd seroprevalence varies from 0-82.9%. Herd number two has the highest prevalence compared to other positive goat farms; it is managed indoors, while the others have a mixed management system (indoor and outdoor). The prevalence within positive sheep herds varies from 23.1% to 57.1%. No test is ideal (sensitivity and specificity 100%); the true prevalence was calculated based on a formula as follows: True prevalence = (Observed prevalence + Sp - 1)/(Se + Sp - 1). IDvet ELISA test is reported to have a sensitivity and specificity of 91.7% and 98.9%, respectively, according to Nowicka et al. (2014).

In each sheep flock, an average of 13 blood samples were collected. The distribution of flocks was as follows: 12 herds (63.15%) did not have any positive animal; one herd (5.26%) had less than 30% positive of tested animals; five herds (26.30%) had between 30 and 50% of positive animals; one herd (5.26%) had 50 and 90% of positive animals. From 413 collected samples, 91 showed positive results in the diagnostic test. The observed individual prevalence was 22% (95% CI: 18.11–25.95), while the herd prevalence was 44.26% (CI 95%: 42.36–46.15). By species, 56 goats (33.5%) and 35 sheep (14.2%) were positive. The observed and true herd seroprevalence of SRL in sheep and goats, CAE in goats, and MV in sheep herds are shown in Tables 3-5.

Discussion

Sheep and goat breeding is vital in Albania's agricultural sector, contributing significantly to its economy. However, no studies have been conducted to assess the prevalence of Small Ruminant Lentivirus (SRLV) in the country, nor have any programs been implemented to control or eradicate the disease. This study reports, for the first time, the presence and the prevalence of SRLV infection in sheep (MV) and goats (CAE) in the territory of the Korça region. Considering the sensitivity (91.70%) and specificity (98.90%) of the diagnostic test used, the true herd prevalence in this region was 48.6% (95% CI: 42.3–54.9). The observed herd prevalence was 44% (95% CI: 29.0–59.0). The prevalence was higher in goat herds, 66.7% (95% CI: 43.1–90.2) than in sheep's herds, 36.8% (95% CI: 18.2–55.1). Except for New Zealand and Australia, SRLV infection is ubiquitous worldwide. Few countries, for example, Island, achieved disease-free status after long and vigorous eradication campaigns.

The high seroprevalence is reported in Finland, Greece, Italy, and Spain, where the reported prevalence at herd level was 97% in the northeast of Spain (Luján et al., 1993), 71.4% in Italy (Salvatori et al., 2002), and 77% in Finland (Sihvonen et al., 1999). In Kosovo, the MV individual prevalence in sheep was 35%, and the flock prevalence was 85%, with a 40% within average flock prevalence for sheep, while in goats, the overall individual prevalence was 15%, and the flock prevalence was 35%, with a 29% within flock prevalence for goats (Cana et al., 2019). In North Macedonia, the seroprevalence of Maedi-Visna is reported at 60.3%, while CAEV seroprevalence was 55.8% (Dine et al., 2009).

Considering the sensitivity (91.70%) and specificity (98.90%) of the diagnostic test used, the true herd prevalence in this region was 48.6% (95% CI: 42.3–54.9). In the USA, the disease is known as ovine progressive pneumonia (OPP), and the herd prevalence was reported to be 48% (Cutlip et al., 1992), while in Canada, the herd prevalence was estimated to be 19% (Simard and Morley, 1991). Based on our study data, the individual mean prevalence was 22% (95% CI: 18.11–25.95). It is higher in goats, 33.5% (95% CI: 29.9–37.2) than in sheep, 14.2% (95% CI: 12.0–16.5) (Tables 3-5 and Figures 1-2). Based on test sensitivity and specificity, the true prevalence was higher than the observed prevalence (Tables 3-5).

Some studies found a similar incidence in goat flocks, whereas others found a lower prevalence, particularly for individual prevalence. In Croatia, the apparent seroprevalence was reported at 10% (Pavlak et al., 2022). SRLV infection is common in many developed countries; however, countries with mandatory national control programs (such as Switzerland) have controlled the infections, and the prevalence of both MVV and SRLV is relatively low (3.04%) (Thomann et al., 2017). Albania has never implemented an official program to control either Maedi-Visna or Caprine Arthritis Encephalitis. Despite the global significance of small ruminants, research on the prevalence of SRLV is sporadic and inconsistent. No gold-standard diagnostic tests are available, and serological tests are the most widely used.

It's important to note that testing positive for a virus doesn't always mean that an animal will show signs of the disease. Similarly, just because an animal tests negative doesn't necessarily mean it's free of infection. For instance, in some cases, such as early-infected animals, e.g., lambs infected by colostrum ingestion, animals may not test positive, as seroconversion can take months after being infected. Additionally, the effectiveness of

ELISA tests in diagnosing SRLV strains can be limited due to the SRLV antigenic variability.

We have analyzed several risk factors, including animal species, flock size, management system, and external biosecurity (if the animal species are managed in closed or open herds). Albanian sheep and goat farming is mostly semi-extensive, where animals graze during the day and are collected at night in stables or high-density fences. Traditional rearing methods are widely used, and management practices are consistent nationwide. A species analysis revealed a link between SRLV infection and the species. Goat flocks had a higher probability of infection than sheep herds. There was a significant association between the animal species and positive test results (<0.0001), with goats having 2.36 times the odds of testing positive than sheep (odds ratio 95% CI: 1.48-3.76). In Croatia, Pavlak and colleagues identified location and animal breed as the main risk factors (Pavlak et al., 2022). We did not investigate the age risk factor because the inclusion criteria for tested animals required all sampled animals to be older than two years old. This was based on the best author's knowledge and the findings of other studies, which discovered that animals over two years old had a substantially higher risk of being seroconverted and were more than twice as likely to be infected. This could be due to lifetime exposure to the pathogen, which can determine the infection of animals who have never been infected. It is also reported that the condition's late seroconversion can influence laboratory positives and delay diagnosis. The last outbreaks in Norwegian sheep herds indicate a need to use strategic serological tests and develop new methods to detect all affected herds and individuals (Jerre et al., 2023).

Flock size appears to be statistically related to SRLV infection. The average farm size of a positive goat and sheep herd was 121.8 milking goats and 234.3 milking sheep, while negative farms were 71.5 and 126 milking goats and sheep, respectively. These findings have been reported in several different epidemiological investigations (Ghanem et al., 2009; Herrmann-Hoesing, 2010; Lago et al., 2012; Kaba et al., 2013; Junkuszew et al., 2016; Illius et al., 2020). Both risk variables are identified in the literature as having a significant impact on SRLV infection (Leginagoikoa et al., 2006). Commonly, larger flocks are also produced more intensively, with greater population density, facilitating the transmission of the virus between animals (Leginagoikoa et al., 2006; Junkuszew et al., 2016). According to the literature, SRLVs infect mixed sheep and goat flocks more commonly than single-species flocks (Ghanem et al., 2009; Lago et al., 2012).

In this investigation, contact between various small ruminant flocks was not investigated. Despite this, we know that it can play a significant role in the spread of various diseases, including SRLVs (Ghanem et al., 2009). Flocks in the study areas are grassing in common pastures and spending the night in a stable, posing an infection risk (Junkuszew et al., 2016). Purchasing animals from other flocks may also expose the flock to disease transmission (Thomann et al., 2017). One goat herd (Herd No. 2) was handled indoors, and the prevalence of CAE was highest (82.9%), suggesting that an indoor-rearing approach may increase CAE virus transmission. This is consistent with earlier data; for example, the overall seropositive rate of CAE in goats in Taiwan was 61.7%, with 98.5% of goat farms testing positive (Yang et al., 2017).

Natural feeding management was found to be substantially related to SRLV infection. Lambs and goat kids, which ingest colostrum and milk from positive animals, are among the common transmission routes, as reported in other studies (Alvarez et al., 2005). No measures in place in the study herds interfere with SRLV transmission (colostrum pasteurization, colostrum replacement, etc.).

In conclusion, our preliminary investigation shows that both MVV and CAEV are present in the Korça region. The positive rate is moderate to high, and large-scale testing is required to assess the prevalence and develop conclusions based on scientific evidence; for a better understanding of the SRLV variations in this region and country, molecular and phylogenetic investigations are required.

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Authors contribution. TRP study conception and design, sampling and data collection: EO data collection, manuscript preparation: ID manuscript editing, statistical data analyses; AK laboratory test performing, data collection, SÇ laboratory test performing and data collection, KM and VV sample and data collection, XhK draft manuscript preparation, interpretation of results, statistical analyses: All authors reviewed the results and approved the final version of the manuscript.

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