Small Ruminant Research 111 (2013) 16–22

Contents lists available at SciVerse ScienceDirect

Small Ruminant Research

journal homepage: www.elsevier.com/locate/smallrumres

Genetic risk assessment for atypical scrapie in Turkish native sheep breeds

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ARTICLE INFO

Article history:
Received 5 March 2012
Received in revised form 29 August 2012
Accepted 29 August 2012
Available online 5 October 2012

Keywords:
Atypical scrapie
Genetic risk
PRNP gene
Turkish native sheep breeds

ABSTRACT

Scrapie, a fatal transmissible spongiform encephalopathy (TSE), occurs in two phenotypes; classical and atypical. The aim of this study was to assess the genetic risk and identify the PRNP polymorphisms for atypical scrapie in a total of 1110 healthy sheep from 18 Turkish native sheep breeds. There were 10 alleles and 23 genotypes observed based on codons 136, 141, 154 and 171 of PRNP gene. The ALRQ allele was predominant for all breeds. The AFRQ allele, associated with the susceptibility to atypical scrapie, was detected in only İvesi. The other susceptible allele, ALHQ, was found at low frequencies in Akkaraman, Kangal Akkaraman, Güneykaraman, Kıvırcık, Sakız, Dağlıç and Gökçeada breeds. Generally, the ALRQ/ALRQ genotype, which is resistant to atypical scrapie, was predominant in all breeds. Among the most susceptible genotypes to atypical scrapie, only ALHQ/ALHQ was found in this study. In addition, the ARR/ARR genotype, which has been reported in lots of atypical scrapie positive sheep from various countries, was detected in almost all Turkish native sheep breeds. According to our results, it is propounded that the susceptibility to atypical scrapie increased from eastern to western part of Turkey. Although it seems that Turkish native sheep breeds are safe from atypical scrapie, the occurrence of susceptible genotypes should be taken into consideration.

1. Introduction

Scrapie is a fatal nervous disease that affects small ruminants and is the prototype of transmissible spongiform encephalopathies (TSEs) or prion diseases. It is characterized by the accumulation of an abnormal, protease-resistant isoform (PrP^{Sc}) of the cellular prion protein (PrP^{C}) in some tissues of infected animals (Prusiner, 1998). In sheep, susceptibility to classical scrapie has been largely proven to be controlled by polymorphisms of the PRNP gene at codons 136, 154 and 171. Sheep with VRQ were highly susceptible to classical scrapie and had a short survival period after challenge with scrapie; whereas sheep with ARR were resistant to classical scrapie under field and laboratory conditions (Hunter, 1997; Goldmann, 2008).

In 1998, a new type of scrapie called scrapie Nor98 was detected in Norway and has become known as Nor98, Nor98-like or atypical scrapie (Benestad et al., 2003). After this time, atypical scrapie cases have been diagnosed not only in several European countries including Germany, France, Belgium, Sweden, Ireland, Portugal, Great Britain, Switzerland, Poland and Italy (Buschmann et al., 2004; De Bosschere et al., 2004; Gavier-Widén et al., 2004; Onnasch et al., 2004; Orge et al., 2004; Everest et al., 2006; Saunders et al., 2006; Lühken et al., 2007; Mazza et al., 2010), but also in USA (Loiacono et al., 2009), the Falkland Islands (Epstein et al., 2005), Canada (Mitchell et al., 2010) and New Zealand (Kittelberger et al., 2010). Atypical scrapie cases differ from classical scrapie in several features, including the neuroanatomical distribution of the histopathological lesions and of PrP^{Sc} in the brain, and the pattern of PrP^{Sc} deposits (Benestad et al., 2003). In 2005, the European

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http://dx.doi.org/10.1016/j.smallrumres.2012.08.013

Food Safety Authority (EFSA) defined diagnostic criteria for classical scrapie and atypical scrapie, based on the results of Western blot pattern of the pathogenic prion protein, histopathology, immunohistochemistry, age and epidemiology (EFSA, 2005).

As a contagious disease, classical scrapie is often clustered within flocks and regions. Infected animals usually die at the end of the clinical course of the disease when they are between two and four years of age. In contrast to classical scrapie, atypical scrapie is usually detected in older (5 to >10 years of age) animals (Benestad et al., 2008; Fediaevsky et al., 2010a). While sheep carrying PrP genotypes with VRQ and/or ARQ alleles are considered most susceptible to classical scrapie (Hunter, 2007), PrP genotypes that include alleles AHQ and/or AFRQ are more susceptible to atypical scrapie (Benestad et al., 2003; Moum et al., 2005; Arsac et al., 2007; Moreno et al., 2007; Fediaevsky et al., 2010b).

One of the first full descriptions of the PrP genetics for atypical scrapie was provided by Moum et al. (2005). Performing four codon genotyping (codons 136, 141, 154, and 171) on 38 cases of atypical scrapie, they came to three major conclusions. Firstly, all animals were of AA_{136} PrP genotype. The VRQ allele conferring susceptibility to classical scrapie was completely absent from Nor98 cases. Secondly, there was an over-representation of animals carrying the AHQ allele, in HH_{154} homozygous and HR_{154} heterozygous genotypes. Thirdly, the $AF_{141}RQ$ allele appeared to confer higher susceptibility to atypical scrapie than the $AL_{141}RQ$ allele. Indeed, the $AF_{141}RQ$ allele conferred a higher risk than the AHQ allele.

A case–control study was designed to study risk factors of atypical scrapie in France (Fediaevsky et al., 2009). According to this study, PrP genotypes were linearly classified by levels of genetic risk for atypical scrapie as five different groups. Group 1 was thought to be most resistant to atypical scrapie whereas group 5 was thought to be most susceptible. Fediaevsky et al. (2009) revealed that they did not find any risk factor associated with an infectious origin of scrapie and atypical scrapie could be a spontaneous disease influenced by genetic and metabolic factors.

The results of another case–control study in France demonstrated that there were no atypical scrapie cases among the ALRR/VLRQ, ALRQ/ALRH, ALRQ/VLRQ, and VLRQ/VLRQ genotypes. The ALHQ/ALHQ, AFRQ/ALHQ and AFRQ/AFRQ genotypes were associated with the highest risks of atypical scrapie compared to ALRQ/ALRQ. Within classical scrapie cases, the VLRQ/VLRQ animals presented the highest risk compared to ALRQ/ALRQ. In addition, the authors detected a significant risk of atypical scrapie for sheep carrying the ALRR/ALRR genotype (Fediaevsky et al., 2010b).

The earliest evidence of sheep domestication was found in certain parts of the Near East, with Turkey as an area of major importance. Archeological data suggest two different areas with independent sheep domestication events in Turkey: the upper Euphrates valley in eastern Turkey (particularly, the Çatal Höyük and Aşıklı Höyük sites). The Zagros Mountains on the border of Turkey and Iran is also recognized as a primary center of sheep domestication (Bruford et al., 2003; Zeder, 2008). Thus, it is likely that the Turkish native sheep breeds of today are one of the oldest living descendants of their first domesticated ancestors and Anatolian (Turkish) native breeds may be special in maintaining very valuable genetic diversity. Therefore they must be explored with regard to genetic markers. In Turkey, there have been no official reports about the cases of classical and atypical scrapie. Although there were a few studies on PrP genotyping for classical scrapie (Ün et al., 2008; Alvarez et al., 2011; Meydan et al., 2012), we could not come across any studies about the atypical scrapie in Turkish native sheep breeds. The aim of this study was to genotype all eighteen Turkish native sheep breeds in order to determine polymorphisms of the PRNP gene and evaluate the genetic susceptibility to atypical scrapie.

2. Materials and methods

2.1. Sampling and DNA extraction

In this study, a total of 1110 unrelated healthy sheep were randomly (regardless of age and sex) sampled from 18 Turkish native breeds, İvesi (Awassi, $n = 100$), Akkaraman ($n = 100$), Kangal Akkaraman ($n = 100$), Morkaraman ($n = 100$), Güneykaraman ($n = 30$), Kıvırcık ($n = 140$), Norduz ($n = 35$), Karakaş ($n = 35$), Sakız (Chios, $n = 50$), Herik ($n = 45$), Hemşin ($n = 55$), Dağlıç ($n = 40$), Karayaka ($n = 45$), Tuj (Tushin, $n = 45$), Çine Çaparı ($n = 40$), Gökçeada (Imroz, $n = 50$), Karagül (Karakul, $n = 50$) and Zom ($n = 50$) breeds.

Blood samples were collected from the jugular vein into EDTA containing tubes, transported to the laboratory and stored at −20 °C until genomic DNA extraction, which was carried out using a salting-out method (Miller et al., 1988).

2.2. PCR assay and DNA sequencing

The fragment of 771 bp in length, which covered open reading frame of PRNP gene and codons 136, 141, 154 and 171, was amplified by PCR with forward (5′-ATG GTG AAA AGC CAC ATA GGC AGT-3′) and reverse (5′-CTA TCC TAC TAT GAG AAA AAT GAG-3′) primers suggested by Sipos et al. (2002). PCR products resolved by electrophoresis on 2% agarose gels. After gel electrophoresis, the amplicons were purified using a Qiamp Mini Kit (QIAGEN, Valencia, CA, USA). The purified samples were sequenced by a Big Dye Terminator Chemistry on an ABI 3100 Avant Automated DNA Sequencer (Applied Biosystems, Foster City, CA, USA). The DNA sequences were analyzed using the Sequencing Analysis Software Version 3.3 (Applied Biosystems, Foster City, CA, USA).

2.3. Statistical analysis

Genotype (X_{ij}) and gene ($\hat{x}_i$) frequencies were estimated as following formulas (Nei, 1987);

$$X_{ij} = \frac{n_{ij}}{n} \quad \text{and} \quad \hat{x}_i = \frac{2n_{ii} + \sum n_{ij}}{2n}$$

where X_{ij} is genotypic frequency of A_iA_j; n_{ij} and n_{ii} are the number of individuals for heterozygous (A_iA_j) and homozygous (A_iA_i) genotypes, respectively; $\hat{x}_i$ is the gene frequency of A_i and n is the total number of individuals sampled from the population.

3. Results

The alleles and genotypes observed based on codons 136, 141, 154 and 171 of PRNP gene and their frequencies are summarized in Table 1. The most frequent allele in each of the eighteen breeds was ALRQ with the frequencies ranging from 0.445 to 0.757. The AFRQ allele, associated with the susceptibility to atypical scrapie, was detected in only İvesi with the frequency of 0.006. The other susceptible allele to atypical scrapie, ALHQ, was detected in Akkaraman (0.005), Kangal Akkaraman (0.010), Güneykaraman

Table 1
The genotype and allele frequencies of PRNP gene for atypical scrapie in Turkish native sheep breeds.

Group[a]		IVE $n=100$	AKK $n=100$	KAK $n=100$	MRK $n=100$	GNK $n=30$	KVR $n=140$	NRD $n=35$	KRK $n=35$	SKZ $n=50$
	Genotype frequency									
1	ALRR/ALRQ	0.040	0.230	0.220	0.220	0.242	0.407	0.706	0.703	0.260
1	ALRR/VLRQ					0.034	0.007			
1	ALRQ/ALRQ	0.530	0.410	0.270	0.520	0.277	0.329	0.265	0.270	0.260
1	ALRH/ALRQ	0.190	0.080	0.090	0.040	0.069		0.029		0.100
1	VLRQ/ALRQ	0.010					0.014			
2	ALRR/ALRR	0.030	0.040	0.100	0.080	0.069	0.093			0.180
2	ALRR/ALRH	0.040	0.160	0.060	0.030					0.120
2	VLRQ/VLRQ						0.007			
3	ALHQ/ALRH[b]									
3	VLRQ/ALHQ						0.007			
3	ALRH/AFRQ[b]									
3	ALRH/ALRH	0.090	0.070	0.130					0.027	
3	VLRQ/AFRQ[b]									
3	VLRQ/ALRH									0.020
4	ALRR/ALHQ		0.010			0.034	0.029			
4	ALRR/AFRQ[b]									
4	ALHQ/ALRQ			0.020		0.034	0.093			0.020
4	AFRQ/ALRQ	0.010								
5	ALHQ/ALHQ						0.014			
5	ALHQ/AFRQ[b]									
5	AFRQ/AFRQ[b]									
nc	ALRR/TLRR			0.010						
nc	ALRR/TLRQ			0.060		0.069				0.020
nc	ALRQ/TLRQ	0.030		0.020	0.090	0.172				0.020
nc	TLRQ/TLRQ									
nc	ALRR/ALRK									
nc	ALRH/ALRK				0.020					
nc	ALRQ/ALRK	0.030								
nc	ALRH/TLRH			0.020						
	Allele frequency									
	ALRR	0.070	0.240	0.275	0.205	0.259	0.315	0.353	0.351	0.380
	ALRQ	0.680	0.565	0.445	0.695	0.535	0.586	0.632	0.622	0.460
	AFRQ	0.005								
	ALRH	0.210	0.190	0.215	0.045	0.034		0.015	0.027	0.120
	ALHQ		0.005	0.010		0.034	0.078			0.010
	VLRQ	0.005				0.017	0.021			0.010
	TLRR			0.005						
	TLRQ	0.015		0.040	0.045	0.121				0.020
	TLRH			0.010						
	ALRK	0.015			0.010					

Group[a]		HRK $n=45$	HMS $n=55$	DGL $n=40$	KRY $n=45$	TUJ $n=45$	CCP $n=40$	GOK $n=50$	KRG $n=50$	ZOM $n=50$
	Genotype frequency									
1	ALRR/ALRQ	0.222	0.255	0.358	0.430	0.089	0.172	0.367	0.292	0.260
1	ALRR/VLRQ									
1	ALRQ/ALRQ	0.423	0.564	0.410	0.205	0.490	0.585	0.552	0.375	0.360
1	ALRH/ALRQ	0.156	0.109	0.051	0.023	0.222	0.122		0.104	0.220
1	VLRQ/ALRQ				0.023		0.024			
2	ALRR/ALRR	0.133	0.036		0.023	0.044	0.049	0.041	0.104	0.040
2	ALRR/ALRH			0.026	0.023	0.022	0.024		0.083	0.020
2	VLRQ/VLRQ									
3	ALHQ/ALRH[b]									
3	VLRQ/ALHQ									
3	ALRH/AFRQ[b]									
3	ALRH/ALRH	0.022	0.018						0.021	0.020
3	VLRQ/AFRQ[b]									
3	VLRQ/ALRH									
4	ALRR/ALHQ							0.020		
4	ALRR/AFRQ[b]									
4	ALHQ/ALRQ			0.026				0.020		
4	AFRQ/ALRQ									
5	ALHQ/ALHQ									
5	ALHQ/AFRQ[b]									
5	AFRQ/AFRQ[b]									

Table 1 (*Continued*)

Group[a]		HRK $n=45$	HMS $n=55$	DGL $n=40$	KRY $n=45$	TUJ $n=45$	CCP $n=40$	GOK $n=50$	KRG $n=50$	ZOM $n=50$
nc	ALRR/TLRR									
nc	ALRR/TLRQ	0.022			0.045					
nc	ALRQ/TLRQ			0.077	0.205					
nc	TLRQ/TLRQ				0.023					
nc	ALRR/ALRK			0.026						
nc	ALRH/ALRK		0.018			0.022				
nc	ALRQ/ALRK	0.022		0.026		0.111	0.024		0.021	0.080
nc	ALRH/TLRH									
	Allele frequency									
	ALRR	0.256	0.165	0.205	0.273	0.100	0.146	0.235	0.292	0.180
	ALRQ	0.622	0.745	0.679	0.546	0.700	0.757	0.745	0.583	0.640
	AFRQ									
	ALRH	0.100	0.081	0.038	0.022	0.133	0.073		0.115	0.140
	ALHQ			0.013				0.020		
	VLRQ				0.011		0.012			
	TLRR									
	TLRQ	0.011		0.039	0.148					
	TLRH									
	ALRK	0.011	0.009	0.026		0.067	0.012		0.010	0.040

[a] Genotypes were grouped by levels of genetic risk for atypical scrapie according to Fediaevsky et al. (2009).
[b] These genotypes were not detected in this study.
nc, not classified in any risk group by Fediaevsky et al. (2009).
IVE, İvesi [Awassi]; AKK, Akkaraman; KAK, Kangal Akkaraman; MRK, Morkaraman; GNK, Güneykaraman; KVR, Kıvırcık; NRD, Norduz; KRK, Karakaş; SKZ, Sakız [Chios]; HRK, Herik; HMS, Hemşin; DGL, Dağlıç; KRY, Karayaka; TUJ, Tuj [Tushin]; CCP, Çine Çaparı; GOK, Gökçeada [Imroz]; KRG, Karagül [Karakul]; ZOM, Zom.

(0.034), Kıvırcık (0.078), Sakız (0.010), Dağlıç (0.013) and Gökçeada (0.020) breeds.

The ALRQ/ALRQ genotype was predominant in all breeds, except for in Kıvırcık, Norduz, Karakaş and Karayaka breeds. The AFRQ/ALRQ genotype was found in only İvesi breed (0.010) and deposited in GenBank with the accession number of JX187526. The ALHQ/ALHQ genotype, one of the most susceptible genotypes to atypical scrapie, was found in only Kıvırcık with the frequency of 0.014. Other two most susceptible genotypes to atypical scrapie, ALHQ/AFRQ and AFRQ/AFRQ, were not found in this study. In addition, the ARR/ARR genotype, which has been reported in lots of atypical scrapie positive sheep from various countries, was detected in almost all breeds.

4. Discussion

The identification of PrP genotypes for classical and atypical scrapie is very important for every country in order to develop and implement scrapie breeding program. Many European countries have identified their sheep breeds for classical scrapie (O'Doherty et al., 2000; Vaccari et al., 2001; Arnold et al., 2002; Drögemüller et al., 2004; Acin et al., 2004; Gama et al., 2006) and atypical scrapie (Buschmann et al., 2004; Saunders et al., 2006; Moreno et al., 2007; Fediaevsky et al., 2010a). In Turkey, scrapie control breeding programs have not been established for both classical and atypical scrapie. Although, there are a few studies about the identification of PrP genotypes for classical scrapie, we could not come across any studies about the atypical scrapie in Turkish native sheep breeds. In this study, all Turkish native sheep breeds were identified for atypical scrapie based on the polymorphisms in PRNP gene.

A new strain of scrapie, Nor98, first reported in five AHQ/AHQ and two AHQ/ARQ sheep in Norway, was found to have an unusual PrP^{Sc} distribution and glycoform (Benestad et al., 2003). A further report from Norway (Moum et al., 2005) found that 38 Nor98 cases were associated strongly with AFRQ and ALHQ alleles. In addition, the results of a few studies from different countries suggested that AFRQ and ALHQ alleles were associated with susceptibility to atypical scrapie (Buschmann et al., 2004; Arsac et al., 2007; Moreno et al., 2007; Lühken et al., 2007; Fediaevsky et al., 2009). In addition to these reports, one study in Great Britain showed that animals carrying any homozygous or heterozygous combination of ALRR, ALHQ or ALRQ alleles or one of these alleles when paired with AFRQ were susceptible to atypical scrapie infection (Saunders et al., 2006). Also, a few studies showed that sheep with ARR/ARR genotypes were susceptible to atypical scrapie (Buschmann et al., 2004; Arsac et al., 2007; Lühken et al., 2007; Fediaevsky et al., 2010b).

As we did not have Nor98 cases and there was no official report about Nor98 cases in Turkey, we could not carry out a case–control study. We just tried to evaluate the genetic susceptibility to atypical scrapie in Turkish native sheep breeds. According to our results, the predominant allele in Turkish native sheep breeds was ALRQ with the frequencies ranging from 0.445 (Kangal Akkaraman) to 0.757 (Çine Çaparı). It was reported that the risk of atypical scrapie was very low for ALRQ allele (Moreno et al., 2007; Fediaevsky et al., 2009, 2010b). The most susceptible alleles to atypical scrapie, AFRQ and AHQ, were found at low frequencies in 1 and 7 breeds, respectively (Table 1). Although both susceptible alleles were detected, only AHQ/AHQ genotype, one of the most susceptible genotypes to atypical scrapie, was observed in Kıvırcık. Other susceptible genotypes (AHQ/AFRQ and AFRQ/AFRQ) were not found in Turkish native sheep breeds. We also detected

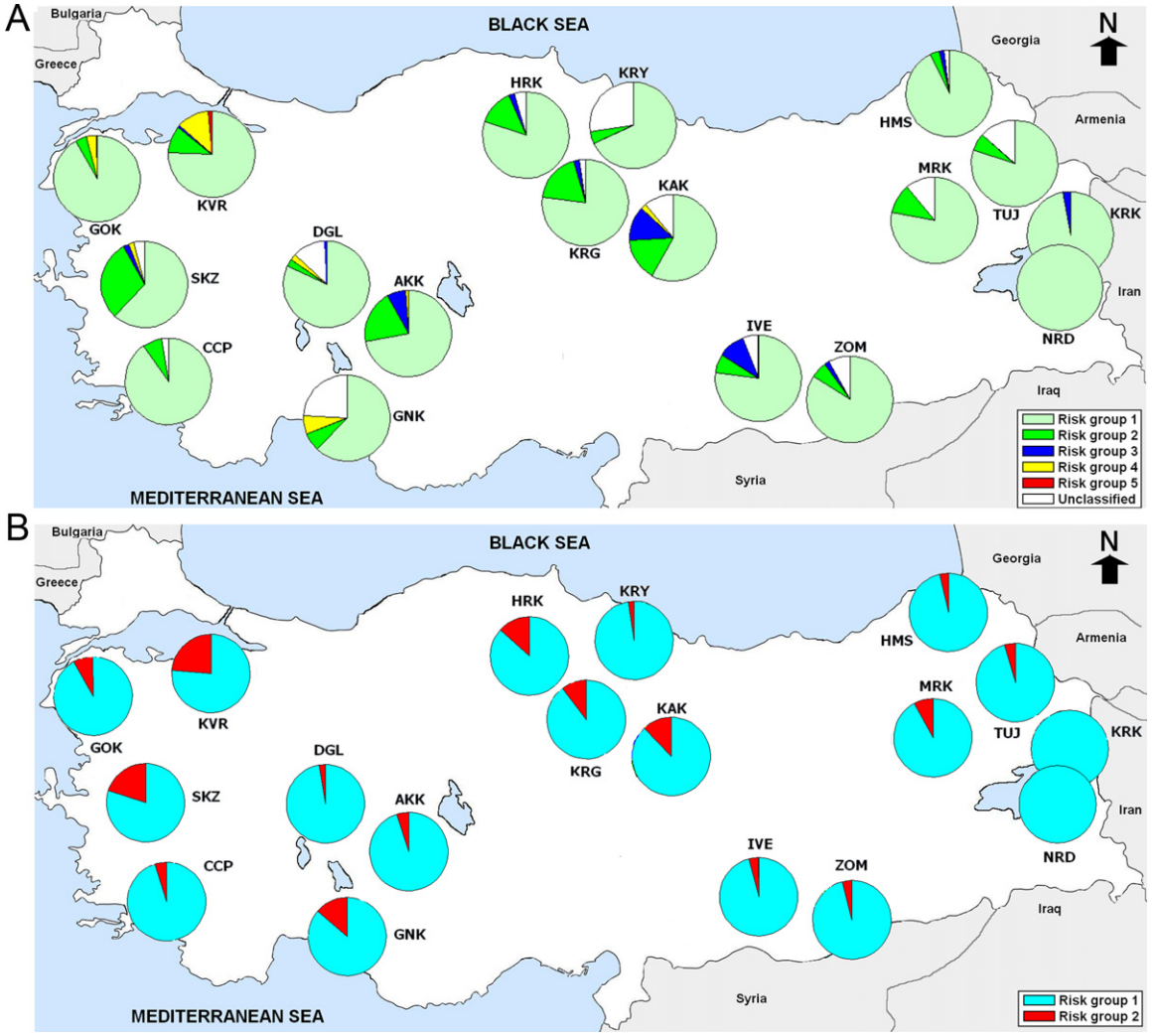

Fig. 1. Distributions of risk group in all Turkish native sheep breeds for atypical scrapie. (A) Distributions of risk group according to Fediaevsky et al. (2009). (B) Risk group 2 includes the genotypes of ALRR/ALRR, ALHQ/ALRQ, AFRQ/ALRQ and ALHQ/ALHQ that are associated with the highest risk of atypical scrapie. Risk group 1 includes the other genotypes. IVE, İvesi (Awassi); AKK, Akkaraman; KAK, Kangal Akkaraman; MRK, Morkaraman; GNK, Güneykaraman; KVR, Kıvırcık; NRD, Norduz; KRK, Karakaş; SKZ, Sakız (Chios); HRK, Herik; HMS, Hemşin; DGL, Dağlıç; KRY, Karayaka; TUJ, Tuj (Tushin); CCP, Çine Çaparı; GOK, Gökçeada (Imroz); KRG, Karagül (Karakul); ZOM, Zom.

ALRQ/AFRQ genotype, member of risk group 4 (Fediaevsky et al., 2009) in only İvesi. The ALRQ/ALRQ genotype, which is resistant to atypical scrapie and corresponded to a risk group 1, was predominant genotype in Turkey with the frequencies ranging from 0.205 to 0.585. Moreover, most of the sheep studied were belong to risk group 1 (Fediaevsky et al., 2009) for atypical scrapie. In addition to these genotypes, we detected additional genotypes which were not classified in any risk group (Table 1). Because these additional genotypes did not carry both AFRQ and ALHQ alleles, they might be thought to be resistant to atypical scrapie.

Previous study on PRNP genotyping in Turkey, one sheep carrying AFRQ allele was found in 100 sheep from five Turkish sheep breeds (Alvarez et al., 2011). This result is similar to our results. Also Ün et al. (2008) reported that they did not found AFRQ allele in 107 sheep from three Turkish sheep breeds. In these studies, the frequency of the AFRQ allele was found much lower than expected compared to non-Turkish breeds. Until now, more than 2000 sheep with AFRQ allele were identified in European, Asian and American sheep breeds. The low frequency of the AFRQ allele reduces the susceptibility of Turkish breeds to atypical scrapie.

In this study, the ARR/ARR genotype was present in almost all breeds with the frequency of 0.064 in total. It is well known that the ARR/ARR is most resistant genotype to classical scrapie. But it has been reported that six atypical scrapie positive sheep (6.8%) carried the ARR/ARR genotype in Germany (Lühken et al., 2007), nine atypical cases (13.0%) with ARR/ARR genotype were found in Great Britain (Saunders et al., 2006) and six of the atypical scrapie cases (11.8%) were ARR/ARR genotype in France and Norway (Arsac et al., 2007).

The VRQ allele was detected at low frequencies in İvesi (0.006), Güneykaraman (0.017), Kıvırcık (0.021), Sakız (0.010), Karayaka (0.011) and Çine Çaparı (0.012). The VRQ/VRQ genotype was also found in only Kıvırcık (0.007). It is well known that the VRQ allele has been associated with the highest susceptibility to classical scrapie. The classical form of the disease most frequently occurs in sheep with ARQ/VRQ, ARH/VRQ and VRQ/VRQ genotypes (Baylis and Goldmann, 2004), but there were no atypical scrapie cases with VRQ/VRQ genotype. It is suggested that the VRQ allele confers partial or complete resistance to atypical scrapie, whereas it is highly susceptible to classical scrapie (Moum et al., 2005; Saunders et al., 2006).

According to our results, Turkish native sheep breeds belong to risk group of 1 (77.4%) followed by risk group 2 (10.5%). Kıvırcık, in western part of Turkey, had 13.6% of the sheep in high-susceptible groups (risk groups 4 and 5) to atypical scrapie and 9.3% of the sheep with ARR/ARR genotype, compared with the other breeds sampled in this study. On the other hand, almost all sheep of Norduz and Karakaş breeds, in eastern part of Turkey, were in high-resistance group (risk group 1). Also both breeds had not ARR/ARR genotype. It is propounded that the susceptibility to atypical scrapie increased from eastern part to west part of Turkey. While none of the breeds from eastern part of Turkey had the sheep in high-susceptible groups, almost all breeds from western part of Turkey had the sheep in high-susceptible groups (Fig. 1A). The frequencies of susceptible genotypes in western breeds (Kıvırcık, Gökçeada, Sakız, Güney Karaman, Herik) were higher than in eastern breeds (Fig. 1B). This result could be explained that the breeds reared in western part of Turkey might have relationship to European breeds where the sheep in high-susceptible has been described previously. Further researches are needed to argue and confirm this result.

5. Conclusion

All Turkish native sheep breeds were identified for the PRNP polymorphism for atypical scrapie in this study. This study may be first report about genetic risk assessment for atypical scrapie in Turkish native sheep breeds. Allele frequencies at the PRNP locus showed a predominance of the ALRQ allele. The most susceptible alleles (AFRQ and ALHQ) and one of the most susceptible genotypes (ALHQ/ALHQ) to atypical scrapie were observed in this study. Although it seems that Turkish native sheep breeds are safe from atypical scrapie, the occurrence of susceptible genotypes should be taken into consideration. Especially the breeds reared in western part of Turkey seem to be more susceptible to atypical scrapie than other breeds.

The ARR/ARR, most resistant genotype to classical scrapie, was present in almost all Turkish native sheep breeds. But this genotype has been reported in lots of atypical scrapie positive sheep from various countries. The susceptibility of ARR/ARR genotype has been a major concern because national breeding and eradication plans for classical scrapie in EU member states are inadvertently creating a high frequency of ARR/ARR animals. Based on the observed resistance to TSE in homozygous ARR animals, a breeding program for resistance to scrapie has been implemented in several EU countries to control human exposure to TSE risk. This unusual susceptibility of small ruminants believed to be genetically resistant to TSE could lead to a reevaluation of such a policy (Arsac et al., 2007; Benestad et al., 2008). Atypical scrapie occurrence appears to be heavily dependent on the PRNP genotype, possibly modulated by some environmental risk factors that are to be further explored. Even if the open reading frame of the PRNP gene has a strong influence on the occurrence of atypical scrapie it might not be the unique genetic factor of susceptibility. Other regions of the PRNP or other genes could be involved either independently or in synergy and this hypothesis is also worth to be investigated (Fediaevsky et al., 2010b).

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

Authors would like to thank Dr. B. Yüceer and R. Değirmenci for their assistance in the collection of samples. We are also grateful to Dr. W. Goldmann, The Roslin Institute & Royal (Dick) School of Veterinary Studies, University of Edinburgh, UK, for his comments on an earlier version of the manuscript. This study was partially supported by a grant from Scientific Research Projects (BAP) of Ankara University (Project No: BAP-09B4347007; Project Coordinator: Dr. M.M. Özkan).

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