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The Polymorphism of Insulin-Like Growth Factor-1 Receptor Gene and Its Associations with Live Weight Traits and Birth Type in Akkaraman Lambs

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The insulin-like growth factor 1 receptor (*IGF1R*) gene is a potential candidate gene as it is involved in several physiological processes related to yield charecteristics. We conducted this study to investigate a polymorphism (g.195C>T) in the *IGF1R* gene, identified using the RsaI enzyme, and its associations with live weight gain from birth to weaning and birth type in the Akkaraman sheep breed. A total of 397 male Akkaraman breed lambs were examined. The samples analyzed have revealed three distinct genotypes (AA, AB, BB) in terms of the g.195C>T polymorphism as a result of the utilized polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). As a result of Chi-square analysis using genotypic data, it was determined that the examined samples were not in Hardy-Weinberg equilibrium for *IGF1R*-RsaI polymorphism. Throughout the growth period from birth to 90 days, slight differences in growth rates were observed due to the effects of birth type and *IGF1R* genotypes. However, these differences were not statistically significant across genotypes in terms of live weight gain. Additionally, it was observed that the BB genotype had a higher frequency in single-born lambs, and there was a statistically significant relationship between *IGF1R*-RsaI polymorphism and lamb birth type ($p<0.01$). The results have considered that it was necessary to suggest that new studies might be planned to investigate the relationship between *IGF1R*-RsaI polymorphism and other yield characteristics, especially birth type, in sheep.

Key Words: *Weight, Birth type, IGF1R, PCR-RFLP, Sheep*

Akkaraman Kuzularında İnsülin Benzeri Büyüme Faktörü-1 Reseptör (IGF1R) Gen Polimorfizmi ile Canlı Ağırlık Özelliklerinin ve Doğum Tipinin İlişkisi

İnsülin benzeri büyüme faktörü 1 reseptörü (*IGF1R*), verimle ilgili birçok fizyolojik sürece katıldığı için potansiyel bir aday gendir. Bu çalışmada, Akkaraman koyun ırkında *IGF1R* geninde bulunan ve *Rsa*I enzimi ile belirlenen polimorfizm (g.195C>T) ile kuzuların doğumundan sütten kesimine kadarki canlı ağırlık artışı ve doğum tipi arasındaki ilişkisi araştırılmıştır. Araştırmada 397 baş Akkaraman ırkı erkek kuzu incelenmiştir. Yapılan polimeraz zincir reaksiyonu-restriksiyon fragment uzunluk polimorfizmi (PCR-RFLP) sonunda incelenen örneklerde g.195C>T polimorfizmi yönünden üç farklı genotipin (AA, AB, BB) bulunduğu görülmüştür. Genotipik veriler kullanılarak yapılan Ki-kare analizi sonunda incelenen örneklerin *IGF1R*-RsaI polimorfizmi için Hardy-Weinberg dengesinde olmadığı tespit edilmiştir. Mevcut çalışmada, canlı ağırlık ile genotip arasındaki ilişkide doğum tipinin önemli bir faktör olduğu bulunmuştur. Ek olarak, incelenen örneklerden tekiz doğan kuzularda BB genotipinin daha yüksek bir frekansa sahip olduğu, *IGF1R*-RsaI polimorfizmi ile kuzuların doğum tipi arasında istatistiksel olarak önemli bir ilişkinin olduğu görülmüştür ($p<0.01$). Sonuçlar, koyunlarda *IGF1R*-RsaI polimorfizmi ile başta doğum tipi olmak üzere diğer verim özellikleri arasındaki ilişkinin araştırılacağı yeni çalışmaların planlanmasının gerekli olduğunu düşündürmektedir.

Anahtar Kelimeler: *Ağırlık, Doğum tipi, IGF1R, PCR-RFLP, Koyun*

Introduction

Sheep (*Ovis aries*) have been raised since the Neolithic era, during which they were domesticated across different regions, including Anatolia (1, 2). Most breeders worldwide prefer sheep due to their disease resistance, adaptability to harsh climates, ability to effectively use low-yielding pastures, and ease of care and feeding (3). Sheep population of Türkiye, despite a decrease of approximately 6% over the past year, has a huge number of about 42 million, ranking seventh in the world (4, 5). Indigenous breeds are essential to sustainable sheep breeding because they have evolved to be well-suited to the local environment (6). Akkaraman, known for its fat-tailed characteristic, is a commonly bred indigenous sheep breed in Türkiye (7). Further breeding investigations are warranted concerning the growth performance traits of the Akkaraman sheep breed, characterized by a daily live weight gain ranging from 187 to 229 grams from birth to weaning (8). In order to improve the Akkaraman sheep breed in terms of significant production traits, investigations on selection and crossbreeding have been conducted and continue to be conducted for this aim (9). The German Mutton Merino breed has been crossbred in Türkiye to improve the meat production of Akkaraman sheep. German Mutton Merino × Akkaraman (Central Anatolian Merino) crosbred sheep were

not very popular among breeders and could not become widespread in the region because hybrid breeds could not adapt to local breeding conditions (10, 11). Consequently, the current population of the Akkaraman breed needs improvement to increase both yield and quality per animal unit via effective selection methods (12). A few growth performance traits, such as average daily weight gain, live weight at slaughter age, and body measurements, are essential for sheep breeding to be economically profitable (13). The delayed slaughter of lambs due to lower growth performance results in higher maintenance and feeding costs for the sheep enterprise. This situation consequently reduces the profitability of the sheep enterprise (14).

There is a need for further research to reveal the genetic potential of indigenous sheep breeds in Türkiye with regards to yield traits (11). It is believed that selecting animals with the desired genotype for candidate genes related to yield traits will enhance the success of breeding programs (15). The improvement of genetic values in indigenous sheep breeds may be facilitated by selection studies utilizing known candidate genes with a relationship with growth, a polygenic trait (16). Hence, there is an increasing interest in identifying polymorphisms within potential candidate genes associated with crucial growth performance traits in the sheep genome and exploring their utilization options in selection (17).

The somatotropic axis, including key components such as the insulin-like growth factor 1 *(IGF1)* gene and the growth hormone *(GH)* gene, contains promising candidate genes related to meat production traits in livestock (18). *IGF1* plays a significant role in various physiological and metabolic processes, including the enhancement of glycolysis uptake, increased lipid synthesis, stimulation of myogenesis, inhibition of apoptosis, and promotion of cell proliferation (19). Additionally, IGF1 is a significant gene for growth and development in both intrauterine and postnatal life (20). The *insulin-like growth factor 1 receptor (IGF1R),* activated by *IGF1*, is a transmembrane receptor containing tyrosine kinase that regulates birth weight in addition to cell growth and differentiation (21). According to a study conducted by Louvi et al. (22), it was shown that offspring mice with the silenced-IGF1R gene silenced had birth weights that were around 45% lower and experienced postnatal growth retardation. Studies conducted on various farm animals, such as cattle, buffalo, sheep, pigs, and chickens, have reported that the *IGF1R* gene is associated with growth performance traits such as periodic body weight and daily weight gain (18, 21, 23-25). On the other hand, it has been proposed that the *IGF1R* gene plays a significant role in the function of granulosa cells in mice, hence its association with fertility in females (26). Furthermore, in a study conducted by Yang et al. (27), it was reported that the *IGF1R* gene is associated with superovulation in cattle.

The *IGF1R* gene, which includes 21 exons and 20 introns, is located on the 18th chromosome in sheep. The sheep *IGF1R* gene encodes a polypeptide containing 1367 amino acids, and it plays a crucial role in promoting cell proliferation and facilitating postnatal growth (28, 29). Ding et al. (30) have reported the *IGF1R* gene as a candidate gene for improving early-stage live weights in sheep. Previous studies have shown that the g.195C>T polymorphism in the 12th intron of the IGF1R gene affects live weight gain in different sheep breeds (23, 31). This study was conducted to determine the polymorphism of *IGF1R*-RsaI (g.195C>T) located in the 12th intron and to compare the early live weight from birth to weaning age and birth type in the Akkaraman breed in Türkiye.

Materials and Methods

Research and Publication Ethics: All animal procedures were accepted by the Local Ethics Committee for Animal Experiments at University of Erciyes (#13/130-13.11.2013).

In the present study, we used 397 male Akkaraman breed lambs on four farms in the Kayseri province of Türkiye. These farms raise sheep with the same feeding, care, and environmental conditions. All lambs were also tagged with a small plastic ear tag after birth. All data, such as the weight and birth type of the lambs, were recorded according to the numbers on the ear tags.

Animals and DNA Extraction: The weight of the lambs was measured at birth, 30th, 60th, and 90th days. K_3EDTA tubes containing an anticoagulant were used to take about 10 ml of blood from the jugular vein. Genomic DNA used in genetic analyses was isolated from total blood samples using the phenol-chloroform extraction method.

Molecular Genetic Analyses: A primer pair of the *IGF1R* gene (NCBI Accession number: KJ140106.1) recommended by Proskura and Szewczuk (23) was utilized in the PCR process (forward; 5'TCC CAA GTG GAG GTG AGT CT3'; reverse; 5'ATA AGC CAG CTT CCT GCA CAC3'). PCR amplification was carried out in total volume of samples 20 µL, containing 1.5 mM MgCl2, 200 µM each primer, 250 µM dNTPs, 10×PCR buffer, 1.5 U Taq DNA polymerase, 50 ng DNA template, and deionized water. The thermal cycling PCR conditions included initial denaturation at 94 °C/5 min, followed by 33 cycles consisting of denaturation at 94 °C/50 sec, annealing at 59.5 °C/1 min, extension at 72 °C/50 sec, and a last extension at 72 °C/5 min. The presence of PCR products with a length of 206 base pairs (bp) was confirmed by using 2% agarose gels. The obtained PCR products were digested by incubating at 37°C for at least 5 hours with 5 U of the RsaI restriction endonuclease enzyme (Thermo Scientific). Following the digestion process, the DNA restriction fragments were separated in 2% agarose gels. The results of gel electrophoresis separations were visualized under UV light.

Statistical Analyses: The allele and genotype frequencies of the population in terms of *IGF1R* gene polymorphism were calculated manually. Chi-Square (χ^2) test was used to identify the Hardy-Weinberg equilibrium

of the population. The statistical significance of the relationship between lamb birth type (single or twin) and genotypes (AA, AB, BB) was tested using the Chi-Square analysis. In this study, the effects of IGF1R genotypes on the live weight of Akkaraman lambs were evaluated using the Generalized Linear Model (GLM). The model incorporates genotypes and other control variables to assess their impact on live weight. The mathematical representation of the model is as follows:

$$Y_i = \beta_0 + \beta_1 X_{i1} + \beta_2 X_{i2} + \beta_3 X_{i3} + \beta_4 X_{i4} + \epsilon_i$$

Where:
Y_i: The live weight of the i-th lamb (dependent variable)
X_{i1}: The genotype of the i-th lamb (categorical independent variable)
X_{i2}: The birth type of the i-th lamb (categorical independent variable: single or twin birth)
X_{i3}: The birth weight of the i-th lamb (continuous independent variable)
X_{i4}: The farm where the i-th lamb was raised (categorical independent variable)
$\beta_0, \beta_1, \beta_2, \beta_3, \beta_4$: Model parameters
ϵ_i: Random error term for the i-th observation.

The β coefficients represent the effects of independent variables on live weight, estimated through GLM analysis. Each coefficient reflects the average effect of the respective variable on live weight.

Additionally, Pearson correlation coefficients were calculated to assess the relationship between genotypes and live weights at different growth periods (birth, 30th day, 60th day, and 90th day). The correlation values between genotypes (AA, AB, BB) and live weights, along with other calculations, were generated using JMP software (SAS Institute Inc., Cary, NC). These correlations provide important insights into how different genotypes influence growth rates at various stages of lamb development.

Results

PCR amplification of the relevant region of the *IGF1R* gene resulted in amplicons of 206 base pairs in length (Figure 1). Following digestion of the obtained amplicons with the RsaI restriction enzyme, individuals with the BB genotype showed two bands at 139 and 67 base pairs in length; individuals with the AB genotype showed three bands at 206, 139, and 67 base pairs in length; while individuals with the AA genotype showed a single band at 206 base pairs in length (Figure 2).

The analysis revealed that the AB genotype (0.49) was the most prevalent genotype, while the AA genotype (0.20) was the least common genotype. The analyses of the population indicated that the B allele (0.56) exhibited the highest prevalence among alleles, as shown in Table 1. Akkaraman lambs were found not to be in Hardy-Weinberg equilibrium regarding the IGF1R-RsaI polymorphism.

Correlations of genotypes according to live weights at different growth times are given in Table 2. When analyzing the relationship between birth type (single or twin) and IGF1R genotypes, distinct effects of different genotypes on birth weight and subsequent live weights were observed. The study identified and statistically supported differences in weight gain based on the AA, AB, and BB genotypes of lambs, alongside their birth types. For single-born lambs, weight differences based on genotypes were noted. The average birth weights for AA, AB, and BB genotypes were recorded as 4557 g, 4617 g, and 4644 g, respectively. For twin-born lambs, AA genotype lambs weighed 4750 g, while AB genotype lambs weighed 4621 g at birth. Despite these differences, the variations in birth weight were not statistically significant (p>0.05). At 30 days, the average weight of single-born AA genotype lambs was 12.503 g, while AB and BB genotype lambs had average weights of 12.505 g and 12.156 g, respectively. For twin-born lambs, AA genotype lambs reached an average weight of 12.972 g, and AB genotype lambs weighed 13.170 g. However, the differences in 30-day weights between genotypes were also not statistically significant (p=0.5398). By day 60, the average weight of single-born AA genotype lambs was 22.281 g, while AB genotype lambs weighed 21.591 g, and BB genotype lambs reached 21.004 g. For twin-born lambs, AA genotype lambs averaged 22.523 g, while AB genotype lambs weighed 22.344 g. As with previous periods, the differences in 60-day weights were not statistically significant (p>0.05). At 90 days, single-born AA genotype lambs reached an average weight of 33.023 g, AB genotype lambs 31.809 g, and BB genotype lambs 31.637 g. For twin-born lambs, AA genotype lambs weighed 33.909 g, and AB genotype lambs reached 31.500 g. Again, there were no statistically significant differences between the 90-day weights of different genotypes (p>0.05).

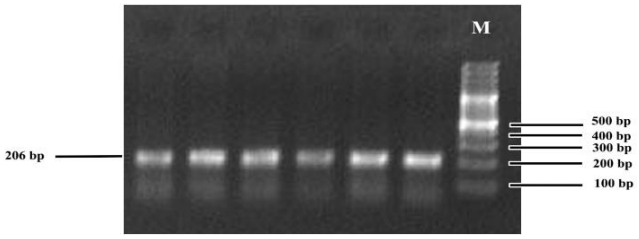

Figure 1. Electrophoretic pattern of the PCR amplicons, which are 206 base pairs in length in the *IGF1R* gene, M: 100 bp DNA Ladder

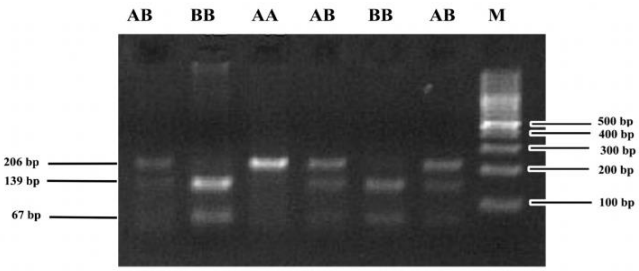

Figure 2. Electrophoretic pattern of RFLP fragments for *IGF1R*-RsaI polymorphism, AA: 206 bp, BB: 139, 67 bp, AB: 206, 139, 67 bp, M: 100 bp DNA Ladder

Table 1. Allele and genotype frequencies of *IGF1R*-RsaI polymorphism in Akkaraman lambs

n	Genotype						Allele Frequency		Chi-Square (df=1)
	AB		AB		BB		A	B	
397	Obs (Exp)	F	Obs (Exp)	F	Obs (Exp)	F	0.44	0.56	χ2=66.25
	38 (78.02)	0.20	276 (195.94)	0.49	83 (123.02)	0.31			*p*<0.001

n: Number of animals; Obs: Observed frequency; Exp: Expected frequency; F: Frequency; df: Degrees of freedom; χ2: Chi-Square; *p*:Probability value

Table 2. Correlations of genotypes according to live weights at different growth times

		Birth Weight	30th Weight	60th Weight	90th Weight
Birth Weight	AA	1.0000	0.3194	0.2696	0.1397
	AB	1.0000	0.2320	0.2747	0.3169
	BB	1.0000	0.0082	0.0692	0.1432
30th Weight	AA	0.3194	1.0000	0.8749	0.6919
	AB	0.2320	1.0000	0.8695	0.7047
	BB	0.0082	1.0000	0.8629	0.7560
60th Weight	AA	0.2696	0.8749	1.0000	0.8693
	AB	0.2747	0.8695	1.0000	0.8742
	BB	0.0692	0.8629	1.0000	0.9130
90th Weight	AA	0.1397	0.6919	0,8693	1,0000
	AB	0.3169	0.7047	0,8742	1,0000
	BB	0.1432	0.7560	0,9130	1,0000

A GLM analysis was performed to analyze the impact on birth weight and the weights at the 30th, 60th, and 90th days based on the data reported in Table 3. All models were computed via the highest likelihood technique. The farm factor exerted the most substantial influence on birth weight (LogWorth=19.047, *p*<0.0001). Furthermore, the weight at 30 days markedly affected the delivery weight (LogWorth=2.250, *p*=0.0056). The effects of the allele, 60th day weight, birth type, and 90th day weight were not statistically significant. The model was substantially affected by the farm variable (*p*<0.0001), but the allele variable exhibited questionable significance. The parameter estimates revealed that the AB allele exerted a favorable influence (estimate=108.133, *p*=0.0472), whereas the AA allele was not statistically significant (estimate=-86.806, *p*=0.2740). The farm component was found to be significant for the weight on the 30th day (LogWorth=22.602, *p*<0.0001). Alleles, birth type, and 90th-day weight were not significant in the model; however, birth weight was significant. The parameter estimates revealed that the weight on the 30th day was strongly influenced by farm 1 (estimate=-1004.637, *p*<0.0001), whereas farm 3 exerted a considerable positive effect (estimate=1199.090, *p*<0.0001). The AA allele was not significant, whereas the AB allele (estimate=-162.642, *p*=0.0882) exhibited marginal significance. For the weight at day 60, the weight at day 30 was the most important variable (LogWorth=38.125, *p*<0.0001), and the farm factor was also noteworthy (LogWorth=22.602, *p*<0.0001). Birth weight, allele, and birth type were found to be statistically insignificant. The AB allele had a positive and significant influence on parameter estimates (estimate=218.564, *p*=0.0309), while the AA allele was not significant (estimate=11.042, p=0.9404). The farm component exerted a substantial influence (LogWorth=9.260, *p*<0.0001), with the weight on the 60th day identified as the most important variable affecting the weight on the 90th day (LogWorth=55.143, *p*<0.0001). The model indicated that birth type (LogWorth=0.856, p=0.1394), allele (LogWorth=0.697, *p*=0.2010), and 30th-day weight (LogWorth=0.107, *p*=0.7818) were not statistically significant. According to parameter estimates, Farm 1 exhibited a positive and substantial influence (estimate=1244.934, *p*<0.0001), whereas Farm 3 demonstrated a negative and significant impact (estimate=-1343.843, *p*<0.0001). The AB allele showed a marginally significant negative impact (estimate=-297.512, *p*=0.0755).

The study conducted on the Akkaraman population revealed a higher prevalence of the BB genotype among lambs with a single birth type, as indicated in Table 4.

Table 3. Generalized Linear Model (GLM) Results for the Effect of IGF1R Farm, Genotypes and Birth Weight on the Live Weights of Akkaraman Lambs

Efffects	Farm	Allel	Birth Type	Birth Weight	30th Weight	60th Weight
Birth Weight	91.8046***	3.9467	0.3239			
30th Weight	108.3364***	5.2299	0.1605	7.6689**		
60th Weight	14.2488**	7.4667	1.7005	0.4456	169.9740***	
90th Weight	46.0666***	3.2090	2.1850	0.00117	0.07672	247.9679***

Table 4. Distribution of *IGF1R* genotypes among birth types of Akkaraman lambs

Genotype	Birth Type	
	Single	Twin
AA (n=38)	%71,05 (n=27)[a]	%28,95 (n=11)[a]
AB (n=276)	%77,90 (n=215)[a]	%22,10 (n=61)[a]
BB (n=83)	%91,57 (n=76)[b]	%8,43(n=7)[b]
Chi-Square / p	χ2=9.6368 / p=0.008	

n: Number of animals; χ2: Chi-Square; *p*: Probability value; a,b,c: Percentage values with different small letters in the same column are significantly different (*p*<0.01).

Discussion

The present study observed that AB genotype was the most common genotype (0.49) in terms of IGF1R-RsaI polymorphism in the Akkaraman breed lambs examined, followed by BB (0.20) and AA (0.31) genotypes, respectively. Additionally, it was determined that the B allele (0.56) was more prevalent compared to the A allele (0.44) in terms of allele frequencies. The SNP (g.195C>T) was examined in a study conducted by Karadağ (31) on several breeds, such as Alman Karabaş x Kıvırcık, Hampshire Down x Merino, Kıvırcık, Karacabey Merino, and Ramlıç. The research findings revealed that the AB genotype had a higher frequency in the investigated breeds, with recorded values of 0.49, 0.49, 0.47, 0.49, and 0.49, respectively. A study examining the same SNP (g.195C>T) in Pomeranian Coarsewool sheep bred in Poland named the allele names as T and C, reporting that the TT genotype (0.47) was the most prevalent genotype (23). In the current study, it was observed that the Akkaraman sheep population was not in Hardy-Weinberg equilibrium (HWE) for *IGF1R*-RsaI polymorphism, which was speculated to be attributed to the selection studies conducted.

The effects of polymorphisms in the *IGF1R* gene on growth traits have also been investigated in studies conducted on different livestock species. A study investigating Hereford cattle breeds reported that *IGF1R* variants were significantly associated with body weight and body measurement traits, while another study investigating Angus cattle breeds reported a significant association with weaning weight (18, 32). The *IGF1R* gene variant has been linked to the body weight and measurement traits of yaks in China (33). A significant *IGF1R* variant has been reported in Egyptian buffaloes, associated with high daily live weight gain from birth to 6 months (24). The investigated *IGF1R* variant in Wanbai and Yorkshire pig breeds has been reported to be associated with higher body weight at birth, 2 months, and 6 months (25). According to a study conducted on chickens, it was found that the *IGF1R* gene has a significant effect on early growth traits (34). A study conducted on Japanese quails reported that the *IGF1R* gene is significantly associated with 10-week live weight and average live weight gains at different periods (35). Studies conducted on sheep have also reported associations between the *IGF1R* gene and growth traits. In Makooei sheep, the *IGF1R* gene has been reported to be associated with average daily weight gain from birth to 6 months (36). A study on a Merino-derived sheep breed in Poland investigated the SNP (c.654G>A) in the 3rd exon of *IGF1R*, revealing an association between the gene and average weight gain from 56–78 days after birth (29). Another study conducted on Hulun Buir sheep reported a significant association between *IGF1R* and various growth traits (30). In a study of Pomeranian Coarsewool sheep breed in Poland, the investigated SNP (g.195C>T) was reported to be significantly associated with body weight on days 1, 33, and 90 post-birth, as well as with average daily weight gain between days 1-33, 33-90, and 1-90 (23). Similarly, Karadağ (31) reported that in Alman Karabaş × Kıvırcık, Hampshire Down × Merino, Kıvırcık, Karacabey Merino, and Ramlıç breeds in Türkiye, lambs carrying the AB genotype have higher birth weights. In this study, the IGF1R genotype was found to have no statistically significant effect on lamb weights across all measured periods (birth, 30th, 60th, and 90th days). However, birth type (single or twin) and farm conditions were identified as significant factors affecting weight gain in all measurement periods. These findings highlight the need to consider both genetic and environmental factors when evaluating the growth performance of lambs.

Yang et al. (27) established a relationship between the *IGF1R* gene and superovulation in cattle. The literature review shows that in addition to studies on the effects of the *IGF1* gene on the twinning trait, there is also a need for studies on *IGF1R*, the receptor gene of IGF1. In addition to growth, the twinning rate is a crucial economic trait that could be utilized for sheep breeding objectives. In this study investigating the *IGF1R*-RsaI polymorphism in sheep, it was observed that the BB genotype was more prevalent in single-birth lambs. The findings of this study suggest that future studies investigating the relationship between *IGF1R*-RsaI polymorphism and twinning are necessary. In summary, this study found that *IGF1R*-RsaI polymorphism was effective on live weight in lambs according to birth type. Future research may investigate the *IGF1R* gene for more growth traits or use a larger population of Akkaraman sheep breeds. Additional to these findings, the fact that the BB genotype was more prevalent in single-birth lambs might prove an important area for future research for the purpose of establishing a possible link with lambing. These findings are a foundational investigation of genetic factors that affect growth and lambing traits in Akkaraman sheep, highlighting the complexity of genetic effects on these traits and the necessity for more comprehensive studies.

References

1. Deng J, Xie XL, Wang DF, et al. Paternal origins and migratory episodes of domestic sheep. Curr Biol 2020; 30: 4085-4095.
2. Stiner MC, Munro ND, Buitenhuis H, Duru G, Özbaşaran M. An endemic pathway to sheep and goat domestication at Aşıklı Höyük (Central Anatolia, Turkey). Proc Natl Acad Sci USA 2022; 119: e2110930119.
3. Morris ST. Economics of sheep production. Small Ruminant Res 2009; 86: 59-62.
4. Sevim S. Aydın İli Hayvancılığının Mevcut Durumu. Hayvan Bilimi ve Ürünleri Dergisi 2022; 5: 48-61.
5. TUİK. "Hayvansal Üretim İstatistikleri, 2023". https://data.tuik.gov.tr/Bulten/Index?p=Hayvansal-Uretim-Istatistikleri-2023-49681/ 09.02.2024.
6. Kizilaslan M, Arzik Y, White SN, Piel LMW, Cinar MU. Genetic parameters and genomic regions underlying growth and linear type traits in Akkaraman sheep. Genes 2022; 13: 1414.

7. Behrem S. Effects of environmental factors growth traits of Akkaraman sheep in Çankırı province. Livest Sci 2021; 61: 22-27.
8. Ceyhan A, Şekeroğlu A, Duman M. Niğde İlinde Yetiştirilen Akkaraman ırkı koyunların bazı döl verim özellikleri ve kuzuların büyüme performansı. Turkish Journal of Agriculture - Food Science and Technology 2019; 7: 1509-1514.
9. Üçtepe A. Koyunlarda Besi özelliklerini geliştirmek amacıyla Türkiye'de yapılan melezleme çalışmalarının kantitatif olarak değerlendirilmesi. J Tekirdag Agric Fac 2016; 13: 75-84.
10. Sönmez R, Kaymakçı M, Eliçin A, et al. Türkiye koyun islahı çalışmaları. Uludağ Üniversitesi Ziraat Fakültesi Dergisi 2009; 23: 43-65.
11. Kaymakçı M, Taşkın T. Türkiye koyunculuğunda melezleme çalışmaları. Hayvansal Üretim 2008; 49: 43-51.
12. Saygili E, Turkyilmaz D, Ekinci K, et al. Associations between MSTN/HaeIII polymorphism and reproductive and growth characteristics in Morkaraman sheep. Kafkas Univ Vet Fak Derg 2022; 28: 717-722.
13. McGovern FM, McHugh N, Fitzmaurice S, et al. Phenotypic factors associated with lamb live weight and carcass composition measurements in an Irish multi-breed sheep population. Transl Anim Sci 2020; 4: txaa206.
14. Gascoigne E, Lovatt F. Lamb growth rates and optimising production. In Pract 2015; 37: 401-414.
15. Goddard ME, Hayes BJ. Mapping genes for complex traits in domestic animals and their use in breeding programmes. Nat Rev Genet 2009; 10: 381-391.
16. Bayram D, Akyüz B, Arslan K, et al. DGAT1, CAST and IGF-I gene polymorphisms in akkaraman lambs and their effects on live weights up to weaning age. Kafkas Univ Vet Fak Derg 2019; 25: 9-15.
17. Kalds P, Zhou S, Gao Y, et al. Genetics of the phenotypic evolution in sheep: a molecular look at diversity-driving genes. Genet Sel Evol 2022; 54: 61.
18. Szewczuk M, Zych S, Wójcik J, Czerniawska-Piątkowska E. Association of two SNPs in the coding region of the insulin-like growth factor 1 receptor (IGF1R) gene with growth-related traits in Angus cattle. J Appl Genet 2013; 54: 305-308.
19. De la Rosa Reyna XF, Montoya HM, Castrellón VV, et al. Polymorphisms in the IGF1 gene and their effect on growth traits in mexican beef cattle. Genet Mol Res 2010; 9: 875-883.
20. Maghnie M, Loche S, Cappa M, Ghizzoni L, Lorini R. Hormone resistance and hypersensitivity: From genetics to clinical management. In: Walenkamp MJE, Losekoot M, Wit JM. (Editors). Molecular IGF-1 and IGF-1 Receptor Defects: From Genetics to Clinical Management. Italy: Genoa 2012; 24: 128-137.
21. Jin S, Chen S, Li H, et al. Associations of polymorphisms in GHRL, GHSR, and IGF1R genes with feed efficiency in chickens. Mol Biol Rep 2014; 41: 3973-3979.
22. Louvi A, Accili D, Efstratiadis A. Growth-promoting interaction of IGF-II with the insulin receptor during mouse embryonic development. Dev Biol 1997; 189: 33-48.
23. Proskura WS, Szewczuk M. The polymorphism in the IGF1R gene is associated with body weight and average daily weight gain in pomeranian coarsewool ewes. Pak Vet 2014; 34: 514-517.
24. El-magd MA, Saleh AA, Nafeaa AA, El-komy SM, Afifi MA. Polymorphisms of the IGF1 gene and their association with growth traits, serum concentration and expression rate of IGF1 and IGF1R in buffalo. J Zhejiang Univ Sci B 2017; 18: 1064.
25. Wang W, Ouyang K, Su X, Xu M, Shangguan X. Polymorphism of insulin-like growth factor 1 receptor gene in 12 pig breeds and its relationship with pig performance traits. Asian Australas J Anim Sci 2006; 19: 1541-1545.
26. Baumgarten SC, Armouti M, Ko C, Stocco C. IGF1R expression in ovarian granulosa cells is essential for steroidogenesis, follicle survival, and fertility in female mice. Endocrinology 2017; 158: 2309-2318.
27. Yang WC, Yang LG, Riaz H, et al. Effects in cattle of genetic variation within the IGF1R gene on the superovulation performance and pregnancy rates after embryo transfer. Anim Reprod Sci 2013; 143: 24-29.
28. Froesch ER, Schmid C, Schwander J, Zap J. Actions of insulin-like growth factors. Annu Rev Physiol 1985; 47: 443-467.
29. Grochowska E, Lisiak D, Akram MZ, et al. Association of a polymorphism in exon 3 of the IGF1R gene with growth, body size, slaughter and meat quality traits in Colored Polish Merino sheep. Meat Sci 2021; 172: 108314.
30. Ding N, Tian D, Li X, et al. Genetic polymorphisms of IGF1 and IGF1R genes and their effects on growth traits in Hulun Buir sheep. Genes 2022; 13: 666
31. Karadag O. The polymorphism of insulin-like growth factor-1 receptor (IGF-1R) gene in meat-type Lambs in Turkey: I. Effect on growth traits and body measurements. Small Ruminant Res 2022; 215: 106765.
32. Szewczuk MA, Kulig H. Association of selected polymorphic sites in the IGF1R gene with body weight and conformation of Hereford cattle. Scientific Annals of the Polish Society of Animal Production 2020; 16: 17-26.
33. Liang C, Yan P, Yao Y, et al. A novel single nucleotide polymorphism (SNP) of the IGF1R gene and the association with growth traits in yak (Brief Report). Arch Anim Breed 2010; 53: 626-628.
34. Lei M, Peng X, Zhou M, et al. Polymorphisms of the IGF1R gene and their genetic effects on chicken early growth and carcass traits. BMC Genet 2008; 9: 1-9.
35. Moe HH, Shimogiri T, Kamihiraguma W, et al. Analysis of polymorphisms in the insulin-like growth factor 1 receptor (IGF1R) gene from Japanese quail selected for body weight. Anim Genet 2007; 38: 659-661.
36. Pasandideh M, Rahimi G, Hemati V. Effect of Single nucleotide polymorphisms in IGF-1R Gene on growth rate traits in Makooei sheep. Iran J Appl Anim 2019; 9: 669-675.