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Polymorphisms in the Leptin Receptor (LEPR) Gene and Their Association with Growth and Reproductive Traits in Indonesian Sheep

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ABSTRACT

The leptin receptor (LEPR) gene is a potential gene associated with growth and reproductive traits in livestock. However, studies on local Indonesian sheep are very rarely conducted. This study aimed to investigate the LEPR gene polymorphism and its association with growth and reproductive traits in Indonesian sheep. A total of 553 DNA samples were used to identify LEPR gene polymorphisms in Indonesian sheep populations. The sheep population used was 313 crossbred lambs (Garut × Garut, Dorper × Garut, Batur × Garut, and Suffolk × Garut) observed to determine the association of the LEPR gene with growth traits, while 240 Garut ewes were also examined to determine the association of the LEPR gene with reproductive traits. The genetic variation of sheep breeds was assessed using the PCR-RFLP technique with the restriction enzyme *Aci1*. The correlation of growth and reproductive Traits associated with Genotypes was assessed using a General Linear Model (GLM). The result indicated that the LEPR gene was polymorphic in Indonesian sheep breeds and produced two alleles (A and C) and three genotypes (AA, AC, and CC) according to the Hardy-Weinberg Equilibrium. The polymorphisms of the LEPR gene were statistically significant in association with the weight of the lamb at birth and the weight of the lamb at weaning ($p<0.05$). The lambs that were homozygous AC had significantly higher births and weaning weights ($p<0.05$) than those lambs with the AA genotype. The LEPR polymorphisms were not found to be associated with average litter size or offspring mortality. These findings indicate that the LEPR gene is a promising candidate marker for improving growth performance, particularly birth weight and weaning weight, in Indonesian sheep.

Keywords: growth; LEPR gene; reproductive; sheep, polymorphisms

INTRODUCTION

Sheep are an important livestock commodity, providing animal protein and income for farmers in Indonesia. Sheep meat production increased by 1.09% despite a relative decline in sheep population from 2013 to 2023 (National Food Agency, 2023). Sheep in Indonesia are primarily raised by small-scale farmers, with local breeds constituting the majority of the national sheep population (Tiesnamurti *et al.*, 2020). Local sheep play a vital role in rural community development, providing income and employment, as well as opportunities for religious practices. However, the main issue raised in this study is the low productivity of local sheep breeds, characterized by slow growth rates, small birth sizes, and high offspring mortality rates, which limit the increase in sheep population and production. This study addresses this gap by designing a targeted breeding strategy that uses genetic selection to produce sheep with fast growth rates, the ability to give birth to 2-3 lambs, and low lamb mortality rates. Gunawan *et al.* (2011) noted that improved management and controlled breeding programs would enable increased local sheep production.

Sheep productivity in Indonesia still faces various challenges, one of which is genetic factors that are directly related to the growth and reproduction processes of animals. Studies have reported high genetic correlations between birth weight and weaning weight, as well as growth rate and meat characteristics (Şirin *et al.*, 2024). In addition, weaning weight has a significant correlation with the weight of one-year-old livestock and carcass weight (Lopes *et al.*, 2016). Strategies that can help increase productivity also include the use of prolific ewes (i.e., ewes capable of producing more than one lamb per birth) (Gebreselassie *et al.*, 2020; Yang *et al.*, 2024) and preventing lamb mortality, both of which influence the potential profitability of the farm and the productive capacity of ewes (Bashir *et al.*, 2020). Improvements in growth and reproductive traits in sheep are still limited because traditional selection relies on several generations. Selection using genomic markers to identify genetic variation is essential for improving livestock productivity (Khaerunnisa *et al.*, 2016).

Therefore, the application of genomic technology to determine the relationship between phenotypic traits and specific gene variants has the potential to improve the efficiency of the selection process compared to traditional methods. The SNP identification was used for marker-assisted selection (MAS) to improve carcass quality and growth performance, particularly by optimizing muscle mass and carcass traits in cattle (Khasanah *et al*., 2016). The marker-assisted selection (MAS) can be a more viable selection method, especially as a result of the need to maximize genetic diversity, as well as maximize growth and reproductive traits in sheep (Mucha *et al*., 2022)..

Growth and reproductive traits are controlled by multiple genes in specific chromosomal regions known as quantitative trait loci (QTL). A total of 331 QTLs associated with production traits and 101 QTLs associated with reproductive traits have been identified in sheep, leading to the identification of several important candidate genes that can be utilized for breeding programs (Gebreselassie *et al.,* 2020; Ma *et al.,* 2022). The candidate gene for growth and reproductive traits refers to the Leptin Receptor (LEPR) gene. The LEPR gene plays a role in regulating energy balance, metabolism, and reproduction (Saxton *et al.,* 2023; Childs *et al.,* 2021). Genetic diversity at specific SNPs can serve as markers for molecular-based selection (Gunawan *et al*., 2021). This approach accelerates genetic improvement and efficiently increases the productivity of local Indonesian sheep (Li *et al.,* 2025).

Genetic diversity is crucial for evolution. It provides a pool of alleles available for natural selection to exploit in producing organisms better adapted to climate change (Zhulan *et al.,* 2022). Molecular analyses, such as PCR-RFLP analysis, can identify the level of genetic diversity found among samples obtained from a population and characterize the genetic variation found among breeds. Conservation of a species must be based on the conservation of local genetic diversity (Sutarno *et al.,* 2019; Sèzonlin *et al.,* 2020). The proper implementation of conservation and sustainable management programs requires a framework that is informed by sufficient information on the structure of biologically diverse populations, including examining the genetics of individual animals within populations or breed groups (Rodríguez-Quilón *et al.,* 2016; Hohenlohe *et al*., 2020). The evaluation of genetic diversity in Barki sheep has revealed that LEPR gene polymorphisms are found in exon 19 – specifically at the c.2800G>A and c.2978C>G loci, which are correlated with growth traits, including average daily weight gain (ADG) and body length (Ibrahim, 2021). Furthermore, identifying genetic diversity associated with reproductive performance, including litter size and offspring mortality, is crucial if the current and future genetic capacity of locally adapted sheep populations is to be developed and maintained (Liu *et al.,* 2024; Abuzahra *et al.,* 2025).

Various studies have found significant correlations between polymorphisms in the LEPR gene and body weight in pigs (Pérez-Montarelo *et al.,* 2015), cattle (Guo *et al.,* 2008), and mice (Breit *et al.,* 2023), as well as empirical findings from various sheep breeds, such as Romane sheep related to body fat reserves (Macé *et al.,* 2022), and Indonesian sheep related to fatty acid nutrition (Gunawan *et al.,* 2019). In addition, the LEPR gene was also found to be associated with the onset of puberty and ovulation rate in Mongolian sheep (Ji *et al.,* 2023) and the total number of litters and live births in pigs during their reproductive period (Sun *et al.,* 2018). Brickell *et al.* (2010) also found that several SNPs in the leptin gene were associated with the incidence of perinatal mortality in Holstein-Friesian cattle. However, the identification of LEPR gene polymorphisms and their correlation with growth traits, birth weight, and weaning weight, as well as reproductive traits, litter size, and mortality in Indonesian sheep have not been studied. The LEPR gene polymorphisms are hypothesized to be associated with growth and reproductive traits in Indonesian sheep. Therefore, this study aims to identify LEPR gene diversity and evaluate its correlation with growth and reproductive traits in local Indonesian sheep. We revealed significant effects of different LEPR genotypes on birth weight and weaning weight. Information on the diversity of LEPR genes and their effects on growth and reproductive traits will provide a scientific basis for the application of molecular selection in breeding programs.

MATERIALS AND METHODS

Animals

Blood samples were used as a source of total DNA from 553 sheep. Specifically, growth traits were evaluated in 313 crossbred lambs (77 males and 238 females) aged 9–15 months, while reproductive traits were assessed in 240 Garut ewes aged 1.5–3 years. The lambs used in this study were crossbred Garut x Garut (n=192), Dorper x Garut (n=81), Batur x Garut (n=30), and Suffolk x Garut (n=10) (Figure 1). This study was conducted in the Laboratory of Animal Molecular Genetics, Faculty of Animal Science, IPB University. The phenotypic data on growth and reproductive traits were collected between 2023 and 2025 from the premium sheep breeding center of IPB University and UPTD-BPPTDK Margawati Garut (Technical Implementation Unit of the Livestock Breeding and Animal Diagnostics Development Center). The traits observed were birth weight (aged 1 day), weaning weight (aged 90 days), litter size (parity 1-3), and mortality (parity 1-3). These animals were raised under an integrated management system that included controlled feeding with forage and concentrates, ad libitum access to water, adequate housing and infrastructure, proper sanitation, processing of waste into compost and biogas, and comprehensive disease prevention and control measures. Blood samples were taken from the jugular vein using a 3 mL syringe, then preserved in a 10 mL EDTA tube as an anticoagulant and stored at −4 °C before DNA extraction (Barra *et al.,* 2025). All procedures involving animals were approved by the Animal Ethics Committee of IPB University (approval number: 117-2018 IPB).

DNA Extraction and Amplification

The DNA extraction followed the Genomic DNA Mini Kit Buffy Coat protocol (Geneaid). The blood

Figure 1. The crossbred lambs of Garut x Garut (a), Dorper x Garut (b), Batur x Garut (c), and Suffolk x Garut (d).

extraction procedure comprised five stages: (1) Sample Preparation, (2) Cell Lysis, (3) DNA Binding, (4) Wash, and (5) DNA Elution. Extracted DNA was stored at -20 °C. The g.40761672 A>C SNP, along with the Forward primer (5′-GGA GGA ATC AGG GCA TTT TC-3′) and Reverse primer (5′-CCC CTA TCC TTA CGC AAT CC-3′), was used for amplification according to Gunawan *et al.* (2019), and analyzed following the approach described by Azizah *et al.* (2020), producing a fragment of 432 bp. The SNP (g.40761672 A>C) in the LEPR gene is located in intron 19 on chromosome 1.

The DNA amplification was carried out in two stages. In the first stage, 2 μL of extracted DNA was aliquoted into 0.2 mL tubes, followed by the addition of a reaction mixture consisting of 6.1 μL nuclease-free water (NFW), 0.2 μL of forward and reverse primers, and 7.5 μL of MyTaq HS Red Mix. The mixing of the materials proceeded until they were entirely homogenized in the centrifuge. In the second step, the combined materials underwent DNA amplification using a Biored thermocycler. The amplification process started with an initial denaturation step at 95 ºC for 1 minute. The following 35 cycles consisted of denaturation at 95 ºC for 15 seconds, primer annealing at 60 ºC for 15 seconds, and extension at 72 ºC for 10 seconds. The last step was a terminal extension at 72 ºC for 1 minute.

PCR-RFLP Analysis of LEPR Gene Polymorphism

Identification of LEPR gene polymorphisms using the PCR-RFLP method, referring to Tarach (2021). A 5 μL PCR product sample was added with 2 μL of a mixture (1 μL of nuclease-free water (NFW), 0.7 μL of enzyme buffer, and 0.3 μL of enzyme), and incubated at 37 °C for four hours. All PCR-RFLP products were electrophoresed on a 2% agarose gel for 25-35 minutes at 100 volts. The restriction fragment pattern based on the *Aci1* enzyme consisted of three bands, namely the CC genotype: 432 bp, the AA genotype: 140 bp and 292 bp, and the AC genotype: 140 bp, 292 bp, and 432 bp.

Statistical Analysis

Descriptive analyses of growth and reproductive parameters were performed to summarize the general characteristics of the study data. The analyses of polymorphism and Hardy–Weinberg Equilibrium, genotype frequencies, and allele frequencies were performed using the software PopGen32. The association between the LEPR gene and growth and prolificacy traits was analyzed using a GLM analysis of variance in Minitab 17. Allele and genotype frequencies were analyzed using the methodologies described by Nei & Kumar (2000).

$$\mathcal{X}_{\mathrm{i}} = \frac{(2nii+\sum j\neq jn_{jj})}{2N}\,\mathcal{X}_{ii} = \frac{n_{ij}}{N}$$

where X_i was the frequency of the allele, X_{ii} was the frequency of genotype, nii was the total number of individuals with genotype ii, nij was the total number of individuals with genotype ij, and N was the total population size**.**

The Hardy–Weinberg equilibrium was assessed using the Chi-square (χ^2) test, following the methodology described by Hartl & Clark (1997).

$$\chi 2 = \sum \frac{(\mathrm{O}-\mathrm{E})^2}{\mathrm{E}}$$

where χ^2 was chi-square, Σ was the sum of analyzed classes O was the observed value, and E was the expected value.

The association of the LEPR gene with phenotypic traits in Indonesian sheep was analyzed using the GLM described by Chen *et al.* (2004). The statistical model for growth traits used was as follows:

$$\Upsilon_{ijkl} = \mu + G_i + B_j + S_k + e_{ijkl}$$

where Υ_{ijkl} was the observed values variable, μ was the overall mean, G_i was the effect of the i-th genotype (i=2 levels), B_j was the effect of the j-th breed (j=4 levels), S_k was the effect of the k-th sex (k=2 levels), and e_{ijkl} was the residual error.

Another model was used to detect the effect of genotype on the reproductive traits as follows:

$$\Upsilon_{ijkl} = \mu + G_i + P_j + R_k + e_{ijkl}$$

where Υ_{ijkl} was the observed values variable, μ was the overall mean, G_i was the effect of the i-th genotype (i=3 levels), P_j was the effect of the k-th parturition (k=3 levels), R_k was the effect of the j-th ram (j=4 levels), and e_{ijkl} was the residual error.

The analyses were performed on each growth and reproductive trait separately. When a significant difference was found ($p<0.05$), the Tukey test was used to assess differences among genotypes for the traits examined.

RESULTS

Descriptive Statistics of Growth and Reproductive Phenotypic Traits

Descriptive analysis shows variation in growth and reproductive performance among Indonesian sheep breeds. The GG breed (n=192) had the highest average birth weight of 2.85±0.04 kg. The DG breed (n=81), BG breed (n=30), and SG breed (n=10) showed lower average birth weights of 2.46±0.06 kg, 2.43±0.10 kg, and 2.34±0.28 kg, respectively. Weaning weight performance showed a pattern consistent with birth weight. The GG group (n=192) had the highest average weaning weight of 13.90±0.21 kg. The DG (n=81), BG (n=30), and SG (n=10) groups had average weaning weights of 12.50±0.43 kg, 13.02±0.78 kg, and 12.77±1.07 kg, respectively. In terms of reproduction, Garut ewes (n=240) had an average litter size of 1.75±0.05 lambs, ranging from 1 to 5 lambs. Meanwhile, the mortality rate was recorded at 28.99±2.62%. The results of the descriptive analysis of growth and reproduction characteristics are presented in Table 1.

Identification of the LEPR Gene Polymorphism

The LEPR gene was successfully screened using the PCR-RFLP method with the AciI restriction enzyme. Three genotypes were observed, namely AA, AC, and CC, which represent homozygous and heterozygous combinations of the A and C alleles. Restriction DNA fragments at the g.40761672 A>C locus of the LEPR gene showed that the homozygous CC genotype produced a 432 bp fragment, the homozygous AA genotype produced 292 bp and 432 bp fragments, while the heterozygous AC genotype produced fragments of 140 bp, 292 bp, and 432 bp (Figure 2). The AA genotype had the highest frequency (n=438; 0.79), followed by AC (n=111; 0.20) and CC (n=4; 0.01). The A allele was

Table 1. Descriptive statistics of growth and reproductive traits in Indonesian sheep

Trait category	Trait	Breed	N	Mean	SE	Min	Max
Growth	Birth weight (kg)	GG	192	2.85	0.04	1.04	4.54
		DG	81	2.46	0.06	1.00	3.75
		BG	30	2.43	0.10	1.20	3.40
		SG	10	2.34	0.28	1.20	3.88
	Weaning weight (kg)	GG	192	13.90	0.21	5.80	23.63
		DG	81	12.50	0.43	6.66	23.00
		BG	30	13.02	0.78	6.20	21.60
		SG	10	12.77	1.07	7.60	17.80
Reproduction	Litter size (n)	Garut	240	1.75	0.05	1.00	5.00
	Offspring mortality (%)	Garut	240	28.99	2.62	0.00	100.00

Note: N = number of samples, GG = Garut x Garut, DG = Dorper x Garut, BG = Batur x Garut, SG = Suffolk x Garut, SE = standard error, Min = Minimum, Max = Maximum.

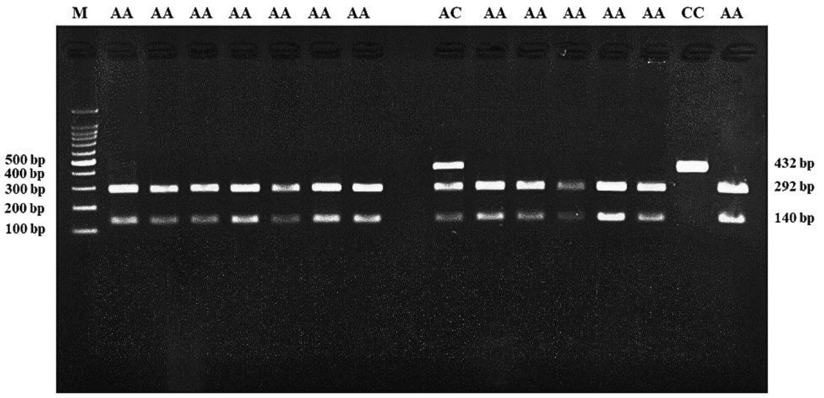

Figure 2. Visualization of PCR-RFLP products using 100 bp DNA markers and 2% agarose gel separated by the restriction enzyme *Aci1*. The horizontal axis represents the sample lane, which consists of M (DNA marker) followed by individual samples with AA, AC, and CC genotypes. The vertical axis represents the size of the DNA fragments (base pairs, bp).

dominant, with a frequency of approximately 89%, while the C allele had a frequency of approximately 11%. Chi-square test analysis showed that the LEPR gene locus was in Hardy–Weinberg equilibrium, with a value of 1.13 (Table 2).

Association of the LEPR Gene with Growth Traits

The SNP at the g.40761672 A>C locus of the LEPR gene showed a significant association with differences in birth weight and weaning weight in the Indonesian sheep population ($p<0.05$). Individuals with the AC genotypes had higher birth weight and weaning weight than those with the AA genotypes ($p<0.05$). Breed and sex differences have been included in the correction factors to reduce bias in observing the effect of genotype on birth weight and weaning weight in Indonesian sheep. The association result is shown in Table 3.

Association of the LEPR Gene with Reproductive Traits

The LEPR gene polymorphism showed no significant correlation with litter size ($p>0.05$). The number of lambs born in this sheep population ranged from 1 to 5. Additionally, there was no association ($p>0.05$) between the LEPR gene polymorphism and offspring mortality. Other factors, such as differences in parturition and rams, affect litter size and offspring mortality, but both factors have been included in the statistical model as correction factors so that the results of this study are purely due to genotype differences. The association results are presented in Table 4.

DISCUSSION

Descriptive analysis shows that the GG breed has a higher birth weight than the DG, BG, and SG breeds in this study. The average birth weight was greater than that reported by Gowane *et al*. (2011) at 1.82±0.03 kg, but smaller than that reported by Nurlela *et al*. (2024) at 2.96±0.43 kg. Birth weight is influenced by several factors, such as genetics and maternal nutrition during pregnancy (Wong *et al.*, 2021). In addition, relatively similar results also show that the weaning weight of the GG breed is greater than that of the DG, BG, and SG breeds. The average weaning weight in this study is also greater than that reported by Somanjaya *et al*. (2025) of 12.85±2.86 kg, but smaller than that reported by Athifa *et al.* (2022) at 14.15±2.94 kg and Lusi *et al.* (2023) at 14.06±6.17 kg. The body weight traits at various ages are positively correlated, indicating that selection at one growth phase can lead to improved performance at subsequent stages (Hasan *et al*., 2014). The differences in sheep body weight are influenced by the genetic potential of the breed as well as the breeding strategies applied (Sharif *et al*., 2022).

Garut ewes have a larger birth size than that reported by Habtegiorgis *et al.* (2022), which is 1.57±0.02. The average litter size in this study is relatively high for local sheep breeds. This indicates the presence of genetic potential that can be improved through selection (Jayadi & Jan, 2024). Ghiasi & Abdollahi-Arpanahi (2021) stated that several sheep breeds have the potential to increase the number of lambs per birth. The offspring mortality rate in this study was relatively high, averaging 28.99%. Several factors, such as the condition of the mother during pregnancy and genetic factors from the parents, contribute to offspring mortality at birth (Wong *et al.*, 2021; Souza *et al.*, 2024).

The LEPR gene in the Indonesian sheep population was amplified using the PCR method and found a specific size with a length of 432 bp. The successful PCR amplification with specific fragment sizes indicated that the method used was optimal and could support genetic variation analysis (Rusdin *et al.*, 2020). The

Table 2. Allele frequencies, genotype frequencies, and Hardy-Weinberg equilibrium of the LEPR gene

Gene	N	Genotype frequency			Allele frequency		Chi square (x^2)
		AA (438)	AC (111)	CC (4)	A	C	
LEPR	553	0.79	0.20	0.01	0.89	0.11	1.13

Note: N = Number of samples, x^2 (0.05) = 1.13

Table 3. Association of the LEPR gene with growth traits in Indonesian sheep

Variables	N	Genotype of LEPR gen ($\bar{x}$± SE)			p-Value
		AA (245)	AC (68)	CC (0)	
Birth weight (kg)	313	2.64^b±0.43	2.89^a±0.68	-	0.041*
Weaning weight (kg)	313	13.15^b±0.23	14.39^a±0.33	-	0.029*

Note: N = number of samples, $\bar{x}$ = mean, SE = standard error, a,b = different superscripts indicate a significant difference ($p<0.05$), (*) = significantly different ($p<0.05$).

Table 4. Association of the LEPR gene with the reproductive traits in Indonesian sheep

Variable	N	Genotype of LEPR gen ($\bar{x}$± SE)			p-Value
		AA (193)	AC (43)	CC (4)	
Litter size (n)	240	1.77±0.06	1.72±0.13	1.50±0.28	0.71
Mortality (%)	240	31.04±3.01	22.48±5.64	0.00±0.00	0.21

Note: N = number of samples, $\bar{x}$ = mean, SE = standard error

PCR-RFLP method was successfully used to identify the LEPR gene variant (g.40761672A>C) in the Indonesian sheep population. The results showed that the LEPR gene has genetic polymorphism in the Indonesian sheep population, represented by three genotypes: AA, AC, and CC. Gunawan *et al.* (2021) stated that an SNP can be polymorphic if it has more than one allele, with a frequency of at least 1%. The A allele has a higher frequency than the C allele. The Hardy-Weinberg equilibrium is observed in the allele frequencies of a sheep population. Allele frequencies are considered to be in Hardy-Weinberg equilibrium if the Chi-square value is less than 3.84 (Komarudin *et al.*, 2024). A sheep population is also said to be in Hardy-Weinberg equilibrium when the genotype and allele frequencies remain constant from generation to generation due to random mating and a large population (Sutikno *et al.*, 2018).

The LEPR gene genotype plays a role in controlling energy metabolism, lipolysis, and reproductive function. Azizah *et al.* (2020) found a positive correlation between the AC genotype and fat quality and meat characteristics in Indonesian local sheep. In Romane female sheep, the TT variant of the LEPR gene is associated with higher fat reserves and better body condition during the reproductive cycle compared to the CC and CT genotypes (Macé *et al.*, 2022). The p.P1019S allele variant of the LEPR gene affects the rate of oocyte maturation and ovulation in Davisdale sheep (Montgomery, 2024). Leptin signaling through the LEPR gene triggers the release of LH in response to GnRH, linking the LEPR gene to metabolic and reproductive mediators (Younis *et al.*, 2019).

This study shows that genetic variation in the LEPR gene has a significant effect on birth weight and weaning weight in Indonesian sheep. In addition, sheep with the AC genotype have a higher body weight than those with the AA genotype, indicating that the LEPR gene is a critical factor in early growth. These findings are consistent with the research by Ma *et al.* (2022), which identified the c.240C>T and c.279C>T mutations in the LEPR gene of Mongolian and Ujimqin sheep, indicating that these specific genetic polymorphisms affect embryo growth regulation. Zhao *et al.* (2022) also reported that the LEPR gene plays an essential role in controlling cell proliferation and other physiological processes in pigs. In addition, genetic variation in the LEPR gene is associated with fatty acid nutrient composition in sheep (Gunawan *et al.*, 2019), which is related to energy homeostasis and metabolic efficiency that are important for sheep growth processes (Li *et al.*, 2025). These findings indicate that the LEPR gene plays a role in the early stages of sheep development until weaning.

Genetic variation in the LEPR gene is not associated with litter size or mortality. The LEPR gene is responsible for regulating energy use in the body through leptin and is associated with the function of the hypothalamus, pituitary gland, and gonads; however, its influence on litter size is relatively limited (Herdis *et al.*, 2025). There are major genes that influence reproduction, particularly litter size in sheep, such as the BMPR1B and BMP15 genes, which affect oocyte number and ovulation rate to enable larger litter sizes in sheep (Wang *et al.*, 2024; Wen *et al.*, 2021). Genetic variation in the LEPR gene also does not appear to influence offspring mortality directly. Du *et al.* (2024) noted that there are many factors that influence offspring mortality, including management, genetics, and environmental effects such as the season of birth, and the physiological condition of the ewes are more likely to be associated with offspring mortality (Abdelqader *et al.*, 2017; Tüfekci & Sejian, 2023; Ceyhan & Kozaklı, 2023).

The LEPR gene is an important regulator in energy metabolism and animal growth processes (Raza *et al.*, 2020), especially its effect on birth weight and weaning weight, which are indicators of growth performance in Indonesian sheep. Additionally, the LEPR gene has physiological effects on metabolic regulation and reproductive function, but does not directly influence litter size or offspring mortality (Lakhssassi *et al.*, 2020). Therefore, to improve reproductive performance, the use of a combination of genes that can directly influence litter size and offspring mortality is necessary. This study demonstrates the potential of the LEPR gene in breeding programs to enhance birth weight and weaning weight, which are indicators of growth traits in Indonesian sheep.

CONCLUSION

The LEPR gene exhibits diverse polymorphisms in local Indonesian sheep populations. Genetic variation in the LEPR gene is associated with birth weight and weaning weight. However, LEPR gene diversity does not correlate with litter size and offspring mortality. The AC genotype shows higher birth weight and weaning weight than the AA genotype. Therefore, the LEPR gene has the potential to be a candidate genetic marker in sheep selection and breeding programs to improve growth traits. Further research is needed to analyze the mRNA expression of the LEPR gene to validate its biological role.

CONFLICT OF INTEREST

C. Sumantri and A. Gunawan serve as editors of the Tropical Animal Science Journal but have no role in the decision to publish this article. The authors declare that they have no financial, personal, or institutional conflicts of interest with any individuals or organizations related to the content of this manuscript.

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DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

The authors of this article used ChatGPT by OpenAI (version 4), Consensus (version 5), and Grammarly (version 1.2), which were used only to fix grammar errors, correct vocabulary errors, and improve the overall clarity of the writing through better sentence structures. After using these tools, the authors carefully edited and improved their work for readability and accuracy; therefore, the authors are entirely responsible for the quality and validity of the content contained in this publication.

REFERENCES

Abdelqader, A., Irshaid, R., Tabbaa, M. J., Abuajamieh, M., & Titi, H. (2017). Factors influencing Awassi lambs survivorship under field conditions. Livestock Science, 199, 1–6. https://doi.org/10.1016/j.livsci.2017.03.007

Abuzahra, M., Wijayanti, D., Effendi, M., Mustofa, I., Munyaneza, J., & Moses, I. (2025). Improved litter size in thin-tailed Indonesian sheep through analysis of TGIF1 gene polymorphisms. Veterinary Medicine International, 2025, 1–9. https://doi.org/10.1155/vmi/7778088

Athifa, I. R., Sari, A. P. Z. N. L., Maharani, D., Budisatria, I. G. S., Bintara, S., Noor, Y. G., Hidayat, R., & Panjono. (2022). The pre-weaning growth of lambs from crossbreeding between Garut ewes and Dorper rams. Biodiversitas, 23(11), 5738–5743. https://doi.org/10.13057/biodiv/d231125

Azizah, D., Noor, R. R., & Gunawan, A. (2020). Investigasi hubungan keragaman gen leptin receptor (LEPR) dengan karakteristik karkas dan kualitas daging domba. Jurnal Ilmu Produksi dan Teknologi Hasil Peternakan, 8(3), 124–130. https://doi.org/10.29244/jipthp.8.3.124-130

Bashir, I., Rather, M., Rather, J., Hajam, I., Baba, J., Shah, M., & Haq, Z. (2020). Study of mortality pattern in an organized farming sector amongst Kashmir Merino sheep. International Journal of Current Microbiology and Applied Sciences, 9(4), 1570–1578. https://doi.org/10.20546/ijcmas.2020.904.184

Breit, S. N., Manandhar, R., Zhang, H. P., Lee-Ng, M., Brown, D. A., & Tsai, V. W. W. (2023). GDF15 enhances body weight and adiposity reduction in obese mice by leveraging the leptin pathway. Cell Metabolism, 35(8), 1341–1355.e3. https://doi.org/10.1016/j.cmet.2023.06.009

Brickell, J., Pollott, G., Clempson, A., Otter, N., & Wathes, D. (2010). Polymorphisms in the bovine leptin gene associated with perinatal mortality in Holstein-Friesian heifers. Journal of Dairy Science, 93(1), 340-7. https://doi.org/10.3168/jds.2009-2457

Ceyhan, A., & Kozaklı, Ö. (2023). The survival analysis of some environmental factors associated with lamb mortality in Awassi sheep. Tropical Animal Health and Production, 55(6), 409. https://doi.org/10.1007/s11250-023-03821-y

Chen, C. C., Chang, T., & Su, H. Y. (2004). Characterization of porcine leptin receptor polymorphisms and their association with reproduction and production traits. Animal Biotechnology, 15(1), 89–102. https://doi.org/10.1081/ABIO-120037903

Childs, G. V., Odle, A. K., MacNicol, M. C., & MacNicol, A. M. (2021). The importance of leptin to reproduction. Endocrinology (United States), 162(2), 1–18. https://doi.org/10.1210/endocr/bqaa204

Du, B., Hu, H., Zhang, J., Cai, B., Ma, Y., Cai, X., & Ma, Y. (2024). Estimation of genetic parameters of Holstein calf survival. Tropical Animal Health and Production, 56(1), 44. https://doi.org/10.1007/s11250-023-03874-z

Gebreselassie, G., Berihulay, H., Jiang, L., & Ma, Y. (2020). Review on genomic regions and candidate genes associated with economically important production and reproduction traits in sheep (*Ovis aries*). Animals, 10(1). https://doi.org/10.3390/ ani10010033

Ghiasi, H., & Abdollahi-Arpanahi, R. (2021). The candidate genes and pathways affecting litter size in sheep. Small Ruminant Research, 205, 106546. https://doi.org/10.1016/j.smallrumres.2021.106546

Gowane, G. R., Chopra, A., Prince, L. L., Mishra, A. K., & Arora, A. L. (2011). Genetic analysis for growth traits of prolific Garole × Malpura (GM) sheep. Tropical Animal Health and Production, 43(2), 299-303. https://doi.org/10.1007/s11250-010-9718-8

Gunawan, A., Listyarini, K., Harahap, R. S., Jakaria, Roosita, K., Sumantri, C., Inounu, I., Akter, S. H., Aminul Islam, M., & Uddin, M. J. (2021). Hepatic transcriptome analysis identifies genes, polymorphisms and pathways involved in the fatty acids metabolism in sheep. PLoS ONE, 16(12), 1–26. https://doi.org/10.1371/journal. pone.0260514

Gunawan, A., Pramukti, F. W., Listyarini, K., Abuzahra, M. A., Jakaria, J., Sumantri, C., Inounu, I., & Uddin, M. J. (2019). Novel variant in the leptin receptor (LEPR) gene and its association with fat quality, odour and flavour in sheep. Journal of the Indonesian Tropical Animal Agriculture, 44(1), 1–9. https://doi.org/10.14710/ jitaa.44.1.1-9

Gunawan, A., Sari, R., Parwoto, Y., & Uddin, M. J. (2011). Non-genetic factors effect on reproductive performance and preweaning mortality from artificially and naturally bred Bali cattle. Journal of the Indonesian Tropical Animal Agriculture, 36(2), 83–90. https://doi.org/10.14710/jitaa.36.2.83-90

Guo, Y., Chen, H., Lan, X., Zhang, B., Pan, C., Zhang, L., Zhang, C., & Zhao, M. (2008). Novel SNPs of the bovine LEPR gene and their association with growth traits. Biochemical Genetics, 46(11–12), 828–834. https://doi.org/10.1007/s10528-008-9197-z

Habtegiorgis, K., Haile, A., Getachew, T., Jimma, A., & Gemiyo, D. (2022). Litter size, litter weight, and lamb survivability of Doyogena sheep managed under a community-based breeding program in Ethiopia. Heliyon, 8(11), e11576. https://doi.org/10.1016/j.heliyon.2022.e11576

Hartl, D. L., & Clark, A. G. (1997). Principles of population genetics. Sinauer Associates.

Hasan, F., Jakaria, & Gunawan, A. (2014). Genetic and phenotypic parameters of body weight in Ettawa Grade goats. Media Peternakan, 37(1), 8–16. https://doi.org/10.5398/medpet.2014.37.1.8

Herdis, H., Inounu, I., Santoso, S., Anwar, R. I., Hayanti, S. Y., Hudaya, M. F., Mahari, D. A., Lupitasari, F. B. I., Hafid, A., & da Costa, M. A. (2025). Reproductive integration of leptin and kisspeptin in small ruminants: Mechanisms, biomarker potential, and prospects for precision breeding. Veterinary World, 18, 1614–1633. https://doi.org/10.14202/vetworld.2025.1614-1633

Hohenlohe, P., Funk, W., & Rajora, O. (2020). Population genomics for wildlife conservation and management. Molecular Ecology, 30(1), 62 - 82. https://doi.org/10.1111/mec.15720.

Ibrahim, A. (2021). Polymorphisms in hormone-sensitive lipase and leptin receptor genes and their association with growth traits in Barki lambs. Veterinary World, 14(2), 515–522. https://doi.org/10.14202/vetworld.2021.515-522

Jayadi, S., & Jan, R. (2024). Study fenotip dan litter size bibit domba ekor gemuk di Kabupaten Lombok Timur. i-SAPI, 1(1), 1–7. https://doi.org/10.29303/i-sapi.v1i1.4975

Ji, X., Cao, Z., Hao, Q., He, M., Cang, M., Yu, H., Ma, Q., Li, X., Bao, S., Wang, J., & Tong, B. (2023). Effects of new mutations in BMPRIB, GDF9, BMP15, LEPR, and B4GALNT2 genes on litter size in sheep. Veterinary Sciences, 10(4). https://doi.org/10.3390/vetsci10040258

Khaerunnisa, I., Pramujo, M., Arief, I. I., Budiman, C., Gunawan, A., Jakaria, & Sumantri, C. (2016). Polymorphism of the T4842G myostatin gene is associated with carcass characteristics in Indonesian chickens. International Journal of Poultry Science, 15(8), 316–324. https://doi.org/10.3923/ijps.2016.316.324

Khasanah, H., Gunawan, A., Priyanto, R., Ulum, M. F., & Jakaria. (2016). Polymorphism of myostatin (MSTN) promoter gene and its association with growth and muscling traits in Bali cattle. Media Peternakan, 39(2), 95–103. https://doi.org/10.5398/medpet.2016.39.2.95

Komarudin, Listyarini, K., Budiman, C., Sumantri, C., & Gunawan, A. (2024). The association of IGFBP7 gene polymorphism on lamb meat quality in Javanese Thin-Tailed sheep. Tropical Animal Science Journal, 47(4), 448–455. https://doi.org/10.5398/tasj.2024.47.4.448

Lakhssassi, K., Serrano, M., Lahoz, B., Sarto, M. P., Iguácel, L. P., Folch, J., Alabart, J. L., & Calvo, J. H. (2020). The LEPR gene is associated with reproductive seasonality traits in Rasa Aragonesa sheep. Animals, 10(12), 1–15. https://doi.org/10.3390 /ani10122448

Li, R., Bai, Y., Zhao, M., Zhang, X., Wang, H., Feng, B., Zhang, S., Zhang, H., Ren, G., Wang, X., et al. (2025). Fine mapping genetic variants affecting birth weight in sheep: A GWAS of 3007 individuals using low-coverage whole genome sequencing. Journal of Animal Science and Biotechnology, 16(1), 1–12. https://doi.org/10.1186/s40104-025-01251-4

Liu, K., Liu, Y., & Chu, M. (2024). Detection of polymorphisms in six genes and their association analysis with litter size in sheep. Animal Biotechnology, 35(1), 1–10. https://doi.org/10.1080/10495398.2024.2309954

Lopes, F. B., Da Silva, M. C., Magnabosco, C. U., Narciso, M. G., & Sainz, R. D. (2016). Selection indices and multivariate analysis show similar results in the evaluation of growth and carcass traits in beef cattle. PLoS ONE, 11(1), 1–21. https://doi.org/10.1371/journal.pone.0147180

Lusi, D., Yurmiati, H., & Ramdani, D. (2023). Pengaruh sistem pemeliharaan terhadap produktivitas induk domba Garut. Jurnal Produksi Ternak Terapan, 3(2), 73. https://doi.org/10.24198/jptt.v3i2.42288

Ma, S., Ji, X., Cang, M., Wang, J., Yu, H., Liu, Y., Zhang, W., Wu, Y., Zhao, S., Cao, G., et al. (2022). Association analysis between novel variants in LEPR gene and litter size in Mongolia and Ujimqin sheep breeds. Theriogenology, 183, 79–89. https://doi.org/10.1016/j.theriogenology.2022.02.014

Macé, T., González-García, E., Foulquié, D., Carrière, F., Pradel, J., Durand, C., Douls, S., Allain, C., Parisot, S., & Hazard, D. (2022). Genome-wide analyses reveal a strong association between LEPR gene variants and body fat reserves in ewes. BMC Genomics, 23(1), 1–15. https://doi.org/10.1186/s12864-022-08636z

Montgomery, G. W. (2024). Genetic regulation of ovulation rate and multiple births. Reproduction, Fertility and Development, 36(14), 1-14. https://doi.org/10.1071/RD24083

Mucha, S., Tortereau, F., Doeschl-Wilson, A., Rupp, R., & Conington, J. (2022). Animal Board Invited Review: Meta-analysis of genetic parameters for resilience and efficiency traits in goats and sheep. Animal, 16(3), 100456. https://doi.org/10.1016/j.animal.2022.100456

National Food Agency. (2023). Livestock Commodity Outlook: Goats and Sheep. Center for Agricultural Data and Information Systems, Ministry of Agriculture, Indonesia. https://satudata.pertanian.go.id/details/publikasi/611

Nei, M., & Kumar, S. (2000). Molecular evolution and phylogenetics. Oxford University Press. https://doi.org/10.1093/oso/9780195135848.001.0001

Nurlela, H., Indrijani, H., & Heriyadi, D. (2024). Growth curve modeling of Garut sheep at UPTD-BPPTDK Margawati Garut. Jurnal Ilmu Ternak, 24(2), 195–201. https://doi.org/10.24198/jit.v24i2.53454

Nyam, Y. S., Matthews, N., & Bahta, Y. T. (2020). Improving livelihoods of smallholder farmers through region-specific strategies: A case study of South African sheep production. Agrekon, 59(1), 1–15. https://doi.org/10.1080/03031853.2019. 1639205

Pérez-Montarelo, D., Rodríguez, M. C., Fernández, A., Benítez, R., García, F., Silió, L., & Fernández, A. I. (2015). Haplotypic diversity of porcine LEP and LEPR genes involved in growth and fatness regulation. Journal of Applied Genetics, 56(4), 525–533. https://doi.org/10.1007/s13353-015-0284-7

Raza, S. H. A., Liu, G. Y., Zhou, L., Gui, L. S., Khan, R., Jinmeng, Y., Chugang, M., Schreurs, N. M., Ji, R., & Zan, L. (2020). Detection of polymorphisms in the bovine leptin receptor gene affects fat deposition in two Chinese beef cattle breeds. Gene, 758, 144957. https://doi.org/10.1016/j.gene.2020.144957

Rodríguez-Quilón, I., Santos-Del-Blanco, L., Serra-Varela, M., Koskela, J., González-Martínez, S. C., & Alía, R. (2016). Capturing neutral and adaptive genetic diversity for conservation in a highly structured tree species. Ecological Applications, 26(7), 2254–2266. https://doi.org/10.1002/eap.1361

Rusdin, M., Solihin, D. D., Gunawan, A., Talib, C., & Sumantri, C. (2020). Genetic variation of eight Indonesian swamp-buffalo populations based on cytochrome b gene marker. Tropical Animal Science Journal, 43(1), 1-10. https://doi.org/10.5398/tasj.2020.43.1.1

Saxton, R. A., Caveney, N. A., Moya-Garzon, M. D., Householder, K. D., Rodriguez, G. E., Burdsall, K. A., Long, J. Z., & Garcia, K. C. (2023). Structural insights into the mechanism of leptin receptor activation. Nature Communications, 14(1), 1–10. https://doi.org/10.1038/s41467-023-37169-6

Sèzonlin, M., Fassinou, A., Koukpo, C., Baba-Moussa, L., & Akogbeto, M. (2020). PCR-RFLP and genetic diversity in Anopheles coluzzii populations in Benin (West Africa). Journal of Entomology and Zoology Studies, 8(5), 400–407. https://doi.org/10.22271/j.ento.2020.v8.i5f.7537

Sharif, N., Ali, A., Dawood, M., Khan, M. I. ur R., & Do, D. N. (2022). Environmental effects and genetic parameters for growth traits of Lohi sheep. Animals, 12(24), 3590. https://doi.org/10.3390/ani12243590

Şirin, E., Şen, U., Aksoy, Y., Çiçek, Ü., Ulutaş, Z., & Kuran, M. (2024). The effect of birth weight on fattening performance, meat quality, and muscle fibre characteristics in lambs of the Karayaka native breed. Animals, 14(5), 704. https://doi.org/10.3390/ ani14050704

Somanjaya, R., Fuah, A. M., Rahayu, S., Abdullah, L., & Setiadi, M. A. (2025). Post-natal Indonesian Garut sheep performance fed with sorghum–Indigofera–mixed feed and stimulated with pregnant mare serum gonadotropin hormone. Journal of Medical Veterinary, 8(1), 63–73. https://doi.org/10.20473/jmv.vol8.iss1.2025.63-73

Souza, J. P., Day, L. T., Rezende-Gomes, A. C., Zhang, J., Mori, R., Baguiya, A., Jayaratne, K., Osoti, A., Vogel, J. P., & Campbell, O. (2024). A global analysis of the determinants of maternal health and transitions in maternal mortality. The Lancet Global Health, 12(2), e306–e316. https://doi.org/10.1016/S2214-109X(23)00468-0

Sun, C., Wang, L., Jiang, D., & Zhang, B. (2018). Missense mutations in exon 2 of the porcine leptin receptor gene and their associations with litter size and body weight. Czech

Journal of Animal Science, 54(5), 210–216. https://doi.org/10.17221/1663-CJAS

Sutarno, S., Zahrah, S., Astirin, O. P., Herawati, E., & Setyawan, A. D. (2019). Genetic diversity of Ongole Grade, Aceh, and Sumbawa cattle based on polymorphism on ND-5 fragment mitochondrial DNA using PCR-RFLP technique. Biodiversitas Journal of Biological Diversity, 20(3), 724–731. https://doi.org/10.13057/biodiv/d200324

Sutikno, S., Priyanto, R., Sumantri, C., & Jakaria, J. (2018). Polymorphism of ADIPOQ and EDG1 genes in Indonesian beef cattle. Journal of the Indonesian Tropical Animal Agriculture, 43(4), 323–332. https://doi.org/10.14710/jitaa.43.4.323-332

Tarach, P. (2021). Application of polymerase chain reaction-restriction fragment length polymorphism (RFLP-PCR) in the analysis of single nucleotide polymorphisms (SNPs). Acta Universitatis Lodziensis. Folia Biologica Et Oecologica, 17, 48–53. https://doi.org/10.18778/1730-2366.16.14

Tiesnamurti, B., Sinulingga, S. E., & Gatenby, R. M. (2020). Small ruminant community breeding program in Indonesia. Indonesian Bulletin of Animal and Veterinary Sciences, 30(3), 163. https://doi.org/10.14334/wartazoa.v30i3.1935

Tüfekci, H., & Sejian, V. (2023). Stress factors and their effects on productivity in sheep. Animals, 13(17), 2769. https://doi.org/10.3390/ani13172769

Wang, J., Liu, Y., Guo, S., Di, R., Wang, X., He, X., & Chu, M. (2024). Polymorphisms of the BMPR1B, BMP15 and GDF9 fecundity genes in four Chinese sheep breeds. Archives Animal Breeding, 67(1), 51–60. https://doi.org/10.5194/aab-67-51-2024

Wen, Y. L., Guo, X. F., Ma, L., Zhang, X. S., Zhang, J. L., Zhao, S. G., & Chu, M. X. (2021). The expression and mutation of BMPR1B and its association with litter size in small-tail Han sheep (*Ovis aries*). Archives Animal Breeding, 64(1), 211–221. https://doi.org/10.5194/aab-64-211-2021

Wong, J. T., Vance, C., & Peters, A. (2021). Refining livestock mortality indicators: A systematic review. Gates Open Research, 5, 13228. https://doi.org/10.12688/gatesopenres.13228.1

Yang, H., Zhu, M., Wang, M., Zhou, H., Zheng, J., Qiu, L., Fan, W., Yang, J., Yu, Q., Yang, Y., & Zhang, W. (2024). Genome-wide comparative analysis reveals selection signatures for reproduction traits in prolific Suffolk sheep. Frontiers in Genetics, 15, 1–12. https://doi.org/10.3389/fgene.2024.1404031

Younis, L. S., Al-Mutar, H. A. A., & Abid, A. A. (2019). Effect of leptin gene polymorphism on reproductive efficiency in Awassi ewes. Advances in Animal and Veterinary Sciences, 7(1), 17–23. https://doi.org/10.17582/journal.aavs/2019 /7.1.17.23

Zhao, Y. X., Gao, G. X., Zhou, Y., Guo, C. X., Li, B., El-Ashram, S., & Li, Z. L. (2022). Genome-wide association studies uncover genes associated with litter traits in the pig. Animal, 16(12), 100672. https://doi.org/10.1016/j.animal.2022.100672

Zhulan, N., Yongli, R., Lirong, Z., Rui, G., & Jie, W. (2022). Analysis of population genetic diversity and genetic structure of Schizothorax biddulphi based on 20 newly developed SSR markers. Frontiers in Genetics, 13, 908367. https://doi.org/10.3389/fgene.2022.908367