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EFFECT OF FASN AND ANXA9 GENE POLYMORPHISM ON GENETIC VARIATION, QUANTITATIVE AND ECONOMIC IMPACT OF LAMB'S WEANING WEIGHT

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ABSTRACT

The objective of the current study was to investigate the effect of FASN AND ANXA9 gene polymorphism on genetic variation, quantitative and economic influences, and the extent of their contribution to the variation in the weaning weight of Awassi lambs based on the genetic polymorphism of their dams. New equations were designed and modified to calculate the contribution of both genes to the weight and price of the lambs. The contribution of both genes to the heritability of lamb's waning weight and the expected quantitative and price values to be inherited by the next generation were also estimated. Results revealed that the AA genotype of the FASN gene was superior to its hetero genotype AT counterpart in price and quantitative values. Moreover, the FASN gene was superior to the ANXA9 gene in both counterpart values. In conclusion, The FASN gene can be adopted as linked to the lamb's weight. It is considered an influential and effective gene in the studied trait and can be relied upon in selecting the dam ewes in the sheep flocks.

Key words: heritability, quantitative values, price values, sheep.

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INTRODUCTION

The fatty acid synthase (FASN) gene is located on chromosome 19 in sheep and consists of 42 coding regions (National Center for Biotechnology Information [NCBI], n.d.-a) This gene encodes a multifunctional enzyme that catalyzes the synthesis of medium-chain fatty acids in mammals (Ronti et al., 2006). It also plays a crucial role in the body’s energy balance and the formation of milk fat during lactation (Chirala et al., 2003). The ANXA9 gene is located on chromosome 1 in sheep. It has 14 coding regions (NCBI, n.d.-b), encodes a protein of a similar name, and has a crucial role in cytoplasmic transport across membranes of mammals. It is responsible for the transport of calcium through special channels and as a binding agent for phosphorylated lipids, as well as resistance to cell inflammation (Calvo et al., 2006; Pecka-Kiełb et al., 2021; Symeou, 2021; Senkal et al., 2023). Selecting ewes to be dams in the flock is an important matter. Dams were evaluated based on their lambs' weaning weight (Shrestha et al., 2002; Hamad Senkal et al., 2022). Many genetic improvement programs depended on detecting genetic variation in the flock and were designed as a guide for selection (Rönnegård et al., 2013; Karim et al., 2023). The genes that directly affect the trait are known as candidate genes, and it is principal to choose them as selection markers (Zhu & Zhao, 2007). Therefore, this study is designed to investigate the quantitative and economic values resulting from the genetic polymorphism of the FASN and ANXA9 genes through modified equations.

MATERIALS AND METHODS

This experiment was conducted at Al-Fayha Breeding Station (55 km south of Baghdad) using 52 Awassi ewes and their lambs to study the effect of genetic polymorphism of the FASN and ANXA9 genes on the genetic variation in the weaning weight and calculate the actual impact (quantitative) of the genes of weaning weight in the current generation and the inherited value in next generation. The price impact of the gene on the total animal price calculated as kilogram, according to new equations designed, was also investigated. Primers were identified for the FASN gene (A>180 G SNP Intron 23) by Zhao, Li (2022), and for the ANXA9 gene (intron 4 G>844 C SNP) by Pecka-Kiełb, Kowalewska-Łuczak (2021).

1. The equations for the following values were applied according to Falconer and Mackay (1996):

a. Average effect of allele A = $q[a+d(q-p)] = \alpha A$

Average effect of allele B = $-p[a+d(q-p)] = Ab$

The average replacement represents the difference between the two values.

b. Breeding values were as follows:

$AA = 2\alpha 1$, $AB = \alpha 1 + \alpha 2$, $BB = 2\alpha 2$

c. Dominant deviations:

$AA=-2q^2d$, $AB=2pqd$, $AA=-2p^2d$

The different variances were extracted as follows:

$=\alpha^2$, $VD=4p^2q^2d^2$, $VG=VA+VD$ $VA=2pq$

2. The following values were calculated from equations designed previously by Senkal et al. (2023) with some modifications.

The heritability in the wide sense (h^2g) = $2pq\alpha^2 + 4p^2q^2d^2/\sigma^2$

The heritability in the narrow sense (h^2g) = $2pq\alpha^2/\sigma^2$

a. The value of the actual (real) effect of the gene (or quantitative effect) $=\sqrt{vA + vD}$

b. The value of the price effect of the gene $=\sqrt{vA + vD}$ x price

c. The percentage of the actual (real) effect of the gene $\sqrt{VA + VD}/m$

d. The percentage of the price effect of the gene $\sqrt{VA + VD}/m$ x price

e. The actual (real) effect of the gene in next generation $\sqrt{VA}$

f. The value of the price effect of the gene in next generation $=\sqrt{vA}$ x price

g. The percentage of the actual (real) effect of the gene in next generation = $\sqrt{VA}/m$

h. The percentage of the caloric effect of the gene in next generation = $\sqrt{VA}/m$ x price

RESULTS AND DISCUSSION

Table (1) revealed the A allele's superior Mean and substitution effects for the FASN gene (0.46 and 3.34, respectively), representing the deviation of individuals carrying this allele from the Mean. The substitution mean represents the amount of variation in the value of the weight at weaning for the individuals whose dams carry the A allele over the other alleles (Falconer & Mackay, 1996). The superiority extended to the A allele of the FASN gene over the alleles of the ANXA9 gene with both T and G alleles, whose effect was minimal (Table 1). This result was consistent with the fact that the FASN gene is active and influential in the production of lipids (Zhang et al., 2021). The ANXA9 gene does not affect weight as it regulates several vital activities, such as transporting calcium across cell membranes (Lizarbe et al., 2013).

Table 1. Mean and substitution effects of FASN and ANXA9 alleles.

FASN alleles	Mean effect of allele	Mean of allele substitution
A	**0.46**	**3.34**
T	**-2.87**	**-3.34**
ANXA9 alleles	**Mean effect of allele**	**Mean of allele substitution**
T	**-0.125**	**-0.44**
G	**0.323**	**0.44**

values were calculated according to Falconer and Mackay (1996).

The AA genotype of the FASN gene is superior to both TA and TT genotypes for the similar gene in breeding value, which is the summation result of the gene mean effect that the individual carries (Salim et al., 2019). It is also expressed as twice the deviation of the offspring from the overall mean (Huțu et al., 2020). In general, it is a value that attempts to show the genetic content or the actual susceptibility of the individual, away from the increase or decrease in the value of the trait's appearance due to the interaction between alleles. Thus, ewes carrying the AA genotype are at the forefront when designing selection programs for the weaning weight of their lambs. For the ANXA9 gene, the ewes carrying the pure wild-type TT had the highest percentage compared to the AA and TA genotypes of the same gene, meaning that the ewes carrying the TTAA genotype (for FASN and ANXA9 genes) were the best in selection programs for the individuals that would be the sires of the next generation. For the dominance deviation values, they were the opposite, as pure mutant individuals had precedence in both genes (Table 2). Dominance deviation explains the inheritance of traits, especially in hybrid individuals (Visscher et al., 2002; Al-Samarai et al., 2019). The Additive variation (AV) was higher for the FASN and ANXA9 genes than the dominance variation (DV), namely 2.69 and 0.08 for the two genes, respectively (Table 2), which supports the adoption of these two genes within selection programs because the real value that an individual inherits is the additive variance. Dominance results from the interaction of alleles carried by an individual, and it varies from generation to generation. The FASN gene outperformed the ANXA9 gene obviously (6.92 and 0.0805, respectively), which confirms its effect on weaning weight. In general, the variance represents the extent to which values fluctuate from the overall mean for the trait (Gagnon & Barber, 2018). This superiority can be explained in two ways; the first is that the FASN gene plays a vital role in fat synthesis (Michal et al., 2006), and thus, this is reflected in weight. The second is the absence of the pure mutant genotype of this gene, which creates a large discrepancy in weaning weight.

Table 2. Breeding values, dominant deviations, genetic variance, and its components for weight at weaning based on FASN and ANXA9 genes information.

FASN genotype	Trait	Mean	Adjusted mean	Breeding value	Dominance deviation	AV	DV	GV
AA	Weaning weight	18.98	19.707	20.64	19.54	2.69	2.23	6.92
AT		18.03		17.3	21.76			
TT		0		13.96	32.34			
ANXA9 genotype	**Trait**	**Mean**	**Adjusted mean**	**Breeding value**	**Dominance deviation**	**AV**	**DV**	**GV**
TT	Weaning weight	18.37	18.5	28.24	18.49	0.08	0.0005	0.0805
TG		18.83		18.69	18.51			
GG		19.25		19.14	18.52			

***Values were calculated according to Falconer and Mackay (1996).**

AV: Additive variance; DV: Dominant variance; GV: Genetic variance.

The heritability of the weight at weaning was calculated based on the genetic variance calculated in Table (2) and divided by the total variance of the trait. This study included only two genes from the total genes controlling the weaning weight. The value of the heritability is less than the expected value that can be obtained by one of the traditional methods, which depends on the regression of the offspring on one of the parents or their mean, which is often between 20 and 40% (Getabalew et al., 2019). The heritability value calculated based on the variance of both genes was around 0.02 (Table 3). The advantages of calculating the genetic equivalent in this way clarify the percentage of each gene's contribution to the inheritance of the weaning weight. Thus, the importance of these genes can be revealed.

Table 3. Heritability of weaning weight based on genetic variation for the FASN and ANXA9 genes

Heritability of weaning weight	FASN	ANXA9	FASN and ANXA9
Broad heritability	0.019	0.011	0.0225
Narrow heritability (based on VA)	0.008	0.0001	0.009

Values were calculated by Senkal et al. (2023) with modification

The FASN gene is superior in the value of the quantitative effect of the gene, which represents the root of genetic variation and the amount of increase or decrease in weight when adopting the desired genotype, which is the pure wild type over the pure mutant genotype. The mutation in this gene causes a deterioration in the animal's weight, as the increase expected in the case of the wild-type formula is 2.572 kg. The contribution of the wild-type for the ANXA9 gene is about 0.28 kg. The mutant genotype deletes this value from the weight. Thus, animals carrying the AATT genotype increase their lambs by approximately 3 kg. If the price value is calculated based on live weight (10,000 dinars per kilogram), the FASN gene is responsible for 2,572 dinars of the animal's price, while the ANXA9 gene represents 2,828 dinars of the animal's value. The rest of the value goes back to the remaining unstudied genes and their interaction with the environment, considering the weaning weight is a quantitative characteristic. The FASN gene contributes 138 grams to every kilogram of animal weight, while the ANXA9 gene contributes 0.151 grams to every kilogram of meat. Together, they contribute 1,381 and 151 dinars, respectively, to the price of a kilo of meat (Table 4).

Table 4. Quantitative and price measurements based on genetic variation of the FASN and ANXA9 genes

Measurements based on genetic variation		
Measurements of the actual and relative values of gene	**FASN**	**ANXA9**
The value of the gene's quantitative effect.	**2.572**	**0.282**
The total price value	**25720**	**2828.42**
Actual effect percentage of gene (per kg)	**0.138**	**0.0151**
Price effect of gene (per kg)	**1381**	**151**

Values were calculated by Senkal et al. (2023) with modification

The value inherited by the next generation is based on the additive variance because the dominance variance varies with every new combination, that is, with every generation (Jiang et al., 2017). On this basis, the contribution of the FASN gene to the inherited weight of the offspring is approximately 1640 grams, and for the ANXA9 gene is approximately 283 grams, meaning 16,400 dinars and 2,837 dinars for the two genes, respectively (Table 5). For calculations based on each kilogram of live weight in the next generation, FASN contributes with a weight of 0.088 grams, and the ANXA9 gene contributes with a weight of 0.015 grams and a price value of 880 and 152 dinars for the two genes, respectively (Table 5).

Table 5. Quantitative and price measurements based on additive variation for the FASN and ANXA9 genes

Measurements based on additive variation (expected genotype values)		
Measurements of the actual and relative values of gene	**FASN**	**ANXA9**
Actual additive inherited effect (kg)	**1640**	**0.2837**
Inherited price value (total)	**16400**	**2837.25**
Percentage of true heritable additive effect (per kg)	**0.088**	**0.015**
Percentage of the inherited price value (per kg)	**880.79**	**152.363**

Values were calculated by Senkal et al. (2023) with modification :Although both genes significantly affect the weight characteristic at weaning, the effect of the FASN gene was superior to the ANXA9 gene in terms of genetic variation, the actual quantitative impact of the gene, and the actual inherited additive effect. Also, this superiority was reflected in the price value inherited by the next generation. Therefore, the FASN gene can be adopted as linked to the weight trait and considered an influential and effective gene in weaning weight. It can be relied upon when selecting the ewes that will be dams in the flock. The current quantitative and economic calculations (Tables 3, 4, and 5) can also be adapted to compare the effect of a group of genes that jointly affect a specific trait. Adopting the weight and price could be a language that producers and breeders understand. It gives them a better understanding of the importance of genetic improvement of their flocks by relying on genetic markers, thus increasing cooperation among breeders and researchers in the field of genetic improvement of farm animals.

CONCLUSION

The integration of molecular genetics with quantitative economic analysis reveals that both the FASN and ANXA9 genes are significant markers for weaning weight, though their contributions differ substantially. The FASN gene emerges as the primary driver of genetic gain, demonstrating a superior additive effect (1.64 kg) and a higher contribution to genetic variance (6.92) compared to ANXA9.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHORS' DECLARATION

The authors declare that this manuscript is original, has not been published previously, and is not currently under consideration by any other journal. All figures and tables are original and prepared by the authors. Any material obtained from third parties has been included with the required permissions. All authors have read and approved the final manuscript.

AUTHORS' CONTRIBUTION STATEMENT

All authors made equal contributions to the study design, methodology, experimental work, data analysis, and manuscript writing. All authors reviewed and approved the final version of the manuscript.

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تأثير تعدد المظاهر الوراثية لجيني FASN وANXA9 على التباين الوراثي والتأثيرات الكمية والاقتصادية في وزن الحملان عند الفطام

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المستخلص

ان الهدف من الدراسة الحالية هو لبيان تأثير تعدد المظاهر الوراثية لجيني FASN وANXA9 في التباين الوراثي والتأثيرات الكمية والاقتصادية ومدى مساهمتها في تباين وزن الفطام للحملان العواسي على أساس التباين الوراثي لأمهاتها. تم تصميم وتعديل معادلات جديدة لحساب مساهمة كلا الجينين في وزن وسعر الحملان. كما تم حساب مساهمة كلا الجينين في المكافئ الوراثي لصفة الوزن عن فطام الحملان والقيم الكمية والسعرية المتوقع توريثها للجيل القادم. بينت النتائج تفوق المجموعة الوراثية AA للجين FASN على نظيرتها AT في القيمتين السعرية والكمية. علاوة على ذلك، كان جين FASN متفوقًا على جين ANXA9 في كلا القيمتين النظيرتين. يمكن الاستنتاج باعتماد جين FASN لارتباطه بوزن الحمل. ويعتبر من الجينات المؤثرة والفعالة في الصفة المدروسة ويمكن الاعتماد عليه في انتقاء النعاج في قطعان الأغنام.

الكلمات المفتاحية: **المكافئ الوراثي، القيم الكمية، القيم السعرية، الأغنام.**