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Single Nucleotide Polymorphisms of the Growth Hormone Gene and Their Association with Growth Traits in Sheep: A Systematic Review

Khadija Salka[1,2], Veronica Margareta Ani Nurgiartiningsih[2], Asrullah As[2], Sohaib Akram[2,3], Irida Novianti[2], Marjuki Marjuki[2], and Suyadi Suyadi[2]*

[1]*Pir Mehar Ali Shah Arid Agriculture University, Rawalpindi, 43490, Pakistan*
[2]*Faculty of Animal Science, Universitas Brawijaya, Malang, 65145, Indonesia*
[3]*University of Veterinary and Animal Sciences, Lahore, Pakistan*

*Corresponding author's Email: suyadi@ub.ac.id

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ABSTRACT

Growth hormone (GH) is synthesized and secreted by the pituitary gland. It is regulated by the *GH* gene, located on chromosome 11 in sheep, and is crucial for regulating postnatal growth and development in sheep. Single-nucleotide polymorphisms (SNPs) in the *GH* gene are associated with substantial differences in weight and body size in sheep. This study aimed to systematically evaluate SNPs of the *GH* gene and their association with growth parameters such as weaning weight (WW), yearling weight (YW), average daily gain (ADG), and linear body conformation in sheep. A total of 71 studies were extracted from January 2011 to March 2026. The results identified 25 distinct SNPs (with 15 SNPs reported on exon 5), of which five SNPs, A781G, A1544G, C1765A, T1772A, and G1769C, were detected in more than one breed. Eighteen SNPs were found to be significantly associated with growth traits; these associations were not uniform, as individual SNPs were linked to single or multiple traits, including body weight, birth weight, pre-weaning gain, weaning weight, 6-month weight, daily live weight gain, yearling weight, and morphometric traits. In conclusion, polymorphism at the *GH* gene influences growth traits in sheep, and several SNPs such as C1776G, A1544G, A1678G, A1558G, C1765A, G1550A, T1772A, G1769C, G1756C, 476G>A, 480 G>A, 55G>A, G871A, G1383A, A1509G, A781G, C408G and T735A associated with growth traits are promising candidate markers after validation in larger breed-specific and trait-specific validation.

Keywords: Breeding program, Growth hormone gene, Marker-assisted selection, Sheep growth, Single nucleotide polymorphism

INTRODUCTION

Globally, demand for small ruminant meat is increasing in line with population growth and changing dietary preferences toward a high-protein diet and increased red meat consumption, underscoring the urgency of improving productivity traits in sheep populations (OECD-FAO, 2025). Economically important growth traits in sheep include body weight (BWT), weaning weight (WW), and average daily gain (ADG), as they directly influence productivity and profitability (Cinar et al., 2023). Growth traits, such as BWT, ADG, WW, 6-month weight (LW6), 9-month weight (LW9), Yearling weight (YW), birth weight (BW), and morphometric traits, are quantitative traits regulated by multiple genes and environmental factors, and therefore, genetic enhancement is a complex but necessary process (Begenova et al., 2025).

Growth hormone (GH), a 191-amino acid polypeptide, is produced and secreted by the somatotrophic cells of the anterior pituitary gland and plays a crucial role in somatic growth, metabolism, protein synthesis, and tissue development (Jia et al., 2014; Bayraktar and Shoshin, 2022). In addition, GH influences major physiological processes, including reproduction, fat metabolism, and body composition (Jia et al., 2014; Bergan-Roller and Sheridan, 2018). Growth hormone is regulated by the growth hormone (*GH*) gene, which is a key candidate gene involved in regulating growth and development in livestock species (Bayraktar and Shoshin, 2022). It has five exons and four introns and is located on chromosome 11 in sheep (Bai et al., 2022). The *GH* gene regulates the synthesis and secretion of GH at the pituitary gland (Bai et al., 2022). The *GH* gene is a central regulator of growth that has been extensively studied as a possible marker to enhance economically significant phenotypes such as WW, ADG, and BWT through marker-assisted selection (Cauveri et al., 2016; Tanış and Keskin, 2025).

Recent advances in molecular genetics have enabled the identification of various single nucleotide polymorphisms (SNPs) associated with growth traits in candidate genes. Such polymorphisms can either alter gene expression or protein activity, thereby affecting phenotypic traits (Xu and Li, 2017). A systematic review of the *GH* gene is important because

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many studies have examined *GH* gene polymorphisms in various sheep breeds and their relationships with growth traits. However, the results are scattered across many studies and inconsistent, with some showing an association of specific SNPs of the *GH* gene with studied growth traits, while others do not (Cauveri et al., 2016; Esen and Elmacı, 2022; Kumar et al., 2024). These inconsistencies can be explained by the breed variations, sample size, environmental conditions, and genotyping techniques. Without a structured synthesis, it is difficult to determine which polymorphisms have a consistent effect on growth traits in sheep or have practical relevance.

There has been an increasing number of publications on *GH* gene polymorphisms in sheep, but few studies have systematically summarized the evidence for the SNPs identified and their association with sheep growth traits. To fill this gap, the aim of this study was to conduct a systematic review of the literature on the SNPs of the *GH* gene and their association with growth traits in sheep. The present review study aimed to combines and evaluates findings from many studies to identify the SNPs of the *GH* gene that are consistently associated with economically important growth traits such as weaning weight and average daily gain. As the *GH* gene plays an important role in growth traits, combining all studies to identify consistent reporting of SNPs will help in marker-assisted selection (MAS) in breeding programs.

MATERIALS AND METHODS

The population, exposure, outcome (PEO) framework is a structured way of designing a research question in a systematic review, particularly in observational studies, to enhance clarity and focus of the review (Moola et al., 2015). In order to design a study question, the PEO components of the study question were identified as explained by Moola et al. (2015), which are called Population, Exposure, and Outcome. The population was "Sheep" with exposure to "Polymorphism", and the outcome was "growth rate/body conformation/morphological traits".

Literature search

A comprehensive literature search was conducted across four databases, including Scopus, PubMed, Web of Science (WOS), and Google Scholar, on the same date from January 2011 to March 31, 2026. The chosen time frame was selected to capture studies during a significant advancement in molecular genetics and the use of more standardized and advanced genotyping methods to increase the reliability of detection of SNPs and association analysis. For each database, the same keywords were used; keywords used for searching include "growth hormone gene/*GH* gene/somatotropin gene", "single nucleotide polymorphism/SNP/polymorphisms /genetic variation", "growth traits/body weight/average daily gain/weaning weight/morphometric/body conformation/ morphological traits/biometric traits", "sheep/ovine". Boolean operators' AND ' and ' OR' were used to refine search results (Rau, 2004). The complete study selection process is shown in Figure 1.

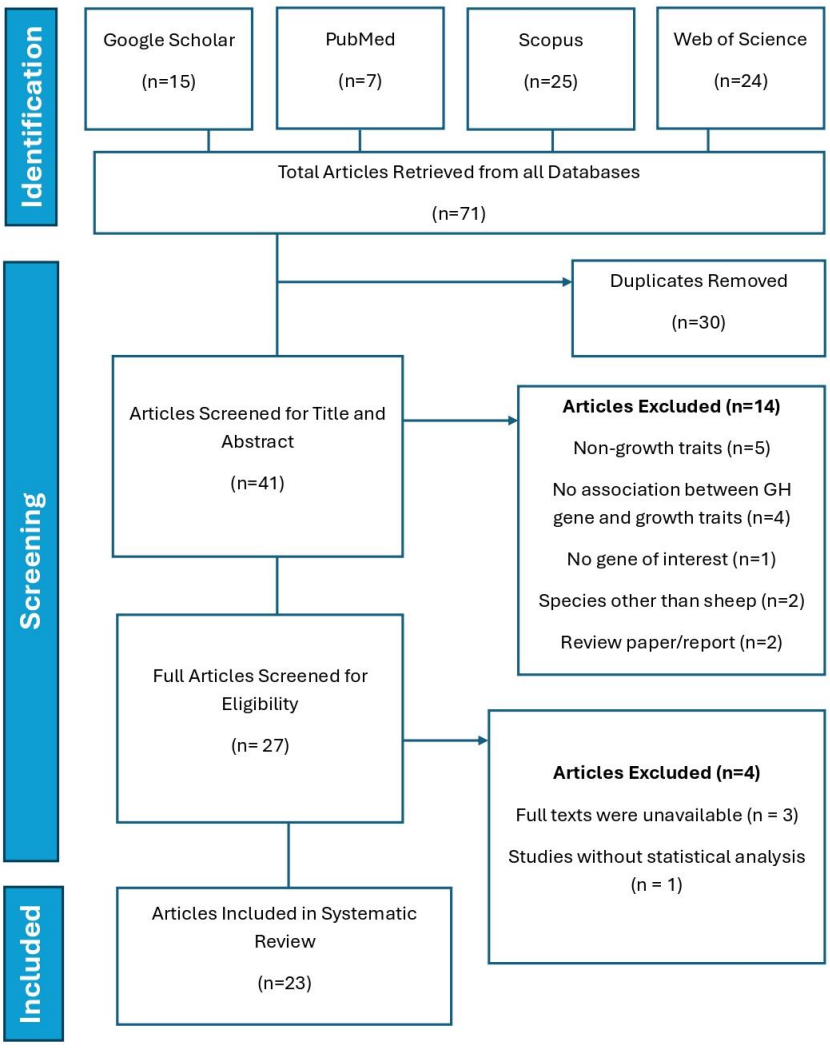

Figure 1. Study selection process for single nucleotide polymorphisms in sheep

Inclusion criteria

Two-step screening was performed, first, title and abstract screening, followed by full text screening. Studies were included based on the following criteria, including *GH* gene under investigation, reported SNPs or genetic variations, and the association between the *GH* gene and growth traits in sheep.

Exclusion criteria

Articles were excluded if they were on non-growth traits, lacked an association between *GH* gene polymorphisms and growth traits, had no gene of interest, were on species other than sheep, were review papers or reports, full texts were unavailable, or studies without statistical analysis.

Data extraction

All retrieved studies from four databases were combined, and duplicate records were removed manually. After that, the remaining articles were screened by one reviewer based on title and abstract, using predefined exclusion and inclusion criteria. After that, full articles were checked for eligibility and excluded if the full text was unavailable or if the study lacked statistical analysis. Data extracted from articles include publication characteristics (first author, journal), publication year, country, population size, sheep breed, SNPs, genomic regions, genotyping methods, genotype and genotype frequencies, allele frequencies, growth traits investigated, and the association between SNPs and growth traits, either significant or non-significant based on statistical results reported in original studies.

Methodological quality assessment

The methodological quality of included studies was assessed using the predefined criteria. Each study was evaluated based on the following criteria of adequate sample size (sample size classification was adapted based on the distribution of sample sizes across included studies, studies with fewer than 100 animals were classified as small, 100-300 as medium, and more than 300 as large), genotypic method used, reporting of genotypic frequencies, reporting of allele frequencies, and statistical analysis for association, which can affect the reliability, transparency, and interpretation of the results of association studies. Studies were divided into low, moderate, and high methodological quality based on these parameters. An adapted methodological quality scoring was used, as indicated by Hooijmans et al. (2014). Previous studies have also used this adapted methodological quality and point based scoring system (Macleod et al., 2004; Van Der Worp et al., 2005). One point was assigned for each criterion met, so the total score ranges from 0 to 5. Studies scoring 4-5 are considered to have a low methodological quality, 2-3 a moderate methodological quality, and 0-1 a high methodological quality (Macleod et al., 2004; Van Der Worp et al., 2005). Studies with a small sample size are not considered low methodological quality, even if other criteria are met, due to reduced statistical power (Zepeda Batista et al., 2018).

Study selection methodology

After searching the literature, a total of 71 articles were retrieved for this systematic review from the following electronic databases, including Google Scholar (n = 15), WOS (n = 24), Scopus (n = 25), and PubMed (n = 7). Records were combined, duplicate records (n = 30) were manually removed, and the remaining records (n = 41) were screened according to the inclusion and exclusion criteria. During initial screening of the title and abstract, fourteen (n=14) studies were removed, resulting in twenty-seven (n = 27) papers. Four articles were excluded during the full PDF screening, resulting in twenty-three articles.

Characteristics of included studies

Characteristics of the selected 23 studies are presented in Table 1. Studies included were published between 2013 and 2026. All authors published one article, except one author who published two articles, from each of the 23 studies. The studies were conducted across ten countries. A total of 40 distinct breeds and crossbreeds were investigated across the included studies in these countries. Among these, Awassi was studied in 13% (n = 3) of studies, followed by small-tailed Han sheep in 8.69% (n = 2) of studies. Sample size ranged from 50 to 632 animals, with 73.9% studies (n = 16) ranging from 50 to 192 animals. All studies investigated the *GH* gene polymorphism in relation to growth traits. The most investigated traits were birth weight (60.8%), weaning weight (56.5%), morphometric traits (52.1%), followed by body weight (43.4%), and 6-month weight (39.1%). The most frequently used genotyping method was Polymerase Chain Reaction-Restricted Fragment Length Polymorphism (PCR-RFLP), which accounted for 47.8% (n = 11) of the studies, followed by PCR combined with sequencing in 26% (n = 6) of studies, Polymerase chain reaction single strand conformation polymorphism (PCR-SSCP) in three studies (13%), PCR SSCP combined with sequencing in two studies (8.7%); however, only one study used tetra-primer amplification refractory mutation system PCR (ARMS-PCR).

Distribution of studies by country

The studies were geographically distributed across ten countries, with the highest contribution from Asia. Most of the studies were from Turkey and India (17.3% each), followed by China, Iraq, and Indonesia, each with three studies (13% each). While 8.6 % of the studies were from Russia, the fewest (4.3%) were from Brazil, Egypt, Iran, and Saudi Arabia. Figure 2 shows the distribution of articles by countries.

Distribution of studies by year

The timeline of the publications is presented in Figure 3, which indicates that the researchers' interest in this field has been growing steadily over the years; the latest studies (from 2022 to 2025) have led to the highest number of publications. Most of the articles were published in 2022 (17.4%). While the number of studies was consistent (13 % each year) in 2023 (n = 3), 2024 (n = 3), and 2025 (n = 3), followed by 2014, 2017, and 2019 with two studies each year (8.7 % each year). While one study was published in each of 2013, 2016, 2021, and 2026 (4.3% per year).

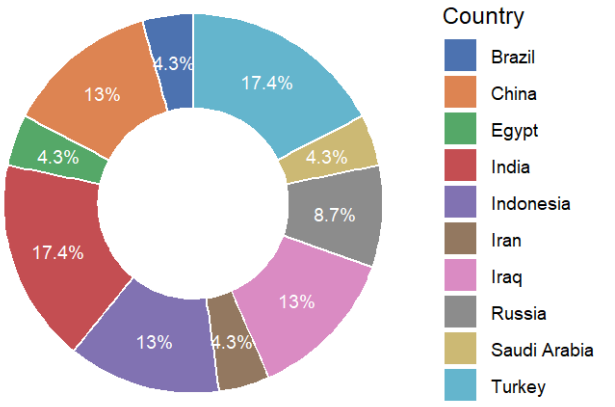

Figure 2. Geographic distribution of studies on the *GH* gene polymorphisms and growth traits in sheep.

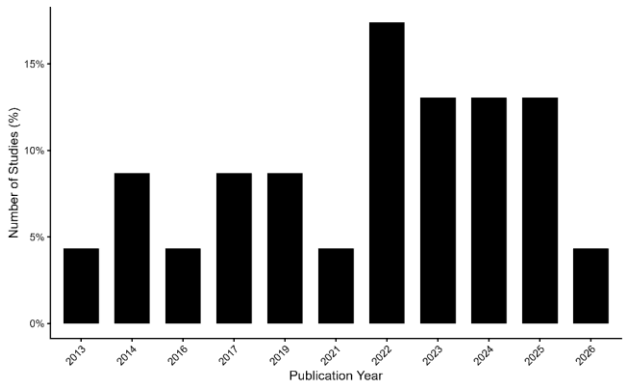

Figure 3. Distribution of studies on the *GH* gene polymorphisms and growth traits in sheep by year (2013-2026).

Distribution of studies by journal

From the findings, 19 studies were each published in one separate journal, while only four studies were published across two journals (8.7% each), as shown in Figure 4.

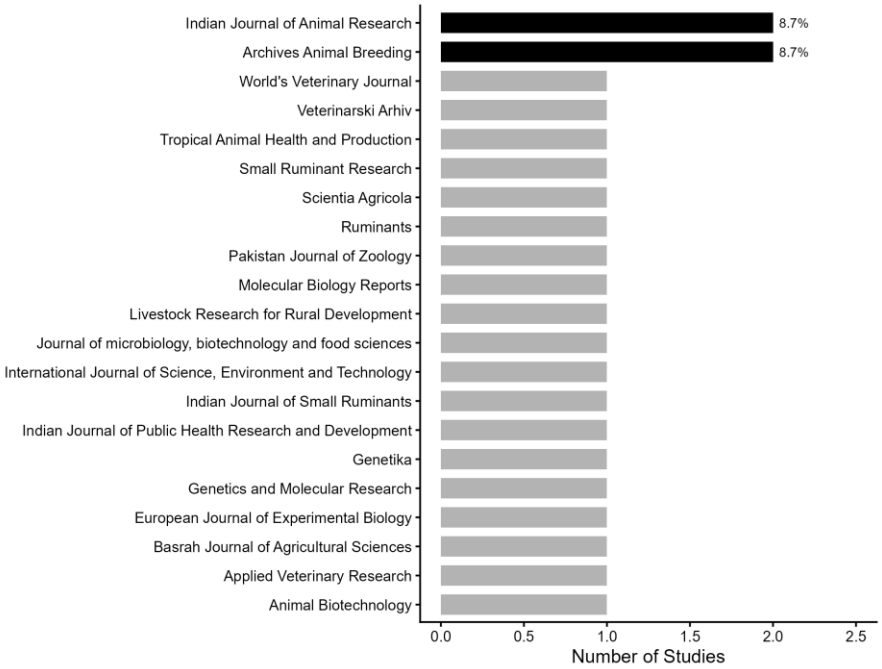

Figure 4. Journal-wise distribution of studies on the *GH* gene polymorphisms and growth traits in sheep published between 2013 and 2026.

Distribution of studies by breed

There was a high level of diversity in sheep populations in the 23 included studies. Findings revealed a total of 40 breeds across the included studies. These breeds include indigenous, commercial, and crossbreed sheep from ten countries. Some articles studied only one breed, whereas others studied more than one breed. From China, one study compared four breeds (Tibetan, Small Tail Han, German Merino, and Polled Dorset), whereas another used two breeds, Charolais and Australian White. Crossbred populations, such as the Rahmani-Barki cross, the Awassi-Suffolk cross, and the Merino cross, were also reported, suggesting that *GH* polymorphism studies were conducted in both purebred and crossbreeding systems. Moreover, certain breeds were reported in multiple studies, such as Awassi in three studies, Merino-related populations (Anatolian Merino, Karacabey Merino, Merino Cross Rams, Soviet Merino, Hampshire Down × Merino crossbreed) in five studies, and the Chinese indigenous breed in two studies. Breeds included in this review are presented in Table 1.

Table 1. Characteristics of 23 included studies on *GH* gene polymorphisms associated with growth traits in sheep

Study references (n = 23)	Breed	Sample size (N)	Year	Country	Genotyping method
Tanış and Keskin (2025)	Akkaraman, Anatolian Merino	73	2025	Turkey	PCR-RFLP
Al Qasimi et al. (2019)	Awassi	68	2019	Iraq	PCR+ sequencing
Bayraktar and Shoshin (2022)	Awassi	150	2022	Iraq	PCR-RFLP
Li et al. (2025)	Charolais, Australian White	632	2025	China	PCR + sequencing
Madikadike et al. (2024)	Dorper	50	2024	Indonesia	PCR-RFLP
Kumar et al. (2024)	Harnali	138	2024	India	PCR-RFLP
Abdelmoneim et al. (2017)	Harri	100	2017	Saudi Arabia	PCR + sequencing
Malewa (2014)	Indonesia fat-tailed	100 (genotyped =70)	2014	Indonesia	PCR-RFLP
Muniasamy et al. (2023)	Kilakarsal	99	2023	India	PCR-RFLP
Esen and Elmacı (2022)	Kıvırcık, Karacabey Merino, Ramlıç, German Black-Head Mutton × Kıvırcık, Hampshire Down × Merino crossbreed	202	2022	Turkey	PCR-SSCP + sequencing
Putra et al. (2024)	Merino Cross Rams	145	2024	Indonesia	PCR-RFLP
Bai et al. (2022)	Mongolia, Small-tailed Han, Tong, Lanzhou large-tailed, Henan large-tailed Han, Yuxi fatty-tailed	300 (50 each)	2022	China	PCR-SSCP
Dagdelen and Esenbuga (2025)	Morkaraman	123	2025	Turkey	PCR-RFLP
Rajith Reddy et al. (2023)	Nellore	50	2023	India	PCR-SSCP
Cauveri et al. (2016)	Nilagiri	60	2016	India	Tetra-primer ARMS-PCR
Skorykh et al. (2023)	North Caucasian Meat Wool, Soviet Merino	60	2023	Russia	PCR + sequencing
Al-Muhsen et al. (2019)	Nuimi, Awassi	63	2019	Iraq	PCR-RFLP
Saleh et al. (2022)	Egyptian sheep: Rahmani, Barki, Rahmani-Barki cross, Awassi-Suffolk cross Ossimi	286	2022	Egypt	PCR + sequencing
Gorlov et al. (2017)	Salsk	50	2017	Russia	PCR-RFLP
Machado et al. (2020)	Santa Ines	192	2021	Brazil	PCR + sequencing
Jia et al. (2014)	Tibetan, Small-tailed Han, German Merino, Polled Dorset	510	2014	China	PCR-SSCP + sequencing
Dagdelen (2026)	Tuj	312	2026	Turkey	PCR-RFLP
Moradian et al. (2013)	Makooei	100	2013	Iran	PCR-SSCP

PCR: Polymerase chain reaction, PCR-RFLP: Polymerase chain reaction restriction fragment length polymorphism, PCR-SSCP: Polymerase chain reaction single strand conformation polymorphism, ARMS-PCR: Amplification refractory mutation system polymerase chain reaction.

Identified single nucleotide polymorphisms and genomic regions

The SNPs and genomic regions identified are listed in Table 2. Results showed that 19 of the 23 articles reported SNPs and genomic regions, with SNPs reported in 10 studies (43.4%) and genomic regions in 20 studies (86.9%). Twenty-five distinct SNPs were identified across 23 studies, of which 18 were associated with growth traits such as BWT, BW, WW, LW6, YW, chest circumference (CC), chest depth (CD), chest width (CW), leg length (LL), hip width (HW), daily live weight gain (DLWG), body height (BH), withers height (WH), body length (BL), rump height (RH), back height, waist height and pre-weaning gain, with some influencing single traits and others influencing multiple traits. Nineteen SNPs were reported in the exonic variant region, of which 15 were in Exon 5. Of the 25 identified SNPs, 4 were in non-coding regions, and the regions for 2 SNPs were not specifically mentioned. Five SNPs, including A781G (Kilakarsal, Harnali), A1544G (Barki, Rahmani-Barki cross), C1765A (Rahmani, Awassi-Suffolk cross), T1772A (Rahmani, Ossimi), and G1769C (Rahmani, Ossimi), were repeated in two different breeds. While all other SNPs occurred only once, this indicates substantial variation in *GH* polymorphisms. As different breeds were studied, this may have contributed to variations in reported SNPs.

Table 2. Identified single nucleotide polymorphisms and corresponding genomic regions in the *GH* gene in sheep

Study References (n=23)	Breed	Sample Size (N)	SNPs	Genomic region
Tanış and Keskin (2025)	Akkaraman, Anatolian Merino	73	-	Intron 2 - 4
Al Qasimi et al. (2019)	Awassi	68	-	-
Bayraktar and Shoshin (2022)	Awassi	150	-	-
Li et al. (2025)	Charolais, Australian White	632	C408G, T364C	-
Madikadike et al. (2024)	Dorper	50	T735A	Exon 4
Kumar et al. (2024)	Harnali	138	A781G	Partial exon 2 Intron 3
Abdelmoneim et al. (2017)	Harri	100	G871A	Intron 2
			G1383A	Exon 4
			A1509G	Intron 4
Malewa et al. (2014)	Indonesia fat-tailed	100 (genotyped = 70)	-	Exon 3, Exon 4, Intron 2 - Intron 4
Muniasamy et al. (2023)	Kilakarsal	99	A781G	Exon 2
Esen and Elmacı (2022)	Kıvırcık, Karacabey Merino, Ramlıç, German Black-Head Mutton × Kıvırcık, Hampshire Down × Merino crossbreed	202	1588C > T 1603A > C 1604G > C 1606A > T 1664C > T	Exon 5
Putra et al. (2024)	Merino Cross Rams	145	55G > A	Exon 2
Bai et al. (2022)	Mongolia, Small-tailed Han, Tong, Lanzhou large-tailed, Henan large-tailed Han, Yuxi fatty-tailed	300 (50 each)	-	Exon 2
Dagdelen and Esenbuga (2025)	Morkaraman	123	-	-
Rajith Reddy et al. (2023)	Nellore	50	-	5′ regulatory region, Exon 4
Cauveri et al. (2016)	Nilagiri	60	480 G > A	Intron 1
			871 G > A	Intron 2
Skorykh et al. (2023)	North Caucasian Meat Wool, Soviet Merino	60	476G > A	Exon 5
Al-Muhsen et al. (2019)	Nuimi, Awassi	63		Exon 2
Saleh et al. (2022)	Rahmani	45	C1776G T1772A G1769C C1765A	Exon 5
	Barki	45	A1544G	
	Rahmani-Barki cross	123	A1678G A1558G A1544G	
	Awassi-Suffolk cross	38	C1765A G1550A	
	Ossimi	35	T1772A G1769C G1756C	
Gorlov et al. (2017)	Salsk	50	-	Exon 3
Machado et al. (2020)	Santa Ines	192	-	Introns 2-4, Exons 3-5
Jia et al. (2014)	Tibetan, Small-tailed Han, German Merino, Polled Dorset	510	-	5′ regulatory region, Exon 4, 3′ untranslated region
Dagdelen (2026)	Tuj	312	-	Exon 5
Moradian et al. (2013)	Makooei	100	-	Exon 4

SNPs: Single nucleotide polymorphisms, -: Not mentioned

Genotype and allele frequencies

Genotype frequencies were reported in 18/23 studies (78.2 %), whereas five studies did not report them. Of the included studies, five studies reported three genotypes per SNP, three studies reported two genotypes per SNP, and one reported one genotype per SNP. The most common genotypic pattern observed was AA, AB, and BB. Moreover, in 18 out of 23 studies (78.2%), allele frequencies were reported, and in 5 studies (21.7%), no allele frequency data were reported. In the included studies, reported allele frequencies range from 0.015 to 1.000. Genotype and allele frequencies of all the reviewed articles are presented in Table 3.

Table 3. Reported genotype and allele frequencies of *GH* gene polymorphisms in sheep

Study references (n = 18)	Breed	SNPs	Genotype frequency[a]	Allele frequency[a]
Tanış and Keskin (2025)	Akkaraman, Anatolian Merino	-	AA = 0.542, AB = 0.429, BB = 0.048; AA = 0.192, AB = 0.426, BB = 0.346	A = 0.738, B = 0.262; A = 0.423, B = 0.577
Bayraktar and Shoshin (2022)	Awassi	-	AA = 0.60, AB = 0.20, BB = 0.20	A = 0.70, B = 0.30
Li et al. (2025)	Charolais, Australian White	C408G	CC=0.01, CG=0.95, GG=0.04 CC=0.00, CG=0.93, GG=0.07	C=0.49, G=0.51 C=0.47, G=0.53
		T364C	TT=0.01, CT=0.95, CC=0.04 TT=0.00, CT=0.90, CC=0.10	T=0.49, C=0.51 T=0.45, C=0.55
Madikadike et al. (2024)	Dorper	T735A	AA = 0.70, AB = 0.30	A = 0.85, B = 0.15
Kumar et al. (2024)	Harnali	A781G	AA = 0.62, AB = 0.38	A = 0.81, B = 0.19
Abdelmoneim et al. (2017)	Harri	G871A	GG = 0.30, GA = 0.22, AA = 0.48	G = 0.41, A = 0.59
		G1383A	GG = 0.18, GA = 0.26, AA = 0.56	G = 0.31, A = 0.69
		A1509G	AA = 0.20, AG = 0.30, GG = 0.50	A = 0.35, G = 0.65
Malewa et al. (2014)	Indonesian fat-tailed: Donggala	-	AA=0.357, AB=0.357, BB=0.286	A=0.536, B=0.464
	Indonesian fat-tailed: East Java		AA=0.464, AB=0.250, BB=0.286	A=0.589, B=0.411
Muniasamy et al. (2023)	Kilakarsal	A781G	AA = 0.29; AB = 0.71	A = 0.65; B = 0.35
Putra et al. (2024)	Merino Cross Rams	55G > A	GG = 0.70; GA = 0.30	G = 0.85, A = 0.15
Bai et al. (2022)	Mongolia	-	AA=0.313, AB=0.375, BB=0.312	A= 0.500; B =0.500
	Small-tailed Han		AA=0.281, AB=0.531, BB=0.188	A= 0.547; B =0.453
	Tong		AA=0.364, AB=0.545, BB=0.091	A= 0.636; B =0.364
	Lanzhou large-tailed		AA=0.311, AB=0.311, BB=0.378	A= 0.525; B =0.475
	Henan large-tailed Han		AA=0.350, AB=0.350, BB=0.300	A= 0.511; B =0.489
	Yuxi fatty-tailed		AA=0.213, AB=0.596, BB=0.191	A= 0.467; B =0.533
Dagdelen and Esenbuga (2025)	Morkaraman	-	AA = 0.504; AB = 0.496	A = 0.752; B = 0.248
Rajith Reddy et al. (2023)	Nellore	-	AA = 0.24, AB = 0.42, BB = 0.34 AA = 0.60, AB = 0.40	A = 0.45, B = 0.55 A = 0.80, B = 0.20
Cauveri et al. (2016)	Nilagiri	480 G > A	GG=0.48, GA=0.43, AA=0.09	G=0.70, A=0.30
		871 G > A	AA=1.00	A=1.00
Skorykh et al. (2023)	North Caucasian Meat Wool	476G > A	CC=53.3%, CT=30.0%, TT=16.7%	C=0.68, T=0.32
	Soviet Merino		CC=53.3%, CT=33.3%, TT=13.4%	C=0.70, T=0.30
Gorlov et al. (2017)	Salsk	-	AA = 57%, AB = 36%, BB = 7%	A ≈ 0.75, B ≈ 0.25
Jia et al. (2014)	Tibetan	-	AA = 0.8175, AB = 0.1111, BB = 0.0714; AA = 0.0872, AB = 0.2461, BB = 0.6667; AA = 0.4286, AB = 0.3095, BB = 0.1032, and AC = 0.1578	A = 0.8532, B = 0.1468; A = 0.4206, B = 0.5794; A = 0.6623, B = 0.2589, C = 0.0788
	Small Tail Han		AA = 0.6071, AB = 0.2858, BB = 0.1071; AA = 0.1429, AB = 0.2500, BB = 0.607; AA = 0.5357, AB = 0.1429, BB = 0.1786, AC = 0.1428	A = 0.6607, B = 0.3393; A = 0.4464, B = 0.5536; A = 0.6786, B = 0.2501, C = 0.0713
	German Merino		AA= 1.000; AA = 0.6111, AB = 0.1667, BB = 0.2222; AA = 0.2222, AB = 0.6111, BB = 0.0000, AC = 0.1667	A = 1.0000; A = 0.7222, B = 0.2778; A = 0.6111, B = 0.3056, C = 0.0833
	Polled Dorset		AA= 1.000; AA = 0.5263, AB = 0.2105, BB = 0.2632; AA = 0.5000, AB = 0.2895, BB = 0.0000, AC = 0.2105	A = 1.0000; A = 0.6579, B = 0.3421; A = 0.6053, B = 0.1447, C = 0.2500
Dagdelen (2026)	Tuj	-	LL = 49.0%, LV = 39.0%, VV = 11.0%	L=0.685, V=0.315
Moradian et al. (2013)	Makooei	-	AA=0.313, AB=0.646, BB=0.01, CC=0.01, CD=0.021	A=0.63, B=0.327, C=0.028, D=0.015

[a] Genotype and allele frequencies are presented as proportions, SNPs: Single nucleotide polymorphisms, -: Not mentioned

Association of *GH* gene polymorphisms with growth traits

Of the included studies, 20 (86.9%) indicated significant associations in one or more traits of interest, while three indicated non-significant associations. Significant and non-significant associations are based on statistical analysis and p-values reported in the original studies. Traits are divided into three standard livestock trait categories, including growth traits (birth weight, weaning weight, 6-month weight, 9-month weight, 12-month / Yearling weight, Body weight at 100,120 and 240 days), growth performance traits (average daily gain, daily live weight gain, Pre and Post-weaning average daily gain, growth rate, Kleiber ratio-feed utilization efficiency of animal compared to its body size), and morphometric traits (withers height, rump height, croup height, body height, back height, sacral height, body length, limb length, leg length, neck length, rump length, chest circumference / thoracic girth, heart girth, paunch girth, cannon bone circumference, abdomen circumference, chest width, thoracic width, croup width, hip width, chest depth, body depth, head width, leg girth, foreleg height). Statistically significant and non-significant findings reported across all studies based on statistical analysis and p-value used in that study are presented in Table 4.

Methodological quality assessment

Table 5 presents the methodological quality assessment for the included studies. Of 23 studies, four were considered of low methodological quality, 17 moderate, and two of high. The predominance of moderate quality studies was primarily due to small or medium sample sizes, despite clear reporting of the genotyping method and statistical analysis. Only a limited number of studies were of low methodological quality because of large sample sizes and comprehensive reporting of genotype methods, genotype frequencies, allele frequencies, and reported associations of *GH* gene polymorphisms with studied growth traits.

Table 4. Association of identified *GH* gene polymorphisms with growth related traits in sheep

Study references (n=23)	Breed	SNPs	Genomic region	Genotypes	Traits	Association
Tanış and Keskin (2025)	Akkaraman, Anatolian Merino	-	Intron 2 - 4	AA, AB, BB	WW, WH, RH, BL, CW, CC	S
					BW, LW6, ADG, KR	NS
Al Qasimi et al. (2019)	Awassi	-	-	CT, TC	BW	S
					WW, LW6, body measurements, growth rate	NS
Bayraktar and Shoshin (2022)	Awassi	-	-	AA, AB, BB	BWT	S
					BL, CD	NS
Li et al. (2025)	Charolais, Australian White	C408G T364C	-	CC, CG, GG TT, CT, CC	BWT, BH, back height, waist height, CC, CD, CW, LML, HW	S
					SH, BL, LL, FW	NS
Madikadike et al. (2024)	Dorper	T735A	Exon 4	AA, AB	WH	S
					BWT, BL, HG, STH, RH	NS
Kumar et al. (2024)	Harnali	A781G	Partial exon 2, Intron 3	AA, AB	BW, WW, LW6, YW, BL, BH, HG, PG	NS
Abdelmoneim et al. (2017)	Harri	G871A	Intron 2	GG, GA, AA	BW, BWT120d, DLWG	S
		G1383A	Exon 4			
		A1509G	Intron 4			
Malewa et al. (2014)	Indonesia fat-tailed	-	Exon 3, Exon 4, Intron 2 - Intron 4	AA, AB, BB	Growth rate, WW	S
					BW	NS
Muniasamy et al. (2023)	Kilakarsal	A781G	Exon 2	AA, AB	YW	S
					BW, WW, LW6, LW9	NS
Esen and Elmacı (2022)	Kıvırcık, Karacabey Merino, Ramlıç, German Black-Head Mutton × Kıvırcık, Hampshire Down × Merino crossbreed	1588C>T 1603A>C 1604G>C 1606A>T 1664C>T	Exon 5	-	BL, RH, CD	S
					BWT, WH, CW, LC	NS

Putra et al. (2024)	Merino Cross Rams	55G > A	Exon 2	GG, GA	BW, CW	S
					BWT120d, BWT365d, Pre-ADG, Post-ADG, HL, HW, WH, BL, CG, RL, RW, CW, leg traits	NS
Bai et al. (2022)	Mongolia, Small-tailed Han, Tong, Lanzhou large-tailed, Henan large-tailed Han, Yuxi fatty-tailed	-	Exon 2	AA, AB, BB	BWT, CW, HH	S
					BH, BL, RH, FH, HL, CC, CBC, RL, NL, HW, CD, HD, HC, AC, waist width, back height	NS
Dagdelen and Esenbuga (2025)	Morkaraman	-	-	AA, AB	WW, ADG	S
					BW	NS
Rajith Reddy et al. (2023)	Nellore	-	5′ regulatory region	AA, AB, BB	BWT, BL, WH, HG	NS
			Exon 4	AA, AB		
Cauveri et al. (2016)	Nilagiri	480 G>A 871 G>A	Intron 1 Intron 2	GG, GA, AA	WW, pre-ADG	S
					BW, LW6, LW9, YW, post-ADG	NS
Skorykh et al. (2023)	North Caucasian meat-wool Soviet Merino	476G>A	Exon 5	CC, CT, TT	WW, growth rate (birth-weaning)	S
					BW: Soviet Merino	S
					BW: North Caucasian	NS
Al-Muhsen et al. (2019)	Nuimi and Awassi	-	Exon 2	AA, Aa, aa	BW, WW	S
Saleh et al. (2022)	Rahmani	C1776G T1772A G1769C C1765A	Exon 5	-	BW, WW, LW6	S
	Barki	A1544G				
	Rahmani-Barki cross	A1678G A1558G A1544G				
	Awassi-Suffolk cross	C1765A G1550A				
	Ossimi	T1772A G1769C G1756C				
Gorlov et al. (2017)	Salsk	-	Exon 3	AA, AB, BB	WW, LW9, ADG	S
					BW	NS
Machado et al. (2020)	Santa Ines	-	Introns 2-4, exons 3-5	-	BWT100d, BWT240d, ADG, WH, CH, BL, TG, LG, TW, CW, BD	NS
Jia et al. (2014)	Tibetan, Small Tail Han, German Merino, Polled Dorset	-	5′ regulatory region, Exon 4	AA, AB, BB	BWT, BL, HG, WH	S
			3′ UTR	AA, AB, BB, AC		
Dagdelen (2026)	Tuj	-	Exon 5	LL, LV, VV	WW, ADG	S
					BW	NS
Moradian et al. (2013)	Makooei	-	Exon 4	AA, AB, BB, CC, CD	WW, LW6, LW9	S
					BW, YW	NS

3′ UTR: 3′ untranslated region, ADG: Average daily gain, ADWG: Average daily weight gain, BWT: Body weight, BWT100: Body weight at 100 days, BWT120: Body weight at 120 days, BWT240: Body weight at 240 days, BWT365: Body weight at 365 days, BW: Birth weight, DLWG: Daily live weight gain, KR: Kleiber ratio, LW6: 6-month weight, LW9: 9-month weight, Pre-ADG: Pre-weaning average daily gain, Post-ADG: Post-weaning average daily gain, WW: Weaning weight, YW: Yearling weight, AC: Abdomen circumference, BD: Body depth, BH: Body height, BL: Body length, CBC: Cannon bone circumference, CC: Chest circumference, CD: Chest depth, CH: Croup height, CG: Chest girth, CW: Chest width, FH: Foreleg height, FW: Frontal width, HC: Hip circumference, HG: Heart girth, HH: Hip height, HL: Head length, HD: Head depth, HW: Hip width, LC: Leg circumference, LG: Leg girth, LL: Leg length, LML: Limb length, NL: Neck length, PG: Paunch girth, RH: Rump height, RL: Rump length, STH: Sternum height, SH: Sacral height, TG: Thoracic girth, TW: Thoracic width, WH: Withers height, S: Significant, NS: Non-significant.

Table 5. Methodological quality assessment of included studies (n = 23) evaluating *GH* gene polymorphisms and growth traits in sheep

Study references (n=23)	Sample size (N)	Genotyping method	Genotyping frequencies	Allele frequencies	Statistics	Methodological quality level
Tanış and Keskin (2025)	Small	PCR-RFLP	Yes	Yes	Yes	Moderate
Al Qasimi et al. (2019)	Small	PCR+ sequencing	No	No	Yes	High
Bayraktar and Shoshin (2022)	Medium	PCR-RFLP	Yes	Yes	Yes	Moderate
Li et al. (2025)	Large	PCR + sequencing	Yes	Yes	Yes	Low
Madikadike et al. (2024)	Small	PCR-RFLP	Yes	Yes	Yes	Moderate
Kumar et al. (2024)	Medium	PCR-RFLP	Yes	Yes	Yes	Moderate
Abdelmoneim et al. (2017)	Small	PCR + sequencing	Yes	Yes	Yes	Low
Malewa (2014)	Small	PCR-RFLP	Yes	Yes	Yes	Moderate
Muniasamy et al. (2023)	Small	PCR-RFLP	Yes	Yes	Yes	Moderate
Esen and Elmacı (2022)	Medium	PCR-SSCP + sequencing	No	No	Yes	Moderate
Putra et al. (2024)	Medium	PCR-RFLP	Yes	Yes	Yes	Moderate
Bai et al. (2022)	Low	PCR-SSCP	Yes	Yes	Yes	Moderate
Dagdelen and Esenbuga (2025)	Medium	PCR-RFLP	Yes	Yes	Yes	Moderate
Rajith Reddy et al. (2023)	Small	PCR-SSCP	Yes	Yes	Yes	Moderate
Cauveri et al. (2016)	Small	Tetra-primer ARMS-PCR	Yes	Yes	Yes	Moderate
Skorykh et al. (2023)	Small	PCR + sequencing	Yes	Yes	Yes	Moderate
Al-Muhsen et al. (2019)	Small	PCR-RFLP	No	No	Yes	High
Saleh et al. (2022)	Medium	PCR+ sequencing	No	No	Yes	Moderate
Gorlov et al. (2017)	Small	PCR-RFLP	Yes	Yes	Yes	Moderate
Machado et al. (2020)	Medium	PCR + sequencing	No	No	Yes	Moderate
Jia et al. (2014)	Large	PCR-SSCP + sequencing	Yes	Yes	Yes	Low
Dagdelen (2026)	Large	PCR-RFLP	Yes	Yes	Yes	Low
Moradian et al. (2013) Moradian et al. (2013)	Medium	PCR-SSCP	Yes	Yes	Yes	Moderate

PCR-RFLP: Polymerase chain reaction restriction fragment length polymorphism, PCR-SSCP: Polymerase chain reaction single strand conformation polymorphism.

DISCUSSION

This systematic review synthesized evidence from 23 studies, identified 25 SNPs, of which 18 were associated with different growth rates, investigating the polymorphism of the *GH* gene in sheep and their association with growth traits.

The compiled Table 4 indicated that *GH* variation was not confined to one location; it was distributed across exonic regions (exons 2, 3, 4, 5), intronic regions (introns 1, 2, 3), the 5′ regulatory region, and the 3′ untranslated region (3′ UTR). One–notable result of this review is the abundance of SNPs in exon 5, which explained most of the observed polymorphisms. This concentration indicates that exon 5 is a highly variable segment of the *GH* gene across sheep populations. Exon 5 is a coding region essential to the GH protein and, therefore, mutations in this region can cause amino acid replacement, which can have effects on protein structure and function. The presence of numerous SNPs in exon 5 might be the reason why several studies have found a relationship between *GH* polymorphisms and growth traits (Esen and Elmacı, 2022; Saleh et al., 2022; Skorykh et al., 2023; Dagdelen, 2026). Since variations in coding regions have more functional implications than those in non-coding regions, they influence phenotypic expression. For example, the study on Turkish meat-type lambs identified several variants in exon 5. It also identified stage-specific variations in body length (BL), rump height (RH), and chest depth (CD). Esen and Elmacı (2022) found a combined SNP effect (1588C > T, 1603A > C, 1604G > C, 1606A > T, and 1664C > T) in exon 5 and discovered breed, growth, and stage-specific correlation with BL, RH, and CD.

The association findings were evidently diverse among breeds, traits, and genomic regions. Some of the studies have reported GH-growth variations in the exon 2 region, such as the study on Nuimi and Awassi sheep by Al-Muhsen et al. (2019), which showed a statistically significant association of GH genotype with BW and WW, in both breeds. Another study on six sheep breeds from China reported an association with BWT, chest width (CW), and hip height (HH; Bai et al., 2022). Similarly, a missense SNP, 55G > A, was reported in merino cross rams by Putra et al. (2024), and it was

associated with BW and CW, with no effect on other body traits, indicating a trait-specific effect. Moreover, polymorphism at Exon 3 was also associated with growth rate in sheep. For instance, Gorlov et al. (2017) identified GH variation in Exon 3, which showed association with WW, ADG, and LW9 in Salsk sheep. Similarly, Malewa et al. (2014) identified a polymorphism in exon 3 associated with growth rate and weaning weight in Indonesian fat-tailed sheep. While variation at the exon 4 region in the *GH* gene was associated with important traits, WW, LW9, and LW6 in Makooei sheep (Moradian et al., 2013). Association of genomic regions with various growth traits in these studies showed the importance of a specific functional region with economically important traits, but these effects are breed and trait specific.

In Nilagiri sheep, of the two identified SNPs, only 480 G > A was reported to be associated with WW and pre-weaning average daily gain (pre-ADG), suggesting an effect on early sheep growth (Cauveri et al., 2016). Similarly, a study on Awassi lambs by Al Qasimi et al. (2019) revealed an effect on BW but no effect on WW, LW6, and other body measurements was observed. Also, in Dorper sheep, SNP T735A was associated with wither height (WH) only, suggesting a limited, trait-specific influence (Madikadike et al., 2024). Polymorphism in a study on Tuj sheep by Dagdelen (2026) showed a statistically significant association of GH genotype with WW and DLWG, but no association with BW or placental traits. Similarly, in Morkaraman sheep, *GH* gene polymorphism has a trait-specific effect, with no association reported with BW, whereas WW and DLWG were influenced by genotype (Dagdelen and Esenbuga, 2025). These variations in the association of SNPs with growth traits showed that association can be trait-specific if one trait is influenced by a specific SNP; other traits may show no association in the same breed.

Moreover, breed specificity is a consistent feature in the literature. Allele frequencies across breeds and genotype frequencies in the 5′ regulatory region, exon 4, and 3′ UTR in the multi-breed study of Tibetan, Small Tail Han, German Merino, and Polled Dorset sheep also supported the notion that *GH* variation is not homogeneous across populations (Jia et al., 2014). Similarly, a SNP 476G > A was reported by Skorykh et al. (2023) to be associated with WW in North Caucasian meat-wool and Soviet Merino. However, BW was significant only in Soviet Merino, indicating a breed-specific effect. According to Li et al. (2025), two SNPs, C408G and T364C, were associated with BWT, CW, BH, CC, CD, LL, HW, back height, and waist height, in Charolais and Australian White sheep breeds; however, the effects were population- and genotype-specific.

Multiple SNPs reported in Egyptian sheep, while three SNPs, A1678G, A1558G, and A1544G, were associated with BW, WW, and LW6 in the crossbred population; however, A1544G was also reported in Barki sheep, but was not associated with growth rate, which showed the effect might be breed-specific or due to the combination of the effects of SNPs (Saleh et al., 2022). One SNP, A781G, reported in two studies, was not associated with any trait in the Harnali breed (Kumar et al., 2024) but was significantly associated with yearling weight in the Kilakarsal breed (Muniasamy et al., 2023), demonstrating breed-specific SNP effects. According to Abdelmoneim et al. (2017), three SNPs, G871A, G1383A, and A1509G, were associated with BW, BWT120d, and DLWG in Harri sheep, indicating that specific SNPs on the *GH* gene have consistent effects in some populations.

Some studies did not report a significant association with growth traits in sheep, such as Machado et al. (2020), who did not find any significant associations following Bonferroni correction in the Santa Inês sheep. Similarly, Rajith Reddy et al. (2023) did not report any statistically significant association of *GH* gene polymorphism with BWT, BL, Withers height (WH), and heart girth (HG) in the Nellore breed, which may show that it does not have an effect in this breed, or maybe linked to the small sample size, which reduces statistical power to detect true effects. Also, in Harnail sheep, no association was observed with growth traits, but the effect on other traits (annual greasy fleece weight) indicates that the effect may be trait-specific (Kumar et al., 2024).

The contribution of the systematic review is to demonstrate an association between the *GH* gene and growth traits in sheep. Based on knowledge, there was a lack of systematic synthesis of the association between the *GH* gene and growth traits in sheep, so this systematic review was conducted. This review suggests that *GH* gene polymorphisms can be useful in MAS programs to enhance sheep productivity. Nevertheless, the inconsistency of SNPs between breeds and the inconsistency in association outcomes imply that *GH* markers must be used with caution. SNPs found in one population are unlikely to affect another population in the same way, due to the interaction between genetics and environment.

CONCLUSION

GH gene polymorphism affects sheep growth traits. However, there are some of the limitations found in the studies in which some studies did not specifically mentioned SNPs, incomplete reporting of allele and genotype frequencies in some studies, identified SNPs were not similar which make it impossible to do meta-analysis, smaller sample sizes in a fraction of the studies (less than 200 animals in 73.9% of studies), heterogeneity in breeds, environments and methodologies. These limitations may have contributed to inconsistent results and hindered a direct comparison across

studies. In 20 of 23 studies, several identified, C1776G, A1544G, A1678G, A1558G, C1765A, G1550A, T1772A, G1769C, G1756C, 476G > A, 480 G > A, 55G > A, G871A, G1383A, A1509G, A781G, C408G and T735A, and unidentified SNPs were reported to be associated with growth traits in sheep. A small number of SNPs were repeated across breeds, but no single SNP was shared across all studies. Findings suggest that the *GH* polymorphism is often significantly associated with growth traits, and effects are highly dependent on breed, trait, and genomic region. Although findings from 23 studies included in this review suggest an association of SNPs of the *GH* gene with growth traits in sheep, practical application in breeding programs requires validation in larger populations, across breeds, and for specific traits. Future studies are needed, with a greater focus on other traits such as reproductive performance.

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Authors' contributions

Khadija Salka wrote the original manuscript. Suyadi Suyadi performed the study conceptualization, methodology development, supervision, and assessment of the manuscript. Sohaib Akram conducted data curation and investigation. Veronica Margareta Ani Nurgiartiningsih made a conceptual contribution that enriched the study. Asrullah, Irida Novianti and Marjuki evaluated and reviewed the manuscript. All authors read and approved the final edition of the manuscript.

Availability of data and materials

The data collected or analyzed during this study are all included in this article.

Competing interests

The authors have not declared any conflict of interest.

Ethical considerations

The authors declare that this manuscript is original and has not been submitted to any other journal for consideration or publication, and have checked the ethical issues, including consent to publish, misconduct, data fabrication, and redundancy. The authors confirmed that no AI tools were used in preparing this study.

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