

# Appropriate growth models to describe early growth of Kejobong goat based on Growth Hormone (GH) gene sequence analysis

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**Submission date:** 26-Jul-2021 09:56AM (UTC+0700)

**Submission ID:** 1624045230

**File name:** Asep\_JITAA\_2021.pdf (342.31K)

**Word count:** 7148

**Character count:** 33456

## Appropriate growth models to describe early growth of Kejobong goat based on Growth Hormone (GH) gene sequence analysis

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Received January 16, 2021; Accepted May 21, 2021

### ABSTRAK

Tujuan penelitian yaitu untuk menemukan model pertumbuhan yang tepat dalam mendeskripsikan pertumbuhan awal kambing Kejobong berdasarkan analisis sekuen gen *Growth Hormon* (GH). Materi penelitian menggunakan 35 sampel DNA dan 1.960 catatan sifat kuantitatif kambing Kejobong. Sampel DNA diamplifikasi dan disekuensing untuk mengidentifikasi SNP yang terdapat pada gen *GH* ekson 3. Pengukuran dan penimbangan bobot badan dan ukuran tubuh dilakukan pada umur 0-14 minggu. Empat model pertumbuhan non-linier diaplikasikan untuk menganalisis pertumbuhan guna membandingkan performan pertumbuhan dari berbagai genotipe dengan menggunakan Non-Linear Mixed model. Mutasi non-sinonim (g1170A→G) pada gen *GH* ekson 3 yang membentuk genotipe GG, AG dan AA secara signifikan berasosiasi dengan sifat pertumbuhan. Kambing Kejobong bergenotipe heterozigot AG menunjukkan sifat pertumbuhan yang lebih tinggi dibandingkan dengan kambing Kejobong bergenotipe homozigot AA. Meskipun demikian, kambing Kejobong bergenotipe homozigot GG memiliki sifat pertumbuhan yang sama dengan kambing Kejobong bergenotipe heterozigot AG dan homozigot AA. Model pertumbuhan yang paling tepat untuk mendeskripsikan bobot badan kambing Kejobong adalah model Von Bertalanffy, sedangkan untuk menggambarkan tinggi badan dan tinggi pinggul adalah model Brody. SNP pada gen *GH* ekson 3 dapat digunakan sebagai penanda genetik untuk perbaikan sifat pertumbuhan kambing Kejobong.

*Kata Kunci : Analisis Pertumbuhan, GH, Kambing, Model Matematika, SNP*

### ABSTRACT

The objectives of this study were to reveal appropriate growth models describing early growth of Kejobong goat based on Growth Hormone (*GH*) gene sequence analysis. A total of 35 DNA samples and 1.960 records of quantitative traits of Kejobong goat were collected. The exon 3 of *GH* gene was amplified and was sequenced to determine the SNP. Body weight and body measurements of the goats were taken at 0-14 weeks of age. Four non-linear growth models were applied for analysis of growth to compare growth performance of different genotypes by Non-Linear Mixed Model. A non-synonymous mutation (g1170A→G) genotyped into GG, AG and AA was significantly associated with growth traits. Animals with heterozygous genotype AG showed higher growth traits than animals with homozygous genotype AA. Nonetheless, animals with homozygous genotype GG had the same growth traits with those animals with heterozygous genotype AG and homozygous genotype AA. The most fitted model for describing body weight was Von Bertalanffy model, while for describing wither height and hip height

was Brody model. SNP at exon 3 of the *GH* gene can be used as genetic marker for improvement of growth traits of Kejobong goats.

*Keywords: GH, Goat, Growth analysis, Mathematical models, SNP*

## INTRODUCTION

Kejobong goat is one of indigenous Indonesian breeds, which only exists in Purbalingga District, Central Java Province, Indonesia, and it is conventionally raised by local farmers. This goat belongs to Southeast Asian lineage and is confirmed to be descendant from crossbred of Kacang and Etawah Grade goats (Kumianto *et al.*, 2012; Kumianto *et al.*, 2013; Lestari *et al.*, 2018<sup>a</sup>; Lestari *et al.*, 2018<sup>b</sup>). As the meat animals, Kejobong goat had 41.30% carcass yield that comprised 67.06% meat and 32.94% bone, while its meat is known to have less cholesterol than meat of Kacang and Etawah Grade goat (Aqsa *et al.*, 2011). Kejobong goat is popular at the district because of its high rate of growth, good reproductive performance, high resistance to local diseases and parasites and ability to survive and growing ability under poor feeding conditions (Kumianto *et al.*, 2012; Febriana *et al.*, 2017). However, the breeders often have difficulty to satisfy the market demand on slaughtering weight. This is probably due to limited information of appropriate breeding strategy for Kejobong goat to accomplish the breeding goal of high meat productivity.

Growth analysis can provide valuable information about mature weight, growth rate and mature time. Growth rate and body weight of animal at different ages influence productivity of meat and have deterministic effects on the profitability of meat production (Kheirabadi and Rashidi, 2019). Particularly, growth rate has large effect on meat producing efficiency up to slaughtering age which is crucial for economic success of animal production (Abbasi *et al.*, 2012). According to Junior *et al.* (2013) and Ripoll *et al.* (2016), animals that have a large frame size of body tend to have higher potential of growth and have a higher proportion of meat. Therefore, besides body weight, body size is also important trait to be considered for performing animal selection. Study of growth analysis has been done by previous researchers (Waheed *et al.*, 2011; Setiaji *et al.*, 2013; Zadeh *et al.*, 2015; Raji *et al.*, 2015; Lupi *et al.*, 2016; Zadeh and Gorbani, 2018; Ghiasi *et al.*, 2018; Rout *et al.*, 2018; Kheirabadi and Rashidi, 2019), however they

were only using phenotypic data into analysis. In this study, conventional growth analysis was modified by including genotype records to growth analysis.

Early growth of kids is an economically important trait that affecting profitability in goat production (Baranzadeh *et al.*, 2012; Moghbeli *et al.*, 2013; Sadeghi *et al.*, 2019). Physiologically, growth of an animal is a result from a complex process of metabolism including a coordinated action of several hormones that controlled by expression of their responsible genes (Mahrous *et al.*, 2018). Growth Hormone (*GH*) gene is one of numerous genes which have large effect on growth performance of an animal. *GH* gene is encoding growth hormone that produces in anterior pituitary and is necessary for postnatal growth and metabolism in vertebrates (Ge *et al.*, 2003). This hormone is known to have a broad impact on biological activity in all body cells, such as controlling and coordinating the flow rate of metabolic process, enhancing glycogen, protein, DNA and RNA biosynthesis and promoting the deposition of fat and the disintegration of fatty acids and glucose in the tissue (Gorlov *et al.*, 2017; Wickramaratne *et al.*, 2010; Othman *et al.*, 2015; Seevagan *et al.*, 2015; Singh *et al.*, 2015). Therefore, *GH* gene is considered to be a prime factor which affects growth performance of an animal.

Based on these backgrounds, effect of *GH* gene on growth traits, especially from a point of genetic improvement is important to build breeding plan for high meat productivity. Prospectively, result of this study is not only suggesting appropriate management practice for improving production for the breeders, but also providing information of genetic marker in Kejobong goat for breeding selection in the future through Marker-Assisted Selection (MAS) and/or Marker-Assisted Introgression (MAI) and appropriate mathematical growth models of Kejobong goat. Therefore, the objective of this study was to reveal appropriate growth models describing early growth of body weight and body measurement of Kejobong goat based on the effect of Growth Hormone (*GH*) gene sequence analysis.

## MATERIALS AND METHODS

### Ethical approval

All procedure involving animals were based on the standard rule of animal treating as appointed in the Republic of Indonesia's law, number 41, 2014.

### Sampling and data collection

A total of 35 blood samples and 1.960 quantitative traits records of Kejobong goat were collected from Purbalingga District, Central Java Province, Indonesia. Quantitative traits records comprised body weight (BW), wither height (WH), chest depth (CD), chest width (CW), hip height (HH), hip width (HW) and heart girth (HG) at 0, 2, 4, 6, 8, 10, 12 and 14 weeks of age.

### DNA extraction, Polymorphism Chain Reaction (PCR) and sequencing

Blood samples for DNA analysis were taken by 3cc sput from jugular venous that previously cleaned with alcohol. The blood was then collected in vacutainer blood collection tubes with an anticoagulant (EDTA). DNA was extracted from whole blood by gSYNC DNA mini kit (Geneaid Biotech, Taiwan) according to the manufacturer's standard protocol for PCR and sequencing analysis.

Forward primer F: 5'-TAGAAATGGGGGTGTGTGGGGT-3' and reverse primer R: 5'-CATCTCCACTGCCATCCAACA-3' (Sigma-Aldrich, Japan) were used to amplify GH gene exon 3. PCR was carried out in total volume 50  $\mu$ L comprising 1  $\mu$ L KOD Plus (Toyobo, Japan), 5  $\mu$ L buffer, 5  $\mu$ L dNTP, 2  $\mu$ L MgSO<sub>4</sub>, 1.5  $\mu$ L forward primer, 1.5  $\mu$ L reverse primer, 32  $\mu$ L PCR water and 2  $\mu$ L DNA template. PCR amplification was running with an initial denaturation at 94°C for 2 min, followed by 40 cycles of denaturation at 94°C for 15 sec, primers annealing 66.8°C for 30 sec and extension at 68°C for 19 sec. PCR products were electrophoresed using 1.3% Agarose gel at 110 V for 20 min. PCR products were then visualized by UV trans-illuminator and was sequenced through Fasmac sequencing service, Japan.

### Data analysis

Allelic and genotypic frequencies were directly calculated. Hardy-Weinberg Equilibrium (HWE) was tested using chi-square statistic ( $\chi^2$ ) as follows:

$$\chi^2 = \sum_{i=1}^k \frac{(o_i - e_i)^2}{e_i}$$

where  $\chi^2$  is the Chi square value;  $o_i$  the observed value of genotype frequency,  $e_i$  the expected value of genotype frequency,  $\chi^2$  the table using 5% significance level for HWE test.

Heterozygosity (H) was calculated as follows:

$$H = 1 - \sum_{i=1}^k p_i^2$$

where H is the value of heterozygosity and  $p_i$  the frequency of the  $i^{\text{th}}$  of  $k$  alleles.

Sequencing result alignment was analyzed by Clustal W (Thompson *et al.*, 1994) with Molecular Evolutionary Genetics Analysis (MEGA6.0) (Tamura *et al.*, 2013) to find out the SNP within animals. Sequencing result then was translated into amino acids form by standard genetic code to identify amino acid alteration that caused by SNP.

Linear Mixed Model (LMM) was used to analyze association between genotype with quantitative traits by MIXED procedure in Statistical Analysis System (SAS 9.3) (SAS Institute Inc, 2011). The model was:

$$y_{ijkl} = \mu + G_i + F_j + u_k + b_1\alpha_{ijkl} + b_2\alpha_{ijkl}^2 + e_{ijkl}$$

where  $y_{ijkl}$  is the observed value of a dependent variable (body weight or body measurements);  $\mu$  the overall mean of the population;  $G_i$  the fixed effect of  $i^{\text{th}}$  genotype ( $i = 1$  for GG, 2 for AG, 3 for AA);  $F_j$  the fixed effect of  $j^{\text{th}}$  farm group ( $j = 1, 2, 3, 4$ );  $u_k$  the random effect of  $k^{\text{th}}$  animal;  $b_1$  and  $b_2$  the linear and quadratic coefficients of partial regression, respectively;  $l^{\text{th}}$  individual measurement,  $\alpha_{ijkl}$  age in days of a covariate and  $e_{ijkl}$  the random residual for  $y_{ijkl}$ . Difference in the least square means of the genotypes was tested by the Tukey-Kramer (Tukey, 1949).

The nonlinear growth models comprised Brody (Brody, 1945), Von Bertalanffy (Bertalanffy, 1938), Logistic (Verhulst, 1838) and Gompertz (Gompertz, 1825) and they were compared by describing animal growth (Table 1). Growth models were analyzed using Nonlinear Mixed Model (NLMM) by NLMIXED procedure of SAS 9.3 (SAS Institute Inc, 2011). Body weight or body measurements as dependent variables are influenced by genotype and age. Therefore, dummy variables were created to assess the effect of qualitative variables on dependent variables according to the method by Filho *et al.* (2014). The NLMIXED procedure

Table 1. Growth equations used to construct the growth model

Model	Function <sup>A</sup>	Inflection weight	Inflection age
Body	$y = a (1 - b \exp^{-kt})$	-	-
Von Bertalanffy	$y = a (1 - b \exp^{-kt})^3$	$y_i = 8a/27$	$t_i = \ln(3b)/k$
Logistic	$y = a / (1 + b \exp^{-kt})$	$y_i = a/2$	$t_i = \ln(b)/k$
Gompertz	$y = a \exp(-b \exp^{-kt})$	$y_i = a/\exp$	$t_i = \ln(b)/k$

<sup>A</sup>y, observed body weight/body measurements; a, the estimated of mature body weight/body measurements; b, the integration constant; k, the growth rate constant; t, the animal age in day and exp, Napier's constant the base of natural logarithm.

was used in this study due to its flexibility in engaging the variance covariance structure which could not be identified by traditional regression approach. Also NLMIXED has ability to handle unbalance data (Aggrey, 2009; Galeano-Risco *et al.*, 2014). This procedure can reduce potential biases despite selective sampling and supply supplemental parameters that characterize variation between individual animals (Craig and Schinkel, 2001).

were well amplified. Sequencing result revealed 5 SNPs as transition mutation in parsimonious form, which were g1121A→G (SNP1), g1148T→C (SNP2), g1160A→G (SNP3), g1170A→G (SNP4) and g1178C→T (SNP5). Genotype frequencies of Kejobong goats were not different from HWE, and the frequency of heterozygosity was 49% (Table 2). The estimated allele of the *GH* gene exon 3 in this study was 57% and 43% for G and A, respectively.

Table 2. Estimated allele and genotype frequency

Variable Measured	Genotype			Allele		H	$\chi^2$
	GG	AG	AA	G	A		
Frequencies	0.37	0.40	0.23				
Observation	13	14	8	0.57	0.43	0.49	1.18
Expectation	11.43	17.14	6.43				

H, Heterozygosity;  $\chi^2$ , Chi square value.

The models were tested for goodness of fit using -2 log likelihood, Akaike Information Criterion (AIC) (Akaike, 1974), Bayesian Information Criterion (BIC) (Schwarz, 1978) and the residual variances ( $\sigma^2_e$ ). AIC and BIC were calculated by the following formula:

$$AIC = n \ln \left( \frac{SSE}{n} \right) + 2k$$

$$BIC = n \ln \left( \frac{SSE}{n} \right) + k \ln(n)$$

where n is the number of observation; SSE the Sum Square Errors and k the number of parameters. Smaller values of AIC, BIC or  $\sigma^2_e$  indicate the best fit of the model to the observations.

## RESULTS

Result showed that a total 117 bp of *GH* gene exon 3 encoding 38 amino acid sequence

Frequencies of genotypes GG, AG and GC were 37%, 40% and 23%, respectively, so that G allele and heterozygous genotype AG were predominant in this locus.

Test of significance showed that the fixed effect of genotype together with effect of farm and linear and quadratic coefficients of age were statistically significant ( $P < 0.05$ ) in BW while the fixed effect of genotype and linear and quadratic coefficients of age were statistically significant ( $P < 0.05$ ) in WH, and the fixed effect of genotype, age of doe and linear and quadratic coefficients of age were statistically significant ( $P < 0.05$ ) in HH. Conversely, the fixed effect of genotype was not significant in CD, CW, HW and HG (Table 3).

Animals of genotype AG demonstrated the highest BW, HW and HH then it followed with animals of genotype GG and AA (Table 4). Comparing genotypes at different periods, BW0 and BW6 in animals of genotype AG (4.35 kg and 8.40 kg) were significantly heavier ( $P < 0.05$ ) than

Table 3. Significance analysis of factor affecting body weight and body measurements

Traits	Effect	Degree of freedom	f-value	p-value
BW <sup>A</sup>	Genotype	2	3.44	0.0335
	Age of doe	3	1.43	0.2355
	Farm	3	5.33	0.0050
	Age (linear)	1	224.97	<0.0001
	Age (quadratic)	1	17.98	<0.0001
WH <sup>B</sup>	Genotype	2	4.14	0.0171
	Age of doe	3	2.59	0.0537
	Farm	3	2.27	0.1021
	Age (linear)	1	238.66	<0.0001
	Age (quadratic)	1	50.99	<0.0001
CD <sup>C</sup>	Genotype	2	0.14	0.8677
	Age of doe	3	0.54	0.6541
	Farm	3	1.00	0.4081
	Age (linear)	1	40.44	<0.0001
	Age (quadratic)	1	10.58	0.0013
CW <sup>D</sup>	Genotype	2	2.41	0.0920
	Age of doe	3	2.66	0.0491
	Farm	3	5.48	0.0043
	Age (linear)	1	36.02	0.0001
	Age (quadratic)	1	9.05	0.0029
HH <sup>E</sup>	Genotype	2	4.25	0.0153
	Age of doe	3	2.64	0.0499
	Farm	3	1.71	0.1879
	Age (linear)	1	267.39	<0.0001
	Age (quadratic)	1	59.44	<0.0001
HW <sup>F</sup>	Genotype	2	1.74	0.1775
	Age of doe	3	0.71	0.5496
	Farm	3	2.27	0.1023
	Age (linear)	1	62.34	<0.0001
	Age (quadratic)	1	13.53	0.0003
HG <sup>G</sup>	Genotype	2	1.69	0.1873
	Age of doe	3	1.62	0.1852
	Farm	3	3.89	0.0192
	Age (linear)	1	347.92	<0.0001
	Age (quadratic)	1	70.55	<0.0001

<sup>A</sup>Body weight; <sup>B</sup>Wither height; <sup>C</sup>Chest depth; <sup>D</sup>Chest width; <sup>E</sup>Hip height; <sup>F</sup>Hip width; <sup>G</sup>Heart girth.

animals of genotype AA (3.40 kg and 6.59 kg), while animals of genotype GG (3.84 kg and 6.97 kg) showed no significant difference with genotype AG and AA. However, there were no significant effect of genotype at BW2, BW4, BW8, BW10, BW12 and BW14.

Significant difference between genotypes for body measurements were observed in wither height (WH6, WH10, and WH14) and hip height (HH12 and HH14). Similar to body weight, animals of genotype AG had significantly (P<0.05) higher wither and hip heights than those

animals of genotype AA, but there was no significant difference between animals of genotype GG with animals of genotype AG and AA (Table 5).

Estimated parameters for body weight, wither height and hip height are presented in Table 6, respectively. Growth analysis showed that Von Bertalanffy model had the lowest -2 log likelihood, and two criteria AIC and BIC compared with the other models indicating this model as the best model for describing growth of body weight in Kejobong goat. On the other hand,

Table 4. Average of body weight and body measurements

Traits	Genotype		
	GG	AG	AA
Body weight (BW)			
BW0	3.75±0.76	4.26±1.02	3.51±1.06
BW2	4.91±0.75	5.39±1.20	4.87±1.20
BW4	6.12±0.89	6.57±1.38	5.84±1.95
BW6	7.39±1.01	7.91±1.63	6.74±2.15
BW8	8.24±1.14	8.87±1.89	7.85±2.62
BW10	9.07±1.21	9.72±2.26	8.64±2.89
BW12	9.87±1.33	10.52±2.56	9.19±3.08
BW14	10.64±1.49	11.36±2.78	9.80±3.10
Wither height (WH)			
WH0	33.93±3.21	35.08±2.49	31.69±4.63
WH2	37.85±2.84	37.72±4.45	36.63±2.92
WH4	40.63±2.55	40.57±4.12	39.33±4.43
WH6	42.34±2.30	43.28±2.48	40.77±5.35
WH8	44.29±2.40	45.09±3.30	42.51±4.88
WH10	45.42±1.85	45.65±3.47	42.85±5.24
WH12	46.35±2.52	47.54±3.29	44.49±4.88
WH14	47.61±2.67	49.06±3.07	45.39±4.98
Hip height (HH)			
HH0	36.57±3.19	37.60±3.40	34.23±4.73
HH2	40.09±3.30	40.78±2.55	38.34±3.55
HH4	42.89±2.85	43.56±3.67	42.00±4.72
HH6	44.84±2.68	46.39±2.52	43.92±5.37
HH8	46.63±3.01	47.67±3.12	45.39±5.02
HH10	48.01±2.00	48.33±2.91	46.03±5.62
HH12	48.99±2.41	50.56±3.08	45.96±4.76
HH14	50.55±2.57	52.15±2.99	47.82±5.75

the highest -2 log likelihood, AIC and BIC were obtained in Logistic model. Brody model in this study showed fit to wither height and hip height well according to its value of -2 log likelihood, AIC and BIC, which was lower than Gompertz, Logistic and Von Bertalanffy model.

Von Bertalanffy model fitted best to body weight, estimated 23.01 kg mature body weight (a), 0.39 integration constant (b) and 0.01389 growth rate (k). The best estimated for wither height and hip height by Brody model were 54.65 cm and 58.91 cm for parameter a; 0.37 and 0.36 for parameter b; 0.01577 and 0.01647 for parameter k. In this study, the estimated parameter b for body weight, wither height and hip height were 0.39, 0.37 and 0.36 respectively.

Furthermore, estimated parameter k of body weight in Von Bertalanffy model was 0.01389. Negative correlation was found between

parameter k and parameter a (Table 7). This result was confirmed by the fact that Brody model in this study had the slowest parameter k (0.006948) in body weight, yet it had the highest estimated parameter a (25.29 kg) among the others. Similarly, the highest parameter k in wither height (0.2606) and hip height (0.02341) had the lowest estimated parameter a (50.78 cm, 56.26 cm) in Von Bertalanffy and Logistic models respectively.

Representing variability among individual animals, estimated animal variance ( $\sigma^2$ ) of the body weight in this study was 5.78. The higher the variance, the greater the difference is realized among animals. Furthermore, residual variance ( $\sigma^2$ ) of the body weight in this study was 0.31 that indicated the gap between predicted value and observed value. Repeatability of body weight by intra-class correlation was 0.95 this study.

Table 5. Estimated genotypic effect for body weight and body measurements for each measurement

Traits	Genotypes		
	GG	AG	AA
Body weight (BW)			
BW0	3.84±0.22 <sup>AB</sup>	4.35±0.20 <sup>A</sup>	3.40±0.27 <sup>B</sup>
BW2	4.84±0.28	5.67±0.26	4.82±0.36
BW4	5.87±0.37	6.97±0.34	5.75±0.46
BW6	6.97±0.43 <sup>AB</sup>	8.40±0.40 <sup>A</sup>	6.59±0.55 <sup>B</sup>
BW8	7.80±0.52	9.43±0.47	7.71±0.66
BW10	8.57±0.59	10.35±0.54	8.54±0.75
BW12	9.29±0.65	11.17±0.60	9.17±0.84
BW14	10.03±0.69	12.03±0.63	9.71±0.88
Wither height (WH)			
WH0	34.27±0.94	35.03±0.87	32.64±1.20
WH2	37.38±1.18	38.41±1.08	36.03±1.51
WH4	39.89±1.07	41.44±0.98	39.08±1.37
WH6	41.88±0.90 <sup>AB</sup>	44.25±0.83 <sup>A</sup>	40.45±1.16 <sup>B</sup>
WH8	43.41±1.04	46.15±0.95	42.14±1.33
WH10	44.15±1.01 <sup>AB</sup>	46.83±0.93 <sup>A</sup>	42.33±1.29 <sup>B</sup>
WH12	45.59±1.03	48.53±0.95	44.34±1.32
WH14	46.69±1.04 <sup>AB</sup>	49.95±0.95 <sup>A</sup>	45.29±1.33 <sup>B</sup>
Hip height (HH)			
HH0	36.95±1.01	37.71±0.93	34.59±1.30
HH2	36.95±1.01	41.11±0.89	38.16±1.23
HH4	42.61±1.12	43.85±1.03	42.02±1.43
HH6	44.55±1.03	47.21±0.94	43.87±1.32
HH8	45.57±1.14	48.65±1.05	44.96±1.46
HH10	46.94±1.00	49.31±0.96	45.48±1.28
HH12	48.58±1.05 <sup>AB</sup>	51.28±0.97 <sup>A</sup>	45.82±1.35 <sup>B</sup>
HH14	49.59±1.09 <sup>AB</sup>	53.08±1.00 <sup>A</sup>	47.57±1.39 <sup>B</sup>

<sup>A,B</sup>In the same row, values with different superscripts are significantly different (P<0.05).

## DISCUSSION

SNP2 of this study was also found in a report analyzing *GH* gene of Chinese goat (An *et al.*, 2010). Among five SNPs in this study, translation result showed SNP4 causing amino acid alteration which changes amino acid sequence in *GH* gene exon 3. SNP4 as non-synonymous mutation changed the first triplet codon of AGC encoding Serin to GGC encoding Glycine (Figure 1) and we used it to distinguished as GG, AG and AA genotypes, whereas the other SNPs were silent mutation (SNP1 CAG>CAA(Gln); SNP2 TCT>TCC(Ser); SNP3 CCA>CAG(Pro); SNP5 AAC>AAT(Asn)). According to Nei and Kumar (2000), most of synonymous amino acid was found due to substitution of nucleotides in the third codon, while substitution of nucleotides in the first and second codon generate non-

synonymous amino acid. Therefore, non-synonymous mutation that change amino acid sequence in exon region may change the peptide sequence of the encoded protein and influence the function of the protein, which was growth hormone in this study. This hormone has substantial metabolic effects on somatic growth, stimulation of protein synthesis and cellular uptake of amino acids and development of body composition (Hjortebjerg *et al.*, 2017).

Result in this study agreed with a result by Dayal *et al.* (2016), in which goats with heterozygous genotype AC had the heaviest body weight among five observed genotypes in Black Bengal goat. Gorlov *et al.* (2017) reported their study in Salsk sheep that sheep with AB genotype significantly had heavier body weight, average daily gain and carcass weight than sheep with AA genotype. A contradictory result was

**1** Table 6. Estimated parameters of growth and goodness of fit for four different growth models

Parameter	Model			
	Brody	Von Bertalanffy	Logistic	Gompertz
<b>Body weight</b>				
a	25.29±1.01	23.01±0.47	21.65±0.30	22.48±0.39
b	0.83±0.01	0.39±0.01	2.56±0.07	1.42±0.03
k	0.006948±0.00101	0.01389±0.00109	0.0277±0.001309	0.01735±0.00114
	9	7		3
y <sub>i</sub>	-	6.82	10.83	8.27
t <sub>i</sub>	-	11.75	33.93	20.10
σ <sup>2</sup> <sub>u</sub>	9.08±2.67	5.78±1.48	4.17±1.03	5.13±1.29
σ <sup>2</sup> <sub>e</sub>	0.32±0.03	0.31±0.03	0.32±0.03	0.31±0.03
GG	-3.6±0.79	-4.2±0.59	-4.64±0.49	-4.37±0.55
AG	-2.01±0.85	-3.03±0.061	-3.63±0.50	-3.26±0.56
AA	-4.53±0.95	-5.06±0.75	-5.3±0.63	-5.18±0.70
-2 Log Likelihood	606.6	605.8	609.5	606.1
AIC	630.6	629.8	633.5	630.1
BIC	649.6	648.8	652.5	649.1
<b>Wither height</b>				
a	54.65±0.94	50.78±0.31	53.59±0.71	55.54±0.81
b	0.37±0.01	1.96±0.08	0.53±0.02	0.44±0.01
k	0.01577±0.002084	0.2606±0.01207	0.02292±0.00226	0.01934±0.00217
			8	1
σ <sup>2</sup> <sub>u</sub>	9.93±2.56	0.0014±0.5954	9.39±2.40	9.62±2.47
σ <sup>2</sup> <sub>e</sub>	3.95±0.36	29.44±1.63	3.97±0.36	3.96±0.36
GG	-3.3±0.82	-6.82±0.50	-3.67±0.77	-5.02±0.79
AG	-2.76±0.81	-6.78±0.47	-3.14±0.76	-4.48±0.78
AA	-5.59±0.92	-11.91±0.64	-5.90±0.88	-7.27±0.90
-2 Log Likelihood	1274.3	2217.3	1276.0	1275.1
AIC	1290.9	2233.3	1292.0	1291.1
BIC	1303.0	2246.0	1304.6	1303.8
<b>Hip height</b>				
a	58.91±0.72	57.73±0.73	56.26±0.56	56.61±0.62
b	0.36±0.01	0.13±0.01	0.50±0.01	0.42±0.01
k	0.01647±0.002009	0.01839±0.00211	0.02341±0.00218	0.01994±0.00209
		2	7	2
σ <sup>2</sup> <sub>u</sub>	8.40±2.20	12.99±0.64	7.91±2.04	8.09±2.10
σ <sup>2</sup> <sub>e</sub>	3.72±0.34	3.71±0.33	3.75±0.34	3.73±0.34
GG	-2.24±0.77	-2.12±0.94	-1.56±0.73	-1.44±0.75
AG	-0.60±0.78	-0.81±0.93	0.12±0.74	0.25±0.75
AA	-4.55±0.89	-4.63±1.08	-3.60±0.86	-3.50±0.87
-2 Log Likelihood	1254.6	1258.2	1256.5	1255.4
AIC	1278.6	1282.2	1280.5	1279.4
<b>1</b> BIC	1297.6	1301.2	1299.5	1298.4

a, the estimated of mature body weight/body measurements; b, the integration constant; k, the growth rate constant; y<sub>i</sub>, body weight (kg) at the point at inflection; t<sub>i</sub>, age (weeks) at the point at inflection; σ<sup>2</sup><sub>u</sub>; additive genetic variance; σ<sup>2</sup><sub>e</sub>, error variance; AIC, akaike information criterion; BIC, bayesian information criterion.

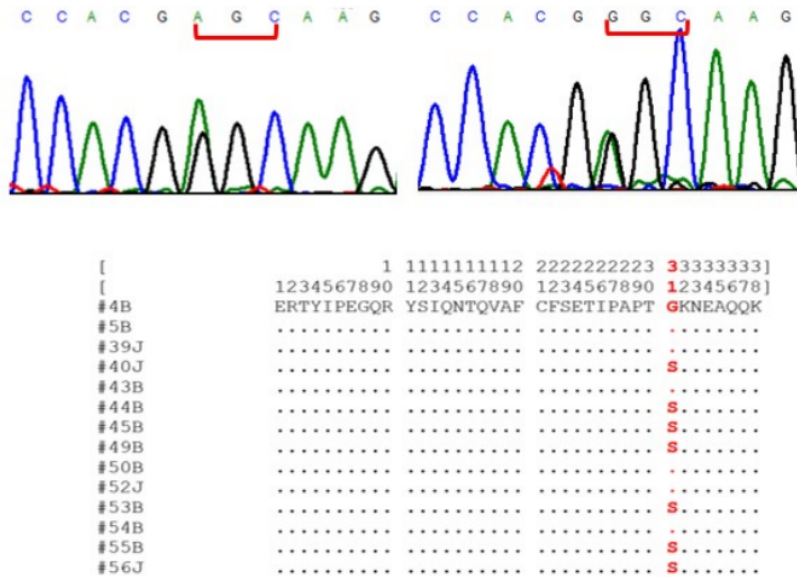


Figure 1. Amino acid alteration caused by SNP g1170A

Table 7. Correlation among growth parameter within traits based on their best model

Growth Parameter	Mature weight (a)		
	BW <sup>A</sup>	WH <sup>B</sup>	HH <sup>C</sup>
Integration constant (b)	0.5564	0.7038	0.6652
Growth rate (k)	-0.7833	-0.8755	-0.8636

<sup>A</sup>Body weight; <sup>B</sup>Wither height; <sup>C</sup>Hip height

reported by An *et al.* (2011) that goats with homozygous genotype AA significantly had higher body weight than those of heterozygous genotype AB at age of one and three months old in Chinese goat, however, wither height showed no significant difference. The different results seem to be due to genetic difference that leads to different structure of *GH* gene and limited number of observations. Therefore, further study is necessary to validate the predominant effect of heterozygote of *GH* gene with a larger number of animals and more sampled observations.

The best model for describing growth of body weight in this study was different with previous study by Kheirabadi and Rashidi (2019), reported that Logistic model fitted worst to body weight, while Brody model fitted most accurately to body weight of Markhoz goat. In this study, estimated

mature body weight (a) was 23.01 kg implying that Kejobong goat had heavier mature body weight than Raeini Cashmere goat (17.97 kg) (Ghiasi *et al.*, 2018) and Nondescipt goat (6.42 to 10.55 kg) (Raji *et al.*, 2015) but lighter body weight than Beetal goat (23.39 kg) (Waheed *et al.*, 2011). Those values of parameter b for body weight, wither height and hip height in this study were described to represent the proportion of mature weight attained after birth, calculated by the initial weight and age value (Lupi *et al.*, 2016). On the other hand, Ghiasi *et al.* (2018) stated that parameter b is a scale parameter that has no biological interpretation. Waheed *et al.* (2011) reported higher estimated values of parameter k (0.1077) in Beetal goat by Brody model. Other researchers estimated parameter k as much as 0.017 in Cashmere goat (Ghiasi *et al.*

2018) and 0.0108 in Repartida goat (Pires *et al.*, 2017) by applying Gompertz model, so that Kejobong goat in this study is considered to attain mature weight later than Beetal and Cashmere goat but earlier than Repartida goat.

Negative correlation between parameter  $k$  and parameter  $a$  indicated the slower growth rate, the larger mature weight, *vice versa*. Previous studies supported this results. Kumianto *et al.* (1998) reported that animals with slower growth rate tended to have estimated heavy body weight at maturity. Brown *et al.* (1976) stated that selection for increasing growth rate tended to decrease mature weight, yet its antagonistic association could be minimized by cross-breeding and improving feed quality. On other hand, previous study by Ghiasi *et al.* (2018) showed lower animal variance (1.29) and higher residual variance (8.01) on growth analysis of Raeni Cashmere goat using Gompertz model than the present study. Repeatability of body weight in this study was higher than repeatability value of South African Angora goat (Snyman and Olivier, 1999) and Boerawa goat (Beyleto *et al.*, 2010). The high repeatability in this study may be resulted by the fact that systematic factors affecting body weight were fitted as many as possible in NLMM and that earlier body weight was a component of latter body weight.

The NLMIXED procedure used in this study has flexibility in engaging the variance covariance structure which could not be identified by traditional regression approach. Also NLMIXED has ability to handle unbalance data (Aggrey, 2009; Galeano-Rasco *et al.*, 2014). This procedure can reduce potential biases despite selective sampling and supply supplemental parameters that characterize variation between individual animals (Craig and Schinkel, 2001). Therefore, this procedure can facilitate growth analysis by including genotype information and estimates accurately the growth performance of Kejobong goats.

## CONCLUSION

SNP g1170A→G in *GH* gene is associated with growth traits and can be used as genetic marker for animal selection to improve goat's growth performance. Animals with heterozygous genotype AG showed higher growth performance than homozygous genotype AA. Nonetheless, animals with homozygous genotype GG showed no difference with either heterozygous genotype

AG or homozygous genotype AA. Model ( $y = 23.01 (1 - 0.39 e^{-0.01389age})^3$ ) by Von Bertalanffy,  $y = 54.65 (1 - 0.37 e^{-0.01577age})$  and  $y = 58.91 (1 - 0.36 e^{-0.01647age})$  by Brody were fitted well to describe body weight, wither height and hip height of Kejobong goat, respectively.

## REFERENCES

- Abbasi, M., R. Abdollahi-Arpanahi, A. Maghsoudi, R. V. Torshizi and A. Nejati-Javaremi. 2012. Evaluation of models for estimation of genetic parameters and maternal effects for early growth traits of Iranian Baluchi sheep. *Small Rumin. Res.* 104: 62-69.
- Aggrey, S. E. 2009. Logistic nonlinear mixed model for estimating growth parameters. *Poult. Sci.* 88: 276-280.
- Akaike, H. 1974. A new look at the statistical model identification. *IEEE Transactions on Automatic Control* 19: 716-723.
- An, X. P., J. X. Hou, L. X. Wang, G. Li, J. G. Wang, Y. X. Song, G. Q. Zhou, D. Han, L. Ling and B. Y. Cao. 2010. Novel polymorphisms of growth hormone gene and their effect on growth traits in Chinese goats. *Meat Sci.* 86: 758-763.
- An, X. P., L. X. Wang, J. X. Hou, G. Li, Y. X. Song, J. G. Wang, M. M. Yang, Y. H. Cui, and B. Cao. 2011. Novel polymorphisms of goat growth hormone and growth hormone receptor genes and their effects on growth traits. *Mol. Biol. Report* 38: 4037-4043.
- Aqsha, G. E., E. Purbowati and A. N. Al-Baari. 2011. Komposisi kimia daging kambing Kacang, Peranakan Etawah dan Kejobong jantan pada umur satu tahun. *Workshop Nasional diversifikasi pangan daging ruminansia kecil.* p: 105-109.
- Baranzadeh, A., S. M. Moghbeli, M. Vatankhah and M. Mohammadabadi. 2011. Estimating non-genetic and genetic parameter of pre-weaning growth traits in Raini Cashmere goat. *Trop. Anim. Health Prod.* 44: 811-817.
- Bertalanffy, L. V. 1938. A quantitative theory of organic growth (Inquiries on growth laws. II). *Hum. Biol.* 10: 181-213.
- Beyleto, V. Y., S. Sumadi and T. Hartatik. 2010. Estimasi parameter genetik sifat pertumbuhan kambing Boerawa di Kabupaten Tanggamus Propinsi

- Lampung. Buletin Peternakan 34: 138-144.
- Brody, S. 1945. Bioenergetics and growth; with special reference to the efficiency complex in domestic animals. Reinhold Publishing Corporation, New York.
- Brown, J. E., H. A. Fitzhugh and T. C. Cartwright. 1976. A comparison of nonlinear models for describing weight-age relationships in cattle. *J. Anim. Sci.* 42: 810-818.
- Craig, B. A. and A. P. Schinckel. 2001. Nonlinear mixed effects model for swine growth. *The Prof. Anim. Sci.*, 17: 256-260.
- Dayal, S., R. Kumari, A. Dey and B. Kumar. 2016. PCR-SSCP of growth hormone gene and its association with body weight in Black Bengal goat. *Indian J. Anim. Sci.* 86: 1283-1286.
- Febriana, A., S. Sutopo and E. Kurnianto. 2017. Identification of BMP15 exon 2 for fecundity traits by PCR-RFLP and nucleotide sequences in Kejobong goat. *J. Indo. Trop. Anim. Agric.* 42: 220-226.
- Filho, R., L. O. Tedeschi, M. T. Rodrigues, L. F. Brito and T. S. Oliveira. 2014. Comparing of growth curves of two genotypes of dairy goats using nonlinear mixed models. *J. Agric. Sci.*, 152: 829-842.
- Galeano-Vasco, L. F., M. F. Ceron-Munoz and W. Narvaez-Solarte. 2014. Ability of non-linear mixed models to predict growth in laying hens. *Revista Brasileira de Zootecnia*, 43: 573-578.
- Ge, W., M. E. Davis, H. C. Hines, K. M. Irvin and R. C. Simmen. 2003. Association of single nucleotide polymorphism in the growth hormone and growth hormone receptor genes with blood serum insulin-like growth factor I concentration and growth traits in Angus cattle. *J. Anim. Sci.* 81: 641-648.
- Ghiasi, H., T. M. Lupi and M. S. Mokhtari. 2018. The estimation of genetic parameters for growth curve traits in Raeini Cashmere goat described by Gompertz model. *Small Rumin. Res.* 165: 66-70.
- Gompertz, B. 1825. On the nature of the function expressive of the law of human mortality and on a new mode of determining the value of life contingencies. *Philosophical Transactions* 115: 513-585.
- Gorlov, I. F., Y. A. Kolosov, N. V. Shirokova, L. V. Getmantseva, M. I. Slozhenkina, N. I. Mosolova, N. F. Bakoev, M. A. Leonova, A. Y. Kolosov and E. Y. Zlobina. 2017. Association of the growth hormone gene polymorphism with growth traits in Salsk sheep breed, M. F. Cezar, M. G. G. Cunha and J. M. P. Filho. 2013. Effect of frame size of performance and carcass traits of Santa Ines lambs finished in a feedlot. *Revista brasileira de zootecnia*, 42: 284-290.
- Kheirabadi, K. and A. Rashidi. 2019. Modelling and genetic evaluation of Markhoz goat growth curve parameters. *Small Rumin. Res.* 170: 43-50.
- Kumianto, E., A. Shinjo and D. Suga. 1998. Analysis of growth in Intersubspecific crossing of Mice using Gompertz model. *Asian-Australasian J. Anim. Sci.* 11: 84-88.
- Kumianto, E., S. Sutopo and E. Purbowati. Penampilan fenotipik dan genotipik kambing Kejobong. Badan Penerbit Universitas Diponegoro, Semarang.
- Kumianto, E., S. Sutopo, E. Purbowati, E. T. Setiatin, D. Samsudewa and T. Permatasari. 2013. Multivariate analysis of morphological traits of local goats in Central Java, Indonesia. *Iranian J. Appl. Anim. Sci.* 3: 361-367.
- Lestari, D. A., E. Purbowati, S. Sutopo and E. Kumianto. 2018<sup>A</sup>. Amino acid sequence based on Cytochrome b gene in Kejobong goat and its genetic relationships among several local goats in Asia. *Vet. World* 11: 1196-1202.
- Lestari, D. A., E. Purbowati, S. Sutopo, and E. Kumianto. 2018<sup>B</sup>. Phylogenetic relationship between Kejobong goat and other goats based on Mt-DNA D-loop sequence analysis. *Trop. Anim. Sci. J.* 41: 85-93.
- Lupi, T. M., J. M. Leon, S. Nogales, C. Barba and J. V. Delgado. 2016. Genetic parameters of traits associated with the growth curve in Segurena sheep. *Anim.* 10: 729-735.
- Mahrous, K. F., S. H. Abdel-Aziem, M. A. M. Abdel-Hafez, M. Abdel-Mordy and H. E. Rushidi, H. E. 2018. Polymorphism of growth hormone gene in three goat breed in Egypt. *Bull. Nat. Res. Center*, 42: 1-7.
- Moghbeli, A. M., A. Baranzadeh, M. Vatankhah and M. Mohammadabadi. 2013. Genetics and non-genetics parameters of body weight for post-weaning traits in Raini Cashmere goats. *Trop. Anim. Health*

- Prod. 45: 1519-1524.
- Nei, M. and S. Kumar. 2000. Molecular evolution and phylogenetics. Oxford University Press, New York.
- Othman, O. E., S. S. Alam, H. A. M. Abd-El-Kader and O. M. Abd-El-Moneim. 2015. Genotyping of growth hormone gene in Egyptian small ruminant breeds. *Biotechnol.* 14: 136-141.
- Pires, L. C., T. M. M. Machado, P. L. S. Carneiro, J. B. L. da Silva, A. D. H. Barbosa and R. A. Torres. 2017. Growth curve of Repartida goats reared in the Caatinga region. *Semina: Ciencias Agrarias*, 38: 1041-1050.
- Raji, A. O., L. G. Asheikh and I. D. Mohammed. 2015. Comparison of growth of male and female kids of Nondescript goats in a semi-arid region of Nigeria. *Iranian J. Appl. Anim. Sci.* 5: 115-120.
- Ripoll, G., P. Alberti, J. Alvarez-Rodriguez, I. Blasco and A. Sanz. 2016. Body size, carcass and meat quality of three commercial beef categories of Serrana de Teruel breed. *Spanish J. Agric. Res.* 14: 1-13.
- Rout, P. K., O. Matika, R. Kaushik, M. S. Dige, G. Dass, M. K. Singh and S. Bhusan. 2018. Genetic analysis of growth parameters and survival potential of Jamunapari goats in semiarid tropics. *Small Rumin. Res.* 165: 124-130.
- Sadeghi, S. A. T., M. Rokouei, M. V. Valleh, M. A. Abbasi and H. Faraji-Arough. 2019. Estimating of additive and non-additive genetic variance component for growth traits in Adani goats. *Trop. Anim. Health Prod.* 52: 733-742.
- Sas Institute Inc. 2011. SAS 9.3 system options: reference, 2<sup>nd</sup> Ed. Cary, USA.
- Schwarz, G. 1978. Estimating the dimension of a model. *The Annals of Statistics*, 6: 461-464.
- Seevagan, M., V. Jeichitra, R. Rajendran and K. G. Tirumurugaan. 2015. Detection of lethal SNP (A781G) in growth hormone (*GH*) gene of Indian sheep. *Small Rumin. Res.* 126: 13-15.
- Setiaji, A., S. Sutopo and E. Kumianto. 2013. Growth analysis in rabbit using Gompertz non-linear model. *J. Indo. Trop. Anim. Agric.* 38: 92-97.
- Singh, P. P., S. S. Tomar, M. S. Thakur and A. Kumar. 2015. Polymorphism and association of growth hormone gene with growth traits in Sirohi and Barbari breeds of goat. *Vet. World*, 8: 382-387.
- Snyman, M. A. and J. J. Olivier. 1999. Repeatability and heritability of objective and subjective fleece traits and body weight in South African Angora goats. *Small Rumin. Res.* 34: 103-109.
- Tamura, K., G. Stecher, D. Peterson, A. Filipski and S. Kumar. 2013. MEGA6: Molecular evolutionary genetics analysis version 6.0. *Mol. Biol. Evol.* 30: 2725-2729.
- Thompson, J. D., D. G. Higgins and T. J. Gibson. 1994. CLUSTAL W: Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. *Nucleic Acids Research* 22: 4673-4680.
- Tukey, J. W. 1949. Comparing individual means in the analysis of variance. *Intl. Biomet. Soc.* 5: 99-114.
- Verhulst, P. F. 1838. Notice sur la loi que la population poursuit dans son accroissement. *Correspond. Math. Physics* 10: 113-121.
- Waheed, A., M. S. Khan, S. Ali and M. Sarwar. 2011. Estimation of growth curve parameters in Beetal goats. *Archiv Tierzucht* 54: 287-296.
- Wickramaratne, S. G. H., B. R. Ulmek, S. P. Dixit, S. Kumar and M. K. Vyas. 2010. Use of growth hormone gene polymorphism in selecting Osmanabadi and Sangamneri goats. *Trop. Agric. Res.* 21: 398-411.
- Zadeh, N. G. H. 2015. Modeling the growth curve of Iranian Shall sheep using non-linear growth models. *Small Rumin. Res.* 130: 60-66.
- Zadeh, N. G. H. and A. Gorbani. 2018. Modelling the growth curves for body weight and some biometric traits in Caspian horses (*Equus ferus caballus*) using non-linear mixed models. *Small Rumin. Res.* 93: 5-12.

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