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Genome-Wide Association Study for Body Weight and Carcass Weight in Sumba Ongole Bulls (*Bos indicus*)

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ABSTRACT

Sumba Ongole (*Bos indicus*) is a native beef cattle that adapts well in Sumba Island of Indonesia. This study was carried out to perform a genome-wide association study for body weight (BW) and carcass weight (CW) in Sumba Ongole (SO) bulls. A total of forty-eight (n=48) SO bulls were used in this study. The data were collected from the slaughterhouse at Bogor City, West Java, Indonesia, and were analyzed using a genomic software of TASSEL 5.0 to obtain the best genetic marker. The result showed that the threshold Manhattan plot ($-Log_{10}P^3$) was used to select SNP markers for BW and CW in SO bulls. The two (2) SNP markers at BTA1, *i.e.*, ARS-BFGL-NGS-3162 (*CEP63* gene) and ARS-BFGL-NGS-78232 were significantly associated with BW and CW, respectively. Nonetheless, the genetic diversity in both SNP markers was low, with a PIC value of less than 0.30. In conclusion, the heterozygous TG bulls in *CEP63* gene have higher CW than homozygous TT bulls.

Keywords: body weight; carcass weight; GWAS; SNP marker; Sumba Ongole bulls

INTRODUCTION

The Sumba Ongole (*Bos indicus*) is one of Indonesian native cattle breeds that originated from Sumba Island. Sumba Ongole (SO) is typical of beef cattle that can produce slaughter and carcass weights of 635.50±6.91 kg and 358.06±15.35 kg, respectively (Agung *et al.*, 2015). As the potential beef cattle of Indonesia, a selection program to increase productivity traits in SO cattle is important. The genome-wide association study (GWAS) is a powerful tool for identifying loci and individual polymorphisms associated with economically important traits in various species of animals (Frayling, 2014; Georges *et al.*, 2019; Tam *et al.*, 2019).

In beef cattle, GWAS can detect loci that are associated with average daily gain, body weight, carcass traits, meat quality traits, and sexual precocity traits in Nellore cattle (Santana *et al.*, 2014; Santana *et al.*, 2015; Espigolan *et al.*, 2015; Magalhaes *et al.*, 2016; Irano *et al.*, 2016); growth traits in Charolais cattle (Jahuey-Martinez *et al.*, 2016); growth and reproductive traits in Braunvieh cattle (Zepeda-Batista *et al.*, 2021; Trujano-Chavez *et al.*, 2022); primal beef cuts and body weight in Simmental cattle (Song *et al.*, 2016; Xia *et al.*, 2017), and fatty acid composition in Simmental and Wagyu cattle of China (Zhu *et al.*, 2017; Wang *et al.*, 2019). In addition, GWAS also detects loci associated with milk quality traits in dairy cattle (Ibeagha-Awemu *et al.*, 2016).

Unfortunately, studies to determine the candidate gene for productivity traits of Indonesian native cattle with GWAS are limited. According to Hartati *et al.* (2015), GWAS has identified the *PLAG1* gene as the candidate gene for the birth weight of Ongole grade cattle. Otherwise, *STXBP6* and *TERT* have been identified as the candidate genes for birth weight in Bali cattle, according to a different study by Sudrajad *et al.* (2023). Additionally, Indonesian Bali cattle (*Bos javanicus*) have had their genetic structure and effective population size evaluated by Sudrajad *et al.* (2022) using GWAS. Presently, the GWAS in productivity traits of SO cattle has not been reported. Hence, this study aimed to maintain the GWAS for body and carcass weight in SO bulls from feedlot farming. This study's results are important for implementing future genetic improvement programs.

MATERIALS AND METHODS

Ethics Statement

The sample collection and study purpose were approved by the Indonesian Code of Practice for the Care and Use of Animals for Scientific Purposes (Approval number: Balitbangtan/Lolitsapi/Rm/08/2018) of the Indonesian Ministry of Agriculture Animal Ethics Committee.

Animals and Phenotypic Data

A total of forty-eight (48) Sumba Ongole (SO) bulls of 3-4 years of age were used in this study, and the SO bulls were collected from the slaughterhouse at Bogor City, West Java, Indonesia. These SO bulls were imported from Sumba Island of Indonesia and kept at the feedlot farm in West Java. The body weight (BW) and hot carcass weight (CW) were taken in each bull for the analysis. Generally, the ranges of BW and CW traits of SO bulls in the present study are presented in Table 1.

SNP Genotyping

Genomic DNA was isolated from whole blood samples taken under aseptic conditions from the jugular vein using the Genomic DNA MiniKit kit (Geneaid, USA) following the manufacturer's protocol. Animal genotyping was performed using Illumina 50 K SNP Bead Chip through a commercial laboratory service (Macrogen, South Korea). Initial processing of the genotyping results was performed using the Genome Studio 2.0 software (Illumina Inc., CA, USA).

Filtering and Selecting of SNP Markers

The SNP markers were filtered with TASSEL 5.0 software (https://www.tassel.bitbucket.io) with PLINK format of pad and map files (Bradbury *et al.*, 2007). SNP markers with no chromosomal or physical localization were removed from the study, and SNP with a minor allele frequency (MAF) of less than 5% were removed from the full dataset. Hence, a total of 9,111 SNP markers were used for further analysis. The SNP markers with highly significant values were detected using the quantile-quantile (Q-Q) plot graphic computed by the Mixed Linear Model (MLM) with PCA + Kinship method. In addition, the Manhattan plot was performed in this study with MLM method to detect the significance of SNP markers. A Bonferroni-corrected threshold ($-Log_{10}P^3$) was adopted to declare significant SNP markers. Therefore, SNP markers were selected according to Bonferroni-corrected threshold and coefficient of determination (R^2marker) values.

Gene Annotation and Data Analysis

Mapping of gene location in the selected SNP markers was performed with the Genome Data Viewer Program in the NCBI database (https://www.ncbi.nlm.nih.gov). The genetic diversity parameters of genotypic and allelic frequencies (Nei & Kumar, 2000), observed heterozygosity / H_o, expected heterozygosity / H_e (Weir, 1996), polymorphic informative content / PIC (Hildebrand *et al.*, 1992), number of effective allele / n_e and Chi-square / χ^2 (Nei & Tajima, 1981) were calculated in each selected SNP marker. Therefore, a General Linear Model (GLM) was performed by the SAS program (SAS, 2013) for association study and calculated using a mathematical formula referring to Falconer & Mackay (1989) as follows:

$$Y_{ij} = \mu + \beta_i + \varepsilon_{ij}$$

where Y_{ij} is the observed trait; μ is the common mean; β_i is the i^{th} genotype, and ε_{ij} is the experimental error.

RESULTS

Generally, the body weight and carcass weight data of SO cattle in this study are presented in Table 1. The mean of body weight and carcass weight of SO cattle were 456.1±49.4 kg and 229.5±28.8 kg, respectively. The highest percentage of carcasses was 52.5%, obtained from cattle in the range of 585-615 kg, while the lowest, 48.6%, was obtained from cattle in the range of 368-398 kg.

The diversity of SNP markers for BW and CW traits in SO bulls was low. Hence, the Q-Q plot of SNP markers for both traits is under the threshold line, as illustrated in Figure 1. However, the Manhattan plot analysis revealed that two SNP markers of ARS-BFGL-NGS-3162 and ARS-BFGL-NGS-78232 were detected as the genetic markers for BW and CW traits of SO bulls (Figure 2). According to the GenBank database, an SNP marker of ARS-BFGL-NGS-3162 (T/G) is located at the intron9 of *Centrosomal protein 63* (*CEP63*) gene. This gene located at BTA1 from 134,765,156th to 134,839,171th nucleotide was significantly associated with BW traits of SO bulls (p=1.58E-4), as presented in Table 1. In contrast, a SNP marker of ARS-BFGL-NGS-78232 (C/T) is not located at the gene region. Nonetheless, this SNP marker was significantly associated with BW (p=2.41E-4) and CW (p=5.08E-4) traits of SO bulls. The genetic diversities in both SNP markers are classified into low category (PIC<0.30) with one common allele (Table 2). Thus, genetic diversity in an SNP marker of ARS-BFGL-NGS-3162 is under Hardy-Weinberg equilibrium. The association study revealed that both SNP markers were significantly associated with economic traits (Table 3). According to the SNP marker of ARS-BFGL-NGS-3162, the BW of heterozygous (TG) bulls (510.11±61.20 kg) are higher than homozygous (TT) bulls (443.64±37.05 kg). In comparison, an SNP marker of ARS-BFGL-NGS-78232 revealed that the TT genotype has the highest BW and CW traits compared to the other genotypes (Table 4).

DISCUSSION

Carcass weight is one of the most critical quantitative traits affecting beef cattle production. Body weight

Table 1. The average of body weight and carcass weight in Sumba Ongole bulls

Body weight range (kg)	N	Carcass weight (kg)	Carcass percentage (%)
368-398	3	184.3± 8.6	48.6±1.2
399-429	14	208.5±10.3	50.1±2.2
430-460	12	225.1±10.3	50.7±2.4
461-491	8	237.5±11.0	50.0±1.8
492-522	7	253.6±12.1	50.3±2.4
523-553	2	270.5± 2.1	50.6±0.4
585-615	2	312.5±16.3	52.5±2.9

Note: N: number of animals.

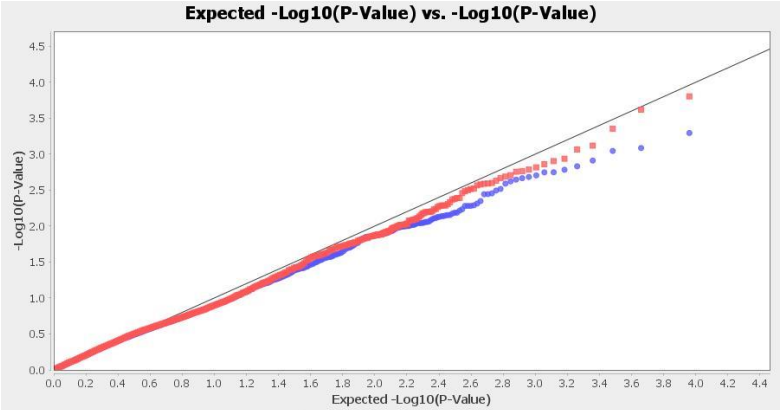

Figure 1. Quantile-quantile plot of the selected p values (-$Log_{10}P^3$) for individual SNP marker. The line indicates the expected values when confirming the null hypothesis of the absence of associations. ■ =BW, body weight; ● = CW, carcas weight; ── = expected values.

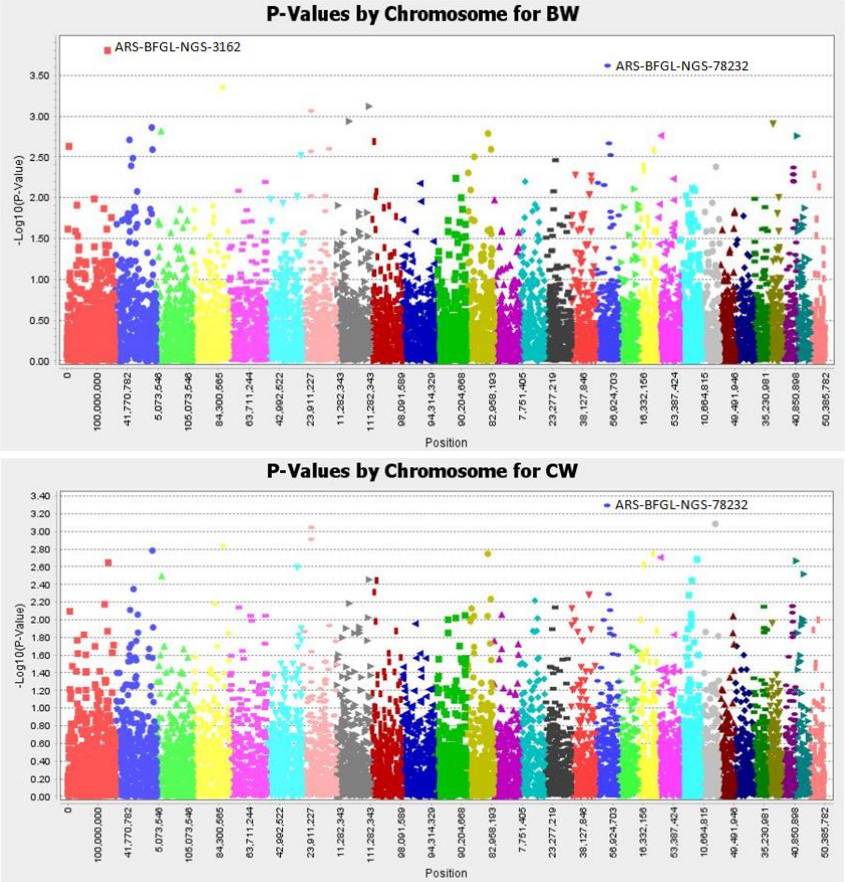

Figure 2. The potential SNP markers for the body weight (BW) and carcass weight (CW) in Sumba Ongole bulls (*Bos indicus*) based on Manhattan plot. Plots with different colors at 1-29 indicate the chromosome number.

and carcass weight were affected by genetics and environmental factors (Irshad *et al.,* 2013). The results of this study indicate that most of the body weight of SO cattle has not reached optimal slaughter weight; this is indicated by the lowest body weight of SO cattle in the range of 368-398 kg with a carcass percentage of 48.6%. Agung *et al*. (2015) reported that the carcass percentage of SO cattle ranged from 52.89%-53.43% with a slaughter weight ranging from 351-475 kg. Adhikari *et al*. (2023) reported that the mean carcass weight of beef cattle in Hawai'i is 201-273 kg and lower than animals under study. The highest body weights obtained in this study ranged from 585-615 kg, with a carcass percentage of 52.5%.

In general, the SNP markers in the present study are under the threshold line (-$Log_{10}P^3$). In GWAS for heat stress adaptation in Egyptian sheep, Aboul-Naga *et al.* (2022) obtained the SNP markers plots under the threshold line (-$Log_{10}P^3$). Niciura *et al.* (2022) selected SNP markers for *Haemonchus contortus* resistance

Table 2. The main SNP markers for body weight and carcass weight in Sumba Ongole bulls (*Bos indicus*)

SNP Marker	BTA	Position	Trait	P-value	R^2 Marker	Additive effect	Dominance effect	Gene	Region	Location
ARS-BFGL-NGS-3162	1	134808305	BW	1.58E-4	0.39	-	-	*CEP63*	Intron 9	134765156 - 134839171
ARS-BFGL-NGS-78232	17	38144582	BW	2.41E-4	0.47	-7.87E1	-2.82E1	-	-	-
			CW	5.08E-4	0.43	-4.50E1	-1.69E1			

Note: BTA= *Bos taurus* autosom; BW= body weight; CW= carcass weight.

Table 3. Genetic diversity in the selected SNP marker

SNP Marker / Genotype	Frequency (N)	Allele frequency	H_o	H_e	PIC	n_e	χ^2
ARS-BFGL-NGS-3162 (g.43150K)							
TT	0.81 (39)	T (0.91)	0.19	0.17	0.16	1.2	0.51
TG	0.19 (9)	G (0.09)					
GG	0.00 (0)						
ARS-BFGL-NGS-78232							
CC	0.88 (42)	C (0.92)	0.08	0.15	0.14	1.18	9.92
CT	0.08 (4)	T (0.08)					
TT	0.04 (2)						

Note: N= number of observations; Ho= observed heterozygosity; He= expected heterozygosity; PIC= polymorphic informative content; ne= number of effective alleles. χ^2= Chi-square value.

Table 4. Association between selected SNP markers with body and carcass weight of Sumba Ongole bulls (*Bos indicus*)

Trait	Selected SNP Marker				
	ARS-BFGL-NGS-3162		ARS-BFGL-NGS-78232		
	TT (N=39)	TG (N=9)	CC (N=42)	CT (N=4)	TT (N=2)
Body weight (kg)	443.64±37.05[a]	510.11±61.20[b]	445.79±36.75[a]	495.00±57.23[a]	595.00± 1.41[b]
Carcass weight (kg)	-	-	224.62±22.52[a]	252.38±29.12[a]	312.50±16.26[b]

Note: N= number of observations; [a,b]Means in the same row with different superscripts differ significantly ($p<0.05$).

phenotype in Morada Nova sheep using a similar threshold line ($-Log_{10}P^3$). Abdalla *et al.* (2023) identified two SNP markers in the BTA1 of Chinese Holstein cattle, ARS-BFGL-NGS-18743 (*MYH15* gene) and BTB-00074122, which were substantially related to body height and body depth, respectively. Furthermore, two SNP markers in BTA1, ARS-BFGL-NGS-98203 and ARS-BFGL-NGS-115015, were found to be strongly linked with age at first calving in Hanwoo heifers (Hyeong *et al.*, 2014). Thus, two other SNP markers in BTA1, *i.e.,* ARS-BFGL-NGS-57889 (*VEPH1* gene) and ARS-BFGL-NGS-115015, were significantly associated with height at withers of indigenous Beninese cattle and sperm abnormalities of Angus bulls, respectively (Vavanhossou *et al.*, 2020; Butler *et al.*, 2022). Therefore, Wagner *et al.* (2021) obtained three SNP markers in BTA1 that were significantly associated with mastitis pathogens resistance traits in Friesian Holstein cows, *i.e.,* ARS-BFGL-NGS-60721, ARS-BFGL-NGS-26782, and Hapmap23088-BTA-151194 (*HACL1* gene). Despite three SNP markers in the BTA1 of cattle, *i.e.,* ARS-BFGL-NGS-78259 (*CD47* gene), ARS-BFGL-NGS-97095 (*SLC51A* gene), and ARS-BFGL-NGS-114968 (*HES1* gene), were significantly associated with milk yield trait (da Cruz *et al.,* 2021). Moreover, previous studies reported that the BTA1 of cattle has many candidate genes that affect growth traits (Akanno *et al.,* 2015), carcass weight (Adhikari *et al.,* 2023), and meat quality, *i.e., MME* and *PIGP* (Kelly *et al.,* 2014).

The BTA17 of the animal under study has an SNP marker significantly associated with BW and CW traits. However, previous studies reported that BTA17 of cattle has many candidate genes for genetic improvement in dairy cattle, such as *ABCE1, MIR130B*, *MIR301B*, *AIFM3*, *LZTR1*, *KLHL22,* and *CDC45* genes (Qanbari *et al.,* 2010; Ibeagha-Awemu *et al.,* 2016). Despite this, BTA17 of cattle has many candidate genes, *i.e., ARHGAP10*, *LARP1B*, *ABHD18*, *MFSD8*, *PLK4*, *HSPA4L*, *SLC25A31,* and *INTU* genes, which are significantly associated with economic traits of beef cattle (Vahedi *et al.,* 2022).

The current study revealed that the *CEP63* gene is a candidate gene that influences BW in SO bulls. *The bovine CEP63* gene is located at BTA1 with exons along 74.016 bp (GenBank: NC_037328.1). This gene plays a role in the regulation of centriole duplication. The mouse embryonic fibroblast with a deficiency of *CEP63* protein reduces the centriole number and microcephaly (Brown *et al.,* 2013). Lee & Shin (2018) reported that the substitution rate of the *CEP63* gene in Hanwoo was higher than in Friesian Holstein cattle (7.49E-11 vs 5.70E-11). The *CEP63* gene has been identified as a potential gene for milk phosphorus content (Chen *et al.,* 2018) and feed intake (Salleh *et al.,* 2018) in dairy cattle. Rowan *et al.* (2021) also identified *CEP63* as the

candidate gene for birth weight and environmental adaptation in Simmental cattle. However, a mutation in the human *CEP63* gene causes dyslexia (Einarsdottir *et al.*, 2015) and familial short stature (Lin *et al.*, 2017) disorders. The genetic diversity in livestock animals can be affected by selection, migration, inbreeding, and cross-breeding (Falconer & Mackay, 1989). Despite its low frequency in the current study, the G allele of the *CEP63* gen may positively affect the BW characteristic. As a result of its low genetic diversity, the *CEP63* gene cannot be exploited for molecular selection. In the future, in-depth genomic research involving a large number of samples and records data is important to obtain the candidate genes accurately.

CONCLUSION

In this study, two SNP markers of ARS-BFGL-NGS-3162 (T/G) and ARS-BFGL-NGS-78232 (C/T) were selected as the genetic marker for BW and CW traits in SO bulls according to the thresholds line -$Log_{10}P^3$. An SNP marker of ARS-BFGL-NGS-3162 (T/G) was significantly associated with BW traits of SO bulls, while an SNP marker of ARS-BFGL-NGS-78232 (C/T) was significantly associated with BW and CW traits of SO bulls. A SNP marker of ARS-BFGL-NGS-3162 is mapped at the intron 9 of the *CEP63* gene (BTA1) that was previously identified as the candidate gene for birth weight in beef cattle.

CONFLICT OF INTEREST

We certify that there is no conflict of interest with any financial, personal, or other relationships with other people or organizations related to the material discussed in the manuscript.

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