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Research Article

Identification of genetic loci associated with live body weight and carcass weight in red brown Korean native chickens

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ABSTRACT

Body weight is an important quantitative trait controlled by genetic and environmental factors. The identification of genetic mechanisms influencing weight gain is important for improving the production of chicken meat. Thus, the aim of this study was to identify genetic loci associated with live body weight and carcass weight at the age of 10 weeks in the Red Brown Korean chickens. The body weight of 541 chickens was measured before slaughter. On the other hand, carcass weights for 637 chickens were obtained after slaughter. DNA samples were genotyped using the 60K Illumina SNP panel. Genome-wide association studies for the two traits were conducted separately using the mixed linear model. Two suggestively significant SNPs in chromosome 11 were associated with live body weight. As for carcass weight, seven suggestively significant SNPs were identified in chromosomes 1, 3 and 10. Several candidate genes, including the *GLG-1, FHOD1* and *AGRP,* were associated with live body weight. Likewise, the genomic regions associated with carcass weight harboured notable genes, including *HMG20A, TSPAN3, NRG4* and *TBC1D2B*. Furthermore, the identified SNPs were in QTL regions associated with growth traits in chickens. The results of this study provided insights into the genetic mechanisms influencing live body weight and carcass weight at 10 weeks of age in the Red Brown Korean native chickens. Further studies are warranted to verify the candidate genes' role in the regulation of growth and weight gain in chickens.

Keywords: Live body weight; Carcass weight; GWAS; Korean Native Chicken; SNP

INTRODUCTION

Growth is a complex process yet an economically important trait in livestock. The growth rate in animals is estimated by measuring body weight at different stages of life (Guixin et al., 2022). Over the years, many quantitative trait loci (QTLs) linked to body weight traits have been identified in chickens. The animal QTL database has 2,863 QTLs associated with body weight in chickens (https://www.animalgenome.org/QTLdb). These QTLs are distributed in almost all chromosomes except chromosomes (GGA) 30, 31, 32 and W. However, most of the QTLs were discovered in crossbred chickens. There is limited information on the QTLs and genetic variants influencing growth in pure indigenous chickens.

Indigenous chickens have a slower growth rate than the hybrid lines making them less competitive in commercial production systems (Ariza et al., 2021). However, the change in consumer preferences and increased awareness of biodiversity conservation have stirred new interest in indigenous chicken products (Ariza et al., 2022). The demand for indigenous chicken meat is increasing due to its unique characteristics (Jeon et al., 2010). The Red Brown Korean native chickens are known to have a high level of meat flavouring compounds in their muscles making them a potential genetic resource in high-quality chicken meat production in Korea (Kim et al., 2023). Therefore, understanding the genetic architecture

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underlying production traits in these indigenous chickens is necessary.

Genome-wide association studies (GWAS) have been utilised to find genetic variants affecting various economically important traits in chickens (Zhang et al., 2020; Marchesi et al., 2021; Yang et al., 2021). GWAS involves the statistical association of numerous single nucleotide polymorphisms (SNPs) with phenotypes to find the most significantly influential variants on a particular trait. It has proved to be a useful tool for elucidating the genetic mechanisms underlying important phenotypes in livestock.

Genomic regions affecting body weight traits have been reported in various breeds of chickens (Wei et al., 2020; Zhang et al., 2021). The detected causal loci for body weight tend to vary with the age at which the association was done. In Korean native chickens (KNC), QTLs influencing body weight at different ages were mapped in GGA 3, 4 and 19 using microsatellite markers (Cahyadi et al., 2016). Using SNP markers, Cha et al., (2021) found 12 SNPs associated with body weight at the age of 8 weeks in the red and yellow KNC. The significant SNPs were in GGA 2, 3, 4, 12 and 18. The Red Brown KNC chickens are marketed for slaughter at 10 weeks. However, no studies have been conducted to identify genetic loci affecting body weight at this age. Thus, this study aimed to find genetic loci influencing the live body and carcass weight at 10 weeks of age in Red Brown KNC.

MATERIALS AND METHODS

Animals and sample collection

The experiments and sampling procedures applied in this study were approved by the Institute of Animal Care and Use Committee of the National Institute of Animal Science (NIAS) (Approval number: NIAS 20212219). The samples used in this study were collected from the Red Brown KNC population kept at the National Institute of Animal of Science, Republic of Korea. The chickens were raised in battery cages and fed on commercial feeds *ad libitum*.

Sampling was done from four generations, between the years 2019 to 2023. The live body weight of the chickens was measured at the age of 10 weeks before slaughter. Blood samples for DNA extraction were obtained from the wing vein. The birds were then killed through decapitation. The carcass weight was measured after defeathering and evisceration. After phenotype data preprocessing, live body weight information for 541 chickens and carcass weight measurements for 637 chickens were available for further analysis.

Genotyping and data quality control

DNA samples were obtained from blood using a commercial kit (GeNet Bio, Daejeon, Korea). The quality of the DNA was checked using a nano spectrophotometer. The DNA samples were genotyped using the Illumina 60K SNP panel (Illumina Inc., San Diego, CA, USA). The quality control of the genotype information was done by filtering out markers with a call rate < 0.9, minor allele frequency (MAF) < 0.02 and Handy Weinberg equilibrium (HWE) P-value < 1.0×10^{-6}. Markers in sex chromosomes (Z and W) and linkage groups (LGE64 and LGE22C19W28_E50C23) were excluded from further analysis. After quality control, 42,872 SNPs were available for analysis.

Statistical analysis

Statistical analysis was conducted separately for the two traits. Firstly, the genomic relationship matrix (GRM) was calculated using the genome-wide complex trait analysis software (GCTA v.1.93). Secondly, the variance components for each trait were computed using the restricted maximum likelihood method (REML). Finally, a genome-wide association study was conducted by fitting a mixed linear model, leaving one chromosome out (MLMA-loco) as follows; -

$$y = a + bx + g^{-} + e$$

Where y is the vector of phenotypes, a is the mean term, b is the additive effect of the SNP genotype x coded as 0,1 and 2, g^{-} is the cumulative effect of the genomic relationship matrix excluding markers on the chromosome that is left out, and e is the residual effect (Yang et al., 2014). Additionally, sex, generation and the first two principal components were fitted as fixed effect covariates. The significant threshold was set based on the number of independent markers determined by linkage disequilibrium (LD) blocking (Dugall et al., 2008). Within a window size of 1000 variants, SNPs with $r^2 < 0.5$ were considered amounting to 19,451 independent SNPs. Consequently, a suggestive significant threshold was set at a nominal p-value ($1/19,451 = 5.141124 \times 10^{-5}$). To minimise false positive results, a genome-wide significant threshold was set following Bonferroni correction ($0.05/19,451 = 2.570562 \times 10^{-6}$). The LD-based adjustment of significance threshold was done to minimise the number of false negative tests due to the stringency of Bonferroni correction.

Functional analysis

Significant SNPs were retrieved and annotated using the chicken reference genome (GRCg6a) and the animal QTL database. Genes and QTLs within the range of 1 Mb around the significant SNPs were considered for functional analysis. The functions of genes within the significant regions were determined through literature review and gene ontology analysis in DAVID software(https://david.ncifcrf.gov/). Additionally, QTL enrichment analysis within the significant genomic zones was done using the GALLO r package.

RESULTS AND DISCUSSION

A GWAS was conducted to find genetic loci influencing live body weight and carcass weight at 10 weeks of age in the Red Brown KNC. Table 1 and 2 shows descriptive statistics for live body weight and carcass weights across the generations analysed. Partitioning of the traits' statistics based on sex revealed that males were heavier than females, as shown in Table 3. The distribution pattern of phenotypic values is illustrated in Figure 1. The variance components of the two traits are shown in Table 4 The heritability of the live body and carcass weights were 0.18 and 0.49, respectively. The marked difference in the heritability of live body weight and carcass weight could be due to the differences in sample sizes used in computation. A low heritability for growth rate at around 10 weeks in Korean native chickens was reported in a previous study (Manjula et al., 2018).

Table 1. Descriptive statistics for live body weight per generation

Generation	No	Min	Mean	Max	SD
2019	158	620	803.64	1185	93.77
2022	191	555	1031.23	1455	162.86
2023	192	640	986.94	1350	83.22

No, Number of samples; SD, Standard deviation

Table 2. Descriptive statistics for carcass weight per generation

Generation	No	Min	Mean	Max	SD
2019	158	358	532.32	744	67.07
2021	96	544	706.56	936	98.36
2022	191	340	696.40	976	115.57
2023	192	404	638.50	870	83.22

No, Number of samples; SD, Standard deviation

Table 3. Summary statistics of live body weight and carcass weight partitioned based on sex

	Live body weight (g)		Carcass weight (g)	
	Male	Female	Male	Female
No	191	350	222	415
Min	555	620	340	358
Max	1,455	1,215	976	801
Mean	1,084.82	874.67	731.64	590.29
SD	142.19	116.52	107.92	83.08

No, Number of samples; SD, Standard deviation

Table 4. Variance components for live body weight and carcass weight

	Live body weight	Carcass weight
Phenotypic variance (Vp)	14,096.40 (891.76) *	12,363.47 (779.42)
Genetic variance (Vg)	2,577.56 (1,195.96)	6,174.92 (1,143.30)
Heritability (h2)	0.18 (0.08)	0.49 (0.07)

* Standard error

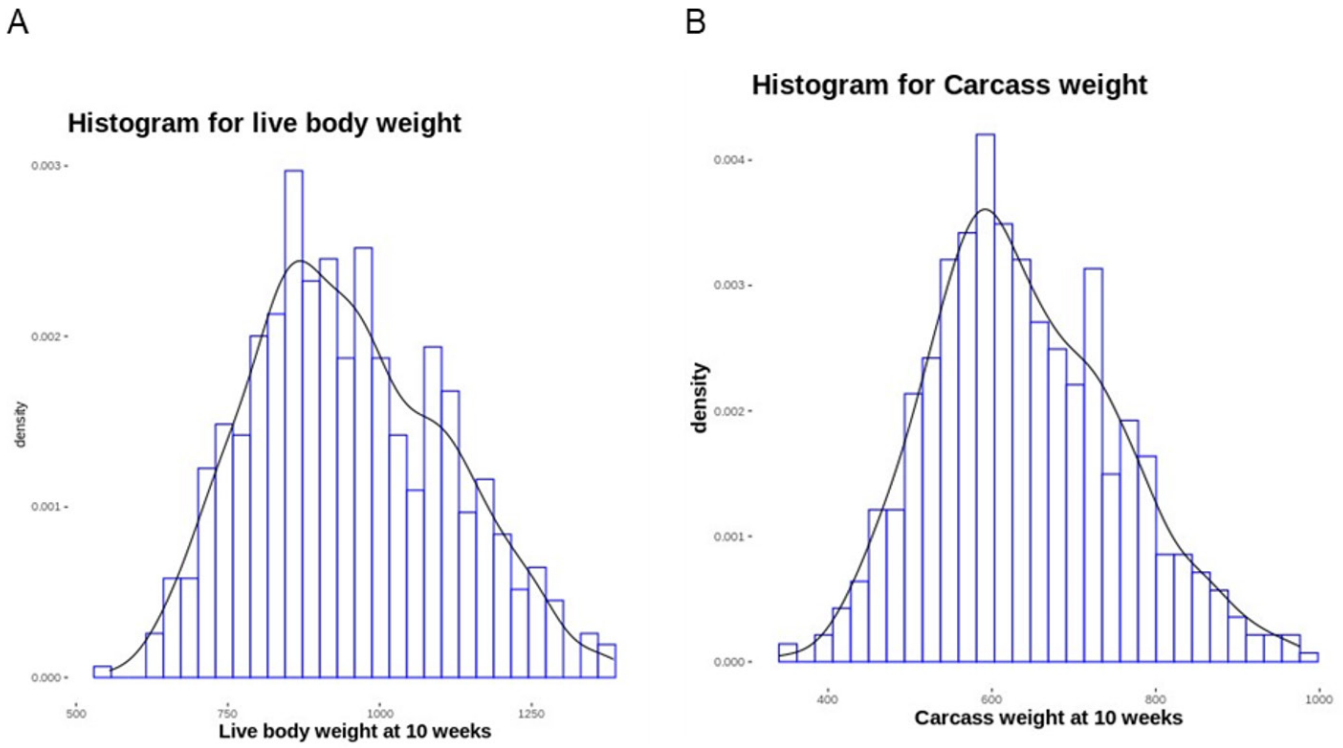

Figure 1. Distribution of body weight traits in the Red Brown Korean native chicken. Live body weight values (A). Carcass weight values (B).

No SNPs reached the significance threshold set after Bonferroni correction for both traits (Figure 2A-D). However, two SNPs, GGaluGA074605 and GGaluGA074596 in GGA 11 reached the suggestive threshold for live body weight (Table 5). The two SNPs were approximately 14 bp apart and in high LD (r^2= 0.74), as shown in Figure 3. The two SNPs were in a genomic region having QTLs for live body weight, carcass weight, and abdominal fat weight. Zhang et al. (2020) discovered a haplotype close to this region that was significantly associated with growth traits in broilers.

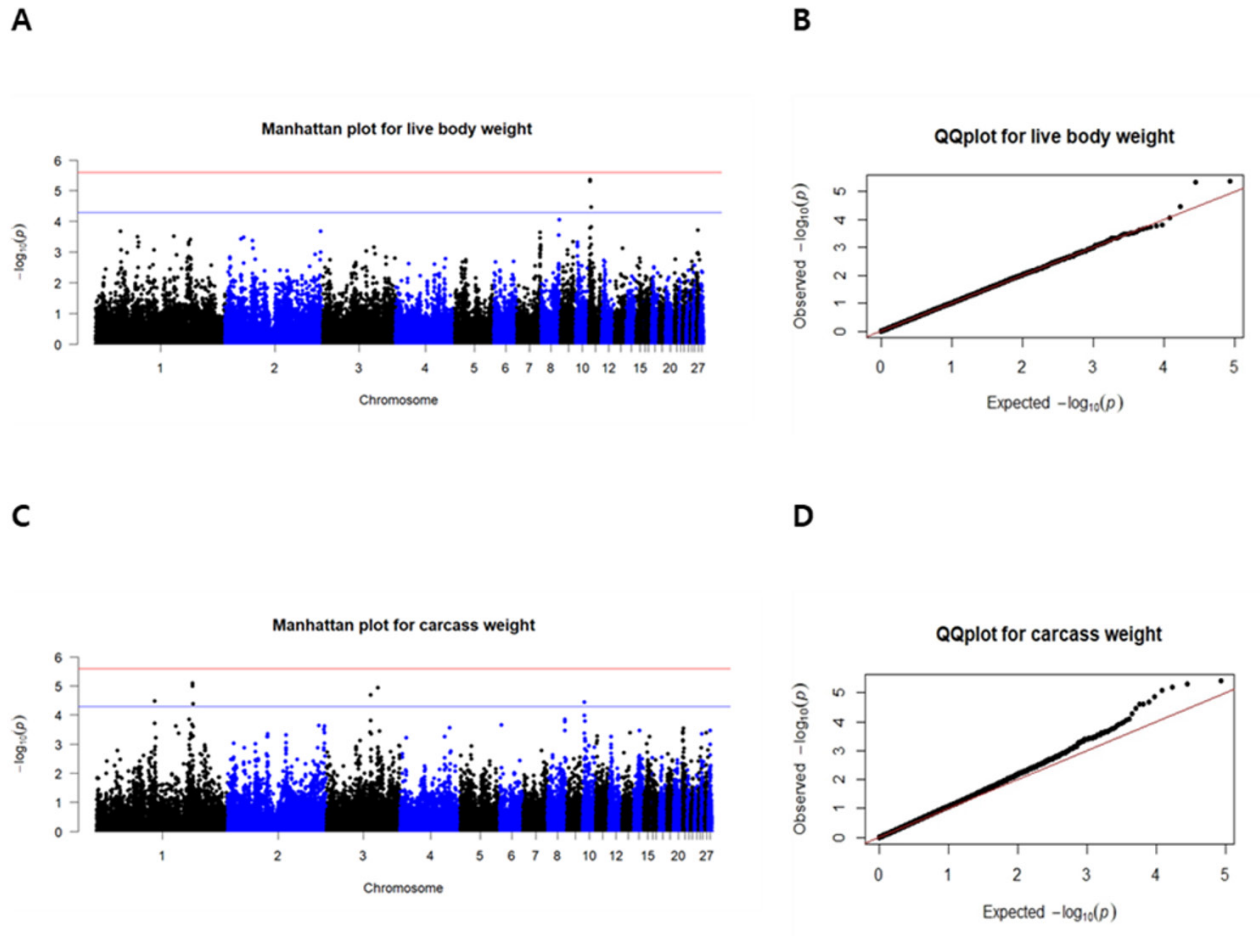

Figure 2. Manhattan plots and Q-Q plots of genome-wide association study (GWAS) of live body weight and carcass weight. Manhattan plot for GWAS of live body weight(A). Q-Q plot of GWAS P-values for live body weight (B). Manhattan plot for GWAS of carcass weight(C). Q-Q plot of GWAS P-values for carcass weight (D).

Table 5. Summary statistics for single nucleotide polymorphisms associated with live body weight and carcass weight

Trait	SNP	CHR	Position (bp)	Beta (Se)	PVE (%)	P-value
LBW	GGaluGA074605	11	1,849,774	-38.16 (8.30)	0.67	4.289×10^{-6}
	GGaluGA074596	11	1,843,788	-35.75 (7.82)	3.34	4.807×10^{-6}
CW	Gga_rs13897753	1	87,563,814	-21.74 (5.24)	2.8	3.298×10^{-5}
	GGaluGA048470	1	144,833,042	24.01 (5.38)	2.57	8.219×10^{-6}
	Gga_rs13950462	1	144,320,962	-23.67 (5.36)	1.90	1.003×10^{-5}
	Gga_rs13951568	1	145,391,453	-21.75 (5.30)	1.99	4.073×10^{-5}
	GGaluGA229805	3	76,955,418	23.28 (5.31)	2.99	1.169×10^{-5}
	Gga_rs14369983	3	65,872,040	-29.07 (6.82)	3.22	2.038×10^{-5}
	GGaluGA066621	10	3,823,440	22.98 (5.57)	4.46	3.654×10^{-5}

SNP, Single nucleotide polymorphism; CHR, Chromosome; Se, Standard error; PVE, Proportion of Phenotypic variance explained by the SNP; LBW, Live body weight; CW, Carcass weight

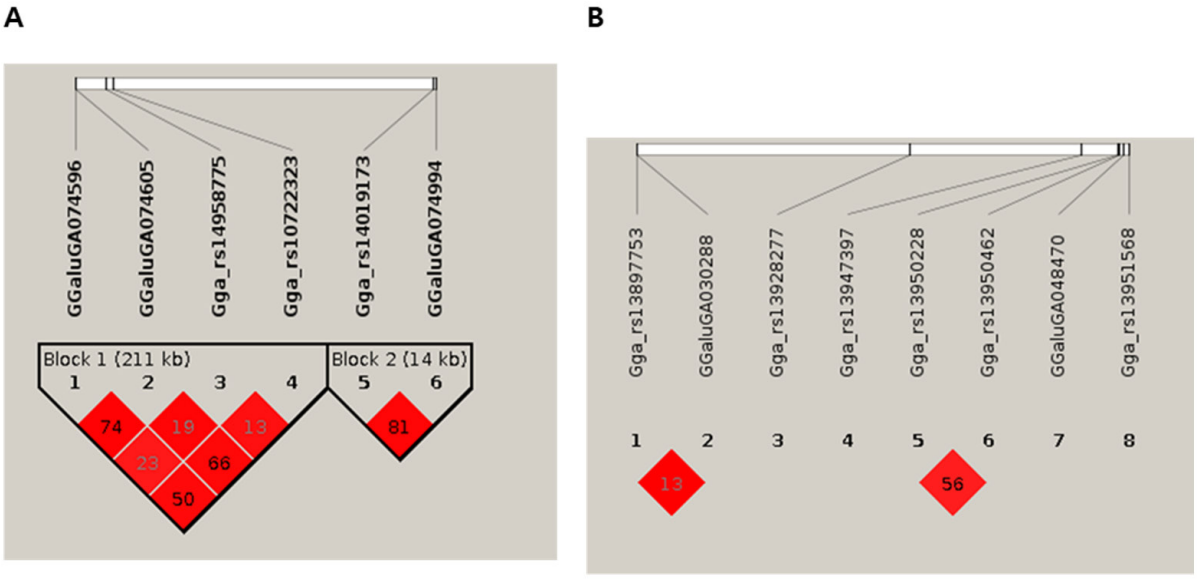

Figure 3. Linkage disequilibrium plots for suggestive single nucleotide polymorphisms (SNPs). Linkage disequilibrium block for the topmost significant SNPs associated with live body weight on GGA 11 (A). Linkage disequilibrium plots for topmost significant SNPs associated with carcass weight on GGA 1 (B).

Table 6 shows the candidate genes within the vicinity of the suggestive SNPs. The nearest genes to the two SNPs included *GLG-1*, *FHOD1*, *AGRP* and *FA2H*. The Glycoprotein-1 gene (*GLG-1*) encodes for a protein that binds to the transforming growth factor (*FGF*) which regulates bone morphogenesis (Luo et al., 2021). This gene was found to be differentially expressed in Bighead carps with different growth rates. The FH1 domain-containing protein 1 (*FHOD1*) gene regulates smooth muscle fibre arrangement and elongation. Genomic regions overlapping the *FHOD1* have been associated with growth and carcass traits in chickens, pigs and beef cattle (Zhao et al., 2015; Chen et al., 2019 & Sood et al., 2023). The V-type proton ATPase subunit d 1 (*ATP6V0D1*) and Agouti Related Neuropeptide (*AGRP*) regulate feed intake and thus may influence weight gain in chickens (Miroslaw et al., 2019, Dadousis et al., 2021).

Table 6. Genes found near the suggestive single nucleotide polymorphisms associated with live body weight and carcass weight

Trait	CHR	Position (Mb)	Genes
LBW	11	1.335 – 2.386	*SLC9A5*[d], *FHOD1*[d], *HSD11B2*[d], *ATP6V0D1*[d], *AGRP*[d], *SETD6*[u], *CNOT1*[d], *SNORA50A*[u], *SLC38A7d*, *GOT2d*, *CALB2d*, *CMTR2*[u], *HYDIN*[d], *VAC14*[d], *MTSS2*[d], *SF3B3*[d], *COG4*[d], *ST3GAL2*[d], *PDPR*[u], *GLG1*[i], *RFWD3*[u], *MLKL*[u], *FA2H*[u], *WDR59*[u], *ZNRF1*[u], *CTRB2*[u], *BCAR1*[d], *CFDP1*[u], *TMEM170A*[u], *NUP93*[u], *MT4*[u], *BBS2*[u], *OGFOD1*[u], *NUDT21*[u], *AMFR*[u], *GNAO1*[u], *CBFB*[u]
CW	1	87.48 – 88.06	*ALCAM*[u], *CBLB*[u]
	1	144.10 – 145.27	*ERCC5*[u], *BIVM*[u], *POGLUT2*[u], *TEX30*[u], *METTL21C*[u], *TPP2*[u], *FGF14*[u], *ITGBL1*[i], *NALCN*[u], *TMTC4*[u]
	1	144.93 – 145.89	*TMTC4*[d], *GGACT*[i], *PCCA*[u], *ZIC2*[u], *ZIC5*[u], *CLYBL*[u]
	3	65.39 – 66.35	*LAMA4*[d], *FYN*[u], *REV3L*[u], *MFSD4B*[u], *SLC16A10*[u]
	3	76.45 – 77.31	*SLC35A1*[u], *SMIM8*[d], *ZNF292*[d], *CGA*[d], *HTR1E*[d], *SYNCRIP*[d], *SNX14*[i], *NT5E*[u], *TBX18*[u]
	10	3.42 – 4.31	*HMG20A*[d], *PEAK1*[d], *TSPAN3*[d], *PSTPIP1*[d], *RCN2*[d], *SCAPER*[d], *ISL2*[d], *ETFA*[i], *TMEM266*[u], *NRG4*[u], *FBXO22*[u], *UBE2Q2*[u], *CHRNA3*[u], *CHRNA5*[u], *PSMA4*[u], *HYKK*[u], *IREB2*[u], *CRABP-1*[u], *WDR61*[u], *DNAJA4*[u], *ACSBG1*[u], *IDH3A*[u], *CIB2*[u], *TBC1D2B*[u]

[u] SNP is upstream of the gene, [i] SNP is intragenic, [d] SNP is downstream of the gene
CHR, Chromosome; LBW, Live body weight; CW, Carcass weight; SNP, Single nucleotide polymorphism

The Fatty acid -2 hydroxylase (*FA2H*) gene, which is essential for galactosphingolipid synthesis, was found near the suggestive SNPs. The knockout of this gene in mice was shown to cause growth retardation (Jacinto et al., 2021). Additionally, the suggestive region harboured the Bardet-Biedl Syndrome 2 (*BBS2*) and Glutamic-Oxaloacetic Transaminase 2 (*GOT2*) genes, which regulate intramuscular fat deposition (Ge et al., 2012). The two genes have been linked to obesity in humans (Benzinou et al., 2006; Cao et al., 2021).

As for carcass weight, seven SNPs reached the suggestive threshold on GGA 1, 3 and 10. The SNPs were within QTLs associated with body and carcass weight traits (Figure 4). Three suggestive SNPs, GGaluGA048470, Gga_rs13950462 and Gga_rs13951568 on GGA 1 associated with carcass weight were close to each other within a region of 1.07 Mb. However, the SNPs were not linked (Figure 3B). The genomic region overlapping these SNPs housed several genes, including the *FGF14*, *ITGBL1*, *TMTC4*, *ZIC2* and *ZIC5* genes.

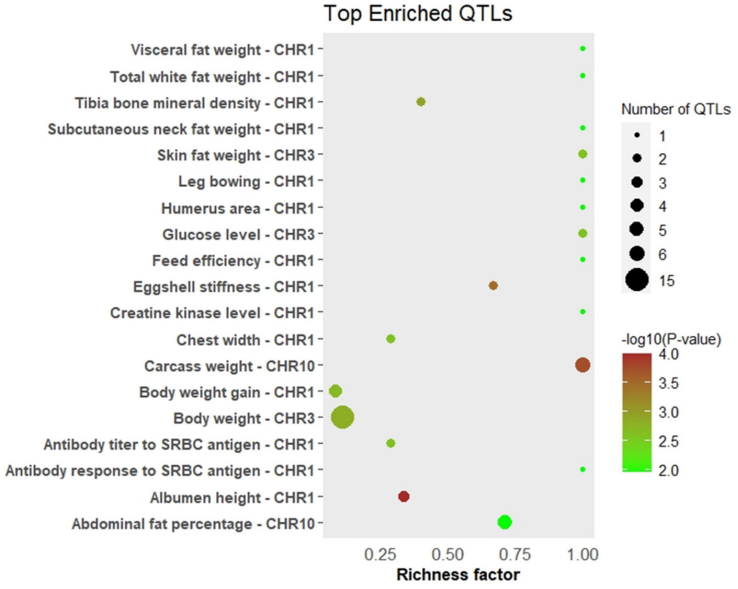

Figure 4. Quantitative trait loci (QTL) enrichment plot in the suggestive candidate regions associated with carcass weight. Enrichment was based on adjusted P-value < 0.05.

The fibroblast growth factor14 (*FGF14*) associated with growth factor activity and neuromuscular activity is believed to affect growth in chickens (Hu et al., 2013). The Integrin beta-like protein 1 (*ITGBL1*) promotes cell adhesion and migration and has been associated with muscle growth and development in sheep (Claire et al., 2013). Dumas et al. (2016) showed that *ITGBL1* regulates heart development by modulating cellular response to collagen. Within the same region, were the Transmembrane O-Mannosyltransferase Targeting Cadherins 4 gene (*TMTC4*) and Zinc finger protein ZIC 5 (*ZIC5*) which have been associated with body weight in sheep (Li et al., 2023).

In GGA 3, two suggestive SNPs reached the suggestive threshold. The two SNPs, Gga_rs14369983 and GGaluGA229805 were located at 65.87 Mb and 76.95 Mb, respectively. The SNPs were in a region having QTLs associated with body weight and feed conversion ratio in chickens. The 1 Mb regions encompassing the SNPs housed genes such as *REV3L, MFSD4B, SMIM8, HTR1E* and *TBX18.* In humans, the mutations of the REV3 Like, DNA-directed polymerase zeta catalytic subunit (*REV3L*) gene have been linked to developmental anomalies characterised by growth retardation. This suggests that the gene is important in growth and development (Halas et al., 2021).

The Small Integral Membrane Protein 8 (*SMIM8*) gene has been reported to influence myofiber formation in pigs (Li et al., 2024). Also, a genomic window harbouring the *SMIM8* gene was associated with growth traits in Hanwoo cattle (Masoumeh et al., 2020). The 5-hydroxytryptamine receptor 1E (*HTR1E*) is highly expressed in the pituitaries and pancreas of chickens, implying that it might have a role in the regulation of the secretion of various hormones such as insulin that can influence body weight gain (Sun et al., 2021). However, further studies are necessary to elucidate the functions of this gene in chickens.

The Major Facilitator superfamily domain-containing protein 1 gene (*MFSD4B)* encodes for glucose and fructose transporters that regulate lipogenesis and fat accumulation in muscles (Betti et al., 2022). The gene was detected in a genomic region associated with body weight in yaks (Wang et al., 2022). Also found in the same suggestive region, was the T-box 18 gene (*TBX18*), which is highly expressed in the somatic mesoderm of chick embryos (Haenig & Kispert 2004). The gene has been reported as a candidate for average daily gain in pigs (Park, 2024).

In GGA 10, there was one suggestive SNP located at 3.82 Mb. The SNP was located within a QTL region associated with carcass weight (Figure 4). The 1 Mb region around the suggestive SNP harboured genes, including the *HMG20A, TSPAN3, NRG4, FBXO22* and *TBC1D2B.* The tetraspanin-3 (*TSPAN3*) located 0.24 Mb upstream of the suggestive SNP is an important modulator of bone formation and its knockdown in mice resulted in reduced bone mass (Xing et al., 2022). In chickens, the *TSPAN3* gene was detected in a candidate region associated with growth traits (Dekkers et al., 2024).

The high mobility group protein 20A (*HMG20A*) has been associated with body weight in turkeys and is believed to regulate adipogenesis and intramuscular fat deposition in pigs (Li et al., 2022). The suggestive SNP was also near the Neuregulin-4 (*NRG4*) gene, a positive cellular proliferation regulator. The gene has been reported as a candidate for body weight in pigs (Liangyu et al., 2022). The electron transfer flavoprotein subunit alpha gene (*ETFA*) encodes for the electron transfer flavoprotein, that catalyses fatty acid metabolism in muscles. The gene has been associated with carcass quality traits in cattle and pigs (Yoon et al., 2016; Bergamaschi et al., 2020).

The results of gene ontology analysis are summarised in Table 7. Most candidate genes were not clustered in any significant ontological terms (P-value < 0.05). Two candidate genes (*MT3* and *MT4*) were enriched in a biological process linked to cellular responses to copper and zinc ions. The metallothionein genes are involved in various biological processes, including metal ion metabolism, detoxification, and protection against oxidative stress (Davis et al., 2000). Metal ions including copper and zinc are important in the growth and development of bones and skeletal muscles. Thus, the Metallothionein genes may influence body weight in chickens.

Table 7. Gene ontology analysis for the candidate genes associated with live body weight and carcass weight

Trait	GO	Term	Genes	P-value	FDR
Live body weight	Biological process	Cellular response to copper ion	*MT3, MT4*	4.81×10^{-3}	0.22
	Biological process	Detoxification of copper ion	*MT3, MT4*	4.81×10^{-3}	0.22
	Biological process	Cellular response to zinc ion	*MT3, MT4*	1.20×10^{-2}	0.33
	Biological process	Cellular response to cadmium ion	*MT3, MT4*	1.44×10^{-2}	0.33
	Biological process	Cellular zinc ion homeostasis	*MT3, MT4*	3.78×10^{-2}	0.70
Carcass weight	Molecular function	Acetylcholine-gated cation-selective channel activity	*CHRNA3, CHRNA4, CHRNA5*	1.46×10^{-3}	0.12
	Biological process	Chemical synaptic transmission	*HTR1E, CHRNA3, CHRNA5, CHRNA4*	4.86×10^{-3}	0.12
	Biological process	Nervous system process	*CHRNA3, CHRNA4, CHRNA5*	7.99×10^{-3}	0.27
	Biological process	Regulation of membrane potential	*CHRNA3, CHRNA4, CHRNA5*	1.12×10^{-2}	0.27
	Kegg pathway	Neuroactive ligand-receptor interaction	*HTR1E, CHRNA3, CHRNA5, CHRNA4, CGA*	3.97×10^{-2}	1.00

GO, Gene ontology category; FDR, False discovery rate

As for carcass traits, the Neuronal acetylcholine receptor subunit alpha genes (*CHRNA 3,4* and *5*) genes were enriched in biological process terms related to acetylcholine signalling. These genes regulate neurological development and may affect body weight through modulation of muscle functions and development (Brachman 1968). Two candidate genes, 5-hydroxytryptamine receptor 1E (*HTR1E*) and the glycoprotein hormones, alpha polypeptide (*CGA*), were significantly enriched in the KEGG pathway associated with neuroactive ligand-receptor interaction. The neuroactive ligand-receptor interaction is essential in modulating cellular response to external stimuli such as neurotransmitters and hormones (Ge, 2023). The two candidate genes could be important in regulating the cellular response to hormones that stimulate growth.

CONCLUSION

GWAS was conducted to identify the candidate genomic regions influencing live body weight and carcass weight in the Red Brown KNC. Several suggestive SNPs were associated with the two traits in different chromosomes. The genomic regions around the suggestive SNPs housed candidate genes that potentially regulate body weight gain in chickens. As for live body weight, *GLG-1*, *FHOD1*, *AGRP* and *FA2H* were detected as potential candidate genes. Additionally, several genes, such as *HMG20A*, *TSPAN3*, *NRG4 and TBC1D2B* were associated with carcass weight at the age of 10 weeks. A detailed analysis of these genes may provide deeper insights into their role in the growth of chickens. However, it is important to note that this association study was statistically underpowered probably due to the small sample size. Since growth traits are largely polygenic, future studies may require larger data sizes to identify more significant variants. The results of this study provide a foundational understanding of genetic variants influencing live body and carcass weight in Red Brown Korean chickens.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the current manuscript.

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DATA AVAILABILITY STATEMENT

The data used in this study can be availed upon request to the corresponding author.

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