UNIVERSITI PUTRA MALAYSIA

TELOMERE LENGTH AND REGULATORY GENES DIVERSITY AS NOVEL WELL-BEING BIOMARKERS IN BROILER CHICKENS (Gallus gallus domesticus Linnaeus)

BADMUS KAZEEM AJASA

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By

BADMUS KAZEEM AJASA

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Doctor of Philosophy

February 2021

DEDICATION

*To my lovely parents and my beloved wife (*Adebayo Modinat Olawumi*) who had series of sleepless night praying for me to achieve my goal*

To Federal republic of Nigeria and Malaysia and
To all my family members and friends who supported me during the journey

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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Chairman : Mamat Hamidi Kamalludin, PhD
Faculty : Agriculture

Telomeres are nucleoprotein (*TTAGGG* repeats) structures that shield the end of chromosomes from degeneration. Telomere length and its regulatory genes have not been well characterized and used for biomarkers of stress in chicken and hence the reason for this study. This study is aimed at focusing on the how telomere length and its regulatory genes could be altered and used as novel well-being biomarkers under the influence of both acute stress (feed restriction and heat stress) and chronic stress (corticosterone administration). The study was conducted at the Institute of Tropical Agriculture and Food Security, University Putra Malaysia. In the experiment 1, fourty (40) birds of equal sizes (1700 ± 100g) were selected from 300 Cobb 500^{TM} broiler chickens and subjected to both feed restriction (60% of the ad-libitum) and heat stresses (34ºC for 6 hours) in group of five (5) replicated 2 times and their controls. Body weight (BW) and body conformation traits (BCT) were significantly ($P < 0.05$) reduced by feed restriction and heat stress. Both chickens under feed restriction and heat stresses revealed significant ($P < 0.05$) telomere attrition at week 1. The loss in telomere length was not observable in heat stressed chickens at week 2 but was observed in the feed restricted birds ($p < 0.05$) at the same week. In the experiment 2, total of one hundred (100) day old Cobb 500^{TM} broiler chickens were used. Five (5) replicates of ten (10) chickens each were fed 30mg/kg diet of corticosterone from two weeks of age for 4 weeks (Cort group) while the rest 50 chickens were made control of the same replicates. Plasma level of corticosterone of Cort fed chickens was evaluated. Feed conversion ratio (FCR) and biweekly body weight were recorded and two chickens from each replicate were sampled from the two groups (corticosterone and control) for organ's weight determination and histopathology of small intestine, liver, and muscle fibre. In the same experiment, DNA samples were extracted from the whole blood and tissues (muscle, liver, and heart) and used for telomere length determination. RNA samples were extracted from muscle, liver, and heart for the expression profiles of telomere length regulatory genes such as telomeric repeat factor 1(*TRF1*), chicken telomerase (*chTERT*), telomere maintenance gene 2 (*TELO2*), telomeric repeat containing RNA (*TERRA*) and heat shock transcription factor 1 (*HSF1*) and

mitochondria DNAs such as uncoupling protein 3 (*UCP3*), cytochrome C oxidase (*COX6A1*). RNA was also extracted from hypothalamus for the expression profiles of serum amyloid a (*SAAL1*) and C-reactive protein (*CRP*). The meat quality traits were measured from the meat sample collected from both groups (Cort fed chickens and control). No significant differences were observed in the plasma Cort level of both groups at week 2 but a substantial difference was reported at week 4. At week 2 and 4 of the stress, body weights of the Cort fed chickens were significantly ($P < 0.05$) suppressed with increase in feed conversion ratio compared to the control ($P < 0.05$). The relative weights of liver, small intestine, heart and gizzard were significantly ($P < 0.05$) higher in the Cort fed chickens compared to their control. Duodenal and the jejunal villi height were both significantly higher in the Cort fed chickens than in the control. The liver morphology of the Cort fed chickens showed sign of apoptosis and unhealthy conditions (liver fibrosis) in both week 2 and 4. Muscle myofibril revealed significantly ($P < 0.05$) lower diameter in the Cort fed chickens than in the control at both weeks 2 and 4 of the stress. Telomere length revealed significant ($P < 0.05$) attrition at both week 2and 4 in the whole blood of the Cort chickens. Significant ($P < 0.05$) telomere length attrition was revealed at week 2 and 4 of the stress duration in all the tissues except in the liver and heart at week 4. It is observed in this study that *TRF1*, *chTERT, TELO2 and HSF1* were significantly ($P < 0.05$) upregulated in liver and heart of the Cort fed chickens at week 4 but they were all significantly ($P < 0.05$) upregulated in the liver at week 2. However, they were all significantly ($P < 0.05$) downregulated in the muscle at both week 2 and 4. *TRF1* and *TELO2* were upregulated ($P < 0.05$) in the heart at week 2 while *TERRA* and *HSF1* were downregulated ($P < 0.05$). Mitochondria DNAs were significantly ($P < 0.05$) upregulated in all the tissues at week 2. Acute phase protein factors were significantly ($P < 0.05$) upregulated in the Cort fed chickens. The meat pH of the Cort fed chickens was significantly ($P < 0.05$) reduced at week 2 whereas at week 4, it was significantly higher compared to the control. Drip loss was significantly higher at both week 2 and 4 in the Cort fed chickens compared to the control. The meat of the Cort fed chickens showed significantly ($P < 0.05$) higher redness and lowered lightness at week 4. The shear force of the Cort fed chickens was significantly ($P < 0.05$) higher than that of the control at week 4. The correlation between telomere length of the chickens used in this study revealed that there is strong and positive relationship ($r = 0.62$, $P < 0.05$) between telomere length and the pH and the correlation between telomere length and the drip loss was significant and negative ($r = -0.59$, $P < 0.05$) at week 4. The results of the meat quality obtained in this study revealed that the Cort fed chickens possess poor meat quality and these could be responsible for the telomere attrition. The regression model indicated that pH could be used to predict the telomere integrity. The present findings demonstrated that telomere length is well characterized and shortened with stresses (acute and chronic). Telomere length was shortened with feed restriction at 60% of the ad-libitum feed, heat stress at 34 ºC temperature for 6 hours per day and corticosterone feeding at 30mg/kg diet. Therefore, telomere length could be used as a novel well-being biomarker in broiler chicken.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

KEPELBAGAIAN PANJANG TELOMER DAN GENE PENGANWALSELIA SEBAGAI PENTANDA BIOLOGI NOVEL KESEJAHTERAAN AYAM

Oleh

BADMUS KAZEEM AJASA

Februari, 2021

Pengerusi : Mamat Hamidi Kamalludin, PhD
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Telomere adalah struktur nukleoprotein (pengulangan *TTAGGG*) yang melindungi hujung kromosom dari degenerasi. Panjang telomere dan gen pengawalseliaan tidak digunakan sebagai petanda biologi tekanan pada ayam sekaligus menjadi keperluan untuk kajian ini dijalankan. Kajian ini bertujuan untuk memfokuskan bagaimana panjang telomere dan gen pengawalseliaannya dapat diubah dan digunakan sebagai petanda biologi kesejahteraan baru di bawah pengaruh tekanan akut (sekatan makanan dan tekanan panas) dan tekanan kronik (pemberian kortikosteron). Kajian ini dijalankan di Institut Pertanian Tropika dan Keselamatan Makanan, Universiti Putra Malaysia. Dalam eksperimen 1, empat puluh (40) ekor ayam dengan ukuran berat yang sama (1700 ± 100 g) dipilih dari 300 ekor Cobb 500 dan dikenakan catuan makanan (60% dari ad-libitum) dan tekanan suhu (34ºC selama 6 jam) dalam kumpulan sepuluh ekor (10) dengan 2 replikasi dan kumpulan kawalan. Berat badan (BW) dan sifat konformasi badan (BCT) secara signifikan ($P < 0.05$) menurun oleh sekatan makanan dan tekanan haba. Kedua-dua kumpulan ayam di bawah sekatan makanan dan tekanan haba menunjukkan penurunan ($P < 0.05$) ukuran telomere pada minggu 1. Kekurangan panjang telomere tidak signifikan pada ayam yang mengalami tekanan suhu pada minggu kedua tetapi diperhatikan pada ayam yang dicatu makanan ($p < 0.05$) pada minggu yang sama. Dalam eksperimen 2, seratus (100) ekor anak ayam berumur sehari Cobb 500 telah digunakan. Lima puluh (50) ekor ayam dibahagikan kepada 5 replikasi yang mengandungi 10 ekor ayam diberi diet 30mg / kg kortikosteron dari usia dua minggu selama 4 minggu (kumpulan Cort) sementara 50 ekor ayam lainnya digunakan sebagai kumpulan kawalan dengan replikasi yang sama. Tahap kortikosteron plasma ayam Cort dinilai. Nisbah penukaran makanan (FCR) dan berat badan dua minggu sekali dicatat dan dua ekor ayam dari setiap replikasi diambil sebagai sampel dari dua kumpulan (kortikosteron dan kawalan) untuk penentuan berat badan dan histopatologi usus kecil, hati dan serat otot. Dalam eksperimen yang sama, DNA diekstrak dari sampel darah dan tisu (otot, hati dan jantung) dan digunakan untuk penentuan panjang telomere. Sampel RNA diekstrak dari tisu yang sama dan hipotalamus untuk profil ekspresi gen pengawalselia panjang telomere seperti faktor ulangan telomerik 1 (*TRF1*), telomerase ayam (*chTERT*), gen penyelenggaraan telomere 2 (*TELO2*),

ulangan telomere yang mengandungi RNA (*TERRA*) dan faktor transkripsi kejutan haba 1 (*HSF1*) dan DNA mitokondria seperti mencabut protein 3 (*UCP3*), sitokrom C oksidase (*COX6A1*), amiloid serum a (*SAAL1*) dan protein C-reaktif (*CRP*). Ciri-ciri kualiti daging diukur dari sampel daging yang dikumpulkan dari ayam yang diberi makan Cort dan kumpulan kawalan. Tidak terdapat perbezaan yang signifikan ($P < 0.05$) pada tahap plasma Cort untuk kedua kumpulan pada minggu ke-2 tetapi perbezaan yang ketara ($P < 0.05$) dilaporkan pada minggu ke-2. Pada minggu 2 dan 4, penurunan berat badan ayam yang diberi makan Cort secara signifikan ($P < 0.05$) dengan peningkatan nisbah penukaran makanan berbanding dengan kawalan ($P < 0.05$). Berat relatif organ hati, usus kecil, jantung dan pedal meningkat dengan ketara ($P < 0.05$) pada burung yang diberi makan Cort berbanding dengan kumpulan kawalan. Ketinggian villi duodenal dan jejunal adalah jauh lebih tinggi pada ayam yang diberi makan Cort daripada kawalan. Morfologi hati ayam yang diberi makan Cort menunjukkan tanda apoptosis dan keadaan tidak sihat (fibrosis hati) pada kedua minggu ke-2 dan ke-4. Myofibril otot menunjukkan diameter yang lebih rendah ($P < 0.05$) dengan diameter yang lebih rendah pada ayam yang diberi makan Cort daripada pada kawalan pada minggu 2 dan 4. Panjang telomere menunjukkan penurunan yang ketara ($P < 0.5$) pada kedua minggu ke-2 dan ke-4 untuk sampel darah kumpulan Cort. Pengurangan panjang telomere yang ketara ($P < 0.05$) diperhatikan pada minggu ke-2 dan ke-4 dari tempoh tekanan pada semua tisu kecuali di hati dan jantung pada minggu ke-4. Pada masa ini, diperhatikan dalam kajian ini bahawa ekspresi *TRF1*, *chTERT*, *TELO2* dan *HSF1* secara signifikan ($P < 0.05$) meningkat pada hati dan jantung ayam yang diberi makan Cort pada minggu ke-4 tetapi meningkat secara signifikan ($P < 0.05$) di hati pada minggu ke-2. Walau bagaimanapun, pada kedua minggu ke-2 dan ke-4, penurunan regulasi secara signifikan ($P < 0.05$) diperhatikan pada otot. Ekspresi *TRF1* dan *TELO2* meningkat ($P < 0.05$) di jantung pada minggu ke-2 sementara *TERRA* dan *HSF1* menurun ($P < 0.05$). DNA mitokondria secara signifikan ($P < 0.05$) diatur secara berlebihan di semua tisu pada minggu ke 2. Faktor protein fasa akut secara signifikan ($P < 0.05$) meningkat pada ayam yang diberi makan Cort. pH daging ayam yang diberi makan Cort secara signifikan ($P < 0.05$) menurun pada minggu ke-2 sedangkan pada minggu ke-4, peningkatannya secara signifikan dibandingkan dengan kawalan. Kehilangan cecair jauh lebih tinggi pada minggu ke-2 dan ke-4 pada ayam yang diberi makan Cort berbanding dengan kawalan. Daging ayam yang diberi makan Cort menunjukkan kemerahan yang lebih tinggi ($P < 0.05$) lebih tinggi dan penurunan warna pada minggu ke 4. Kekuatan ricih daging ayam yang diberi makan Cort secara signifikan ($P < 0.05$) lebih tinggi daripada kawalan pada minggu ke-4. Korelasi antara panjang telomere ayam yang digunakan dalam kajian ini menunjukkan bahawa ada hubungan kuat dan positif ($r = 0.62$, $P < 0.05$) antara panjang telomere dan pH dan korelasi antara panjang telomere dan kehilangan cecair adalah signifikan dan negatif ($r = -0.59$, $P <0.05$) pada minggu ke-4. Hasil kualiti daging yang diperoleh dalam kajian ini menunjukkan bahawa ayam yang diberi makan Cort mempunyai kualiti daging yang lebih rendah dan ini boleh menyebabkan terjadinya penurunan panjang telomere. Model regresi menunjukkan bahawa pH dapat digunakan untuk meramal integriti telomere. Penemuan ini menunjukkan sifat panjang telomere dan dipendekkan akibat tekanan (akut dan kronik). Panjang telomere dipendekkan dengan sekatan makanan pada 60% makanan ad-libitum, tekanan panas pada suhu 34 ºC selama 6 jam sehari dan pemberian kortikosteron pada diet 30mg / kg. Oleh itu panjang telomere dapat digunakan sebagai biomarker kesejahteraan pada ayam pedaging.

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This thesis was submitted to the Senate of Universiti Putra Malaysia has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of Supervisory Committee were as follows:

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Date: 11 November 2021

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) were adhered to.

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AMSA	American meat science association
AOAC	Association of official analytical chemist
a*	Meat redness
b*	Meat yellowness
BCT	Body conformation traits
BW	Body weight
BL	Body length
BG	Body girth
β-Actin	Beta actin
CCSTEL	Cort fed Chickens with short telomere
Cort	Corticosterone
Cooklos	Cooking loss
Cort wk2	Corticosterone at 2 weeks of administration
Cort wk4	Corticosterone at 4 weeks of administration
COX6A1	Cytochrome C oxidase 1
CST	Cds13/Stn1 /Ten1
CSCs	Cardiac stem cells
chTERT	Chicken telomerase
CT	Threshold cycle
CRP	C-reactive protein
DNA	Deoxyribonucleic acid
DL	Drumstick length
Driploss	Drip loss
EDTA	Ethyline diamine tetra acetic acid

ELISA	Enzyme Linked Immunosorbent Assay
FC	Fold change
FR	Feed restriction
FRC	Feed restriction control
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase
GCs	Glucocorticoids
H	Heat stress
H_2S0_4	Sulphuric acid
HC	Heat stress control
IACUC	Institutional Animal Care and Use Committee
L*	Meat Lightness
NAFL	Non-alcoholic fatty liver
NH_3	Ammonia
NTC	Non template control
NCBI	National Centre for Bioinformatics
MC%	Percent moisture content
POT1	Human Protection of telomeres 1
PBS	Phosphate buffer saline
pHu	Ultimate pH
PCR	Polymerase chain reaction
qPCR	Quantitative polymerase chain reaction
RAP1	Repressor activator protein 2
REE	Resting energy expenditure
RGD	Rat genome database
Rat1	Ribonucleic acid trafficking

RNASE H2	Ribonuclease H2
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SAAL1	Serum amyloid alpha 1
SAS	Statistical analysis software
SCG	Single copy gene
ShForce	Shear force
SE	Standard error of means
SD	Standard deviation
SL	Shank length
TBE	Tris boric ethylene diamine tetraacetic acid
TPP1(ACD)	Adrenocortical dysplasia homolog
TeloWK4	Telomere week 4
Telo2	Telomere maintenance 2
Telo	Telomere
TERRA	Telomeric repeat containing RNA
TRF1	Telomeric repeat binding factor 1
TRF2	Telomeric repeat binding factor 2
TIN2	TRF1-interacting protein 2
WHC	Water holding capacity
W1	Initial weight
W2	Final weight
G	Gram
Mg	Milligram
Kg	Kilogram

Cm	Centimeter
ng/mol	Nanogram/mole
Kb	Kilobase
µl	Microlitre
µM	Micromolar

CHAPTER 1

GENERAL INTRODUCTION

1.1 Background of the study

Animal industry particularly the poultry section is constantly faced with controversies surrounding animal stress and welfare. Broilers especially are prone to many welfare issues related to genetic differences and environmental challenges. Adapting broilers to these challenges has becomes the subject of many discussions in the animal industries. Generally, there are varieties of external and internal stresses chickens are usually subjected to and these may include stocking density, temperature, transportation, feed restriction, feed contamination, fear, and disease (Keles et al., 2010; Zulkifli et al., 2009). The reproductive and growth performance of the poultry birds are usually suppressed by these stressors. Thus, there is an increasing demand for reliable biomarkers to stress and well-being of poultry. Biological indicators for monitoring physiological problems are usually hematological values and plasma corticosterone (Mashaly et al., 2004). Also, immunological conditions of birds under stress are measured with recently introduced cytokine such as interleukin 4 and 6 (*IL-4* and *IL-6*) and inducible nitric oxide synthase (Mashaly et al., 2004). It is known that most commonly used among biomarkers of stress are hematological values and plasma corticosterone levels (De Jong et al., 2002). However, these biomarkers are not reliable as they are characterized by several irregularities due to environmental influences. Rushen (1991) revealed that plasma levels of corticosteroid is not a good predictor of physiological problems. The reason behind this might be because plasma corticosteroid level is highly episodic and irregular.

However, telomere length and its regulatory genes are recently shown to be consistently correlated with stress response. Telomeres are nucleoprotein structures of tandem DNA repeat situated at the tail ends of chromosomes and are subject to attrition at each cycle of cell division (Houbon et al., 2007). Telomere transcription factors and regulators are the upstream signaling pathways sensing the free radical generation and trigger a wide array of response to stress. Telomeric DNA quantity, DNA damage, and expression profiles of regulatory factors could be good candidates for physiological stress and well-being biomarker. Telomeres which are made up of *TTAGGG* repeat are well conserved in the vertebrate and shortened due to the chronological age of the animals in almost all the vertebrate somatic tissues (Kim et al., 2011). However, findings had reported the worst condition of telomere length attrition during exposure to stress situations (Von Zglinicki, 2002; Richter and Proctor, 2007). Exposure to feed deprivation (Vera et al., 2013) combined with stocking density led to the shortening of telomere length in broiler birds (Sohn et al., 2012). Telomere attrition in fish species raised under higher temperature has also been reported (Simide et al., 2016 and Epel et al., 2004). Moreover, induction of chronic stress conditions and reactive oxygen species (ROS) due to corticosterone administration had a negative impact on the characteristics of the telomere length (Kotrschal et al., 2007; Haussmann et al., 2012) in wild birds. Meanwihle, under normal physiological condition, DNA can show defect which increases under critical stress factors. Feed restriction at 60% feeding (Azad et al., 2013), heat stress at 34 ºC (Somaia, 2019) and 30 mg/Kg diet corticosterone administration (Hu et al., 2010) had been reported to affect performances and

physiological traits of broiler chickens but information on how they affect telomere length in broiler hickens at the same levels of exposure are scanty and this called for the present findings.

Telomere regulatory genes, mitochondria DNA and acute phase protein genes could be useful in the assessment of animal welfare as they have direct links with telomere length maintenance. Telomere length mediators such as shelterin and Cdc 13/ Stn 1/ Ten1 (CST) are also proteins of non-DNA components that facilitate the T-Loop formation of telomere length protection and regulates telomerase action at the telomere (Motevalli, 2014). Among the shelterin genes, telomeric repeat binding factor 1 (*TRF1)* facilitates the recovery and supports the sheltering of the telomeric DNA in T-loop formation (Bianchi et al. 1997 and Ye et al., 2004). *TRF1* may be able to facilitate the restoration of the telomeric DNA in T-loop system through other telomeric binding proteins such as *TIN2, TPP1*, and *POT1* (Bianchi et al. 1997). *TRF1* forms links between other shelterin components and the telomeric DNA (Ye et al., 2004). Ye et al. (2004), reported that higher administration of doxorubicin (drugs made of corticosterone) intensely reduces the upsurge of *TRF2* while improving *TRF1* activation, thus determining early cell-death (apoptosis).

Apart from shelterin complex, telomerase forms an important basis of telomere regulation and it is usually regulated by the shelterin complex. Telomerase, an enzyme that stabilizes telomere length by the addition of new telomeric DNA to the end of chromosomes (Greider, 1995). Stem cells of germ line usually have their telomere length maintained as they have a high amount of telomerase. However, somatic stem cells show progressive telomere shortening with each round of replication due to low telomerase (Lansdorp, 2008). Telomere maintenance gene 2 (*TELO2*) on the other hand, exerts its action via telomerase and has been predicted to perform a vital role in telomeric DNA binding activity (Gaudet et al., 2011). The expression of telomere maintenance gene 2 has not been examined in the chicken fed with corticosterone. In addition, RNA molecule called telomeric repeat containing RNA (*TERRA*) has been discovered to function in ensuring that very short (or damaged) telomere are substituted in human (Graf et al., 2017). *TERRA* is rapidly detached by the Ribonucleic Acid Trafficking 1 (Rat1) and ribonuclease H2 (*RNASE H2*) proteins at the site of long telomere (Graf et al., 2017). These proteins are usually deficient when the telomere is short. Thereby, this mechanism allows *TERRA* to repair eroded telomeres so that cell can continue to live and keep regenerating. Koskas et al. (2017) noted that human fibroblast showing deficiency in heat shock transcriptional factor 1 (*HSF1*) exhibited telomeric DNA damage (Koskas et al., 2017). This shows that *HSF1* is vital for *TERRA* elevation in cells under heat stress.

Understanding the roles of mitochondria DNAs is vital in the study of oxidative stress due to its impact on telomeric DNA. Higher mitochondria cellular metabolic activities usually results in the generation of reactive oxygen species (ROS) due to electron leakage from oxidative phosphorylation which then forms a superoxide (Jeˇzek and Hlavat'a, 2005 and Kowaltowski et al. 2009). Mitochondria uncoupling protein 3 (*UCP3*) is activated in numerous scenarios involving skeletal muscle deterioration, cancer and glucocorticoids (GCs) feeding (Sun et al., 2019). The complex IV of the inner lining of mitochondria is Cytochrome C oxidase (*COX6A1*). This gene is has been shown as necessary for apoptosis (Newmeyer et al., 1994). Furthermore, acute phase protein genes are recruited during inflammation. Serum amyloid A 1 (*SAA1*) plays a crucial role in fat metabolism,

phargocytosis and regulate inflammation and tumor effects (Sun and Richard, 2016). The upsurge in serum levels of *SAA* is induced by physical injury to the host, including infection, trauma, inflammation and cancer (Buck et al., 2016). *SAA1* prevents cells and tissues from oxidative insult and provides immune cells to the area of inflammation (Buck et al., 2016). On the other hand, C-reactive protein (*CRP*) was observed to be upregulating during inflammatory situations such as rheumatoid arthritis, heart diseases, and infection (Du Clos and Mold, 2004). Negative correlation among *SAA1* and *CRP* and telomere length had been reported by Wong et al. (2014).

The knowledge of how telomere length and these regulatory genes and their associations are affected by chronic stress in various tissues have not been detailed in chickens. Telomere length may effectively represent the individual animal well-being status. It then becomes imperative to evaluate the factors responsible for the variation in the length of telomere and their regulators and how they affect economic traits and adaptation to stressors.

1.2 Statements of problem

1. Feed restriction and heat stress exposed chickens to acute and chronic oxidative stresses. Telomere length is usually reduced with stress but information on how it is affected by feed restriction and heat stress in broiler chicken is not detailed.

2. The knowledge of how telomere length could be used in the place of circulating corticosterone (Cort) level in chicken with pathological symptoms as stress biomarker is not yet clear.

3. How telomere length and the mechanisms underlying its variation in most tissues could be used as stress biomarkers in chicken have not been uncovered.

4. The knowledge of how corticosterone affects meat qualities and the relationship between telomere length and meat qualities is yet to be understood.

1.3 Objectives

The objectives of the study include the following:

1. Evaluation of the effect of feed restriction and heat stress on telomere length of broiler chicken

2. Examination of performances and pathological states of the broiler exposed to Corticosterone administration and association of these states to telomere length attrition.

3. Measurement and characterization of telomere length and its regulatory genes and evaluate their potentials as stress biomarkers in broiler chicken under corticosterone administration.

4. Determination of the effect of corticosterone on the meat quality traits and genetic correlations between telomere length and meat quality traits of the broiler chicken

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LIST OF PUBLICATIONS

Badmus, K.A. Idrus, Z., Goh, Y.M., Qurni, S.A. and Mamat-Hamidi, K. (2021). Telomere Length and Regulatory Genes as Novel Stress Biomarkers and their Diversities in Broiler Chickens (Gallus gallus domesticus) Subjected to Corticosterone Feeding. Animals, 11(10): 2759. [CrossRef] [PubMed]

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