

The relationship of hematological parameters with adaptation and reproduction in sheep; A review study

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Abstract

Sheep possess desirable characteristics for farmers such as resistance to disease, good acclimation to environmental fluctuations, and endurance to extreme weather. This may, in part, be due to hematology characteristics and various types of hemoglobin that interact differently to external changes; displaying various reproductive ability in certain environmental conditions. This review aims to investigate the effect of hematology parameters and hemoglobin types on the adaptation and reproductive performance of sheep. Hematological parameters are useful tools for the detection of adaptation and physiological traits of these animals. The reproduction of sheep has depended on the ability of each type and breed to acclimate to different environmental conditions. In addition, hemoglobin types have also been correlated with the environmental adaptability and physiological traits of sheep. Thus, the present review provides useful information on the association of hematology parameters and hemoglobin types in sheep with adaptation and reproductive performance, and could be used as vital tools that help in determining the species or breed of sheep that are more adapted to certain environments or have more reproductive potential.

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Introduction

The blood components are essential indicators that can be used for evaluating and monitoring the health as well as the adaptation and metabolic conditions of the animals (1). One of them, hemoglobin, an important erythrocyte protein that has been reported to be a useful tool for investigating many economic traits in domestic animals (2). In sheep, there are three major Hb types (AA, AB, and BB) caused by Hb A and Hb B genes have been reported (3). Sheep possess very important characteristics that enhance their adaptability to environmental fluctuations, disease resistance, and endurance to extreme weather (4). These important characteristics are, in part, due to hematology parameters and different hemoglobin types. These hematological values are useful tools for the detection of adaptation and physiological status of sheep (5). Moreover, the reproduction potential and fertility of sheep is also associated with health status and

hematological parameters (6). Several hematological parameters could be used to evaluate the productive and reproductive traits of animals (7). Yaqub *et al.* (8) reported that erythrocytes (RBC) and leukocytes (WBC) counts, hematocrit (PCV), and hemoglobin (Hb) are important indicators of animal health and reproductive performance. The hematological parameters of sheep are affected by several factors including age, sex, breed, season, nutritional status, and ability to adapt (9). Moreover, the hematological analysis of sheep is very important for assessing physiological changes, and in managing and improving the production efficiency of herds (10). The variation in the hemoglobin and biochemical characteristics of the blood is a major indicator of the physiological and metabolic status of sheep (11). Therefore, the hematocrit, hemoglobin (Hb), leukocytes count, and whole blood clotting time are important indicators of animal adaptation and reproductive performance (8). Furthermore, hemoglobin represents a

unique system for studying adaptive changes and physiological traits. Sheep that possess HbAA hemoglobin type are more resistant and adapted to extreme environmental conditions while the sheep that possess HbAB and HbBB hemoglobin types are more fertile (12). Although some researchers have studied the environmental factors that affect adaptation and reproductive traits of sheep, little information is known about the hematology parameters and hemoglobin types. Therefore, this review aims to describe the hematology indices, hemoglobin types, and its effects on the adaptation and reproductive traits in sheep.

Hematology parameters and adaptation of sheep

The ability of animals to adapt can be predefined as the capability to survive and reproduce in certain environments (13). Reproduction depends on the ability of each species to acclimate and breed (14). Adaptive factors can be determined by the reproductive performance (15). A species inability to adapt adversely affects sustainable breeding and lead to economic losses for the sheep industry. Therefore, it is necessary to understand the adaptive mechanism of domestic livestock (16). Broadly, adaptation is a combination of non-genetic (phenotype) and genetic (genotype) responses to a challenge (17). The non-genetic response includes the morphological, physiological, and blood biochemical characteristics of an organism (18-20). From these characteristics, physiological and blood biochemical characteristics attract more attention. Blood biochemical characteristics reveal that by the animal might have been affected by non-genetic and genetic factors (21-23). The hematology system is sensitive to non-genetic factors and is a major index of physiological response. Several non-genetic factors such as breed, gender, age, management, physiological status, and environmental fluctuations can influence hematological parameters (14).

Hematological studies assist to understand the responsiveness of blood constituents to the ambient conditions (24). They also help to understand acclimation to high-altitudes (25) and the genetic mechanisms of adaptation (26). Moreover, hematological studies are important for determining the association of hematology features to environmental and physiological adaptation (24). Therefore, it could be a benefit in the selection of animals that are genetically adapted to various ecological conditions (27). Data from many mammals have shown that variation in hemoglobin (Hb) function often plays a major role in regulating the acclimation response (28). Also, enhanced oxygen (O₂) carrying and unloading of hemoglobin are physiological indicators of adaptation (29).

Hemoglobin types and adaptation of sheep

Hemoglobin represents a unique system for examining adaptive responses because these oxygen-loading proteins associate the metabolic necessities of animals and constant environmental changes (30). Therefore, hemoglobin has

acquired numerous complex traits to implement its initial function under extreme variable circumstances (31). The compositional and functional variation of livestock globin sequences is one of these improvements (32). Each hemoglobin molecule is a tetramer composed of four polypeptide globin sequences (Figure 1) (33).

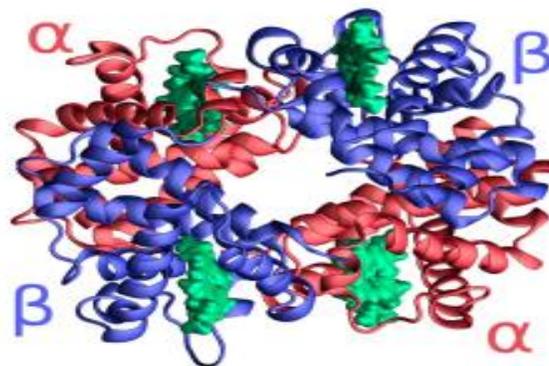


Figure 1: Hemoglobin tetrameric protein composed of four globular subunits, two of each kind, named α and β (33).

The tetrameric hemoglobin includes two alpha and two beta subunits, each consists of eight alpha helices (A-H) (34). Amino acid variations in both α and β subunits seems to be responsible for the adaptive and functional modifications of hemoglobin (32). Furthermore, these adaptive modifications have developed under the impact of natural selection with variation in heme-protein linkage and binding positions of ligands (28). Hemoglobin has been shown to have various forms which correlate with environmental adaptability (35). Two normal hemoglobin (Hb A and Hb B) exist in normal adult sheep, which differ in their β chains (36). Hb A has been found more frequently in animals maintained at higher altitudes and this has been attributed to the greater oxygen affinity Hb A has over Hb B, which has been revealed to be associated with better reproductive traits in animals (12). Pieragostini *et al.* (37) showed that Hb A exists predominantly in sheep that live at, and are more adapted to, high altitude.

Hematology parameters and physiological status in sheep

Hematological parameters are useful indicators for the detection of changes in the health and physiological status of animals (5). These parameters provide the opportunity for more accurate diagnosis and determination of the physiological status of sheep (38). The examination of blood allows investigation of metabolites and other components in the body of sheep and plays a key role in the physiological stages of animals (39). Several studies, such as Bani Ismail *et al.* (38), Frelich *et al.* (40), Jawasreh *et al.* (41), and Etim *et al.* (42), have confirmed that the reference values of hematological parameters could be affected by several

factors, such as breed, age, gender, health conditions, and physiological status. Differences in hematology parameters of animals can also be affected by influences such as altitude, nutrition, and other environmental factors (43). Hematology profiles can be used in the determination and monitoring of the physiological conditions of animals (44), as well as determination genetic adaptation (45). As reported by Isaac *et al.* (27), animals with good hematology constituents may have improved reproductive performance.

Hematological characteristics are important for knowing the health and reproductive traits of sheep (42) and are useful for assessing physiological condition (46). Assessment of various hematology parameters could be utilized to investigate the general health conditions of production livestock (47). Reproductive traits could influence the blood profile of Santa Inês and Morada Nova ewes (48). It is well established that hematological parameters in sheep reveal several differences concerning breeding, age, sex, physiological status, and genotype of the animal (43). Various reports have studied the association of physiological traits with hematology parameters of sheep. Owusu *et al.* (49) reported a significant variation ($P < 0.05$) in some hematological indices of lactating ewes and non-lactating ewes in the Djallonke sheep of Ghana. In addition, Bezerra *et al.* (48) studied the hematological indices of Morada Nova and Santa Inês ewes in different reproductive status.

Hemoglobin types and physiological traits other farm animals

The Hb molecule is made up of two α - globin peptide subunits encoded by the *HBA1* and *HBA2* genes, and two β -globin peptides subunits encoded by the *HBB* gene, with heme moieties needed to transport oxygen (50). These genes contain a greater number of mutations causing variations in amino acid sequence and have been widely investigated for decades (51). Some of these mutations may decrease Hb synthesis and enhance hemolysis. Other variables that influence hemoglobin concentration are present in genes that encode for structural proteins and enzymes in erythrocytes which may influence the structure, function, and survival of erythrocytes, and enhance hemolysis (52). Whole-genome studies have shown a wide range of variants adjusting these phenotypic traits (53). This remarkably diversity includes the synthesis of Hb, iron metabolism, erythropoiesis, erythrocyte function, stability, and Hb production (51). Hemoglobin variants have revealed that even small differences in binding linkages may influence hemoglobin stability and oxygen- packing affinity (32).

The genetic variations of *HBB* have been reported to alter several traits associated with a variety of phenotypes in animals (54). In sheep, analysis of variance revealed that hemoglobin variants had an important effect on reproductive traits. The highest lambing interval was obtained from the HBAA type (55), while the survivability of lambs was greater with hemoglobin type AB (Hb AB). Lambs with Hb

AB should therefore be selected for improved survivability of sheep (56). Furthermore, Nihat *et al.* (57) revealed that Merino ewes possessing Hb AB gave birth to higher weight lambs. The lambing of twins was greater with genotype *HbBB* than *HbAA* (12). Moreover, ewes carrying *Hb BB* have been repeatedly documented to have better fertility than ewes with Hb AA (Figure 2) (58).

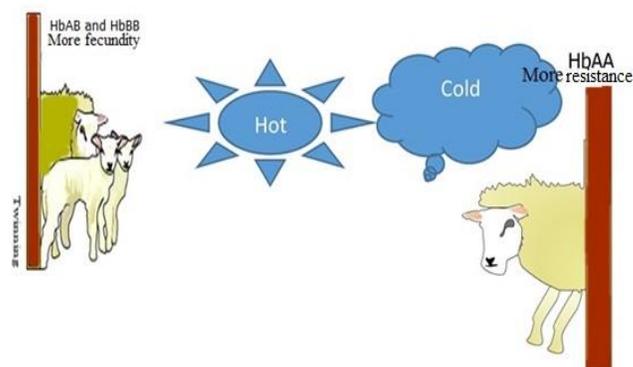


Figure 2: The HbAA genotype of sheep exhibited more resistance to extreme weather while the HbAB and HbBB showed enhanced fertility.

Free hemoglobin and haptoglobin

Although hemoglobin molecules have many important characteristics that make them more affected by the adaptative and physiological traits of animals, excess free Hb is considered toxic for animals (59). The toxicity resulted from free Hb is attenuated by haptoglobin (60). Haptoglobin (Hp) is an abundant plasma protein, which is produced in the liver. It is a high-affinity scavenger for free hemoglobin (Hb) through hemolysis (61). Hp is found in many animals as a two-dimensional protein of 150 kDa. It is composed of two alpha-chains and two beta-chains attached by two disulfide (S-S) bonds between correct pairs of cysteine (Cys) residues connecting the two alpha-chains, producing Hp 1-1 (62). These α and β subunits are believed to be aggregated through (S-S) linkages (34). The Hb: Hp compound provides many protective functions, reducing the toxicity of free Hb on renal function, blood vessels, and peripheral tissues (Figure 3) (59,60,63).

The protection provided by Hp mitigates the major toxic effects of Hb. The large molecular size of the Hb: Hp compound protects kidney function and maintains vascular nitric oxide (NO) homeostasis by inhibiting the arrival of free Hb into the blood vessel wall (64,65). Additionally, the Hb: Hp compound has an anti-oxidative function that prevents the moving of heme to proteins and reactive fats from its globin chains (Figure 4) (60,66). While Hp supplies important protection from free Hb toxicity, it is quickly consumed and released through hemolysis (65). Furthermore, Hp concentration in livestock is not affected by age, sex, or physiological status (67).

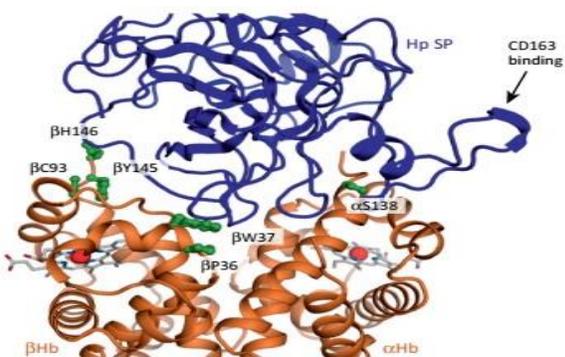


Figure 3. The hemoglobin-haptoglobin (Hb-Hp) complex. Green spheres represent the Hb residues susceptible to oxidation (63).

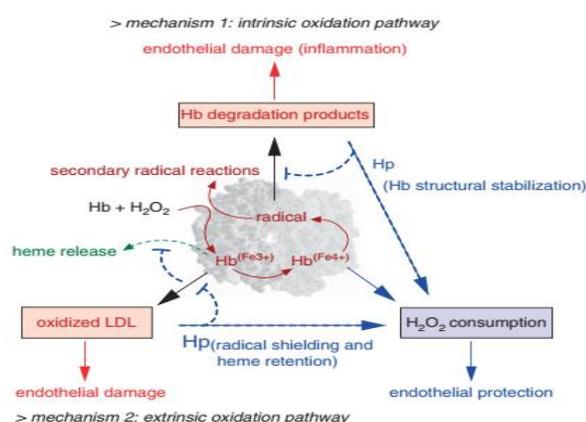


Figure 4: Free hemoglobin (Hb) and protection by haptoglobin (Hp). In the intrinsic oxidation pathway, Hp protects against peroxidative Hb toxicity by stabilizing the Hb structure and by shielding extrinsic molecules against Hb/heme-mediated peroxidative damage in intrinsic oxidation pathway (60).

Conclusion

The present review provides useful information for the association of hematology parameters and hemoglobin types in sheep with adaptive and reproductive performance, and could be used as vital tools that help in discriminating species or breeds of animals that are more adaptive or reproductive. The blood biochemical profiles are considered important in evaluating the adaptive and reproductive performance of animals. Hemoglobin carries out important functions in animals, and for these reasons, hemoglobin types can be linked with certain morphological and production characteristics of animals. Determining the hemoglobin types improves the accuracy of the implementation of the selection process, and thus leads to improvements in sheep production.

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Conflict of interest

The author declares that she has no conflict of interest.

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علاقة معايير الدم بالتكيف والتكاثر في الأغنام؛ دراسة مراجعة

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الخلاصة

تمتلك الأغنام خصائص مرغوبة للمزارعين مثل مقاومة الأمراض، والتأقلم الجيد مع التقلبات البيئية، وتحمل الطقس القاسي. قد يعود هذا، جزئياً، إلى خصائص الدم والأنواع المختلفة من الهيموغلوبين، والتي تتفاعل بشكل مختلف مع التغيرات الخارجية؛ مظهرة قدرة تكاثرية مختلفة في ظروف بيئية معينة. هدفت هذه المراجعة إلى التحري عن تأثير معايير الدم وأنواع الهيموغلوبين على التكيف والأداء التكاثري للأغنام. المعايير الدموية هي أدوات مفيدة للكشف عن التكيف والحالة الفسيولوجية لهذه الحيوانات. يعتمد تكاثر الأغنام على قدرة كل نوع وسلالة على التأقلم مع الظروف البيئية المختلفة. بالإضافة إلى ذلك، ارتبطت أنواع الهيموغلوبين مع التكيف البيئي والصفات الفسيولوجية للأغنام. لذلك، قدمت هذه المراجعة معلومات مفيدة عن ارتباط معايير الدم وأنواع الهيموغلوبين في الأغنام مع التكيف والأداء التكاثري ويمكن استخدامها كأدوات حيوية تساعد في تحديد الأنواع أو سلالات الأغنام الأكثر تكيفاً مع بيئات معينة أو لديها المزيد من القدرة على التكاثر.