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 hematological 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.

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 leucocytes (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), leucocytes count, and whole blood clotting time are important indicators of animal adaptation and reproductive performance (8). Furthermore, hemoglobin represents a
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 hematological 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 hematological 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).](image)

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.
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 interval 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).

**Free hemoglobin and haptoglobin**

Although hemoglobin molecules have many important characteristics that make them more affected by the adaptive 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 Hp: Hb 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 Hp: Hb 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 Hp: Hb 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).
...and thus leads to differences in the adaptative and reproductive performance of animals. Determining the 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.

References

1. Antunović Z, Novoselec I, Klir Ž. Hematological parameters in ewes during lactation in organic farming. Poljoprivreda. 2017;23(2):46-52. DOI: 10.18047/poljic.23.2.7
2. Egena SSA, Alao RO. Haemoglobin polymorphism in selected farm animals: A review. Biotechnol Anim Husbandry. 2014;30(3):377-390. DOI: 10.2298/BAH1403377E
3. Al-Khuzaie HM, Al-Khazaïj WJ. Relationship of hemoglobin types and blood groups with bodyweight and dimensions in unimproved awassi ewes. Adv Anim Vet Sci. 2019;7(6):461-465. DOI: 10.17582/journal.aavs/2019/7.6.461.465
4. Galal S, Gürsoy O, Shaat I. Awassi sheep as a genetic resource and efforts for their genetic improvement-A review. Small Ruminant Res. 2008;79(2-3):99-108. DOI: 10.1016/j.smallrumres.2008.07.018
5. Badawi NM, Al-Hadithy HAH. The hematological parameters in clinically healthy Iraqi Awassi sheep. Platelets. 2014;32:0:12. [available at]
6. Aktas M, Altay K, Dumanli N. Determination of prevalence and risk factors for infection with Babesia ovis in small ruminants from Turkey by polymerase chain reaction. Parasitol Res. 2007;100(4):797-802. DOI: 10.1007/s00436-006-0345-2
7. Al-Hadithy HAH, Suleiman JM. The hematological parameters in clinically normal lactating and ewes affected with mastitis. Kufa J Vet Med Sci. 2014;5(2):46-54. [available at]
8. Yaqub LS, Kauw MU, Ayo JO. Influence of reproductive cycle, sex, age, and season on haematologic parameters in domestic animals:a review. J Cell Anim Biol. 2013;7(4):37-43. [available at]
9. Afolabi KD, Akinsoyinu AO, Abdullah ARO, Olaifade R, Akinleye SB. Haematological parameters of the Nigerian local grower chickens fed varying dietary levels of palm kernel cake. Poljoprivreda. 2011;17(1):74-78. [available at]
10. Opara MN, Udovi N, Okoli IC. Haematological parameters and blood chemistry of apparently healthy West African Dwarf (Wad) goats in Owerri, South Eastern Nigeria. N York Scie J. 2010;3(8):68-72. [available at]
11. Zaher H, El-Zahar H, Al Sharifi S, Shetty T. Alterations in hematological and biochemical parameters affecting the reproductive performance in female camels (Camelus dromedaries). Int J Vet Health Sci Res. 2017;5(1):155-160. DOI: 10.19070/2332-2748-1700032
12. Važić BS, Rogić BS, Drinić MS, Pržulj NM. Relationship between the genetic hemoglobin polymorphism, morphometry and fertility of Pramenka sheep breed from Central Bosnia. Genetika. 2017;49(1):151-160. DOI: 10.2298/GENS1701151V
13. Mirkema T, Duguma G, Haile A, Tibbo M, Okeyo AM, Wurzinger M, Sölkner J. Genetics of adaptation in domestic farm animals:A review. Livestock Sci. 2010;132(1-3):1-12. DOI: 10.1016/j.livsci.2010.05.003
14. Ribeiro MN, Ribeiro NL, Bozzi R, Costa RG. Physiological and biochemical blood variables of goats subjected to heat stress—a review. J Appl Anim Res. 2018;46(1):1036-1041. DOI: 10.1080/09712119.2018.1456439
15. Oliveira WDCD, Araújo MDJ, Edvan RL, Oliveira RL, Bezerra LR. Changes in hematological biomarkers of Nellore cows at different reproductive stages. Acta Scientiarum. Anim Sci. 2019;41 DOI: 10.4025/actascianimsci.v41i1.45725

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).
16. Almeida T, Akeberg D. Adaptation Strategies of Farm Animals to Water Shortage in Desert Areas. Am J Biomed Sci Res. 2019;2(6). DOI: 10.34297/AJBSCR.2019.02.000617
17. Gaughan JB, Sejian V, Mader TL, Dunshea FR. Adaptation strategies: ruminants. Anim Frontiers. 2019;9(1):47-53. DOI: 10.1093/afsfy/209
18. Niyas PAA, Chaidanya K, Shaji S, Sejian V, Bhatta R. Adaptation of livestock to environmental challenges. J Vet Sci Med Diagn. 2015;4:3-2. DOI: 10.4172/2325-9590.1000162
19. Hassan AA, Amin RA, El-Maghrabi NS, Ali J. Effect of vitamin C and acetylsalicylic acid supplementation on some hematological value, heat shock protein 70 concentration and growth hormone level in broiler exposed to heat stress. Iraqi J Vet Sci. 2020;34(2):357-363. DOI: 10.33899/ijvjs.2019.125950.1195

20. Ukweuze C, Akpan ES, Ezekonkw RC, Nwosuh CI, Anene BM. Haematological, oxidative stress and electrolyte alterations in puppies consuming crude oil ingestion in experimental rabbits. African Journal of Experimental Biology. 2020;10(3):171.

21. Crumbliss ML, Jia Y, Banerjee S, Wu G, Kreulen RT, Tsai AL, Bringas M, Petruk AA, Estrin DA, Capece L. Biologica. 2020;54(3):70:13
22. Jentoft S, Andersen D. Functional effect of hemoglobin polymorphism on the haematological pattern of Gentile di Puglia sheep. J Anim Breed Genet. 2006;123(2):122-130. DOI: 10.1111/j.1439-0388.2006.00566.x
23. Bani Ismail ZA, Al-Majali AM, Amireh F, Al-Rawashdeh OF. Metabolic profiles in goat does in late pregnancy with and without subclinical pregnancy toxemia. Vet Clin Pathol. 2008;37(4):434-437. DOI: 10.1111/j.1939-165X.2008.00076.x
24. De BR, William HJ. Association of some five genetic loci influencing the human red blood cell. Natur. 2014;23:24-27. [available at]
25. Ciani E, Alloggio I, Pieragostini E. Intriguing hemoglobin polymorphism in Grey Alpine cattle and functional effect. Large Anim. 2019;34(2):125-129. [available at]
26. Andersen O, Werten OF, De Rosa MC, Andre C, Carelli Alinovi C, Colafranceschi M, Brix O, Colosimo A. Haemoglobin polymorphisms affect the oxygen-binding properties in Atlantic cod populations. Biol Sci. 2008;276(1658):833-841. DOI: 10.1098/rspb.2008.1529
27. Andersen O, De Rosa MC, Yadav P, Piroli D, Fernandez JM, Berg PR, Jen tot S, Andre C. The conserved Phe GHS of importance for hemoglobin intersubunit contact is mutated in gudadu fish. BMC Evol Biol. 2014;14(1):54. DOI: 10.1186/1471-2148-14-54
28. Brinagas M, Petruk AA, Estrin DA, Capece L, Marti MA. Tertiary and quaternary structural basis of oxygen affinity in human hemoglobin as revealed by multiscale simulations. Sci Rep. 2017;7(1):1-10. DOI: 10.1038/s41598-017-11295-0
29. Mollan TL, Jia Y, Banerjees S, Wu G, Kreulen RT, Tsai AL, Olsson JS, Crumbbliss AL. Alayash DA, Redox properties of human hemoglobin in complex with fractionated dimeric and polymeric human haptoglobin. Free Radical Biol Med. 2014;66:265-277. DOI: 10.1016/j.freeradbiom.2014.01.030
30. Peters E, Joseph S, Day S, Garety P. Measuring delusional ideation:the 21-item Peters et al. Delusions Inventory (PDI). Schizophrenia Bull. 2004;30(4):1005-1022. DOI: 10.1093/oxfordjournals.schbul.a007116
31. Hrinca G, Groza M, Fecioru E, Pădeanu I. Association of some biochemical-genetic markers with the reproduction parameters of the botosani karakul ewes. Sci Papers Animi Sci Biotehnol. 2008;41(2):751-757. [available at]
32. Pieragostini E, Rubino G, Bramante G, Rullo R, Petazzi F, Caroli A. Functional effect of haemoglobin polymorphism on the haematological pattern of Gentile di Puglia sheep. J Anim Breed Genet. 2006;123(2):122-130. DOI: 10.1111/j.1439-0388.2006.00566.x
33. Bani Ismail ZA, Al-Majali AM, Amireh F, Al-Rawashdeh OF. Metabolic profiles in goat does in late pregnancy with and without subclinical pregnancy toxemia. Vet Clin Pathol. 2008;37(4):434-437. DOI: 10.1111/j.1939-165X.2008.00076.x
34. Etim NN, Williams ME, Akpabio U, Offiong EE. Haematological parameters and factors affecting their values. Agricultural Science. 2014;2(1):37-47. DOI: 10.1272/jas.v2i1.41
35. Ahmed MN, Humide AO, Muhadi MJ. Haematological state of ewes injected with some mediators during postpartum and lactation period. J Pharmaceut Sci Res. 2018;10(8):1921-1924. [available at]
36. Khan TA, Zafar F. Haematological study in response to varying doses of estrogen in broiler chicken. Int J Poult Sci. 2005;4(10):748-751. [available at]
37. Togun VA, Oseni BSA, Ngundije JA, Arewa TR, Hammed AA, Ajorniebu DC, Mustapha E. Effects of chronic lead administration on the haematological parameters of rabbits-a preliminary study. In Proceedings of the 41st Conferences of the Agricultural Society of Nigeria. 2007;341.
38. Islam MM, Apu AS, Hoque SAM, Ali MY, Karmaker S. Comparative study on the libido, semen quality and fertility of Brahman cross, Holstein Friesian cross and Red Chittagong breeding bulls. Bangladesh J Anim Sci. 2018;47(2):61-67. DOI: 10.320/bjas.472.40236
39. Jawaseh KI, Ismail ZA, Al-Rawai SM, Al-Majali A. Normal haematology and selected serum biochemical values in different genetic lines of Awassi ewes in Jordan. Inter J Poult Sci. 2010;7(2):1-10. [available at]
40. Khan TA, Zafar F. Haematological study in response to varying doses of estrogen in broiler chicken. Int J Poult Sci. 2005;4(10):748-751. [available at]
41. Togun VA, Oseni BSA, Ngundije JA, Arewa TR, Hammed AA, Ajorniebu DC, Mustapha E. Effects of chronic lead administration on the haematological parameters of rabbits-a preliminary study. In Proceedings of the 41st Conferences of the Agricultural Society of Nigeria. 2007;341.
42. Islam MM, Apu AS, Hoque SAM, Ali MY, Karmaker S. Comparative study on the libido, semen quality and fertility of Brahman cross, Holstein Friesian cross and Red Chittagong breeding bulls. Bangladesh J Anim Sci. 2018;47(2):61-67. DOI: 10.320/bjas.472.40236
43. Jawaseh KI, Ismail ZA, Al-Majali A. Normal haematology and selected serum biochemical values in Awassi lambs. Journal of Advanced Vet and Animal Research. 2019;6(2):193. DOI: 10.5455/javar.2019.0331
44. Bezerra LR, Oliveira WD, Silva TP, Torreão JN, Marques CA, Araújo MJ, Oliveira RL. Comparative hematological analysis of Morada Nova and Santa Inês ewes in all reproductive stages. Pesquisa Veterinária Brasileira. 2017;37(4):408-414. DOI: 10.1590/0100-736x2017000400017
45. Owusu M, Abebrese AK, Adzitey F. Hematological Characteristics of ‘Djallonke’ Sheep Reared at Ejura Sheep Breeding Station of Ghana. Vet Res. 2016;16(4):106-109. [available at]
46. Gell DA. Structure and function of haemoglobins. Blood Cells Mol Dis. 2018;70:71-42. DOI: 10.1016/j.bcmd.2017.09.006
47. Schechter AN. Hemoglobin research and the origins of molecular Med. Blood. J Am Soc Hematol. 2008;112(10):3927-3938. DOI: 10.1182/blood-2008-04-078188
48. And X, Mohandas N. Disorders of red cell membrane. Br J Haematol. 2008;141(3):367-375. [available at]
49. Van Der Harst P, Zhang W, Leach IM, Rendon A, Verweij N, Sehnj I, RadhaKrishnan A. Seventy-five genetic loci influencing the human red blood cell. Nature. 2012;492(7429):369-375. DOI: 10.1038/nature11677
كلمة معمارية في الدم بالتكيف والتكاثر في الأغذام: دراسة

الخلاصة

متملك الأغنام خصائص مريحة للمزارعين مثل مقاومة الأموات، والتغلب على الطقس القاسي، وقد يحدث هذا، جزئياً، إلى خصائص الدم والأدوات مختلفة من الهيموغلوبين، والتي تتفاعل بشكل مختلف مع التغيرات الهرمونية. ظاهرة تكاثر وكفاءة الأغنام ترتبط معاً مع الأنواع المختلفة من الهيموغلوبين. هذه المراجعة تمنح هذه الأنواع الأفضل للتكيف والتكاثر والتكافل، مثل الأنواع المختلفة من الهيموغلوبين ودقة الكشف، حيث تأتي مع أنواع الهيموغلوبين، والتي تساعد على التوازن والتكيف والتكافل. بالإضافة إلى ذلك، تعلم المزارعين كيفية استخدام الأنواع المختلفة من الهيموغلوبين والتكافل والتكافل. الدراسات الميدانية تدعم استخدام الأنواع مختلفة من الهيموغلوبين بالتكيف والتكافل. الدراسة تكون استخدامها كأدوات حيوية لتوصيف الأنواع المتغيرة من الأغذام.