Review

Colostrum Induced Passive Immune Transfer in Lambs

Caner Ovet *

Posted Date: 1 August 2023

doi: 10.20944/preprints202307.2111.v1

Keywords: colostrum; passive immunity; sheep; lamb mortality

Review

Colostrum Induced Passive Immune Transfer in Lambs

Caner ÖVET [1,*].

[1] Ministry of Agriculture and Forestry, Edirne, Turkey; ORCID: 0000-0002-8682-0143
* Correspondence: caner.ovet@tarimorman.gov.tr; Tel.: (+90 543 948 6317)

Abstract: During last decades, production and consumption of small ruminant milk has been increased. As a result of it, sheep and goat farming has been developing and scientists are focused on these animal researches both clinical and feeding strategies. By the evolutionary challenges and adaptations, colostrum has a crucial role of immune complementation for litter. As a result of these challenges and adaptations neonatal life is especially more important in ruminants because of it affects their whole life and future of livestock. Passive immune transfer is the main mechanism that explained by biological evolution between dam and lamb and also it is effected by factors up to dam and up to the litter. Today importance of passive immune transfer is well known for the future of livestock economy and animal welfare. In the literature, researchers are focused on correlation between colostrum quality (especially immunoglobulin amounts) and blood serum levels of newborns. Aims of present review are to discuss datas of recent studies, point out different effecting factors in colostrum quality and passive immune transfer, enlighten and give new ideas to researchers.

Keywords: colostrum; passive immunity; sheep; lamb mortality

1. Introduction

The greatest wealth a country can have is its health, and the greatest health any animal can have is its freedom. – Dr. Bernard Rollin

Placental structure of the sheep is chorioallantoic, cotyledonary and villous type [1,2] and due to synepitheliochorial interhemal barrier [2,3], maternal antibodies are considered not transferred in utero to the offspring [4]. Thus, colostrum induced passive immune transfer (PIT) is crucial for the whole life of the lamb. Alongside a strong immunostimulant activity of the colostrum, it is a nutrient rich source for the litter. Newborn lambs bore with quite limited energy reserves thus they need immediate acces to intake colostrum which has enough amount and quality [5]. Colostrum has immunological and nutrient compositon [6,7]. It also has high magnesium content that plays an essential role in peristaltic activation of newborn. Alongside that peristaltic activity, colostrum promotes the remove of meconium, and avoiding the bacterial colonisation in gastrointestinal tract [8,9]. All these properties of colostrum make it an unique life source for the newborn. Immunoglobulin and nutrient amounts are shown in Table 1.

Domestication of the sheep is considered approximately ten thousand years ago during the Neolithic age in Central Asia [10]. Since that age sheep farming has became an important food and animal-by product resource for human beings. Milk and dairy products of small ruminants are quite important for proper human nutrition where cow milk is not readily available or affordable [11].

It is a real challenge for a mammalian litter to transition from intrauterine life to the extrauterine life [12] and that challenge is combined some influences such as behaviour of the litter and mother after birth [5]. According to literature datas, passive immunity in ruminant newborns not only ensure prevent against diseases but also accelerate growth performance [13–15]. Neonatal lamb mortality has no one specifical cause [16]; it has a multifactorial issue. Besides its major function of digestion and absorbtion of nutrients, gastrointestinal tract provides immunological defense against especially pathogens, endotoxins and antigenic substances [17]. In newborn ruminants jejunum is a major intestinal region for IgG absorption [18,19].

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 August 2023 doi:10.20944/preprints202307.2111.v1

Table 1. Concentrations of immunoglobulins and chemical composition of sheep colostrum [20,21].

Component		Amount
Immunoglobulins (mg/ml)	IgG	96.0
	IgA	3.5
	IgM	1.3
Nutrients (%)	Fat	14.04
	Protein	21.24
	Lactose	3.26

2. Why PIT Is Crucial?

Although in some mammals (i.e., human, rabbit, mouse), PIT is mainly completed via placenta [22] in ungulates, it doesn't occurred or considered not to be occurred [23]. Due to placental structure, transfer of maternal antibodies occurs via colostrum not only lambs but also in other neonatal ruminants in 24 hours post partum; thus PIT is related to colostrum quality and its amount intake by the litter. Failure of PIT causes major economical losses in livestocks; it is an important economical concern for producers. Thus PIT is crucial for producers to prevent neonatal mortality and morbidity by monitoring immune status of lambs [24,25]. The nature of PIT is an adaptive natural immunity (Figure 1). As a result of evolutionary adaptation, lambs need to establish PIT to survive.

Lamb mortality is a key factor influencing productivity of ewes and profitability of livestock [26]. Mortality rates are variable by different circumstances (such as management, gestational diseases, common infections, failure of PIT and other) and during last decades the average mortality rate of newborn lambs remained relatively constant by 15% around the world. This rate could be to be higher (up to 30%) in small-scale sheep farming systems in developing countries [16]. According to studies failure of PIT's incidence ranges between 3.4% and 20%; mortality rates are variable between 45% and 50% during 2 weeks of neonatal life [17]. Failure of PIT in neonatal lambs has a significant consequence on neonatal mortality and newborn losses of infectious causes are positively correlated with low concentrations of serum Ig [27,28]. Failure of PIT may happen at different levels; including insufficient concentration of Ig in the colostrum due to lack of specific pathogen exposure or an inability to respond, insufficient intake of colostrum by litter, or lack of transmural Ig transfer from the neonatal intestine to blood. Hence, failure of PIT has been related multiple conditions of lambs, including respiratory disease, diarrhea, septicemia, and commonly omphalophlebitis [29,30]. All these conditions and lack of colostrum intake during first weeks of neonatal life, would affect the litter's whole life [31]. Amount of colostrum is important but also management during the suckling and weaning period; such as stress produced by dam separation, milk quality and suckling frequency, can affect the final immune status of the lambs [32]. Failure of PIT is the most important cause in newborn lamb mortality.

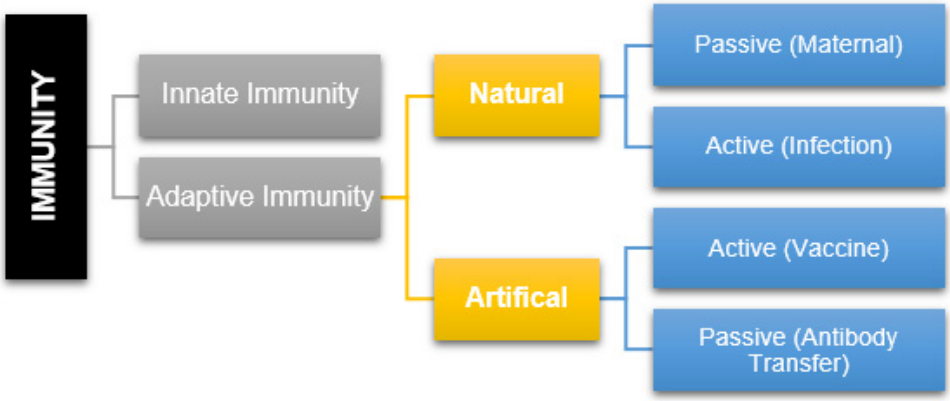

Figure 1. Summarized chart of immunity.

 doi:10.20944/preprints202307.2111.v1

The gastrointestinal tract of newborn lamb is considered sterile and once it's exposured to microorganisms after birth, its development and maturation of the intestinal mucosal immune system start [33]. Although it's not well-explained yet, it is known the mechanism of passive immune transfer from dam to litter occurs by high permeability of intestinal tract of litter to macromolecules pass through especially immunoglobulins in ruminants. This permeability is highest at first 6 hours of birth and it decreases in 24 hours [34–36]. Pinocytosis of enterocytes also have a role in that maternal antibody absorbtion by the newborn [37]. PIT is a complex of reactions by acting together Toll-Like Receptors, Mucins, antimicrobial peptides, and Claudins in intestinal defense during the PIT in newborn lambs [38]. On the other hand, Fc receptor mediated pathways are key mechanism in IgG metabolism [39]. But that high permeability increases also the risk for pathogens to enter as well as macro molecules [40].

3. Effecting Factors of the PIT

3.1. Factors up to Dam

Dam's health is one of the most important factors to produce high-quality colostrum. The healthy udder gland is key to produce high-quality milk in dairy ruminants [41]. Nutrition is a major contributing factor to the quantity and quality of colostrum [42,43]. Sufficient energy to the dam is ingesting and whether that meets its gestational requirements [44,45]. Viola et al. [46] have shown that ewe's diet in the last period of gestation can effect colostral IgG concentration; for instance hazelnut skin in ewe's diet effects positively colostral IgG concentration. Under that condition, colostrum quality is associated directly to the dam's nutrition. In the late gestation, sheeps those supplemented with oat grain had higher colostral protein and IgG and high IgG levels in the blood serum of their lambs [47].

According to some studies, age of dam has no significant effect on growth performance in neonatal lambs [48–51]. Although datas on effect of parity on colostrum quality in sheeps and goats are restricted, some studies reported that primiparous ewes have higher colostral protein and IgG levels [52,53]. But in contrast, Sjoberg and Van Saun [54] reported that parity has no effect on colostral IgG levels. In a study, parity influenced characteristics of colostrum in multiparous dams; they have the lowest concentrations of proteins, glucose, IgG and cortisol, but the highest colostrum IgG level. Also, lambs born from primiparous dams have lower protein, glucose and plasma IgG concentrations than lambs born from multiparous dams [55]. Gokce et al. [15] reported that risk of neonatal mortality and morbidity are higher in dams at first parity than the dams have higher parities because of ewes show mismothering at first lambing. Physiological mechanisms in first pregnancy might play a role in increasing stress in primiparous ewes; they are still growing and need to partition nutrients to sustain their growth physiology and their foetuses [56]. Eventually, parity is one of the important effecting factor on colostrum quality and lamb morbidity-mortality.

In cows, the use of probiotics and prebiotics leads to higher levels of colostral immunoglobulin [57,58]. Also in the sow, dietary probiotics improve colostrum quality and growth performance in piglets [59]. But there is no sufficient data effects of using probiotics on colostrum quality in sheep nutrition. Nouri et al. [99] have demonstrated that prepartum and postpartum feed restriction in fat-tailed dairy sheeps do not affect colostral IgG or lamb serum IgG concentration. Vaccination has important effects on colostrum quality and PIT in newborns; higher serum antibodies in ewes would effect antibody concentrations in colostrum [60].

3.2. Factors up to litter

Not only lambs but also kids and calves need to access colostrum has sufficient amount and quality. In the literature it is controversial the relationship between litter size and colostrum quality. While some studies [61–64] have showned that there is a significant relationship between single and multiple-born lambs, another studies discussed about multiple births may increase the risk of neonatal mortality [65,66]. Alves et al. [67] have showed that lambs demonstrated failure of PIT once their a serum IgG concentration lower than 15 mg/mL at 36th hour post partum. Similarly lambs have

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 August 2023 doi:10.20944/preprints202307.2111.v1

lower serum total protein (TP) concentration at 24th hour post partum show higher morbidity-mortality rates [68]. Management applications and animal charactheristics (i.e., singleton or twin, birth weight, gestationel diseases in ewes) are associated to PIT [51].

Some studies reported that singleton born to ewe lambs are lighter at birth than singletons born to mature ewes [69,70]; lambs born to ewe lambs may have lower survival rate [71].

4. Evaluation Methods

Several methods have been established and they are being using to evaluate PIT in newborn ruminants today. Those methods are mainly divided into direct and indirect methods (Table 2). According to literature datas, most accurate method for evaluate colostrum quality is radial immunodiffusion (RID); also ELISA is a reliable method [72,73]. But RID is an expensive laboratory method and requires time for results. Although it is not well-accurate, in farm-practice the best method is brix refractometry to evaluate colostrum quality because of it is fastest and easiest method [74]. Another method is Split trehalase immunoglobulin G assay (STIGA) that used in bovine colostrum [75]. But in the literature there is no study on evaluate sheep colostrum by STIGA. Besides, radial gel immunodiffusion technique can be used to determine serum and colostral IgG concentration [47].

Table 2. Common direct and indirect methods to evaluate colostrum quality.

Direct Methods	RID ELISA STIGA
Indirect Methods	Refractometer Colostrometer

4.1. Colostral TP and Ig Concentration

Majority of total colostral protein is origined by immunoglobulins; especially IgG in ruminant colostrum. Management, gestational diseases, mastitis, age and parity are factors that affect colostrum quality [76]. Sufficient amount and quality of colostrum are important factors for the PIT. According to ELISA method, values between 29.55 and 53.41 are considered high-quality [67,77]. Brix refractometry can be used in farm practice and values are changeable (Table 3).

Table 3. Brix values of sheep colostrum in different studies.

Brix Values Range (%)	Breed	Reference
14.4 – 17.1	Awassi	[80]
13.0 – 23.5	Crossbreed	[77]
8.6 – 40.0	Santa Inês	[81]
16.8 – 22.6	Lacaune	[82]
15.4 – 40.0	Unknown	[83]
21.6 – 44.7	Merino	[74]
16.8 – 27.0	Unknown	[84]

4.2. Immunoglobulin Levels in Lamb Blood Serum

There are different methods to estimate serum Ig levels. Detection IgG levels by ELISA [78] is one of the common methods. Healthy newborn lambs (in 21 days after birth) have significantly higher serum IgG levels than before they consume colostrum; and also their dams have higher colostral TP levels [68]. Laser-induced breakdown spectroscopy method also can be used evaluation of proteins in sheep colostrum [79]. That method is based on spectroscopic detection and analysis of atomic, ionic and molecular emission of a laser produced plasma; it can be used for in-situ and real time measurements [85]. Another evalution method is Zinc Sulphate Turbidity Test (ZST) that creates

 doi:10.20944/preprints202307.2111.v1

turbidity which is proportional to the quantity of gama globulin in the sample and can be quantified in calorimeter at 525 nm/Spectrophotometer 460 nm. This method was used for the first time in 70s to determine gama globulin levels in calves. According to ZST, neonatal lambs have total serum level is below than 12 are considered to indicate failure of PIT [30]. Enzymatic colorimetric kits can be used for estimate serum TP and albumin concentrations [67].

5. Discussion and Conclusion

According to FAO 2022 report, consumers especially in high-income countries, care more about what they eat and how their food is produced, processed and transported [86]. Sheep farmers produce consumable products (meat and milk) and animal-by products (wool and skins) for national and/or international markets [87]. These economical changes and feeding preferences lead farmers, governments and researches to focus on small ruminant practice. Suckling lambs intake non-immunological factors such as nutrients, vitamines and minerals, hormones, and growth factors alongside colostral IgG [88]. Because of newborn lambs bore with quite limited energy reserves, they need immediate acces to intake colostrum that have enough amount and quality [5]. Today, most of veterinarians use field-based methods in livestocks routinely which lead them to make medical desicions on newborns. There are 2 main reasons to detect PIT in practice: better diagnosis and treatment on newborns and ensure better management [24,25,88]. Immunological differences between species or breeds lead to different strategies on farm-wide or country-wide. There are immunological differences between sheep species; for instance Bighorn Sheep (Ovis canadensis) lambs are more susceptible against Mannheimia haemolytica infections than the other breeds [29]. Although there have been attempts to reduce lamb mortality in recent years (from 1970 to 2014), they have not changed significantly and it's remained at an average of 15% in many countries [16]. Gokce and Atakisi [68] have shown that neonatal losses occured mainly first week of life (84.6% rate). Eventually in the nature, newborn mortality is an inevitable case.

Major keys of PIT are colostral Ig concentration and absorbtion by the litter. In literature, it has demonstrated the role of colostral immunoglobulin concentration in passive immune transfer to newborn kids [89,90]. Gokce et al. [15] have showned that neonatal morbidity and mortality risks are higher in lambs have low birth weight than medium or high birth weight. Birth season may affect mortality rates, but in the literature some studies [76,91–93] assert season has significant affect on mortality and some studies [63,64,94] have showned birth season has insignificant affect. Influence of gender on the neonatal mortality is controversial. While some studies [95–97] have showed higher mortality in male lambs compared to female lambs, Turkson and Sualisu [63] reported higher mortality in female lambs. In a study upon Shaul breed [37], PIT wasn't effected by sex, litter size, parity and birth weight. Yenilmez et al. [78] have showed that twin born affects TP and globuline levels in blood serum, it does not affect IgG levels. Failure of PIT in lambs has a significant effect on neonatal mortality and losses due to infectious causes are positively correlated with low concentrations of serum immunoglobulins [27,28]. Lamb's serum IgG levels at post partum 24th hour are between 21.51 and 81.25 mg/mL [47]. Hunter et al. [98] reported that these concentrations could be in a range of 0 to 102 mg/mL post partum 24th hour. Increased 24th hour serum immunoglubulin levels have significant relationship with growth performance in lambs [15]. Eventually, newborn lambs should consume at least 30 g of IgG in the first 24 h post partum to ensure adequate PIT [67].

In conclusion, important of small ruminant farming has been increasing especially in developed, high-incomed countries. Thus in consideration of economical losses, management and animal welfare have importance and lead us to evaluate PIT and new strategies on that aspect. On the other hand, lambs need to utilize enough maternal IgG via colostrum as well as they consume high-quality colostrum.

Author Contributions: Conceptualization, Associate Professor Doctor Nilay SEYIDOGLU.

References

1. Kaufmann, P.; Burton, G. Anatomy and genesis of the placenta. ln: E Knobil, JD Neill (eds) *The physiology of reproduction*. **1994**.
2. Leiser, R.; Kaufmann, P. Placental structure: in a comparative aspect. *Experimental and Clinical Endocrinology & Diabetes*. **1994**, *102*(03), 122-134.
3. Wooding, F.B.P. The synepitheliochorial placenta of ruminants: binucleate cell fusions and hormone production. *Placenta*. **1992,** *13*(2), 101-113.
4. Prado, M.E.; Prado, T.M.; Payton, M.; Confer, A.W. et al. Maternally and naturally acquired antibodies to Mannheimia haemolytica and Pasteurella multocida in beef calves. *Veterinary immunology and immunopathology*. **2006,** 111.3-4, 301-307.
5. Nowak, R.; Poindron. From birth to colostrum: early steps leading to lamb survival. *Reproduction Nutrition Development*. **2006**, *46*(4), 431-446.
6. Moreno-Indias, I.; Sánchez-Macías, D.; Castro, N.; Morales-delaNuez, A.; Hernández-Castellano, L.E.; Capote, J.; Argüello, A. Chemical composition and immune status of dairy goat colostrum fractions during the first 10 h after partum. *Small Ruminant Research*. ***2012,*** *103*(2-3), 220-224.
7. Övet, C. Cytokines and growth factors in goat colostrum: a short review. Journal of Bahri Dagdas Animal Research. **2023,** 12(1), 89-97
8. García de Jalón, J.A.; De las Heras, M.; Ferrer, L.M.; Sancho, J.F. Síndrome de la boca mojada en corderos. *Medicina Veterinaria*. **1990,** *7*.
9. Barza, H.; Marinescu, M.; Blaga, L. Disorders of foals 0–10 days of age. Part I. *Revista Romana de Medicina Veterinara*. **1993**, *3*, 9-20.
10. Zohary, D.; Tchernov, E.; Horwitz, L. K. The role of unconscious selection in the domestication of sheep and goats. *Journal of Zoology*. **1998,** *245*(2), 129-135.
11. Haenlein, G.F.W. Past, present, and future perspectives of small ruminant dairy research. *Journal of dairy science*. **2001**, *84*(9), 2097-2115
12. Mellor, D.J. Integration of perinatal events, pathophysiological changes and consequences for the newborn lamb. *British Veterinary Journal.* **1998**, *144*(6), 552-569
13. Dewell, R.D.; Hungerford, L.L.; Keen, J.E.; Laegreid, W.W.; Griffin, D.D.; Rupp, G.P.; Grotelueschen, D.M. Association of neonatal serum immunoglobulin G1 concentration with health and performance in beef calves. *Journal of the American Veterinary Medical Association*. **2006**, *228*(6), 914-921
14. Yalçın, E.; Temizel, E.M. Sütten Kesme Öncesi Dönemde Oğlakların Büyüme Performansına Pasif Transfer Durumunun Etkisi. *Uludağ Üniversitesi Veteriner Fakültesi Dergisi*. **2010,** *29*(1), 23-26.
15. Gokce, E.; Atakisi, O.; Kirmizigul, A.H.; Erdogan, H.M. Risk Factors Associated with Passive Immunity, Health, Birth Weight and Growth Performance in Lambs: II. Effects of Passive Immunity and Some Risk Factors on Growth Performance During the First 12 Weeks of Life. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*. **2013a,** *19*(4).
16. dos Santos, J.D.C.; Saraiva, E.P.; Pimenta Filho, E.C.; Neta, G.C.X.; Morais, L.K.C.; Teti, H.S.; Fidelis, S.S. Risk factors for neonatal mortality in sheep farming systems in tropical semi-arid regions. *The Journal of Agricultural Science*. **2023,** 1-44.
17. Turner, J.R. Intestinal mucosal barrier function in health and disease. *Nature reviews immunology*. **2009,** *9*(11), 799-809.
18. Nordi, W.M.; Moretti, D.B.; Lima, A.L.; Pauletti, P.; Susin, I.; Machado-Neto, R. Intestinal IgG uptake by small intestine of goat kid fed goat or lyophilized bovine colostrum. *Livestock Science*. **2012,** *144*(3), 205-210.
19. Yang, Y.; Zhao, X.; Huang, D.; Wang, J.; Qi, Y.; Jiang, L.; Cheng, G. Changes in intestinal proteins induced by colostrum uptake in neonatal calves: Analysis by two-dimensional gel electrophoresis-based proteomics analysis. *Animal Production Science*. **2019,** *59*(8), 1483-1490.
20. Ciuryk, S.; Molik, E.; Kaczor, U.; Bonczar, G. Chemical composition of colostrum and milk of Polish Merino sheep lambing at different times. *Archiv fur Tierzucht*. **2004,** *47*(6; SPI), 129-134.
21. Hurley, W.L.; Theil, P.K. Perspectives on immunoglobulins in colostrum and milk. *Nutrients*. **2011,** *3*(4), 442-474.
22. Gitlin, D.; Kumate, J.; Urrusti, J.; Morales, C. The selectivity of the human placenta in the transfer of plasma proteins from mother to fetus. *The Journal of Clinical Investigation*. **1964,** *43*(10), 1938-1951.

23. Silva, S.R.; Sacarrão-Birrento, L.; Almeida, M.; Ribeiro, D.M.; Guedes, C.; Gonzalez Montana, J.R.; de Almeida, A.M. Extensive sheep and goat production: The role of novel technologies towards sustainability and animal welfare. *Animals*. 2022, *12*(7), 885.
24. Pekcan, M.; Fidanci, U. R.; Yuceer, B.; Ozbeyaz, C. Estimation of passive immunity in newborn calves with routine clinical chemistry measurements. *Ankara Üniversitesi Veteriner Fakültesi Dergisi*. **2013,** *60*(2), 85-88.
25. Elitok, B. Indicators of passive immunity failure in neonatal calves. *Oncol Res Rev*. **2018,** *1*(3), 1-2.
26. Shiels, D.; Loughrey, J.; Dwyer, C. M.; Hanrahan, K.; Mee, J.F.; Keady, T.W. A survey of farm management practices relating to the risk factors, prevalence, and causes of lamb mortality in Ireland. *Animals,*. **2021,** *12*(1), 30.
27. Sallam, A.M. Risk factors and genetic analysis of pre-weaning mortality in Barki lambs. *Livestock Science*. **2019,** *230*, 103818.
28. Ibrahim, N.H.; Badawy, M.T.; Zakzouk, I.A.; Younis, F.E. Kids' survivability as affected by their body weight, blood biochemical indices and maternal and kids' behavior in baladi and shami goats under semi-arid condition. *World's Veterinary Journal*. **2020,** *10*(1), 105-117.
29. Herndon, C.N.; Shanthalingam, S.; Knowles, D.P.; Call, D.R.; Srikumaran, S. Comparison of passively transferred antibodies in bighorn and domestic lambs reveals one factor in differential susceptibility of these species to Mannheimia haemolytica-induced pneumonia. *Clinical and Vaccine Immunology*. **2011,** *18*(7), 1133-1138.
30. Demis, C.; Aydefruhim, D.; Wondifra, Y.; Ayele, F.; Alemnew, E.; Asfaw, T. Maternal Immunoglobulin in the Serum of Newborn Lambs and Its Relation With Neonatal Mortality. *Online Journal of Animal and Feed Research*. **2020,** *10*(3), 119-124.
31. Agenbag, B.; Swinbourne, A.M.; Petrovski, K.; van Wettere, W.H. Lambs need colostrum: A review. *Livestock Science*. **2021,** *251*, 104624
32. Hernández-Castellano, L.E.; Suárez-Trujillo, A.; Martell-Jaizme, D.; Cugno, G.; Argüello, A.; Castro, N. The effect of colostrum period management on BW and immune system in lambs: from birth to weaning. *Animal*. **2015,** *9*(10), 1672-1679.
33. Wesemann, D. R., Portuguese, A. J., Meyers, R. M., Gallagher, M. P., Cluff-Jones, K., Magee, J. M.; Alt, F.W. Microbial colonization influences early B-lineage development in the gut lamina propria. *Nature*. **2013,** *501*(7465), 112-115.
34. Castro-Alonso, A.; Castro, N.; Capote, J.; Morales-delaNuez, A.; Moreno-Indias, I.; Sánchez-Macias, D.; Argüello, A. Apoptosis regulates passive immune transfer in newborn kids. *Journal of dairy science*. **2008,** *91*(5), 2086-2088.
35. Hernandez-Castellano, L.; M Almeida, A.; Castro, N.; Arguello, A. The colostrum proteome, ruminant nutrition and immunity: a review. *Current Protein and Peptide Science*. **2014a,** *15*(1), 64-74.
36. Hernández-Castellano, L.E.; Almeida, A.M.; Ventosa, M.; Coelho, A.V.; Castro, N.; Argüello, A. The effect of colostrum intake on blood plasma proteome profile in newborn lambs: low abundance proteins. *BMC Veterinary Research*, **2014b,** *10*, 1-9.
37. Brujeni, G.N.; Jani, S.S.; Alidadi, N.; Tabatabaei, S.; Sharifi, H.; Mohri, M. Passive immune transfer in fat-tailed sheep: Evaluation with different methods. *Small Ruminant Research*. **2010,** *90*(1-3), 146-149.
38. Zhu, H.L.; Zhao, X.W.; Han, R.W.; Du, Q.J.; Qi, Y.X.; Jiang, H.N.; Yang, Y.X. Changes in bacterial community and expression of genes involved in intestinal innate immunity in the jejunum of newborn lambs during the first 24 hours of life. *Journal of Dairy Science*. **2021,** *104*(8), 9263-9275.
39. Tizard, I.R. *Veterinary Immunology-E-Book*. **2017,** Elsevier Health Sciences.
40. Fischer, A.J.; Villot, C.; van Niekerk, J.K.; Yohe, T.T.; Renaud, D.L.; Steele, M.A. Invited Review: Nutritional regulation of gut function in dairy calves: From colostrum to weaning. *Applied Animal Science,*. **2019,** *35*(5), 498-510.
41. Castro, I.; Alba, C.; Aparicio, M.; Arroyo, R.; Jiménez, L.; Fernández, L.; Rodríguez, J.M. Metataxonomic and immunological analysis of milk from ewes with or without a history of mastitis. *Journal of dairy science*. **2019,** *102*(10), 9298-9311.
42. Banchero, G.E.; Milton, J.T.B.; Lindsay, D.R.; Martin, G.B.; Quintans, G. Colostrum production in ewes: a review of regulation mechanisms and of energy supply. *Animal*. **2015,** *9*(5), 831-837.
43. McGovern, F.M.; Campion, F.P.; Lott, S.; Boland, T.M. Altering ewe nutrition in late gestation: I. The impact on pre-and postpartum ewe performance. *Journal of animal science*. **2015,** *93*(10), 4860-4872.

44. Banchero, G.E.; Clariget, R.P.; Bencini, R.; Lindsay, D.R.; Milton, J.T.; Martin, G.B. Endocrine and metabolic factors involved in the effect of nutrition on the production of colostrum in female sheep. *Reproduction nutrition development*. **2006,** *46*(4), 447-460.
45. Muñoz, C.; Carson, A.F.; McCoy, M.A.; Dawson, L.E.R.; O'Connell, N.E.; Gordon, A.W. Nutritional status of adult ewes during early and mid-pregnancy. 1. Effects of plane of nutrition on ewe reproduction and offspring performance to weaning. *Animal*. **2008,** *2*(1), 52-63.
46. Viola, I.; Tizzani, P.; Perona, G.; Lussiana, C.; Mimosi, A.; Ponzio, P.; Cornale, P. Hazelnut skin in ewes' diet: Effects on colostrum immunoglobulin g and passive transfer of immunity to the lambs. *Animals*,. **2022,** *12*(22), 3220.
47. Castellaro, G.; Ochoa, I.; Borie, C.; Parraguez, V.H. Effects of Strategic Supplementation with Lupinus angustifolius and Avena sativa Grains on Colostrum Quality and Passive Immunological Transfer to Newborn Lambs. *Animals*. **2022,** *12*(22), 3159.
48. Talore, G.D. *On-farm performance evaluation of indigenous sheep and goats in Alaba, Southern Ethiopia* (PHD dissertation, Hawassa University). **2009.**
49. Taye, M.; Abebe, G.; Gizaw, S.; Lemma, S.; Mekoya, A.; Tibbo, M. Growth performances of Washera sheep under smallholder management systems in Yilmanadensa and Quarit districts, Ethiopia. *Tropical animal health and production*. **2010,** *42*, 659-667.
50. Abegaz, S.; Hegde, B.P.; Taye, M. Growth and physical body characteristics of Gumuz sheep under traditional management systems in Amhara Regional State, Ethiopia. *Livestock Research for Rural Development*,. **2011,** *23*(5), 10.
51. Gokce, E.; Atakisi, O.; Kirmizigul, A.H; Erdoğan, H.M. Risk Factors Associated with Passive Immunity, Health, Birth Weight And Growth Performance in Lambs: III. The Relationship among Passive Immunity, Birth Weight Gender, Birth Type, Parity, Dam. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*,. **2013b,** *19*(5).
52. Higaki, S.; Nagano, M.; Katagiri, S.; Takahashi, Y. Effects of parity and litter size on the energy contents and immunoglobulin G concentrations of Awassi ewe colostrum. *Turkish Journal of Veterinary & Animal Sciences*,. **2013,** 37(1), 109-112.
53. Tabatabaei, S.; Nikbakht, G.; Vatankhah, M.; Sharifi, H.; Alidadi, N. Variation in colostral immunoglobulin G concentration in fat tailed sheep and evaluation of methods for estimation of colostral immunoglobulin content. *Acta Veterinaria Brno*. **2013,** *82*(3), 271-275.
54. Sjoberg, A.; Van Saun, R.J. Use of brix refractometer in assessing sheep colostrum. In *American Association of Bovine Practitioners Conference Proceedings*. **2021,** (pp. 273-273).
55. Chniter, M.; Hammadi, M.; Khorchani, T.; Sassi, M.B.; Hamouda, M.B.; Nowak, R. Aspects of neonatal physiology have an influence on lambs' early growth and survival in prolific D'man sheep. *Small Ruminant Research*. **2013,** *111*(1-3), 162-170.
56. Chniter, M.; Salhi, I.; Harrabi, H.; Khorchani, T.; Lainé, A.L.; Nowak, R.; Hammadi, M. Physiological changes in the peri-partum period and colostral IgG transfer in prolific D'man sheep: effects of parity and litter size. *Tropical animal health and production*. **2016,** *48*, 387-394.
57. Sol Morales, M.; Palmquist, D.L.; Weiss, W.P. Milk fat composition on Holstein and Jersey cows with control or depleted copper status and fed whole soybeans or tallow. Journal of Dairy Science. **2000,** 83 (9), 2112-2119.
58. Strusińska, D.; Mierzejewska, J.; Skok, A. Concentration of mineral components β-carotene, vitamins A and E in cow colostrum and milk when using mineralvitamin supplements. Medycyna Weterynaryjna, **2004,** 60 (2), 202-206.
59. Wu, H.; Xu, C.; Wang, J.; Hu, C.; Ji, F.; Xie, J.; Lv, R. Effects of Dietary Probiotics and Acidifiers on the Production Performance, Colostrum Components, Serum Antioxidant Activity and Hormone Levels, and Gene Expression in Mammary Tissue of Lactating Sows. *Animals*. **2023,** *13*(9), 1536.
60. Burezq, H.A.; Khalil, F. Improved vaccination protocol to enhance immunity in lambs of Kuwait farms. *Iraqi Journal of Veterinary Sciences*. **2022,** *36*(2), 539-548.
61. Yapi, C.V.; Boylan, W.J.; Robinson, R.A. Factors associated with causes of preweaning lamb mortality. *Preventive Veterinary Medicine*. **1990,** *10*(1-2), 145-152.
62. Turkson, P.K. Lamb and kid mortality in village flocks in the coastal savanna zone of Ghana. *Tropical Animal Health and Production*. **2003,** *35*, 477-490.
63. Turkson, P.K.; Sualisu, M. Risk factors for lamb mortality in Sahelian sheep on a breeding station in Ghana. *Tropical Animal Health and Production*. **2005,** *37*, 49-64.

64. Mandal, A.; Prasad, H.; Kumar, A.; Roy, R.; Sharma, N. Factors associated with lamb mortalities in Muzaffarnagari sheep. *Small Ruminant Research,*. **2007,** *71*(1-3), 273-279.
65. Nash, M.L.; Hungerford, L.L.; Nash, T.G.; Zinn, G.M. Risk factors for perinatal and postnatal mortality in lambs. *Veterinary Record*. **1996,** *139*(3), 64-67.
66. Holmøy, I.H.; Kielland, C.; Stubsjøen, S.M.; Hektoen, L.; Waage, S. Housing conditions and management practices associated with neonatal lamb mortality in sheep flocks in Norway. *Preventive Veterinary Medicine,*. **2012,** *107*(3-4), 231-241.
67. Alves, A.C.; Alves, N.G.; Ascari, I.J.; Junqueira, F.B.; Coutinho, A.S.; Lima, R.R.; Abreu, L.R. Colostrum composition of Santa Inês sheep and passive transfer of immunity to lambs. *Journal of Dairy science*. **2015,** *98*(6), 3706-3716.
68. Gokce, E.; Atakisi, O. Interrelationships of serum and colostral IgG (passive immunity) with total protein concentrations and health status in lambs. Kafkas Universitesi Veteriner Fakultesi Dergisi. **2019,** 25(4), 387-396.
69. Mulvaney, F.J.; Morris, S.T.; Kenyon, P.R.; Morel, P.C.H.; West, D.M.; Vinoles, C.; Glover, K.M.M. Comparison between the reproductive performance of ewe hoggets and mature ewes following a progesterone-based oestrus synchronization protocol. *New Zealand Journal of Agricultural Research*. **2013,** *56*(4), 288-296.
70. Pain, S.J.; Loureiro, M.F.P.; Kenyon, P.R.; Blair, H.T. The effect of dam age on ewe offspring productive performance and efficiency. In *Proceedings of the New Zealand Society of Animal Production*. **2015,** (Vol. 75, pp. 239-242). New Zealand Society of Animal Production.
71. Pettigrew, E.J.; Hickson, R.E.; Blair, H.T.; Griffiths, K.J.; Ridler, A.L.; Morris, S.T.; Kenyon, P.R. Differences in lamb production between ewe lambs and mature ewes. *New Zealand Journal of Agricultural Research,*. **2021,** *64*(4), 508-521.
72. Lee, S.H.; Jaekal, J.; Bae, C.S.; Chung, B.H.; Yun, S.C.; Gwak, M.J.; Lee, D.H. Enzyme-linked immunosorbent assay, single radial immunodiffusion, and indirect methods for the detection of failure of transfer of passive immunity in dairy calves. *Journal of veterinary internal medicine*. **2008,** *22*(1), 212-218.
73. Cuttance, E.L.; Regnerus, C.; Laven, R.A. A review of diagnostic tests for diagnosing failure of transfer of passive immunity in dairy calves in New Zealand. *New Zealand veterinary journal,*. **2019,** *67*(6), 277-286.
74. Agenbag, B.; Swinbourne, A.M.; Petrovski, K.; van Wettere, W.H. Validation of a handheld refractometer to assess Merino ewe colostrum and transition milk quality. *Journal of Dairy Science,*. **2023,** *106*(2), 1394-1402.
75. Drikic, M.; Windeyer, C.; Olsen, S.; Fu, Y.; Doepel, L.; De Buck, J. Determining the IgG concentrations in bovine colostrum and calf sera with a novel enzymatic assay. *Journal of animal science and biotechnology*. **2018,** 9, 1-9.
76. Swarnkar, C.P.; Gowane, G.R.; Prince, L.L.L.; Sonawane, G.G. Risk factor analysis for neonatal lamb mortality in Malpura sheep. *Indian Journal of Animal Sciences*. **2019,** 89(6): 640–644.
77. Constantin, N.T.; Sipos, A. Passive Transfer of Immunoglobulıns from Ewe to Lamb. *Scientific Works. Series C, Veterinary Medicine*. **2021,** *67*(1).
78. Yenilmez, K.; Arslan, S.; Kılıç, S.; Atalay, H. The effect of twinship on mineral matter, immunoglobulin G and lamb birth weight in late pregnant ewes and their newborn lambs. *Van Veterinary Journal,*. **2021,** *32*(2), 62-68.
79. Abdel-Salam, Z.A.; Abdel-Salam, S.A.M.; Abdel-Mageed, I.I.; Harith, M.A. Evaluation of proteins in sheep colostrum via laser-induced breakdown spectroscopy and multivariate analysis. *Journal of advanced research,*. **2019,** *15*, 19-25.
80. Berge, A.C.; Hassid, G.; Leibovich, H.; Solomon, D.; Haines, D.M. A field trial evaluating the health and performance of lambs fed a bovine colostrum replacement. *J Anim Res Nutr*. **2018,** *Vol*, (3).
81. de Sousa, I.V.P.; Silva, C.B.; Ribeiro, C.V. Influence of the birth order on the total solids concentration of frozen colostrum from Santa Inês ewes. In *55a Reunião Anual da Sociedade Brasileira de Zootecnia, 28° Congresso Brasileiro de Zootecnia, Goiânia, Brasil*, Sociedade Brasileira de Zootecnia-SBZ, Associação Brasileira dos Zootecnistas. **2018.**
82. Torres-Rovira, L.; Pesantez-Pacheco, J.L.; Hernandez, F.; Elvira-Partida, L.; Perez-Solana, M.L.; Gonzalez-Martin, J.V.; Astiz, S. Identification of factors affecting colostrum quality of dairy Lacaune ewes assessed with the Brix refractometer. *Journal of Dairy Research,*. **2017,** *84*(4), 440-443.
83. Kessler, E.C.; Bruckmaier, R.M.; Gross, J.J. Comparative estimation of colostrum quality by Brix refractometry in bovine, caprine, and ovine colostrum. *Journal of dairy science*. **2021,** *104*(2), 2438-2444.

84. Todaro, M.; Maniaci, G.; Gannuscio, R.; Pampinella, D.; Scatassa, M.L. Chemometric Approaches to Analyse the Composition of a Ewe's Colostrum. *Animals*. **2023,** *13*(6), 983.
85. Harmon, R.S.; Senesi, G.S. Laser-induced breakdown spectroscopy–a geochemical tool for the 21st century. *Applied Geochemistry*. **2021,** *128*, 104929.
86. https://www.fao.org/publications/home/fao-flagship-publications/the-state-of-food-security-and-nutrition-in-the-world/2022/en (Accessed on 07 of June 2023).
87. Morris, S.T. Overview of sheep production systems. In *Advances in sheep welfare.* **2017,** (pp. 19-35). Woodhead Publishing.
88. Massimini, G.; Britti, D.; Peli, A.; Cinotti, S. Effect of Passive Transfer Status on Preweaning Growth Performance in Dairy Lambs. *Journal of the American Veterinary Medical Association,*. **2006,** 229, 111-115.
89. Castro, N.; Capote, J.; Alvarez, S.; Argüello, A. Effects of lyophilized colostrum and different colostrum feeding regimens on passive transfer of immunoglobulin G in Majorera goat kids. *Journal of Dairy Science*. **2005,** *88*(10), 3650-3654.
90. Rodríguez, C.; Castro, N.; Capote, J.; Morales-delaNuez, A.; Moreno-Indias, I.; Sánchez-Macías, D.; Argüello, A. Effect of colostrum immunoglobulin concentration on immunity in Majorera goat kids. *Journal of Dairy Science,*. **2009,** *92*(4), 1696-1701.
91. Mukasa-Mugerwa, E.; Lahlou-Kassi, A.; Anindo, D.; Rege, J.E.O.; Tembely, S.; Tibbo, M.; Baker, R.L. Between and within breed variation in lamb survival and the risk factors associated with major causes of mortality in indigenous Horro and Menz sheep in Ethiopia. *Small Ruminant Research*. **2000,** *37*(1-2), 1-12.
92. Tibbo, M.; Mukasa-Mugerwa, E.; Woldemeskel, M.; Rege, J.E.O. Risk factors for mortality associated with respiratory disease among Menz and Horro sheep in Ethiopia. *The veterinary journal*. **2003,** *165*(3), 276-287.
93. Berhan, A.; Van Arendonk, J. Reproductive performance and mortality rate in Menz and Horro sheep following controlled breeding in Ethiopia. *Small Ruminant Research,*. **2006,** *63*(3), 297-303.
94. Piwczyński, D.; Sitkowska, B.; Wiśniewska, E. Application of classification trees and logistic regression to determine factors responsible for lamb mortality. *Small ruminant research,*. **2012,** *103*(2-3), 225-231.
95. Vatankhah, M.; Talebi, M.A. Genetic and non-genetic factors affecting mortality in Lori-Bakhtiari lambs. *Asian-Australasian Journal of Animal Sciences*. **2009,** *22*(4), 459-464.
96. Ahmed, A.; Egwu, G.O.; Garba, H.S.; Magaji, A.A. Studies on risk factors of mortality in lambs in Sokoto, Nigeria. *Nigerian Veterinary Journal,*. **2010,** *31*(1).
97. Abdelqader, A.; Irshaid, R.; Tabbaa, M.J.; Abuajamieh, M.; Titi, H.; Al-Fataftah, A.R. Factors influencing Awassi lambs survivorship under fields conditions. *Livestock Science,*. **2017,** *199*, 1-6.
98. Hunter, A.G.; Reneau, J.K.; Williams, J.B. Factors affecting IgG concentration in day-old lambs. *Journal of Animal Science*. **1977,** *45*(5), 1146-1151.
99. Nouri, M.; Zarrin, M.; Ahmadpour, A.; Castro, N.; González-Cabrera, M.; Hernández-Castellano, L.E. Feed restriction around parturition does not affect colostrum immunoglobulin G concentration in dairy fat-tailed sheep but does affect performance and blood metabolites in newborn lambs. *Journal of Dairy Science*. **2023,** *106*(4), 2980-2988.