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Original Article

Evaluation of serum trace mineral effects on the metabolism of thyroid hormones in lambs

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Abstract

Based on genetic factors, trace minerals are essential for thyroid function and hormone metabolism. For this purpose, serum levels of thyroid hormones and some blood micronutrient concentrations in lambs were determined, compared and their relationships were investigated. A 176 lambs including 70 males under 2 months old and 106 females aged over 2 months were selected from Ghezel and Makui breeds. The 5 ml Jugular blood was prepared and the sera were evaluated for the concentrations of T3, T4, TSH, copper, iron and zinc. Thyroid hormones were determined by ELISA and trace minerals by autoanalyzer method. Mean T3 and TSH in males were higher than females and T4 in females were higher than in males but only TSH was significant. The mean serum concentrations of copper, iron and zinc in males were less than females in that only copper and zinc were significant and iron was not different. TSH in males was 36.3% higher than in females, copper and zinc in females were 12.6% and 7.3% higher than in males, respectively. The T3/T4 ratio was higher in males than in females and overall the T3/T4 ratio was low. Significant negative relationships were found between T3/TSH ($r=-0.36$) and T4/copper ($r=-0.24$) in males but not in females. Significant negative relationship was also found between TSH/T3 ($r=-0.16$) for all lambs. Significant positive relationships were presented between copper/zinc ($r=0.38$) and iron/zinc ($r=0.44$) in males, females and overall ($P<0.01$). In conclusion, the thyroid hormones and micronutrient concentrations in lambs' blood were about the standard level. The amount of thyroid hormones and trace minerals with the exception of T3, were higher in females than in males. The T3/T4 ratio was higher in males than in females. Thyroid hormones were not correlated with trace minerals in males and females except between TSH/Zn and T4/copper which were negative. There were positive and significant relationships between copper/zinc and iron/zinc in males, females and overall samples but copper/iron was not correlated. Finally, mares are predisposing to trace minerals and thyroid hormones sufficiency than females.

Keywords: T3 ‹T4 ‹TSH, Microelements, Lamb

Introduction

Copper (Cu) is considered as a trace element (Jain 1993) and is an essential cofactor for a range of enzymatic reactions (Radostits et al. 2010). It is essential for the function of nutrients such as iron (Fe) (Pop et al. 2021). Copper as a component of metalloenzyme, plays a role in tissue oxidation by complementing the cytochrome oxidase system (Dhanotiya 1999). Copper enzymes include

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ceruloplasmin, cytochrome oxidase, superoxide dismutase, tyrosinase, lysyl oxidase, dopamine beta-hydroxidase and monoamine oxidase (Radostits et al. 2010). It is absorbed in the intestine and then bound to sulfhydryl groups such as albumin and metallothionein to be transported to the liver for storage, so it is necessary in growth, production, and reproduction (Maas & Smith, 1996). Its amount in the ewes' blood must be sufficient for the growth and development of the fetus, otherwise reproductive, congenital and neurological disorders will be occurred (Ayub et al 2013). The most prominent symptoms of Cu deficiency in lambs are enzootic ataxia and cerebral-spinal disorders (Barlow, 1991), so Cu supplements eliminate the deficiency soon (Aliarabi et al 2018, Hasan et al 2019). It has variable relationships with elements such as positive relationship with Fe and negative correlation with Zn and with thyroid hormones as well (Abdel-Mageed et al. 1990). In one study, Cu-deficient ewes showed low levels of Cu and T4 but normal T3, probably means a positive relationship between Cu and T4, so Cu deficiency is associated with T4 deficient ewes (Abd Elghany et al 2017). Pop et al. (2021) and Jain et al. (2014) reported a positive correlation between Cu and thyroid hormones in women. Finally, Fe and Cu are vital for the synthesis of thyroid hormones (Knezevic et al 2020), so Cu evaluation is important in determining the thyroid hormones situation.

Zinc as a metalloenzyme thymidine kinase is an essential micronutrient in growth, production and reproduction (Radostits et al 2010). It is important for energy production through carbohydrate metabolism, protein synthesis for growth and reproduction, enhancing the immune system and cell membrane resistance to microorganism as an antioxidant (Sikiru 2016). It is involved in regulating diodinase activity, thyroid-releasing hormone, and TSH (thyrotrophin) synthesis (Pop et al. 2021). Zinc acts as an inhibitor or cofactor of diodinase enzymes (Severo et al 2019). It also acts as a cofactor for dehydration reactions that convert T4 to T3 (Beserra et al. 2021). Zinc deficiency causes thyroid atrophy, decreased T3 and T4 concentrations, and systemic effects (Gupta et al. 1997). Zinc consumption increases up to 50% in pregnant ewes due to fetus growth, so its decrease is high in last the months of pregnancy and in lambs as well (Lucian et al. 2010). Zinc in forage is hardly hydrolyzed by enzymes in the intestines, so Zn deficiency will occur in ewes in the lack of Zn supplementation (Sikiru 2016). Zinc deficiency is accompanied by increased hematocrit, progesterone changes, decreased immune competition, abnormal platelets and bleeding, and finally, fetal growth retardation (Lucian et al. 2010).

Thyroid hormones including triiodothyronine (T3) and thyroxine (T4) affect the predominant activity of body cells and their role is considered important in terms of cell function and body systems (Sampaio et al. 2021). Thyroid hormones are involved in regulating energy consumption, RNA synthesis, cell oxygen consumption, the body's overall metabolism, and the growth and development of the nervous system. Therefore, the major role of T3 and T4 is vital in maintaining growth and especially milk production, so determining their values will lead the metabolism and nutritional status in animals (Todini et al, 2007). Decreased T3 leads to stimulation of the hypothalamic-pituitary axis to secrete thyroid stimulating hormone (TSH) (Severo et al. 2019), which is also one of the evaluation criteria for thyroid hormones. Iodine is a key in the structure of these hormones and its deficiency (hypothyroidism) in ewes is associated with poor wool growth, milk and weight loss, reproductive system disorder (Schmoelzl and Cowley 2015), decreased sexual activity of rams, abortion and weak births with signs of goiter and increased susceptibility to infections (Sipos et al. 2004), which are also seen in Cu and Zn deficiencies.

The results of genetic factors show that trace minerals such as Cu and Zn are essential for thyroid activity and hormone metabolism (Knezevic et al 2020) as well as some metals have pathogenic effects on the thyroid (Rasic et al 2017). Since Cu and Zn deficiencies have similar signs to hypothyroid hormone depletion in lambs (Kaneko et al. 2008), Secondly, the possibility of micronutrients and thyroid hormones deficiencies is high in lambs due to rapid growth and insufficient nutrition, and thirdly, determining the mutual effect of micronutrients in the metabolism of thyroid hormones and their interrelationships which requires to evaluate their concentration in order to provides the necessities of disease prevention.The results could improve the breeding of small ruminants. The objectives were: 1- To determine and comparison of the serum level of T3, T4, TSH and their ratio in male and female lambs. 2- To determine serum concentrations of Cu, Fe and Zn between genders and 3- To determine the relationships among thyroid hormones and micronutrient indices in lambs.

Matrial and Methods

Animals

The number of 176 lambs including 70 males under 2 months old and 106 females aged over 2 months were selected from Ghezel and Makui ewes' breeds. Ewes had free grazing on pasture consisted of legume and cereal forage without concentrate feeding. The suckling male lambs received milk from ewes twice in the morning and evening. Lambs were clinically healthy and did not have a disease problem. Five ml jugular blood was prepared by syringe from lambs and were transferred to the test tube. After collection, samples were centrifuged at 3000 rpm for 10 minutes to separate the sera and then were frozen in -20 C° for laboratory evaluations.

Tyroid hormones evaluation

T3, T4 and TSH were evaluated by ELISA (Monobind, USA) based on competitive hormone response and hormone-enzyme conjugation to bind to a limited number of anti-hormone monoclonal antibodies. The rate of light absorption of standard samples and sera tested was determined using ELISA Reader (Agilent BioTek 800 TS Absorbance Reade, USA) and calibration curve in terms of nmmol/l. for T3 and T4 hormones and mIU/ml for TSH.

Monobind T3 kit (Product Code 175-300) has a sensitivity of 0.061 nmol/liter and a measurable range of 0.078 to 5 nmol/liter. The coefficient of variation of Inter-assay is 5.52% and Intra-assay is 9.5%.

Monobind T4 kit (Product Code 225-300) has a sensitivity of 0.29 nmol/liter and a measurable range of 0.05 to 12 nmol/liter. The coefficient of variation of Inter-assay is 7% and Intra-assay is 11.2% Trace mineral evaluation.

Monobind TSH kit (Product Code 325-300) has a sensitivity of 0.078 microunits per milliliter and a measurable range of 0.1 to 45 microunits per milliliter. The coefficient of variation of Interassay is 8% and Intraassay is 4%.

According to the manufacturer's instructions, these kits are usable to measure either human or animals such as sheep thyroid hormones.

Concentration of Cu (Byrex Fars Company, Shiraz - Iran, product code BXC0341), Fe (Byrex Fars Company, Shiraz - Iran, product code BXC0232) and Zn (Byrex Fars Company, Shiraz - Iran, product code BXC0462) were determined by Autoanalyzer (Technicon, RA-1000, USA) were measured using the relevant commercial kits of Pars Azmoun, Iran in specific wavelengths. Results were determined in mg/dl.

Statistical analysis method

SPSS23 software program was appropriate to analyze the data. At first, data were tested to their normal distribution using Colmograph, then Case Summaries were used to determine mean, standard deviation, standard error, and range of serum thyroid and micronutrient values. T-test was used to compare the mean of serum thyroid indices and trace minerals in males and females. Chi-square test was applied to determine the significant difference between the ratios of thyroid hormones (T3:T4) in lambs. A value of P less than 0.05 was considered as a significant difference. Pearson correlation test was performed to determine the relationship between serum thyroid indices and micronutrients separately in each group of genders and then in overall data. The results were plotted and interpreted as Tables and Figures for groups of thyroid and trace mineral indices.

Results

The concentration of thyroid hormones and trace minerals in males, females and overall was shown in Table 1. Mean T3 and TSH of males were higher than in females and T4 of females were higher than males but only TSH was significant between gender (P <0.01). The mean serum concentrations of Cu, Fe and Zn in males were lower than in females. Comparison of mean micronutrients showed that Cu and Zn were significantly (P <0.01) less in males than in females but Fe was not different. According to Fig. 1 TSH levels in males were 36.3% higher than in females, Cu and Zn in females were 12.6% and 7.3% higher than in males, respectively (Fig. 2). The ratio of T3:T4 in males was 0.81, for females was 0.66 and overall was 0.71 (Table 2). The above ratio was higher in males than in females, which was not significant on the basis of Student t-test analysis (Fig. 3).

Pearson correlation analysis between thyroid indices and micronutrients showed a significant negative relationship between T3/TSH (r=-0.36) and T4/Cu (r=-0.24) in males but not in females. Overall, significant negative relationship was found between TSH/T3 (r=-0.16). There was a positive and significant relationship between Cu/Zn (r=0.38), Fe/Zn (r=0.44) in males, females and in all samples (P<0.01) but Cu and Fe were not related (Table 3).

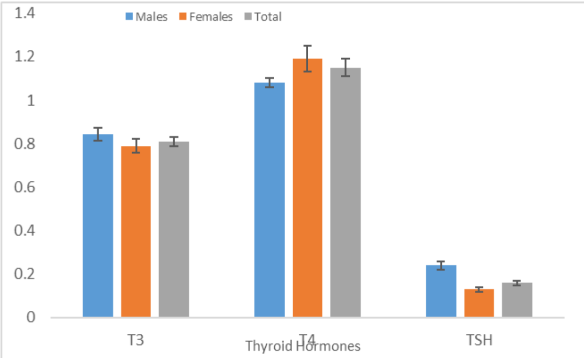

Fig.1: Comparison of mean±SET3, T4 (nmol/l) and TSH (mIU/ml) concentrations in males, females and total lambs' sera

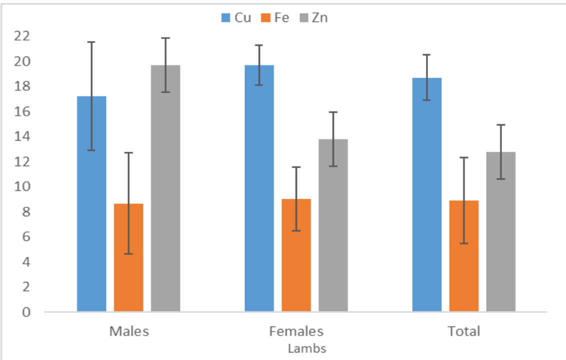

Fig.2: Comparison of mean±SE copper, iron and zinc concentrations (μg/dl) in males, Females and total lambs' sera

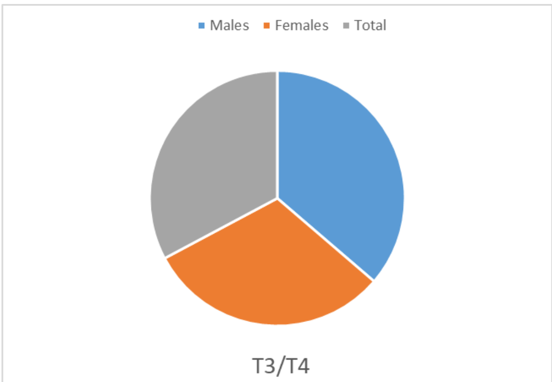

Fig.3: Comparison of serum T3:T4 ratio (nmol/l) in males, females and total lambs

Table 1: Concentrations of serum thyroid hormones and trace minerals in males, females and total lambs

Parameters	Mean	Standard Error	Standard Deviation	Minimum	Maximun
Male lambs (n=70)					
T3[1]	0.842	0.03	026	0.14	1.85
T4[1]	1.08	0.02	0.20	0.57	1.48
TSH[2]	0204	0.02	0.16	0.05	096
Copper[3]	172. 2	4.30	35.9	89.1	290.0
Iron[3]	86.81	1.61	13.4	58.8	142.0
Zinc[3]	115.4	1.81	15.12	89.4	154.0
Female lambs (n=106)					
T3	0.79	0.03	023	0.22	1.48
T4	1.19	0.06	0.57	0.21	2.57
TSH	013	0.01	0.08	0.01	0.56
Copper	197.1	5.34	54.9	83.1	460.0
Iron	90.5	2.53	26.1	35.7	239.0
Zinc	137.7	3.45	35.6	30.2	228.0
Total lambs (n=176)					
T3	0.81	0.02	024	0.14	1.85
T4	1.15	0.04	0.46	0.21	2.75
TSH	016	0.01	0.13	0.01	0.96
Copper	187.1	3.75	49.7	83.1	460.0
Iron	89.1	1.65	21.9	35.7	239.0
Zinc	127.6	2.32	30.8	30.2	228.0

[1] =nml/l [2] -mIU/ml [3] -g/dlμ

Table 2: Mean comparison of T3:T4 ratio (nmol/l) between male and female lambs

Parameters	Male lambs	Female lambs	Total lambs
T3:t4 Ratio	0.80	0.66	0.71
T3:TSH " " " "	4.13	6.10	5.10
T4: TSH " " " "	5.3	9.2	7.2

Table 3: Correlations among serum thyroid hormones and trace minerals in males, females and total lambs

Parameters	T4	TSH	Copper	Iron	Zinc[3]
					Male lambs (n=70)
T3[1]	0.09	-0.36**	-0.11	0.03	0.05
T4[1]		0.15	-0.24*	0.12	-0.19
TSH[2]			0.04	-0.1	-0.15
Copper[3]				-0.06	0.38**
Iron[3]					0.44**
					Female lambs (n=106)
T3	-0.09	-0.03	0.09	-0.01	-0.07
T4		-0.13	-0.11	-0.03	-0.10
TSH			0.14	-0.16	-0.12
Copper				0.04	0.22*
Iron					0.74**
					Total lambs (n=176)
T3	-0.06	-0.16*	-0.01	-0.02	0.03
T4		-0.06	-0.07	-0.04	-0.06
TSH			-0.12	-0.13	-0.19*
Copper				0.04	0.30*
Iron					0.69**

[1] =nml/l [2] -mIU/ml [3] -g/dlμ P<0.05*= P<0.01**=

Discussion

The mean concentration of thyroid hormones in lambs of this study was about normal. The amount of T3 and T4 reported by Kozat (2007) were 2.76 and 0.79, in pregnant ewes were 0.85 and 64.9 (Novoselec et al 2017) and in pregnant and lactating goats were 1.38 and 78.4 nmol/l, respectively (Raoofi et al. 2017), indicates that the concentrations are varies between breeds and age of animals. Thyroid hormones, especially T3, play an important role in the body's metabolism. T3 and T4 affect by TSH, which is secreted by the pituitary gland (Guyton and Hall, 2006). The functions of mentioned hormones are almost the same, T3 in blood and fluids and T4 in the thyroid gland is high, but in terms of speed and intensity of action, T3 is stronger than T4 and stays in the blood for a shorter time. Iodine and selenium (Se) are essential for the synthesis and metabolism of thyroid hormones in converting T4 to T3 (Knezevic et al 2020). Blood Cu and Se levels directly affect thyroid activity (Rasic et al. 2017; Pop et al. 2021). Ruminant feeding in pastures is generally associated with a deficiency of Cu, iodine and Se, which affect the activity of thyroid hormones (Hasan et al. 2019). Therefore, administration of trace minerals as oral, injection, slow release, mineral fertilizers and mineral water in the breeding of small ruminants is inevitable (Grace et al. 2012). In order to balance the regulation of thyroid activity, a definitive level of Cu, Zn, iodine, and Se is necessary (Lopez et al. 2013; Knezevic et al. 2020). Researchers acknowledged that iodine (thyroid indices) and Se are essential for the survival and growth of lambs (Schmoelzl and Cowley 2015). In spite of the macro and trace minerals could affect thyroid hormones, the activity of T3 and T4 also contribute to a variety of factors including pregnancy (Abdollahi et al. 2013), parturition, lactation (Khaled and Illek 2012) and poisoning (Badiei et al 2010), while Nazifi et al. (2010) did not show daily changes in thyroid hormones following consecutive days of sampling.

In this study, the mean T3 of males was higher than in females and the T4 of females was higher than in males, which was not significant, and could indicate a long conversion of T4 to T3 in females or high consumption of T3 in females. Overall, about 93% of thyroid hormones is T4 and the rest is T3. However, all T4 is eventually converted to T3 by deiodinases in tissues, so both T3 and T4 are functionally important (Hall et al. 2017). T4 is a growth factor in lambs and basically, the growth of males is higher than in females (Ramin 1995), which in this study may be the reason for high T3 consumption. Keles et al. (2006) consider thyroid hormone deficiency as the most important factor in delaying calf growth. Since Cu and Se deficiency have been reported in lambs (Kozat 2007), this can directly affect thyroid activity and reduces T3 in the long run (Rasic et al. 2017). Therefore, the low level of T4 in males is probably due to its rapid conversion to T3 for consumption in male growth. However, the difference between these hormones was not significant (Sampaio et al. 2021). According to the results of this study, TSH was significantly higher in males than in females. TSH regulates the activity of T3 and T4, which is released by TRH (Sampaio et al. 2021). TSH is directly inhibited by T4 and stimulated and increased by T3, so a 36.3% increases in TSH may be in response to a slight decrease in T3 in males or, conversely, a decrease in TSH is a reflection of a high T4 in lambs (Article Severo et al. 2019). TSH has been reported to increase by several times in trace minerals deficiencies such as Se, following by decline T3 and enhance T4 (Dalir-Naghadeh et al. 2008). Therefore, supplementation of Se or NanoSe will increase the concentration of thyroid hormones (Rezaeian and Sadeghi, 2017), although some have suggested the opposite explanation (Thomson et al. 2009). However, in Se deficiency, the T3:T4 ratio decreases, meaning that the males of this study are more likely to have Se deficiency (Abd Elghany et al. 2017).

In this study, the T3:T4 ratio in males (0.78) was not significantly higher than in females (0.67) and in all lambs (0.70), which were higher than the findings of Kozat (2007) for lambs (0.35), Novoselec et al. (2017) in pregnant and lactating ewes (0.0125). Determination of T3:T4 ratio is a functional indicator of Se status in human (Pop et al. 2021). The conversion of T4 to T3 can be assessed by monitoring the ratio of T3:T4 in the blood. Progressive reduction of this ratio in human with Se supplementation can be reversed (Pop et al. 2021). The relatively low ratio of T3:T4 in females means that the conversion of T4 to T3 is low, and therefore, the amount of T4 in the blood of females will be higher than in males (Table 1). Konecny et al. (2015), Novoselec et al. (2017) and Kivanç et al. (2021) improved the above ratio in pregnant and lambing ewes by administration of Se.

The mean serum Cu concentration in lambs was in the standard range of 10.2-31.3 µg/l (Silva et al 2018) but was lower in males than in females. The reason is related to the growth difference between genders, in which male grow is high, fast and need more Cu (Ramin 1995). The role of Cu and its metalloenzyme, including cytochrome oxidase, is the most important Cu antioxidants that is vital and essential in lambs' life (Sharifi et al 2017). Therefore, its primary reduction will be associated with enzootic ataxia and pregnancy toxemia (Radostits et al. 2010). Serum Cu cooperates closely with Fe (Jain 2014) and is considered important in males in terms of meat quality and in females in terms of growth, milk production and reproduction (Ayub et al 2013). Copper together with T4 is the most important factor in growth retardation in lambs (Keels et al 2006, Pop et al 2021). Copper with Se is directly involved in thyroid activity (Rasic et al. 2017). Blasig et al. (2016) showed that serum Cu was affected by thyroid hormones in lambs so that hypothyroid in newborns were at risk for Cu deficiency. Nazifi et al. (2009) showed that serum Cu and thyroid hormones were not different in consecutive sampling, have shown a stable status and did not have a competitive effect between them. Abdollahi et al. (2013) reported that thyroid hormones and Cu levels decrease simultaneously during pregnancy, so that T4 and Cu were low in twin pregnancy and T3 and Cu were low in pregnancy with one lamb (et al 2013). These findings indicate that the combined effect of Cu and thyroid hormones need to evaluate in both lambs and ewes. The results reported by scientists on Cu-deficient rats show a decrease in iodine metabolism in the production of thyroid hormones and its accumulation in body tissues. In addition, their results showed that Cu deficiency can has both direct effect on the metabolic process and indirectly disrupt iodine metabolism and severely reduces the production of iodine-binding protein by the thyroid gland (Nazifi et al. 2008).

The mean serum Fe concentration in this study was higher than the normal range of 3.46-3.75µg/l (Silva et al 2018), which was in the optimal range. Iron levels were not different between genders and were consistent with the findings of Silva et al. (2018). It is one of the effective trace minerals in hematopoiesis and has a positive and negative relationships with Cu and Zn, respectively (Abdel-Mageed et al. 1990), while in this study they were positive. Iron and Cu are vital for the synthesis of thyroid hormones (Knezevic et al 2020) and their deficiencies are related with anemia and decreased physiological activity of lambs (Hasan et al 2019). In this study, Fe showed no effect on tyroid hormones activity. Ferritin and homosiderin are the Fe storage compounds (Cihan et al. 2016). In addition to severe anemia, low levels of these minerals are associated with other complications (Radostits et al. 2010). It is frequently affected by pregnancy, parturition, lactation, and its significant reduction has been reported in bleeding and postpartum infections (Abdollahi et al. 2013). The role of Fe in thyroid hormones is unclear and there is no report of their interaction or coordination (Nazifi et al 2009, Abdollahi et al 2013).

The average Zn serum concentration of lambs was in the standard range of 12.3-18.5 µg/l (Silva et al 2018) and was optimal for lambs of this study. Males showed none significantly lower Zn than in females, which is consistent with the results of Silva et al. (2018). It is one of the micronutrients active in protein synthesis, carbohydrate metabolism and many biochemical reactions, its deficiency is associated with skin disorders, low growth, production and reproduction performances (Radostits et al 2010). Zinc deficiency has been reported following pregnancy toxemia, lambing and subclinical ketosis due to decreased appetite, fetal needs, colostrum and milk production (Amouoghli et al. 2011). Decreased co-occurrence of Zn and Cu is related with effects on production, reproduction and increased oxidative stress (Saeed et al 2019, Pop et al 2021). The effect of Zn deficiency on BHB metabolism is due to impaired insulin secretion (Sadegzadeh-Sadat et al 2021). Zinc and thyroid hormones cause neonatal growth retardation (Keles et al. 2006). The levels of Zn and thyroid hormones did not differ between the sampling times, their values were not constant and affected by each other (Nazifi et al 2009), the same as found in this study except for TSH which had a negative effect. Thyroid hormones and Zn levels are affected by pregnancy (Abdollahi et al. 2013), parturition, and lactation (Khaled and Illek 2012). Zinc and Cu are closely related to the secretion of T4 and TSH (Pop et al. 2021). It plays an important role in the conversion of T4 to T3 (Knezevic et al 2020). Sampaio et al. 2021 reported that in Zn-deficient ewes, T3 and T4 were low, meaning that Zn is directly related to thyroid hormones (et al. 2021) while not in this study. In contrast to the above findings, Kececi et al. (2002) reported that Zn supplementation reduces thyroid hormones. Zinc may contrast with Cu, reducing one may cause an increases over another (Abdel-Mageed et al. 1990) while it was positive in this study. Thus, these results emphasize on the use of Zn supplements in food to coordinates with thyroid hormones (Sikiru 2016).

It was predictable to observe a negative relationship between T3 and TSH in males because TSH will increase when T3 decreases in the body (Sampaio et al. 2021), but the lack of such a relationship in females cannot be interpreted, but however, for the overall lambs such a negative relationship is still partially exists with the reduction of coefficient from 0.36 to 0.16, which indicates the effectiveness of females in this correlation. The lack of relationships among the thyroid hormones reveals that T3, T4 and TSH playing a direct function in the body. The existence of a negative relationship between T4/Cu contradicts the positively reported results of Abd-Elghany et al. (2017). Also, the negative relationship between TSH/Zn is not consistent with the positive results of Jain (2014), Pop et al. (2021) and Sampaio et al. (2021). One of the reasons for this difference is that their study was in adult animals and human, while the males of this study were less than 2 months old. Similar results of this study were reported by Blasig et al. (2016) in ewes. Tajik et al. (2010) also reported a positive relationship between tyroid hormones in buffalo and Nazifi et al. (2010) showed no association at all. In this study, no effect or relationship was observed between thyroid hormones and Fe, which can be considered as two different parameters. The positive relationship between Cu/Zn and Fe/Zn in lambs of study is in contradiction with the findings of Abdel-Mageed et al. (1990) who reported a negative relationship among them. In any way, the positive relationship between trace minerals in this study indicates the coordination and support of each other in the physiological activity of the body.

In conclusion, the activity of thyroid hormones and trace minerals in lambs was in the desired range and no deficiencies were expected. T3 level was higher in males and T4 in females but were not significant. TSH in males was significantly higher than in females. The concentrations of Cu and Zn in males were significantly lower than in females, but Fe did not differ. The T3/T4 ratio was not significantly higher in males than in females. Significant negative relationships were found between T3/TSH, T4/Cu and T4/Zn in males but not in females. Overall, significant negative relationship was recorded between TSH/T3. Significant positive relationships were demonstrated between Cu/Zn and Fe/Zn in males, females and overall but not between Cu/Fe. Finally, males probably need more trace minerals concentrations and eventually more thyroid hormones than in females.

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Conflict of interest

The authors declare that there is no conflict of interest.

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References

Abd Elghany, H.; El-khaiat, H.M. & Mahmoud, H.A.Y. (2017). Influence of Experimentally Induced Secondary Copper Deficiency on the Serum Levels of Selenium, Thyroid Hormone and Glutathione Peroxidase in Ossimi Sheep. *Alexandria Journal for Veterinary Sciences*, 52(1): 52-56.

Abdel-Mageed, A.B. and Oehme, F.W. (1990). A review of the biochemical roles, toxicity and interactions of zinc, copper and iron: I. Zinc. *Veterinary and Human Toxicology*, 32(1):34-39.

Abdollahi E.; Kohram, H. and Shahir, M.H. (2013). Plasma concentrations of essential trace microminerals and thyroid hormones during single or twin pregnancies in fat-tailed ewes. *Small Ruminant Research*, 13: 360–364.

Aliarabi, H.; Fadayifar, A.; Alimohamady, R. and Dezfoulian, A.H. (2018). The Effect of Maternal Supplementation of Zinc, Selenium, and Cobalt as Slow-Release Ruminal Bolus in Late Pregnancy on Some Blood Metabolites and Performance of ewes and Their Lambs. *Biological Trace Element Research*, 187: 403–410.

Amouoghli Tabrizi, B.; Hasanpour, A.; Mousavi, G; & Hajialilou, H. (2011). Evaluation of Serum Levels of Copper in Holstein Cows and Their Calves During Colostrum Nourishing Middle-*East Journal of Scientific Research*, 7 (5): 712-714.

Ayub, M.; Zuber, M.; Yousaf, M.; Zahoor, A.F.; Iqbal Khan, Z.; Ahmad, K. & Mansha, M. (2013). Assessment of copper intensity in selected tissues of two different classes of ruminants in Punjab, *Pakistan. African Journal of Pharmacy and Pharmacology*, 7: 1396-1403.

Badiei, K.; Mostaghni, K.; Nikghadam, P. & Poorjafar, M. (2010). The effect of mercury on thyroid function in sheep. *Iranian Journal of Veterinary Medicine*, 4: 34-39.

Barlow, R.M. (1991). Swayback, In: Diseases of sheep W.B. Martin & I.D. Aitken, (Eds), 2nd Edn., PP.:178-81 (Blackwell Scientific Publications, London).

Beserra, J.B.; Morais, J.B.S.; Severo, J.S.; Cruz, K.J.C.; Oliveira, A.R.S.; Henriques, G.S. & Nascimento Marreiro, D. (2021). Relation Between Zinc and Thyroid Hormones in Humans: A Systematic Review. *Biological Trace Element Research*, 199: 4092–4100.

Blasig, S.; Kühnen, P.; Schuette, A.; Blankenstein, O.; Mittag, J. & Schomburg, L. (2016). Positive correlation of thyroid hormones and serum copper in children with congenital hypothyroidism. *Journal of Trace Elements in Medicine and Biology*, 37: 90-95.

Cihan, H.; Temizel, E.M.; Yilmaz, Z. & Ozarda, Y. (2016). Serum Iron Status and Its Relation with Haematological Indexes Before and After Parturition in Sheep. *Kafkas University Veterinary Fak Derg*, 22 (5): 679-683.

Dalir-Naghadeh, B, & Asri-Rezaei, S. (2008). Assessment of serum thyroid hormone concentrations in lambs with selenium deficiency myopathy. *American Journal of Veterinary Research*,. 69: 659-663.

Dhanotiya, R.S. (1999). *Textbook of Veterinary Biochemistry*. S New Delhi: Jaypee Brothers Medical publishers. pp. 235-252.

Grace ND and Knowles SO, 2012. Trace Element Supplementation of Livestock in New Zealand: Meeting the Challenges of Free-Range Grazing Systems. *Veterinary Medicine International*, 41-49.

Gupta, R.P.; Verma, P.C. & Garg, S.L. (1997). Effect of experimental zinc deficiency on thyroid gland in guinea-pigs. *Annals of nutrition and metabolism*, 41: 376–381.

Guyton, A.C. & Hall, J.E. (2006). Textbook of Medical Physiology. *Elsevier Saunders*. pp: 94-99.

Hall, J.E.; Guyton, A.C. (2017). Guyton & Hall Tratado de Fisiologia Médica, 13rd Edn; GEN Guanabara Koogan: Rio de Janeiro, Brasil, 2017.

Hasan Jassim, A.S.T. & Bedawi, A.A. (2019). The effect of different concentrations of copper sulfate on the some physiological and immunological parameters of local male rabbits. *Drug Invention Today*, 12(11): 2654-2657.

Jain, N.C. (1993). Essentials of veterinary Hematology,., PP. :215,254-55 (Lea &Febiger, Philadelphia).

Kaneko, J.J. ; Harvey, J.W. & Brass, M.L. (2008). Clinical biochemistry of Domestic animals, London: Elsevier pub., 669-676, 686-689.

Kececi, T. & Keskin, E. (2002). Zinc supplementation small ruminants. *Acta Veterinaria Hungaria*, 50: 93-100.

Keles, I.; Donmez, N.; Altug, N. & Ceylan, E. (2006). Serum Zinc, Copper and Thyroid Hormone Concentrations in Heifers with Retarded Growth. *Veterinary Fakultacie Derg*, 17:103-105

Khaled, N.F. & Illek, J. (2012). Changes in Selected Blood Minerals, Vitamins and Thyroid Hormones in Barky Ewes during Late Pregnancy, Post-Partum and Early Lactation. *Journal of Applied Biological Sciences.* 6: 5-8.

Knezevic, J.; Starchl, C.; Tmava Berisha, A. & Amrein, K. (2020). Thyroid-Gut-Axis: How Does the Microbiota Influence. *Thyroid Function Nutrients*, 12: 1769 1776.

Konečný, P.; Hasoňová, G.; Trávníček, J. & Samková, E. (2015). Effect of organic selenium and ıodine supplementation on selenium and thyroid hormones status of lactating ewes and lambs. *Acta Veterinaria Beograd*, 65 (4): 477-487.

Kozat, S. (2007). Serum T3 and T4 Concentrations in Lambs with Nutritional Myodegeneration. *Journal Veteterinary International Medicine*, 21:1135–1137.

Lopez-Andre, P.; Luciano, G.; Vasta, V.; Gibson, T.M.; Biondi L. et al, (2013). Dietary quebracho tannins are not absorbed, but increase the antioxidant capacity of liver and plasma in sheep. *British Journal of Nutrition*, 110, 632–639.

Luciano, I.J.; Vasta, V.; Monahan, F.J.; López-Andrés, P.; Biond, L.; et al , (2011). Antioxidant status, colour stability and myoglobin resistance to oxidation of longissimus dorsi muscle from lambs fed a tannin-containing diet. *Food Chemistry*, 124: 1036-1042.

Maas, J. & Smith, B.P. (1996). Copper deficieny in ruminants, In: Large Animal Internal Medicine, B.P. Smith (Ed)., 2ndEdn., PP.: 904-908 (Mosby Company, USA).

Nazifi, S.; Mansourian, M.; Nikahval, B. & Razavi, S.M. (2009). The relationship between serum level of thyroid hormones, trace elements and antioxidant enzymes in dromedary camel (Camelus dromedarius). *Tropical Animal Health and Production*, 41: 129-134

Nazifi, S.; Shahriari, A. & Nazemian, N. (2010). Relationships between thyroid hormones, serum trace elements and erythrocyte antioxidant enzymes in goats. *Pakestan Veterinary Journal*, 30(3): 135-138.

Novoselec, J.; Šperanda, M.; Klir, Z.l Mioč, B.; Steiner, Z. & Antunović, Z. (2017). Blood biochemical indicators and concentration of thyroid hormones in heavily pregnant and lactating ewes depending on selenium supplementation. *Acta Veterinaria Brno*, 86: 353–363.

Pop, V.; Krabbe, J.; Maret, W. & Rayman, M. (2021). Plasma mineral (selenium, zinc or copper) concentrations in the general pregnant population, adjusted for supplement intake, in relation to thyroid function. *British Journal Nutrition*, 125: 71–78.

Radostits, O.M. et al., (2010). Urolithiasis in ruminants. Veterinary Medicine: a textbook of the diseases of cattle, horses, sheep, pigs, and goats. 10th ed. *WB Saunders, Philadelphia*, pp.565-570.

Ramin, A.G. (1995). Physiological Response test and blood profiles in dairy calves and their relationship to growth rates and health parameters. Thesis, University of Queensland, Australia.

Raoofi, A.; Yourdkhani, S. & Bokaie, S. (2017). Comparison of serum triiodothyronine, tetraiodothyronine and thyroid stimulating hormone concentrations in pregnant and lactating Beetal-cross and native goats in Garmsar township. *Iranian Journal Veterinary Medicine*, 11(3): 243-248.

Rasic-Milutinovic, Z.; Jovanovic, D.; Bogdanovic, G.; Trifunovic, J. & Mutic, J. (2017). Potential Influence of Selenium, Copper, Zinc and Cadmium on L-Thyroxine Substitution in Patients with Hashimoto Thyroiditis and Hypothyroidism. *Experimental Clinical Endocrinology Diabetes*, 125(02): 79-85.

Rezaeian-Tabrizi, M. & Sadeghi, A.A. (2017). Plasma antioxidant capacity, sexual and thyroid hormones levels, sperm quantity and quality parameters in stressed male rats received nano-particle of selenium. *Asian Pacific Journal of Reproduction*, 6(1): 29-34.

Sadegzadeh-Sadat, M., Anassori, E.; Khalilvandi-Behroozy, H. & Asri-Rezaei, S. (2021). The effects of Zinc-Methionine on glucose metabolism and insulin resistance during late pregnancy in ewes. *Domestic Animal Endocrinology*, 77, 106647

Saeed, O.A.; Sazili, A.Q.; Akit, H.; Alimon, A.R. & Samsudin, A.A. (2019). Effects of Corn Supplementation into PKC-Urea Treated Rice Straw Basal Diet on Hematological, Biochemical Indices and Serum Mineral Level in Lambs. *Animals*, 9: 781, doi:10.3390/ani9100781

Sampaio, R.A.G.; Riet-Correa, F.; Barbosa, F.M.S.; Gois, D.D.; Lima, R.C.; da Silva I.G. et al (2021). Diffuse Alopecia and Thyroid Atrophy in Sheep, *Animals*, 11(12), 3530.

Schmoelzl, S. & Cowley, F. (2015). The case for pre-parturient selenium and iodine supplementation of ewes for improving lamb survival. *Animal Production Science*, 56(8): 1263-1274.

Severo, J.S.; Morais, J.B.S.; de Freitas, T.E.C.; Andrade, A.L.P.; Feitosa, M.M.; Fontenelle, L.C. (2019). The role of zinc in thyroid hormones metabolism. *International Journal Vitamin Nutritional Research*, 89: 1–9.

Sharifi, R.S.; Sofla, S.S. & Seyedabadi, H.R. (2017). Genetic Diversity and Molecular Phylogeny of Iranian Goats Based on Cytochrome Oxidase I (COXI) Gene Sequences. *Jurnal Veteriner*, 18(4): 565-570.

Sikiru, A.B. (2016). A Review of Zinc Nutrition on Extensive Rangeland. *Jounal Animal Science Advances*, 6: 1737-1743.

Silva, T.R.; Soares, P.C.; Dantas, A.F.; Marques, A.V.; Oliveira Filho, E.F. (2018). Serum and liver copper, iron, molybdenum and zinc concentration in goats and sheep in the state of Paraíba, Brazil. *Pesquisa Veterinária Brazil*, 38: 1313–1316.

Sipos, W.; Miller, I.; Fountoulakis, M.; Schmoll, F.; Patzl M.; Schwendenwein, I. et al, (2004). Hypothyroid Goitre in a Ram: Chemical Analysis gives Indirect Evidence for a Structurally Altered Type of Ovine Thyroglobulin. *Journal of Veterinary Medicine Series A*, 51(2): 90-96.

Tajik, J.; Nazifi, S.; Izadneshan, M. & Naghib, M. (2010). Evaluation of Trace Elements Serum Concentrations and Their Correlation Together, and with Thyroid Hormones in Water Buffalo (Bulbalus bulbalis). *Australian Journal of Basic and Applied Sciences*, 4: 3955-3958.

Thomson, C.D.; Campbell, J.M.; Miller, J.; Skeaff, S.A.; Livingstone, V. (2009). Selenium and iodine supplementation: effect on thyroid function of older New Zealanders. *American Journal Clinical Nutrition*, 90: 1038–1046.

Todini, L. (2007). Thyroid hormones in small ruminants: effects of endogenous, environmental and nutritional factors. *Animal*, 1:7: 997–1008.

Vanderpump, M.P.G. & Tunbridge, W.M.G. (2008). Thyroid diseases. 4th Edi, Oxford University Press, Oxford, 6X2 ^DP, 2008, 1-7.

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مقایسه‌ی تأثیر ریزمغذی‌های خون در متابولیسم هورمون‌های تیروئیدی در بره‌های نر و ماده

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چکیده

بر اساس فاکتورهای ژنتیکی ریزمغذی‌ها برای فعالیت تیروئید و متابولیسم هورمون‌های آن ضروری هستند. به همین منظور مقادیر سرمی هورمون‌های تیروئیدی و غلظت برخی از ریزمغذی‌های خون در بره‌ها تعیین، مقایسه و ارتباط آن‌ها بررسی شد. تعداد ۱۷۶ رأس بره شامل ۷۰ رأس نر شیرخوار زیر ۲ ماهه و ۱۰۶ رأس ماده بین ۲ تا ۸ ماهه از نژاد قزل و ماکویی انتخاب شدند. مقدار ۵ میلی‌لیتر خون وداجی تهیه و سرم‌ها برای T3، T4، TSH، مس، آهن و روی ارزیابی شدند. مقادیر هورمون‌های تیروئیدی با الیزا و ریزمغذی‌ها با اتوآنالیزر تعیین شدند. میانگین T3 و TSH بره‌های نر بیش‌تر از ماده‌ها و T4 بره‌های ماده بیش‌تر از نر بودند اما فقط TSH معنی‌دار بود. میانگین غلظت سرمی مس، آهن و روی در نرها کم‌تر از ماده‌ها بود که فقط مس و روی معنی‌دار بودند و آهن متفاوت نبود. TSH در نرها ۳۶/۳ درصد بیش‌تر از ماده‌ها، مس و روی ماده‌ها به ترتیب ۱۲/۶ درصد و ۷/۳ درصد بیش‌تر از نرها بود. نسبت T3/T4 در نرها بیش‌تر از ماده‌ها بود. در مجموع دام‌ها نسبت T3/T4 پائین بود. بین T3/ TSH (r=-0.36) و T4/Cu (r=-0.24) در نرها رابطه منفی معنی‌داری بود اما در ماده‌ها مشاهده نشد. در مجموع نمونه‌ها بین T3/ TSH (r=-0.16) رابطه منفی معنی‌داری وجود داشت. مس/روی (r=0.38)، آهن/روی (r=0.44) در نرها، ماده‌ها و مجموع نمونه‌ها ارتباط مثبت و معنی‌داری داشتند. نتیجه این که مقادیر هورمون‌های تیروئیدی و ریزمغذی‌های خون بره‌ها در حدود استاندارد بود. مقادیر ریزمغذی‌ها و هورمون‌های تیروئیدی به استثناء T3 در ماده‌ها بیش‌تر از نرها بود. نسبت T3/T4 در نرها بیش‌تر از ماده‌ها بود. بین مس/روی، آهن/روی در نرها، ماده‌ها و مجموع نمونه‌ها ارتباط مثبت و معنی‌داری وجود داشت اما مس و آهن مرتبط نبودند. نتیجه این که بره‌های نر بیشتر از ماده‌ها مستعد به کمبود ریزمغذی‌ها و هورمون‌های تیروئیدی هستند.

کلمات کلیدی: T3، T4، TSH، ریزمغذی‌ها، بره

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