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Original Article

Zinc deficiency in sheep flock in Kerman suburb-Iran: a clinicopathologic study of four cases with a review of literature

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ABSTRACT

Primary zinc deficiency is not common in ruminants, but its occurrence has been documented. This study was conducted on a flock of 45 Kermani sheep during February 2022 to June 2022. The signs of alopecia, pityriasis, infertility, growth retardation, weakness, anorexia, itching, pneumonia, conjunctivitis, and increased risk of infection, which was suspected of zinc deficiency, were observed in 4 sheep. The heart rate, respiration rate, body temperature, and blood indices including PCV, total and differential white blood cell count, and red blood cell count were measured. Hematology results indicated a significant increase in white blood cells in affected sheep. The achieved biopsied cutaneous tissues of the sheep with skin lesions, were stained by Hematoxylin and Eosin method. Pathologically, the parakeratosis was observed in cornified squamous epithelium and therefore zinc deficiency was confirmed. The treatment strategy included oral zinc sulfate tablets with a dose of 250 mg per day for 4 weeks and the use of mineral bricks to continue the treatment process. After 10 weeks, signs of recovery appeared.

کمبود روی در گله گوسفند مبتلا در حومه شهر کرمان_ایران، مطالعه آسیب‌شناسی بالینی در چهار راس گوسفند مبتلا به همراه مروری بر مطالعات صورت گرفته

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چکیده

کمبود اولیه روی در نشخوارکنندگان شایع نیست، اما وقوع آن در گزارش ها ثبت شده است. علائم آلوپسی، شوره، ناباروری، تاخیر رشد، ضعف، بی اشتهایی، خارش، پنومونی، التهاب ملتحمه، افزایش ریسک ابتلا به عفونت در ۴ راس گوسفند که مشکوک به کمبود روی بودند از بهمن ماه سال ۱۴۰۰ لغایت خرداد سال ۱۴۰۱ مورد مطالعه قرار گرفت. ضربان قلب، تعداد تنفس و دمای بدن ثبت گردید و آزمایش خون شامل PCV، شمارش تفریقی گلبول‌های سفید و گلبول‌های قرمز اندازه‌گیری شد. نتایج هماتولوژی در گوسفندان مبتلا افزایش معنی داری در گلبول های سفید را نشان داد. همچنین نمونه های بافتی حاصل از بایوپسی پوست گوسفندان مبتلا، به روش هماتوکسیلین و ائوزین تهیه گردید و از نظر آسیب شناسی، پاراکراتوزیس به همراه شاخی شدن اپیتلیوم سنگفرشی مشاهده گردید که تایید کننده کمبود روی می‌باشد. استراتژی درمانی شامل قرص خوراکی سولفات روی با دوز ۲۵۰ میلی گرم در روز به مدت ۴ هفته و استفاده از آجرهای معدنی برای ادامه روند درمان بود. متعاقب ۱۰ هفته، علائم بهبود ظاهر شد.

واژه های کلیدی: کمبود روی، پاراکراتوز، گوسفند، ایران

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INTRODUCTION

In terms of the abundance of metals in the earth, zinc is the 29th most abundant metal in the earth's crust. This metal is essential for life because it is required for more than 300 enzymes and 1000 transcription factors [8]. Traces of zinc can be seen in almost every biological process of the body [10]. Zinc deficiency is a very important disorder in the body because it can be associated with growth retardation, weakness, anorexia, increased risk of infections, and skin problems [6]. Also, from another point of view, lack of control and excessive exposure to zinc can cause poisoning as it results in metabolic disorders and oxidative damage [12]. So it can be concluded that zinc balance in the body is like a double-edged sword.

Primary zinc deficiency is not common in ruminants, but its occurrence is documented in reports. In this regard, high soil pH (more than 6.5), high soil nitrogen and phosphorus will have a negative effect on plant uptake of zinc [12]. Some elements such as lead, copper, iron and calcium in the gastrointestinal tract interfere with the absorption of zinc and may also play a role in this deficiency. The occurrence of parakeratosis is directly related to the effect of zinc deficiency on the skin. Occurrence of infection and indirect symptoms with immune system can be attributed to zinc deficiency. Parakeratosis occurs bilaterally on the head, face, neck, and limbs. The affected areas have thickened skin and wrinkles. Symptoms such as diarrhea, conjunctivitis, rhinitis, pneumonia, and encephalitis may also occur [3-12]. Zinc binds to sites in proteins and has a catalytic, structural and regulatory role. There are two theories on absorption of zinc from the stomach of ruminants. Some believe that zinc can be absorbed from the rumen wall, but others believe that zinc is stored in the epithelia of rumen and omasum and it is not able to pass through the serosa [3-16]. However, according to the NRC report, zinc absorption is the highest in mammals from the small intestine, and in ruminants; 60-70% of zinc is absorbed from this part (NRC, 2007).The absorption of zinc can be affected by the interaction with other mineral metals such as copper and selenium, on the basis of which zinc absorption can be reduced with metallothioneins, phytate, calcium, phosphorus, copper, cadmium and selenium [3]. Studies show that zinc deficiency can play a role in the storage and release of insulin (NRC, 2007), and it also exerts its harmful effects on the immune system by reducing the level of Zn- interleukin 1. Zinc plays a role in appetite regulation and leptin secretion (hormone secreted by adipocytes) [3].

MATERIAL AND METHODS

The present study was conducted from February 2022 to June 2002 on a Kermani sheep flock. The flock suspected of zinc deficiency with signs of alopecia, pityriasis, infertility, growth retardation, weakness, anorexia, itching, pneumonia, conjunctivitis, and increased risk of infection was examined. In order to further investigate, the involved flock was also subjected to clinical studies. For this purpose, blood samples were taken from sheep via jugular vein.

First, the sampling site was washed with soap and water and the wool was shaved. Then, blood samples were taken from the jugular vein using a 10 cc syringe. They were transferred to tubes containing anticoagulant (to perform hematology tests) and gel tubes (to separate blood serum). The tubes containing the samples were transported to the medical diagnosis laboratory on dry ice. The tissue

samples obtained from biopsy were placed in %10 buffered formalin solution for fixation. Forty-eight hours later, the fixed tissues were processed by a tissue processor machine and then blocked with paraffin. Next, the sections were cut with a thickness of 6µm by a rotary microtome. Finally, the slides were stained with Hematoxylin and Eosin method (H&E) based on a routine protocol. Forty five Blood samples (18 male and 27 female) were taken in order to check the level of zinc in the serum before feeding the sheep in the early morning. Blood samples were taken to the laboratory and Biorexfars ZINC Standard Cat No BXS0462A specialized kit was used to measure the zinc level. The history was taken from the flock owner and the main complaint of the farmer was infertility and lasting infectious problems.

RESULTS

Results of hematological parameters evaluation of the sheep are presented as Mean ± SD in Table 1. On the other hand, the gross appearance of zinc deficiency-related cutaneous lesions in sheep is shown in Figure 1. Moreover, histopathologic changes related to zinc deficiency are described in Figure 2.

Table 1: Hematological indices of 45 samples were taken from a sheep flock in Kerman suburb

hematologic parameters	Mean ± SD	Normal Range	Condition
HCT	22.2± 2.2 %	27-45 (%)	Low
Hb	8.2± 0.9	9-15 (g/dl)	Low
MCHC	28 ±1.4	31-34 (%)	Low
WBC	20.8± 3.4 *	4-8 (x 10^3/µL)	High
Seg Neu	76 ± 12.4 *	0.7-6 (x 10^3/µL)	High
Band	4 ± 0.6 *	Rare (x 10^3/µL)	High
Lymph	20 ± 4.6 *	2-9 (x 10^3/µL)	High
Fibrinogen	650± 46.6 *	100-500 (mg/dl)	High

The hematologic indices show that the MCHC, WBC, Seg Neu, Band, Lymph and fibrinogen increased as well as the HCT decreased. (The * sign indicates the significance of the relationship)

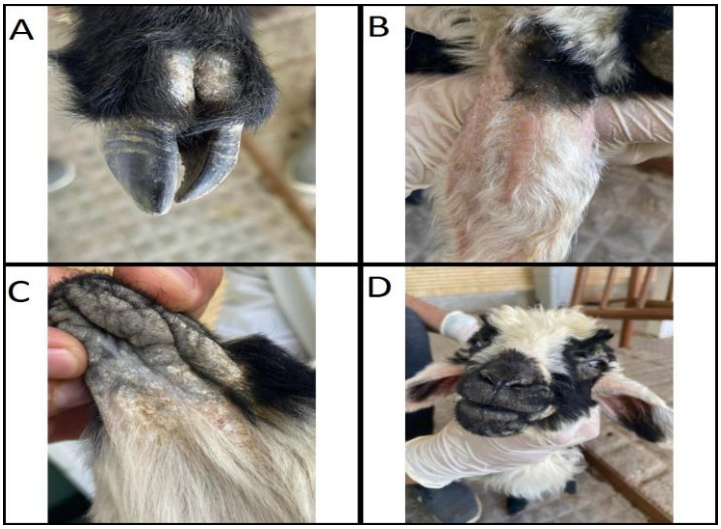

Figure 1: Gross appearance of the sheep affected by Alopecia with parakeratosis and pityriasis in the pastern (A). Thickening of the skin with pityriasis and alopecia in the ear (B). Wrinkled with thickening and parakeratosis in the mandible, accompanied by pityriasis, alopecia (C). Lethargy, weakness and hair loss around the eyes that thicken the skin in the mandible (D).

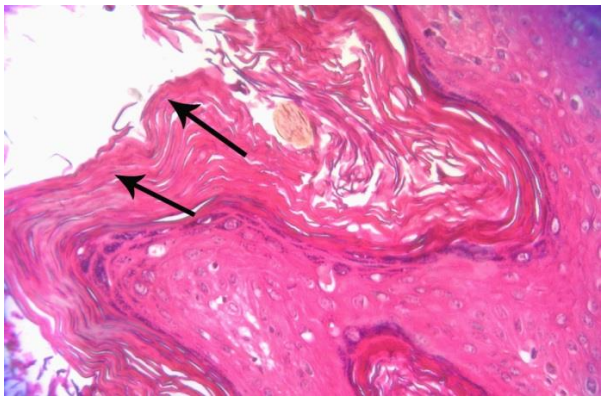

Figure 2: Skin of sheep affected by zinc deficiency. Presence of parakeratosis with abnormal retention of nuclei (arrow) in cornified layers. H&E; ×400.

DISCUSSION

Zinc is one of the most important trace elements required by the body, which is essential for the body's vital functions [11-15], Zinc deficiency is associated with the disorders mentioned in the introduction section. Due to the fact that the source of zinc through feeding is very important in ruminants, therefore the vegetation and soil of the area should also be examined. Kerman province is a vast region in the south and southeast of Iran in the Middle East. Climate changes and differences in soil contents in different regions of the province are significant. There are desert lands in the north of the province and fertile agricultural lands in the south of the province. Soil minerals and vegetation in the area are influenced by mines, factories and the type of vegetation [13]. Also, in the discussion of zinc deficiency, not only the criterion of soil and type of vegetation but also the interaction of minerals should also be considered. As mentioned in the introduction, other minerals such as selenium, copper, cobalt and phytate levels can interfere with zinc absorption [3]. The existence of valuable copper mines as well as soil rich in selenium in Kerman province can create this challenge for zinc absorption. In a study conducted by Stewart et al. in the United States of America, it was found that areas with selenium-rich vegetation are associated with zinc deficiency [14]. In a study conducted by Shayesteh far et al. in Kerman province, Iran, it was found that the level of selenium and arsenic in the soil around copper factories is high, and in this regard, the direction of the wind in moving minerals such as arsenic in the soil has a direct impact. It exists, but it has no significant relationship with the distribution of selenium in the soil [13]. Considering the climate and soil rich in copper and selenium in Kerman province, the competitive effect of these minerals with zinc should be suspected.

Regarding the patient referred to the hospital, an increase in the amount of white blood cells indicates the presence of infection, and abnormal lung sounds (crackle sound and wheezing sound) were also heard during clinical examinations which can indicate the presence of pneumonitis. Other signs that can be suspected of pneumonitis in the herd are coughing, lagging behind the herd, and loss of appetite that was present in the history of the herd. Also, in the studies, the role of zinc in the immune system is documented, in which case, a decrease in the level of zinc in the body can be associated with a malfunction of the immune system, which may be associated with an increased risk of infectious diseases [3]. In the study of Ghazanfari et al., the role of zinc

deficiency in the occurrence of pneumonitis has been discussed, and this deficiency can be cause pneumonitis [5]. An increase in body temperature (39.6 C°) and a decrease in the number of rumen movements (one movement in two minutes) in clinical examinations along with an increase in white blood cells (neutrophils, band cells and lymphocytes) as increase Fibrinogen, indicated infection and inflammation in the body.

Skin is the third tissue rich in zinc in the body and this mineral's role has been described in Keratinocytes, Melanocytes, Mast Cells and Dendritic Cells, Endothelial Cells, T cells, Fibroblasts and Adipocytes [10]. There are traces of zinc deficiency in atopic dermatitis because the function of this mineral metal has been described in the skin's immune mechanisms, skin barriers and finally in maintaining the integrity of the skin. Further, this deficiency can lead to allergic reactions such as pneumonia and allergic rhinitis, which were observed in the referred patient [6]. There are many reports of seborrheic dermatitis caused by zinc deficiency in humans [7], but these reports are insignificant in veterinary medicine. It seems that skin diseases caused by zinc deficiency also occur a lot in small ruminants, but these complications usually occur simultaneously with other deficiencies, especially vitamins A deficiency. A relationship between alopecia and zinc deficiency has been described in cattle [8]. The study of mineral elements and the effect of these elements on animal fertility is one of the interesting topics for researchers in the field of veterinary reproduction. Among domestic ruminants, camels have a lower level of zinc in their serum, and the addition of zinc supplements increased sperm volume, sperm motility, and improved a significant percentage of sperms in terms of morphology males. Also, the effect of this element in females is also associated with proper fertility (Ali et al, 2021). cooperation and interaction in many enzymes, such as angiotensin-converting enzyme (ACE), which is important for testosterone production and spermatogenesis, maintaining the lining of the reproductive organs, regulating the capacitation and acrosome reaction, participation in the production of many of the sex hormones comprising testosterone and GnRH, helping sperm maturation, supporting the function of the accessory sex glands, preventing destruction of spermatozoal DNA, and acting as a cofactor of superoxide dismutase are biological pathways that have been described for zinc in males [4]. Nasr et al. have mentioned that zinc deficiency, along with other mineral elements, is directly related to female infertility [8]. A blood sample was taken from the sheep referred to the veterinary hospital of Shahid Bahonar University in Kerman, and the presence of anemia, a decrease in blood hemoglobin, and a decrease in MCHC were evident. Our results are consistent with Nasr et al.'s study in 2019. According to the clinical symptoms in the sheep referred to the hospital, sampling was done from the sheep herd in order to evaluate the level of zinc in the blood serum of the sheep of this herd. The level of zinc in the serum shows relatively constant values in the reports, as Kargin et al mentioned 80 to 120 µg/dL as a constant standard [1]. In the current study, the level of zinc in the blood serum of the studied sheep was reported to be less than the optimal level, which indicates a chronic deficiency and in some cases severe deficiency. Also, recorded clinical symptoms including pneumonia, infertility, skin disorders, allergic rhinitis, fever and persistent infection in the herd are consistent with zinc deficiency.

CONCLUSION

According to the topics presented and the level of zinc in the blood serum of the studied herd, it seems that this deficiency does not occur initially and there is a possibility of the role of other mineral elements in the occurrence of this deficiency. It should be noted that 4 out of 45 sheep in the herd have zinc deficiency. For treatment, oral tablets of zinc sulfate with a dose of 250 mg per day were used for 4 weeks, and mineral bricks were used to continue the treatment process. To control the infection, taking into account the history of antibiotic use, a more cautious and conservative strategy was adopted, so that for severe cases of infection, broad-spectrum antibiotics were used for several days along with supportive treatment. After 10 weeks, signs of recovery appeared.

ETHICS

Approved.

CONFLICT OF INTEREST

None declared.

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