Biological Trace Element Research (2021) 199:1389–1396
https://doi.org/10.1007/s12011-020-02261-1

Association Between Serum Selenium Level and Subclinical Mastitis in Dairy Cattle

Di Wang [1,2] · Daqing Jia [1,2] · Ronghe He [1,3] · Shuai Lian [1,2] · Jianfa Wang [1,2] · Rui Wu [1,2]

Received: 28 April 2020 / Accepted: 17 June 2020 / Published online: 25 June 2020

Abstract

Selenium is an important element in nutrition, showing great potential in the udder health of dairy cattle and in the control of subclinical mastitis. However, there are few studies on selenium and subclinical mastitis in cows, and the correlation is not clear. A trial was designed to investigate the association between serum selenium levels and the immune and antioxidant capacity of dairy cattle with subclinical mastitis. Fifty cattle in early lactation with similar background information were selected randomly from an intensive dairy farm. Blood samples were collected for the detection of serum selenium levels by ICP-optic emission spectrometer. The cattle were divided into a low-selenium group (< 0.05 mg/L) and three normal selenium groups with different serum selenium levels (0.05–0.08 mg/L). The somatic cell count, immune indexes, and other indexes in the milk of each group were detected. The somatic cell count was found to be negatively correlated with serum selenium level. GSH-Px had a low positive correlation and IL-6 had a low negative correlation with serum selenium level. With a serum glutathione peroxidase < 148 U/L and IL-6 > 451 pg/mL, the risk of subclinical mastitis in dairy cattle increased.

Keywords Dairy cattle · Selenium · Subclinical mastitis · Oxidative stress · Immune system

Introduction

Selenium is an important element in nutrition. Twenty-five selenoproteins have been found in animals, and at least 12 have an extensive immune function, showing great potential in the udder health of dairy cattle and in the control of subclinical mastitis. The susceptibility of mammary glands to bacteria is potentially associated with selenium levels in cows. Studies have shown that after 8 weeks of supplementation with selenium at a dietary level of 0.2 mg/kg, the incidence of mammary gland infection in dairy cows is significantly reduced (up to 60%) [1]. In general, selenium deficiency results in immunosuppression, while supplementation with low doses of selenium could lead to enhanced and/or restored immunologic functions [2]. In a study by Hemingway, 14 of 36 cows who received antibiotics during dry milking developed mastitis, while only five of 36 cows who received 4 mg of selenium during dry milking developed mastitis [3]. Moreover, selenium supplementation induced an unspecified antibacterial activity in milk lactoserum [4], but the mechanism of this antibacterial activity is not clear; however, a higher activity of glutathione peroxidase (GSH-Px) will affect the growth rate of pathogenic microorganisms in whey.

Selenium is a highly effective antioxidant and is incorporated into selenate as GSH-Px [5]. GSH-Px is an important selenoprotein in mammals and acts as a component of the antioxidative defense mechanism in cells. It can remove lipid-damaging peroxides and protect immune cells from oxidative stress–induced damage [6]. Some studies have shown a negative correlation between GSH-Px activity in whole blood and somatic cell count (SCC) in canned milk [7, 8]. After supplementing with selenium, the increase of GSH-Px activity in blood was associated with a decrease in the prevalence of subclinical mastitis in dairy cattle [9].

Reducing the oxidative damage and improving the immune ability of cow mammary glands are important measures for reducing the incidence of recessive mastitis and improving the quality of milk. Trace element selenium plays an important

✉ Rui Wu
fuhewu@126.com

[1] College of Animal Science and Veterinary Medicine, Heilongjiang Bayi Agricultural University, No.5 Xinfeng Road, High and new technology development zone, Daqing 163319, Heilongjiang, People's Republic of China

[2] Heilongjiang Provincial Key Laboratory of Prevention and Control of Bovine Diseases, Daqing 163319, People's Republic of China

[3] Jixi Agricultural and Rural Bureau, Jixi 158100, People's Republic of China

role in enhancing antioxidant capacity and immunity. However, there are few studies on selenium and subclinical mastitis in cows, and the correlation is not clear. Therefore, this experiment investigated the serum selenium content, somatic cell number, antioxidant capacity, and immune capacity of cows in a dairy farm. The correlation between selenium level and various indexes of dairy cows was analyzed to assess the association between serum selenium level and subclinical mastitis.

Methods and Materials

Animals

Fifty cattle in lactation with similar age, lactation period, gestational order, and physiological conditions were selected randomly, total mixed ration (TMR) free feeding. The experimental use of these animals was approved by the Animal Care Committee of Heilongjiang Bayi Agricultural University, and all experiments were performed in accordance with specific guidelines provided by Heilongjiang Bayi Agricultural University.

Sample Collection and SCC

Blood was collected from the jugular vein and the serum was separated, stored at 4 °C for immediate use or stored at − 80 °C for later use. The milk samples were collected during milking, then stored at 4 °C for SCC. SCC were obtained with a Fossomatic FC counter (Foss). 1×10^6/mL > SCC > 5×10^5/mL were regarded as subclinical mastitis.

Serum Selenium Concentration Analysis

Cattle serum (0.4 mL) was placed in a tetrafluoroethylene digestive tube with 8.0 mL HNO_3 (superior purity) and 2.0 mL 30% H_2O_2 (analysis purity). The samples were left in the fume hood for 1 h at room temperature. Then, a cover was added to the digester tube, tightened, and the tubes placed in a rotating body for digestion in a microwave digestion machine. After digestion, the sample was cooled to room temperature and then placed on an acid expeller at 140 °C in the fume hood for about 2 h. The digester tube was cooled to room temperature. Ultrapure water was added to 10 mL, and the sample was stored at 4 °C for trace element detection. Trace elements were determined by ICP-optic emission spectrometer (Optima800, PerkinElmer).

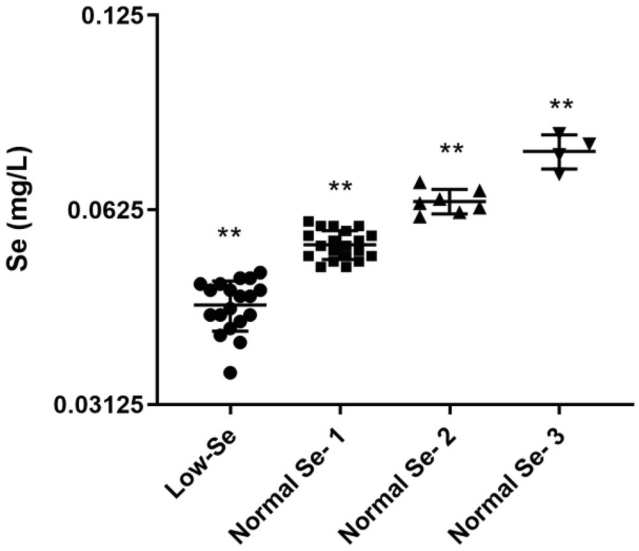

Fig. 1 Total distribution of low to high serum selenium level in dairy cattle, $n = 50$

Detection of Immune and Antioxidant Indexes

The levels of norepinephrine GSH-Px, total antioxidant capacity (T-AOC), Interleukin-1 (IL-1), Interleukin-2 (IL-2), Interleukin-6 (IL-6), Immunoglobulins G (IgG), Immunoglobulins M (IgM), Interferon γ (IFN-γ), and Tumor necrosis factor α (TNF-α) in serum were detected by ELISA kits (USCN, Wuhan, China) according to the manufacturer's protocol.

Statistical Analysis

All experimental data were processed by SPSS 19.0 software for one-way analysis of variance and expressed as the mean ±

Table 1 Serum selenium level in dairy cattle

Groups	*n*	Se (mg/L)	Mean (mg/L)	SD
Low-Se	19	0.00–0.05	0.045[a]	0.0040
Normal Se-1	20	0.05–0.06	0.055[b]	0.0029
Normal Se-2	7	0.06–0.07	0.064[c]	0.0028
Normal Se-3	4	0.07–0.08	0.077[d]	0.0047

Vertical labeling with lowercase letters indicates a significant difference ($P < 0.05$)

Table 2 The correlation between serum selenium and SCC in lactating dairy cows and its influence on the incidence of subclinical mastitis

Groups	*n*	SCC (10^4/mL)	%	Relevance
Low-Se	9/19	57.67 ± 41.6	47.36	$R = -0.28$, $P = 0.045$
Normal Se-1	8/20	52.56 ± 24.92	40.00	
Normal Se-2	2/7	36.96 ± 17.61	28.57	
Normal Se-3	1/4	43.58 ± 39.4	25.00	
Total	21/50	51.39 ± 32.60	42.00	

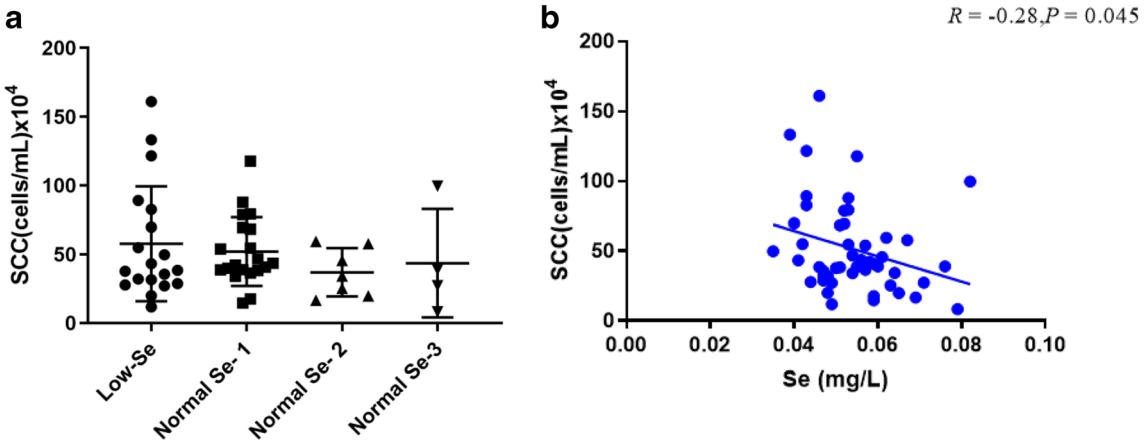

Fig. 2 Effect of different levels of serum selenium on SCC levels in cattle and its changing trend. **a** The effect of different gradient selenium groups on SCC. **b** Changes in serum selenium content and SCC in 50 cows

standard deviation. In the table, lowercase letters were used for longitudinal marking and those with different letters were significantly different ($P < 0.05$); those without letters showed no significant difference ($P > 0.05$). Correlation was analyzed by Pearson's coefficient. A value of $P \geq 0.05$ indicates no significant difference and no correlation; $P < 0.05$ indicates a significant difference and a correlation. A binary logistic regression equation was used to establish the model, and Hosmer–Lemeshow was used to test the degree of fitting. A value of $P > 0.05$ indicated that the model and observed value fitted well. The critical value was determined by ROC curve and the Youden index.

Results

Serum Selenium Level of Dairy Cattle

Table 1 and Fig. 1 show the distribution of serum selenium levels from low to high in all experimental cattle. Groups were divided according to serum selenium level: cattle with serum selenium level below 0.05 mg/L were assigned to the low-selenium group (0–0.05 mg/L, $n = 19$, 0.045 ± 0.004 mg/L); cattle with serum selenium level higher than 0.05 mg/L were assigned to the normal selenium group 1 (Normal Se-1, 0.05–0.06 mg/L, $n = 20$, 0.055 ± 0.0029 mg/L), normal selenium

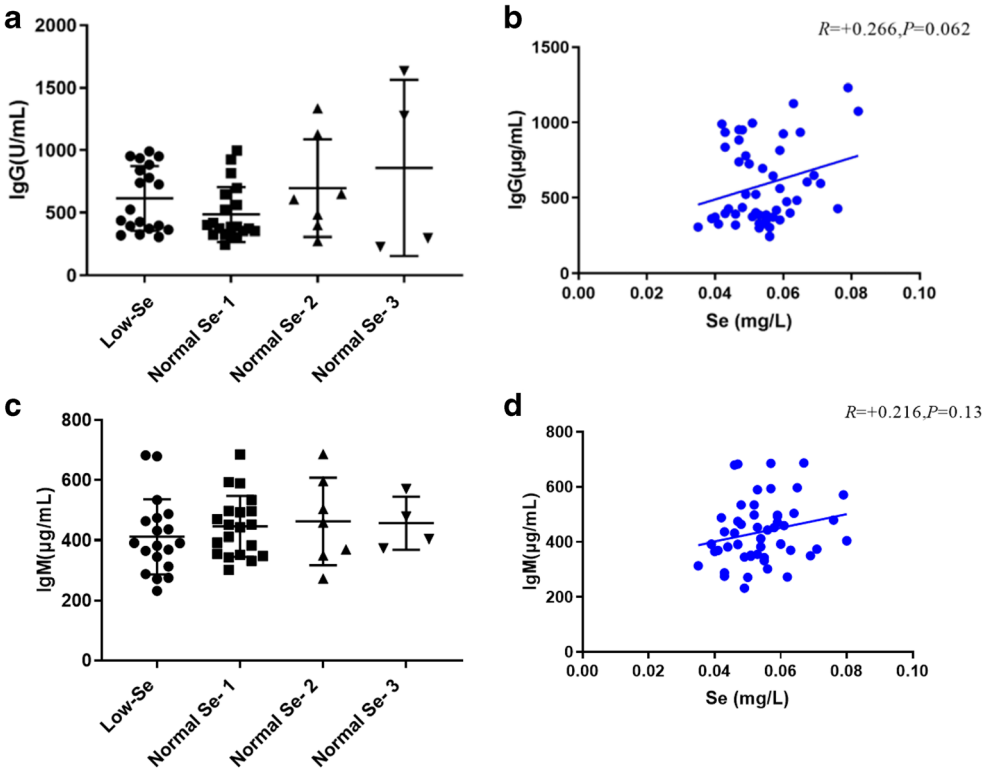

Fig. 3 Effect of different levels of serum selenium on IgG and IgM levels in cattle and its changing trend. **a** The effect of different gradient selenium groups on IgM. **b** Changes in serum selenium content and IgM in 50 cows

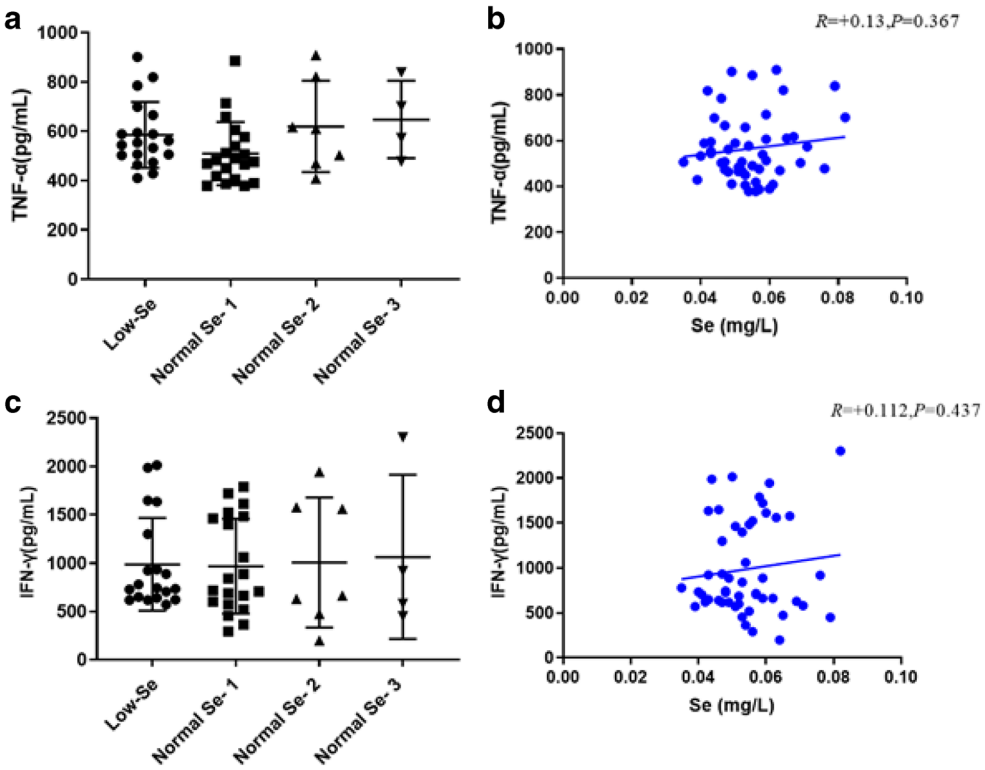

Fig. 4 Effect of different levels of serum selenium on TNF-α and IFN-γ levels in cattle and its changing trend. **a** The effect of different gradient selenium groups on TNF-α. **b** Changes in serum selenium content and TNF-α in 50 cows. **c** The effect of different gradient selenium groups on IFN-γ. **d** Changes in serum selenium content and IFN-γ in 50 cows

group 2 (Normal Se-2, 0.06–0.07 mg/L, $n = 7$, 0.064 ± 0.0028 mg/L), and normal selenium group 3 (Normal Se-3, 0.07–0.08 mg/L, $n = 4$, 0.077 ± 0.0047 mg/L). All indexes in the trial were analyzed according to the above groups, and the correlations between each index and serum selenium level were revealed through data analysis to understand the impact of selenium on the risk of subclinical mastitis in dairy cattle.

Serum Selenium Level and Subclinical Mastitis

As shown in Table 2 and Fig. 2, the prevalence of subclinical mastitis in this batch of experimental cattle was 42%. There was no significant difference in SCC between the normal selenium and the low-selenium group ($P > 0.05$). According to Pearson analysis, the selenium level in cattle serum has a low negative correlation with SCC ($R = -0.28$, $P = 0.045$). With an increase in the level of serum selenium, the incidence of subclinical mastitis in dairy cattle decreased.

Serum Selenium Level and IgG, IgM, TNF-α, IFN-γ, IL-2, and IL-6

The level of IgG in the serum of lactating cattle in the low-selenium group was lower than that in normal selenium groups 2 and 3 (Fig. 3 a and b), but there was no significant difference ($P > 0.05$). Pearson analysis indicated that the serum selenium level of lactating cattle was not correlated with IgG ($R = 0.266$, $P = 0.062$). The IgM level in the serum of lactating cattle in the low-selenium group was lower than that in the normal selenium group (Fig. 3 c and d), but there was no significant difference ($P > 0.05$). Pearson analysis showed that the serum selenium level was not correlated with IgM ($R = 0.216$, $P = 0.132$). Figure 4 a and b demonstrate that the level of TNF-α in the serum of lactating cattle in the low-selenium group was lower than that in normal selenium groups 2 and 3, but there was no significant difference ($P > 0.05$). The serum selenium level was not correlated with TNF-α ($R = 0.13$, $P = 0.367$). The level of IFN-γ in the serum of lactating cattle in the low-selenium group was lower than that in normal selenium groups 2 and 3 (Fig. 4 c and d), but there was no significant difference ($P > 0.05$). The serum selenium level was not correlated with IFN-γ ($R = 0.112$, $P = 0.437$). IL-2 levels in the serum of lactating cattle in the low-selenium group were lower than that in the normal selenium group (Fig. 5 a and b), but there was no significant difference ($P > 0.05$), and Pearson analysis indicated that the serum selenium level was not correlated with IL-2 ($R = 0.133$, $P = 0.356$). IL-6 levels in the serum of lactating cattle in the low-selenium group were higher than that in normal selenium groups 1 and 3, and lower than that in normal selenium group 2 (Fig. 5 c and d), but there was no significant difference ($P > 0.05$). Pearson analysis indicated that the serum selenium level had a low negative correlation with IL-6 ($R = -0.28$, $P = 0.049$); the IL-6 level in the serum of cattle decreased with the increase in selenium levels.

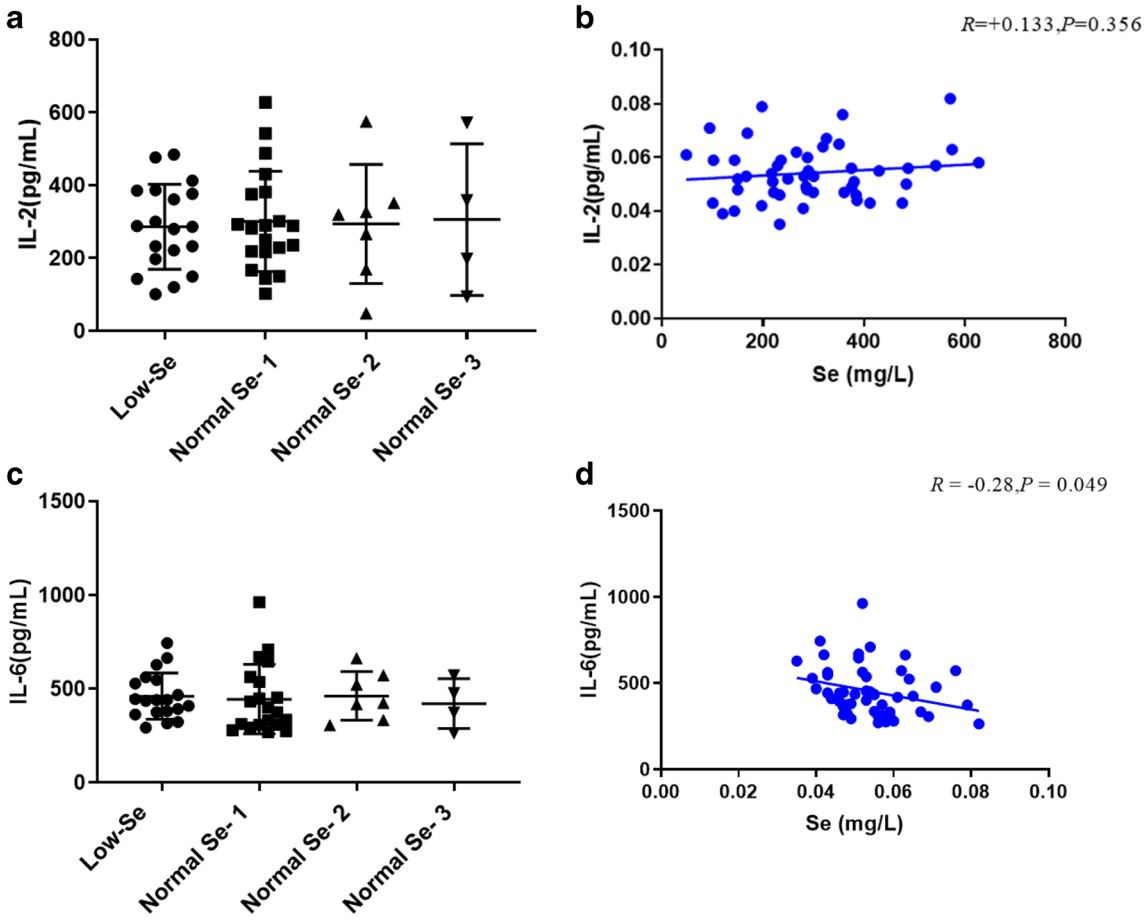

Fig. 5 Effect of different levels of serum selenium on IL-2 and IL-6 levels in cattle and its changing trend. **a** The effect of different gradient selenium groups on IL-2. **b** Changes in serum selenium content and IL-2 in 50 cows. **c** The effect of different gradient selenium groups on IL-6. **d** Changes in serum selenium content and IL-6 in 50 cows

Serum Selenium Level and GSH-Px and T-AOC

As shown in Fig. 6 a and b, the level of GSH-Px in the serum of lactating cattle in the low-selenium group was significantly lower than that in the normal selenium group 2 ($P < 0.05$). Pearson analysis indicated that the serum selenium level had a significantly positive correlation with GSH-Px ($R = 0.395$, $P = 0.010$); the level of GSH-Px tends to increase with the increase of serum selenium. There was no significant difference in the level of T-AOC in the serum of lactating cattle between the low-selenium group and the normal selenium group (Fig. 6 c and d); Pearson analysis showed that the serum selenium level was not correlated with T-AOC ($R = -0.023$, $P = 0.870$).

Binary Logistic Model Predicts Subclinical Mastitis in Dairy Cattle

We established a binary logistic model and predicted the risk of subclinical mastitis in dairy cattle with SPSS biometric software; the model contains GSH-Px, T-AOC, IgG, IL-2, IL-6, and TNF-α. As shown in Table 3, the significance of the fitting degree of Hosmer's binary logistic model was 0.086 ($P > 0.05$), which confirms that the null hypothesis model fitted the observed values. IL-6 and GSH-Px were found to reflect the risk of subclinical mastitis in dairy cattle the best. As shown in Table 4, the optimal threshold was determined by the ROC curve analysis and Youden index as GSH-Px < 148 U/L and IL-6 > 451 pg/mL. The risk of subclinical mastitis in dairy cattle will increase with GSH-Px < 148 U/L and IL-6 > 451 pg/mL.

Discussion

There is a potential relationship between selenium level and susceptibility of dairy cattle to subclinical mastitis. Studies have shown that cattle udder infections decrease significantly (up to 60%) after 8 weeks of supplementation with selenium at a dietary level of 0.2 mg/kg. If the amount of selenium or VE supplementation is higher than the requirement of animals, the immunity of animals will improve [2].

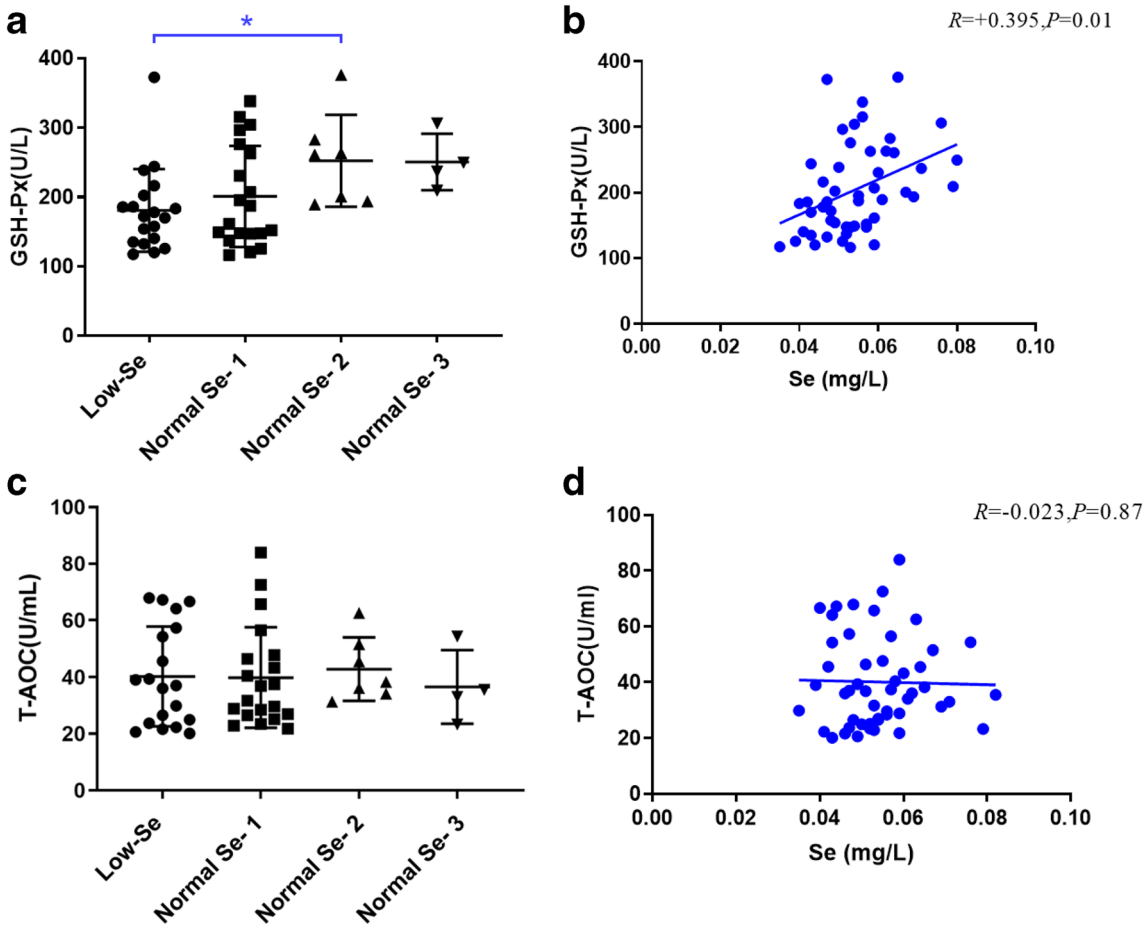

Fig. 6 Effect of different serum selenium levels on GSH-PX and T-AOC levels in cattle and its changing trend. **a** The effect of different gradient selenium groups on GSH-Px. **b** Changes in serum selenium content and GSH-Px in 50 cows. **c** The effect of different gradient selenium groups on T-AOC. **d** Changes in serum selenium content and T-AOC in 50 cows

This is especially important for cattle that are already infected with pathogens. In the study by Hemingway (1999), 14 of 36 dairy cattle who received antibiotics in their udders during the dry period were infected with subclinical mastitis, while only five of 36 who received 4 mg of selenium during the dry period were infected with subclinical mastitis. In this trial, with the increase of selenium level in dairy cattle, the incidence of subclinical mastitis decreased, but there was no significant difference in SCC between the normal selenium group and the low-selenium group ($P > 0.05$). Pearson analysis showed that the selenium level in cattle serum has a low negative correlation with SCC. This trial is consistent with the studies that increasing selenium level plays an important role in reducing the risk of subclinical mastitis [10, 11].

Selenium affects the immune function of cattle mainly through specific and non-specific immunity. Specific immunity includes humoral immunity and cellular immunity, both of which depend on T and B lymphocytes. Selenium can promote the proliferation and differentiation of lymphocytes, and accelerate the secretion of cytokines [12]. IL-2 is an important growth factor in the development of T lymphocytes, it is produced by activated T lymphocytes and then acts on the IL-2 receptor attached to the surface of the T lymphocytes, and it further stimulates the secretion and proliferation of T lymphocytes. Studies have shown that selenium supplementation or

Table 3 Hosmer–Lemeshow test fitting degree of bivariate logistic model

Model	χ^2	DOF	*P* values
1	13.847	8	0.086

Table 4 Boundary value, sensitivity, specificity, and area under the ROC curve

	Boundary	Sensitivity (%)	Specificity (%)	AUC
GSH-Px (U/L)	148	52.40	93.10	0.547, $P = 0.003$
IL-6 (pg/mL)	451	61.90	79.30	0.695, $P = 0.02$

selenium deficiency can alter the expression of the IL-2 receptor in mice. Selenium supplementation can lead to the premature expression of the IL-2 receptor and selenium deficiency can lead to the delayed expression of the IL-2 receptor [13]. Studies have found that selenium supplementation of 1 μg/day and 10 μg/day can significantly increase the level of IL-2 in the serum of mice with low immune function, and selenium supplementation of 1 μg/day can also significantly increase the level of IFN in the serum of mice. A study by Johns et al. also reported that selenium can enhance the secretion of IFN-γ and other cytokines, thereby improving cellular immune function; IFN-γ promotes not only immunomodulation but also antimicrobial and anticancer activity [14]. In humoral immunity, selenium can stimulate the synthesis of immunoglobulin [15], improve the bactericidal activity of serum [16], and significantly improve the level and activity of IL-6 secretion by lymphocytes. IL-6 can affect the secretion of IgM and IgG by mature B cells; therefore, selenium may further affect humoral immunity [17]. TNF-α is a cytokine secreted by macrophages and monocytes that regulates the immune function. In this trial, the levels of IL-2, IgG, IgM, TNF-α, and IFN-γ in the serum of lactating cows in the low-selenium group were lower than those in the normal group, and IL-6 was slightly higher than that in the normal selenium group. Pearson analysis showed that the serum selenium level of lactating cattle was not correlated with IL-2, IgG, IgM, TNF-α, and IFN-γ. The serum selenium level had a low negative correlation with IL-6; this may be because the increasing levels of serum selenium enhance the defense capabilities of the mammary glands' innate immune system in cattle and reduce the entry of pathogenic microorganisms, which cause inflammatory reactions, so the level of IL-6 in serum was reduced. When the level of selenium in cattle serum is decreased, the immune capacity is decreased.

Selenium owes most of its antioxidant properties to GSH-Px [18], an important component of the antioxidant defense mechanism, which removes potentially damaging peroxides and protects immune cells from damage by oxidative stress. Previous studies have shown that the antioxidant function of GSH-Px is the main reason why selenium improves the innate immune response of cattle [19]. Selenium-dependent glutathione peroxidase could protect phagocytes from oxidative damage during respiratory bursts. Moreover, the decreased incidence of dairy cattle subclinical mastitis is related to increased GSH-Px activity in the blood after selenium supplementation. In addition, T-AOC reflects ROS metabolism and the compensatory capacity generated by external stimuli and is an important comprehensive indicator in the antioxidant defense system [7, 20]. The antioxidant defense system of animals is divided into a primary and secondary antioxidant defense system by grade [20]. The primary antioxidant system includes SOD, GSH-Px, CAT, and T-AOC enzymes and trace elements including Se, Cu, Mn, and Zn [21]. Selenium is an essential component of GSH-Px [22], whereas copper, zinc, and manganese are essential components of SOD [23]. Therefore, non-antioxidants are the overall basis of the antioxidant system in animals and the basic conditions for enzymes to function normally. From this perspective, the concentration of antioxidants in body fluids determines the level of total antioxidants in vivo. In the present study, the Pearson correlation coefficient analysis showed that the serum selenium level of cattle had a significantly positive correlation with GSH-Px, but not with T-AOC. The results indicate that when cattle are selenium deficient, the activity of GSH-Px with selenium as the active center changes, the free radical scavenging function is weakened, and the antioxidant defense system is reduced, causing a large amount of ROS and LPO to accumulate, eventually leading to oxidative damage to immune cells, reducing the capacity of the immune system. Therefore, selenium deficiency could cause oxidative stress in lactating dairy cattle and increase the risk.

Conclusion

Selenium has a negative correlation with SCC. The serum selenium level has a significant positive correlation with GSH-Px, while serum IL-6 levels have a low negative correlation with the level of selenium. With a serum level of GSH-Px < 148 U/L and IL-6 > 451 pg/mL, the risk of subclinical mastitis in dairy cattle will increase.

Acknowledgments The authors thank the staff and students of the Heilongjiang Provincial Key Laboratory of Prevention and Control of Bovine Diseases for Animal Care and Data Collection.

Funding information This work was supported by the National Key Research and Development Program (2016YFD0501203) and Heilongjiang Bayi Agricultural University Support Program for San Heng San Zong (ZRCQC201903).

Compliance with Ethical Standards

The experimental use of these animals was approved by the Animal Care Committee of Heilongjiang Bayi Agricultural University, and all experiments were performed in accordance with specific guidelines provided by Heilongjiang Bayi Agricultural University.

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Malbe M, Klaassen M, Fang W, Myllys V, Vikerpuur M, Nyholm K, Sankari S, Suoranta K, Sandholm M (1995) Comparisons of selenite and selenium yeast feed supplements on se-incorporation, mastitis and leucocyte function in Se-deficient dairy cows. J Veterinary Med Ser A 42(1–10):111–121
2. Kiremidjian-Schumacher L, Stotzky G (1987) Selenium and immune responses. Environ Res 42(2):277–303

3. Hemingway R (1999) The influences of dietary selenium and vitamin E intakes on milk somatic cell counts and mastitis in cows. Vet Res Commun 23(8):481–499
4. Ali-Vehmas T, Vikerpuur M, Fang W, Sandholm M (1997) Giving selenium supplements to dairy cows strengthens the inflammatory response to intramammary infection and induces a growth-suppressing effect on mastitis pathogens in whey. J Veterinary Med Ser A 44(1–10):559–571
5. McGrath J (2016) Accelerated pre-weaning growth rates in dairy calves: do antioxidants have a place? Anim Prod Sci 56(8):1275–1284
6. McKenzie RC, Rafferty TS, Beckett GJ (1998) Selenium: an essential element for immune function. Immunol Today 19(8):342–345
7. Weiss W, Hogan J, Smith K, Hoblet K (1990) Relationships among selenium, vitamin E, and mammary gland health in commercial dairy herds. J Dairy Sci 73(2):381–390
8. Ndiweni N, Field T, Williams M, Booth J, Finch J (1991) Studies on the incidence of clinical mastitis and blood levels of vitamin E and selenium in dairy herds in England. The Veterinary record 129(5):86–88
9. Ceballos-Marquez A, Barkema H, Stryhn H, Wichtel J, Neumann J, Mella A, Kruze J, Espindola M, Wittwer F (2010) The effect of selenium supplementation before calving on early-lactation udder health in pastured dairy heifers. J Dairy Sci 93(10):4602–4612
10. Zhang ZB, Guo YF, Li CY, Qiu CW, Guo MY (2019) Selenium influences mmu-miR-155 to inhibit inflammation in Staphylococcus aureus-induced mastitis in mice. Food Funct 10(10):6543–6555
11. Ma J, Zhu S, Guo Y, Hao M, Chen Y, Wang Y, Yang M, Chen J, Guo M (2019) Selenium attenuates Staphylococcus aureus mastitis in mice by inhibiting the activation of the NALP3 Inflammasome and NF-κB/MAPK pathway. Biol Trace Elem Res 191(1):159–166
12. Ru-duan W, Chang-sen W, Zuo-hua F, Yi L (1992) Investigation on the effect of selenium on T lymphocyte proliferation and its mechanisms. J Tongji Med Univ 12(1):33–38
13. Roy M, Kiremidjian-Schumacher L, Wishe HI, Cohen MW, Stotzky G (1994) Supplementation with selenium and human immune cell functions. Biol Trace Elem Res 41(1–2):103–114
14. Lin CF, Lin CM, Lee KY, Wu SY, Feng PH, Chen KY, Chuang HC, Chen CL, Wang YC, Tseng PC, Tsai TT (2017) Escape from IFN-γ-dependent immunosurveillance in tumorigenesis. J Biomed Sci 24(1):10
15. Musa I, Bitto I, Ayoade J, Oyedipe E: Serum immunoglobulins and lipid prof le of sheep as affected by selenium and vitamin E supplementation. 2018
16. Rossi CS, Compiani R, Baldi G, Muraro M, Marden J, Rossi R, Pastorelli G, Corino C, Dell'Orto V (2017) Organic selenium supplementation improves growth parameters, immune and antioxidant status of newly received beef cattle. J Anim Feed Sci 26(2):100–108
17. Tsuji P, Carlson B, Anderson C, Seifried H, Hatfield D, Howard M (2015) Dietary selenium levels affect selenoprotein expression and support the interferon-γ and IL-6 immune response pathways in mice. Nutrients 7(8):6529–6549
18. Yao JK, Reddy RD, Van Kammen DP (2001) Oxidative damage and schizophrenia. CNS drugs 15(4):287–310
19. Salman S, Khol-Parisini A, Schafft H, Lahrssen-Wiederholt M, Hulan H, Dinse D, Zentek J (2009) The role of dietary selenium in bovine mammary gland health and immune function. Anim Health Res Rev 10(1):21–34
20. Miller J, Brzezinska-Slebodzinska E, Madsen F (1993) Oxidative stress, antioxidants, and animal function. J Dairy Sci 76(9):2812–2823
21. Sordillo LM, Aitken SL (2009) Impact of oxidative stress on the health and immune function of dairy cattle. Vet Immunol Immunopathol 128(1–3):104–109
22. He X, Lin Y, Lian S, Sun D, Guo D, Wang J, Wu R (2020) Selenium deficiency in chickens induces intestinal mucosal injury by affecting the mucosa morphology, SIgA secretion, and GSH-Px activity. Biol Trace Elem Res:1–7
23. Wu H, Li R, Liu Y, Zhang X, Zhang J, Ma E (2020) A second intracellular copper/zinc superoxide dismutase and a manganese superoxide dismutase in Oxya chinensis: molecular and biochemical characteristics and roles in chlorpyrifos stress. Ecotoxicol Environ Saf 187:109830