Original article

IMMUNOLOGICAL STATUS OF HIGHLY PRODUCTIVE COWS WITH COMORBID OBSTETRIC-GYNECOLOGICAL AND ORTHOPEDIC PATHOLOGY

V.I. Lutsay, P.A. Rudenko, V.D. Sibirtsev,
A.M. Nefedov, A.A. Rudenko

Abstract Аннотация

Background. Research and clinical observation confirm a significant correlation between postpartum metabolic/obstetric diseases and the development of orthopedic pathology in highly productive cows. In particular, a study supported by the Russian Science Foundation (grant No. 24-26-00172) revealed a clear relationship between the development of purulent-necrotic lesions of the hooves and the occurrence of postpartum endometritis in high-yielding cows. In this study, the following groups of animals were formed by randomization: group 1 (n=28): cows with acute purulent-catarrhal postpartum endometritis; group 2 (n=25): animals with purulent-necrotic lesions of the hooves; group 3 (n=27): cows with a comorbid course of both pathologies; and the control group (n=23): clinically healthy animals. All individuals selected for the study had their jugular venous blood collected on an empty stomach into sterile tubes for subsequent immunological analysis. It was found that the comorbid course of these pathologies is significantly more severe than each of the diseases in isolation. This is evidenced by the immunological screening we conducted. In this regard, when an animal has multiple pathologies, an individual approach is necessary, which dictates the need for a comprehensive study of the clinical course of the main, concomitant, and even previous diseases, their comprehensive diagnosis, and rational treatment.

Purpose. The purpose of the present paper is to study the immunological status of highly productive cows with comorbid obstetric-gynecological and orthopedic pathology.

Materials and methods. To assess the dynamics of the clinical manifestation of hoof diseases, an orthopedic examination was conducted on a monthly basis

throughout the year. During this examination, the following were evaluated: the degree and nature of hoof deformities; the intensity of corneal destruction; the presence of specific lesions such as pockets, delamination, and cracks; and the position of the thoracic and pelvic limbs. In cows with identified purulent-necrotic lesions during the postpartum period, a detailed obstetric and gynecological examination was additionally performed. It included a clinical examination, transrectal palpation, and ultrasound scanning, which was performed using the Scanner Falco device (8 MHz). Ultrasound was used to determine the size, echodensity, tissue homogeneity, and echogenicity of the reproductive structures. For immunological studies, blood was taken from the jugular vein of sick animals and cows from the control group (n=23) in the morning before feeding into sterile tubes. The total protein content in the blood serum of cows was determined using the biuret reaction, and the protein fractions were determined using the nephelometric method, and the A/G ratio was calculated. The amount of C-reactive protein was determined using the immunofluorescence method. The concentration of ceruloplasmin (CP) in the blood serum was determined by the standard method based on the oxidation of p-phenylenediamine with the participation of CP. The level of fibrinogen was determined spectrophotometrically, haptoglobin – by turbidimetric method. The level of circulating immune complexes (CIC) and their fractional composition were analyzed on the basis of determination of their molecular weight. The concentrations of interleukins (IL-1a and IL-8) and tumor necrosis factor-α (TNF-α) were measured by solid-phase enzyme immunoassay using commercial kits of monoclonal antibodies and reagents manufactured by Cytokin LLC, Saint Petersburg, Russia.

Results. According to the Tukey multiple comparison analysis, the most significant increase in the level of CIC was observed in the group of animals with comorbid pathology. This indicates that the combined course of endometritis and hoof diseases leads to a more severe systemic inflammatory response compared to isolated forms of the diseases. This is evidenced by the indicators of protein metabolism, the level of acute phase proteins, the cytokine profile, and the amount of circulating immune complexes in the blood samples of the experimental animals.

Conclusion. Currently, there is an urgent need for a comprehensive fundamental study of comorbidity in veterinary practice. The results of our research demonstrate that the comorbid course of orthopedic and obstetric-gynecological pathologies in high-yielding animals is characterized by a more severe clinical picture compared to isolated forms of monopathologies. This is evidenced by our immunological screening. In this regard, when an animal has multiple pathologies, an individual approach is necessary, which requires a comprehensive study of the clinical course of the main, concomitant, and even previous diseases, as well as their comprehensive

diagnosis and rational treatment. In the future, it is necessary to create a universal tool that allows veterinarians to instantly and easily assess the structure, severity, and possible consequences of concomitant diseases in animals, conduct targeted diagnostics, and then prescribe the correct set of medical measures.

Keywords: factor infections; immunological indicators; endometritis; orthopedic pathology; comorbidity; cows

Научная статья

ИММУНОЛОГИЧЕСКИЙ СТАТУС ВЫСОКОПРОДУКТИВНЫХ КОРОВ С СОПУТСТВУЮЩЕЙ АКУШЕРСКО-ГИНЕКОЛОГИЧЕСКОЙ И ОРТОПЕДИЧЕСКОЙ ПАТОЛОГИЕЙ

*В.И. Луцай, П.А. Руденко, В.Д. Сибирцев,
А.М. Нефедов, А.А. Руденко*

Аннотация

Обоснование. Ветеринарная практика свидетельствует о наличии клинически выраженной связи между акушерскими заболеваниями и ортопедической патологией у высокопродуктивных коров. В частности, исследование, выполненное при поддержке РНФ (грант № 24-26-00172), выявило четкую взаимосвязь между развитием гнойно-некротических поражений копыт и возникновением послеродового эндометрита у высокопродуктивных коров. На примере поголовья ЗАО «Воскресенское» Воскресенского района Московской области в настоящем исследовании были сформированы рандомизировано следующие группы животных: группа 1 (n=28): коровы с острым гнойно-катаральным послеродовым эндометритом; группа 2 (n=25): животные с гнойно-некротическими поражениями копыт; группа 3 (n=27): коровы с коморбидным течением обеих патологий; контрольная группа (n=23): клинически здоровые животные. У всех особей, отобранных в заявленное иссле-

дование, производили забор яремной венозной крови натощак в стерильные пробирки для последующего иммунологического анализа. Было установлено, что коморбидное течение этих патологий протекает значительно тяжелее, чем каждая из болезней в отдельности. Об этом свидетельствует проведенный нами иммунологический скрининг. В связи с этим при ассоциированном течении нескольких патологий у животного необходимо применять индивидуальный подход, что диктует необходимость комплексного изучения клинического течения основных, сопутствующих и даже перенесенных заболеваний, их всесторонней диагностики, а также рационального лечения.

Цель. Цель исследования - изучить иммунологический статус высокопродуктивных коров с сопутствующей акушерско-гинекологической и ортопедической патологией.

Материалы и методы. Для оценки динамики клинической манифестации заболеваний копыт в течение года ежемесячно проводили ортопедический осмотр. В ходе данного осмотра оценивали: степень и характер деформаций копыт; интенсивность разрушения рогового слоя; наличие специфических поражений: карманов, расслоений и трещин, а также положение грудных и тазовых конечностей. У коров с выявленными гнойно-некротическими поражениями в послеродовой период дополнительно выполняли детальное акушерско-гинекологическое обследование. Оно включало клинический осмотр, трансректальную пальпацию и УЗИ-сканирование, которое проводили на аппарате Scanner Falco (8 МГц). С помощью ультразвука определяли размеры, эхоплотность, однородность тканей и характер эхогенности структур репродуктивных органов.

Для иммунологических исследований кровь брали из яремной вены больных животных и коров из контрольной группы (n=23) утром перед кормлением в стерильные пробирки. Содержание общего белка в сыворотке крови коров определяли с помощью биуретовой реакции, белковых фракций - нефелометрическим методом, рассчитывали соотношение A/G. Количество С-реактивного белка определяли методом иммунофлюоресценции. Концентрацию церулоплазмина (ЦП) в сыворотке крови определяли стандартным методом, основанным на окислении п-фенилендиамина с участием ЦП. Уровень фибриногена определяли спектрофотометрически, гаптоглобина - турбидиметрическим методом. Уровень циркулирующих иммунных комплексов (ЦИК) и их фракционный состав анализировали на основе определения их молекулярной массы. Концентрации интерлейкинов (IL-1α и IL-8) и фактора некроза опухоли-α (TNF-α) измеряли методом твердофазного иммуноферментного анализа с использованием коммерческих наборов моноклональных антител и реагентов

производства (ООО «Цитокин», Санкт-Петербург, Россия).

Результаты. Согласно анализу множественных сравнений Тьюки, наиболее значимое повышение уровня ЦИК было зафиксировано в группе животных с коморбидной патологией. Это свидетельствует о том, что сочетанное течение эндометрита и заболеваний копыт приводит к более тяжелой системной воспалительной реакции по сравнению с изолированными формами болезней. Об этом свидетельствуют показатели белкового обмена, уровень белков острой фазы воспаления, цитокиновый профиль, а также количество циркулирующих иммунных комплексов в образцах крови подопытных животных.

Заключение. В настоящее время остро стоит вопрос об общем фундаментальном исследовании коморбидности в ветеринарной практике. Результаты исследования демонстрируют, что коморбидное течение ортопедической и акушерско-гинекологической патологии у высокопродуктивных животных характеризуется более тяжелой клинической картиной по сравнению с изолированными формами монопатологий. Об этом свидетельствует проведенный нами иммунологический скрининг. В связи с этим при ассоциированном течении нескольких патологий у животного необходимо применять индивидуальный подход, что диктует необходимость комплексного изучения клинического течения основных, сопутствующих и даже перенесенных заболеваний, их всесторонней диагностики, а также рационального лечения. В перспективе необходимо создание универсального инструмента, позволяющего ветеринарному врачу мгновенно и легко оценить структуру, тяжесть и возможные последствия сопутствующих заболеваний у животных, провести целенаправленную диагностику, а затем назначить правильный комплекс лечебных мероприятий.

Ключевые слова: факторные инфекции; иммунологические показатели; эндометрит; ортопедическая патология; коморбидность; коровы

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Introduction

The comorbidity of gynecological and orthopedic pathologies in dairy cattle results in substantial economic losses, stemming from diminished milk yield and the elevated expenses of diagnostic, therapeutic, and preventive veterinary measures [1-5]. The high prevalence of reproductive disorders and purulent-necrotic digital lesions necessitates the development of novel methods for

their early diagnosis and management [2; 4; 6-8]. The development of various non-infectious pathologies in cows is multifactorial, stemming from stress, poor management practices, and technical errors. Key contributors include anthropogenic stress, inadequate housing, nutritional imbalances, improper dry-off periods, poor sanitation, antimicrobial misuse, endemic parasites, and mistakes in artificial insemination [1; 9-13]. In high-yielding dairy cows, systemic metabolic disorders frequently lead to the comorbid manifestation of orthopedic, obstetric, and gynecological diseases [14-19]. The prevalence of orthopedic pathology alone is a major concern, affecting 18-80% of herds. This results in a 40-50% decline in milk yield and the premature culling of up to 37% of animals, culminating in severe economic losses for producers [20-24]. The high prevalence of orthopedic pathology is furthermore associated with a significant reduction in the herd's reproductive performance. This is evidenced by impaired fertility, extended postpartum anaphrodisia, and an increased proportion of infertile cows, collectively diminishing overall reproductive efficiency [25; 26].

Existing evidence confirms etiological and pathogenetic links between reproductive and orthopedic disorders in cattle [5; 27-30]. However, the current lack of a holistic, systematic approach results in fragmented and thus less effective treatment and prevention strategies [31; 32]. Therefore, researching common triggers and shared pathological mechanisms is crucial. This will enable the development of reliable diagnostic and prognostic criteria for managing these comorbid conditions.

Consequently, this research aims to establish a foundation for developing targeted therapeutic and preventive strategies, ultimately enhancing cow health and reproductive performance. Based on this rationale, the objective of our study was to characterize the immunological profiles of cows with endometritis, orthopedic pathology, and comorbid presentation of both conditions.

Purpose. This study aims to evaluate the immunological status of high-yielding dairy cows experiencing comorbid obstetric-gynecological and orthopedic pathologies.

Materials and methods

This study was conducted within the herd of JSC Voskresenskoye (Voskresensky District, Moscow Region), which comprised 1,450 cattle, including 830 cows. The research was funded by grant No. 24-26-00172 from the Russian Science Foundation (https://rscf.ru/project/24-26-00172/). The experimental protocol was reviewed and approved by the Bioethics Commission of the Department of Veterinary Medicine at «ROSBIOTEKH», confirming adherence to international standards for the humane treatment of experimental animals, specifically the provisions

of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (ETS 123, 1986). The study cohorts consisted of: high-producing cows with acute purulent-catarrhal postpartum endometritis (n=28); animals with purulent-necrotic diseases in the digits (n=25); cows with comorbid presentation of both endometritis and orthopedic pathology (n=27).

Monthly orthopedic examinations were conducted to assess the severity and type of deformities, the rate of hoof horn deterioration, and the progression of hoof diseases over a one-year period. Evaluations focused specifically on hoof conformation (presence of deformities), the integrity of the hoof horn (detecting pockets, fissures, delamination, and cracks), and the posture and alignment of both thoracic and pelvic limbs. In cows exhibiting purulent-necrotic digital lesions during the postpartum period, comprehensive obstetric and gynecological examinations were performed. These included evaluation of clinical signs, transrectal palpation, and ultrasonography of the reproductive organs using a Scanner Falco device with an 8 MHz transducer. The ultrasonographic assessment measured tissue dimensions, echo density, structural homogeneity, and the echogenic properties of both normal and pathological features.

Blood was collected from the jugular vein of sick animals and cows from the control group (n=23) in the morning before feeding in sterile tubes for immunological studies. The content of total protein in the blood serum of cats was determined by the biuret reaction, protein fractions - by the nephelometric method, the A/G ratio was calculated. The amount of C-reactive protein was determined by the immunofluorescence method. The concentration of ceruloplasmin (CP) in the blood serum was determined by the standard method based on the oxidation of p-phenylenediamine with the participation of CP. The fibrinogen level was determined spectrophotometrically, and haptoglobin - by the turbidimetric method. The total level of circulating immune complexes (CIC) and their fractional composition were determined by molecular weight. The content of interleukins (IL-1α and IL-8) and tumor necrosis factor (TNF-α) was determined using a solid-phase enzyme-linked immunosorbent assay of double antibodies using monoclonal antibody kits and reagents from Cytokine LLC (St. Petersburg, Russia).

The obtained data were subjected to statistical analysis and are presented as tables and figures. All computations were performed using STATISTICA 7.0 (StatSoft, USA) software with conventional statistical methods. Distribution normality was first assessed using ANOVA. The following parameters were calculated: 95% confidence interval (CI), arithmetic mean (Mean), standard error (SE), and standard deviation (SD). Statistical significance of differences was determined using Tukey's test with the following notation: between control and ex-

perimental groups I–III – * p<0.05; ** p<0.01; *** p<0.001; between groups I and II – ◊ p<0.05; ◊◊ p<0.01; ◊◊◊ p<0.001; between groups I and III – ⌐ p<0.05; ⌐⌐ p<0.01; ⌐⌐⌐ p<0.001; between groups II and III – ⁂ p<0.05; ⁂⁂ p<0.01; ⁂⁂⁂ p<0.001.

Results

Clinical observations consistently reveal a clinically significant association between obstetric and orthopedic disorders in high-yielding dairy cattle. Notably, postpartum metritis demonstrates a higher incidence in cows presenting with purulent-necrotic lesions of the distal limbs, whether developed pre-partum or during the early postpartum period. Table 1 presents the protein metabolism parameters evaluated in high-productivity cows exhibiting comorbid endometritis and purulent-necrotic hoof pathology.

Table 1.

Protein metabolism indices in highly productive cows with comorbid course of endometritis and purulent-necrotic diseases in the hoof area

Index	Biometrics	Healthy cows (n=23)	Groups of sick cows			ANOVA test
			I (n=28)	II (n=25)	III (n=27)	
Total protein, g/l	M±SD	78.56±3.62	77.97±5.79	79.60±4.49	81.35±7.20	F=1.93; p<0.5
	95% CI	76.99–80.13	75.73–80.22	77.74–81.45	78.51–84.21	
Albumins, g/l	M±SD	39.09±3.17	35.03±4.92 *	33.39±6.38 ***	34.14±4.65 ***	F=6.27; p<0.001
	95% CI	37.71–40.45	33.12–36.94	30.76–36.02	32.29–35.98	
Globulins, g/l	M±SD	39.47±4.55	42.94±7.38	46.20±7.11 **	47.21±6.90 ***	F=6.79; p<0.001
	95% CI	37.51–41.44	40.08–45.81	43.27–49.14	44.48–49.95	
A\G, units	M±SD	1.00±0.17	0.86±0.28	0.76±0.25 **	0.74±0.17 ***	F=7.34; p<0.001
	95% CI	0.94–1.08	0.75–0.97	0.65–0.86	0.68–0.81	
alpha globulins, g/l	M±SD	9.69±2.06	13.29±4.13 ***	10.14±2.06 ◊◊	16.51±3.52 *** ⌐⌐⁂⁂⁂	F=26.08; p<0.001
	95% CI	8.80–10.58	11.69–14.89	9.29–10.99	15.12–17.91	
beta globulins, g/l	M±SD	11.04±2.23	7.22±1.89 ***	7.90±2.09 ***	7.03±1.79 ***	F=21.02; p<0.001
	95% CI	10.07–12.01	6.48–7.95	7.03–8.77	6.32–7.74	
gamma globulins, g/l	M±SD	18.74±6.19	22.34±6.37	28.16±7.58 ***◊	23.24±7.79	F=7.35; p<0.001
	95% CI	16.06–21.42	19.87–24.82	25.03–31.29	20.16–26.32	
alpha1 proteinase inhibitor, mg/l	M±SD	29.29±5.81	27.34±5.81	30.47±5.35	31.73±3.27 ⌐	F=3.61; p<0.05
	95% CI	26.77–31.80	25.08–29.59	28.26–32.68	30.43–33.01	
alpha2-macroglobulin, g/l	M±SD	1.12±0.09	1.15±0.18	0.89±0.23 **◊◊	0.77±0.87 *** ⌐⌐	F=20.78; p<0.001
	95% CI	1.08–1.16	1.09–1.22	0.79–0.99	0.67–0.88	

Using one-way analysis of variance (ANOVA test), significant changes were found in the parameters of total protein (F=1.93; p<0.5), albumin (F=6.27; p<0.001), globulin (F=6.79; p<0.001), albumin/globulin ratio (F=7.34; p<0.001), alpha-globulins (F=26.08; p<0.001), beta-globulins (F=21.02; p<0.001), gamma-globulins (F=7.35; p<0.001), alpha1-proteinase inhibitor (F=3.61; p<0.05) and alpha2-macroglobulin (F=20.78; p<0.001). In this case, the null hypothesis that the protein metabolism indices in animals of different groups belong to the same general population can be rejected. Subsequently, Tukey's multiple comparisons analysis was performed for a detailed statistical analysis of the differences between the experimental groups of animals. Thus, it was found that the most significant changes in protein metabolism indices occur with the clinical manifestation of the comorbid course of endometritis and purulent-necrotic diseases in the hoof area in highly productive cows. At the same time, a decrease in the amount of albumins by 10.14 times (p<0.001); albumin/globulin ratio by 1.35 times (p<0.001); beta-globulins by 1.57 times (p<0.001) and alpha2-macroglobulins by 1.45 times (p<0.001), against the background of an increase in globulins by 1.19 times (p<0.001) and alpha-globulins by 1.70 times (p<0.001), when compared with the indicators of healthy animals.
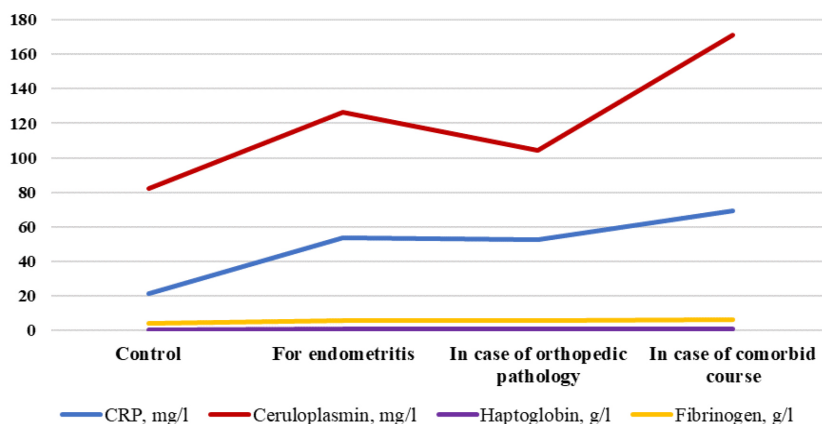
Fig. 1. Level of acute phase inflammation proteins in highly productive cows with comorbid endometritis and purulent-necrotic diseases in the hoof area

One of the main markers of the severity of the inflammatory reaction are acute phase proteins. These proteins are synthesized in the liver, and their concentration depends on the stage of the disease and the extent of damage. High correlation of the concentration of acute phase proteins in the blood with the

activity of the infectious process and its stage distinguishes them favorably from such indicators as an increase in ESR or a shift in the leukocyte formula to the left. In this regard, we also determined the level of acute phase proteins of inflammation in highly productive cows with comorbid endometritis and purulent-necrotic diseases in the hoof area, which is shown in the figure.

The data in the figure indicate that during the clinical manifestation of both individual pathologies and their comorbid course, the indices of acute phase inflammation proteins in the blood serum increase significantly. Thus, in cows with endometritis, a highly reliable (p<0.001) increase in C-reactive protein, fibrinogen, haptoglobin and ceruloplasmin was recorded by 2.50 times, from 21.56±6.63 mg/l to 53.96±17.55 mg/l; by 1.45 times, from 4.09±0.53 g/l to 5.92±0.39 g/l; by 2.04 times from 0.51±0.10 g/l to 1.04±0.18 g/l and by 1.54 times from 82.17±5.19 mg/l to 126.32±11.84 mg/l, respectively, when compared with clinically healthy animals. It was established that with clinical manifestation of purulent-necrotic diseases in the hoof area in highly productive cows, a reliable increase (p<0.001) was observed in the blood serum of C-reactive protein from 21.56±6.63 mg/l to 52.44±10.38 mg/l by 58.9%; fibrinogen from 4.09±0.53 g/l to 5.96±0.63 g/l, by 32.2%; haptoglobin from 0.51±0.10 g/l to 1.01±0.23 g/l, by 49.5% and ceruloplasmin from 82.17±5.19 mg/l to 104.28±12.98 mg/l, by 21.2%. It should be noted that in cows with comorbid endometritis and orthopedic pathology, the most noticeable increase (p<0.001) in acute phase proteins was observed: CRP by 3.21 times, from 21.56±6.63 mg/l to 69.26±6.28 mg/l; fibrinogen by 1.57 times, from 4.09±0.53 g/l to 6.42±1.19 g/l; haptoglobin by 2.39 times, from 0.51±0.10 g/l to 1.22±0.47 g/l; CP by 2.08 times, from 82.17±5.19 mg/l to 171.22±36.53 mg/l, when compared with the indicators of healthy animals.

The level of proinflammatory cytokines in the blood serum of cows with single pathologies, as well as with comorbid course of endometritis and purulent-necrotic diseases in the hoof area is given in Table 2.

Reliable changes in the levels of IL-1alpha (F=146.01; p<0.001), IL-8 (F=254.00; p<0.001) and TNF-alpha (F=130.41; p<0.001) in the blood serum of animals from different experimental groups were established using the one-way analysis of variance (ANOVA test), which made it possible to conduct Tukey's multiple comparisons analysis to identify differences between the experimental groups. It was shown that both in case of single pathologies in cows and in case of comorbid course of two diseases, a highly reliable increase in the level of proinflammatory interleukins was recorded in the blood serum. However, the most significant deviations in the cytokine profile were revealed in animals with comorbid course of endometritis and purulent-necrotic diseases in the

hooves. Thus, in the combined course of obstetric-gynecological and orthopedic pathologies, a reliable increase in the level of IL-1alpha was revealed from 19.44±1.95 pg/ml to 40.15±2.41 pg/ml, by 2.06 times (p<0.001); IL-8 from 13.65±1.27 pg/ml to 39.15±3.37 pg/ml, by 2.86 times (p<0.001); TNF-alpha from 42.04±2.95 pg/ml to 102.33±8.23 pg/ml, by 2.43 times (p<0.001), when compared with clinically healthy cows.

Table 2.

Cytokine profile in highly productive cows with comorbid endometritis and purulent-necrotic diseases in the hoof area

Index	Biomet-rics	Healthy cows (n=23)	Groups of sick cows			ANOVA test
			I (n=28)	II (n=25)	III (n=27)	
IL-1alpha, pg/ml	M±SD	19.44±1.95	33.39±3.81 ***	34.12±5.14 ***	40.15±2.41 *** ⊓⧧⧧⧧	F=146.01; p<0.001
	95% CI	18.59–20.27	31.91–34.87	31.99–36.24	39.19–41.10	
IL-8, pg/ml	M±SD	13.65±1.27	26.04±4.29 ***	29.72±3.20 ***◊◊◊	39.15±3.37 *** ⊓⧧⧧⧧	F=254.00; p<0.001
	95% CI	13.11–14.19	24.37–27.70	28.40–31.03	37.82–40.48	
TNF-alpha, pg/ml	M±SD	42.04±2.95	74.21±17.67 ***	74.68±6.58 ***	102.33±8.23 *** ⊓⧧⧧⧧	F=130.41; p<0.001
	95% CI	40.76–43.32	67.36–81.07	71.96–77.39	99.08–105.59	

The levels of circulating immune complexes in the blood serum of highly productive animals with a single manifestation of the disease, as well as with comorbid course of endometritis and purulent-necrotic diseases in the hoof area are shown in Table 3.

Tukey's multiple comparisons analysis showed that with clinical manifestation of both endometritis and orthopedic pathology in cows, a reliable increase in CIC levels is recorded in the blood, but the most significant increases are noted in the group with comorbid endometritis and purulent-necrotic diseases in the hooves. Thus, in highly productive animals with combined manifestation of endometritis and orthopedic pathology, a highly reliable (p < 0.001) increase in the level of CIC, general was recorded in the blood serum from 288.08 ± 26.9 un. wh. space to 583.56 ± 52.02 un. wh. space, by 2.02 times; CIC, large from 35.78 ± 5.22 un. wh. space to 56.41 ± 12.16 un. wh. space, by 1.57 times; CIC, average from 84.30±5.29 un. wh. space to 107.48±12.15 un. wh. space, by 1.27 times and CIC, small from 168.00±28.51 un. wh. space to 419.67±54.89 un. wh. space, by 2.49 times, when compared with the indicators of healthy cows.

Table 3.

Circulating immune complexes (CIC) in high-yielding cows with comorbid endometritis and purulent-necrotic diseases in the hoof area

Index	Biomet-rics	Healthy cows (n=23)	Groups of sick cows			ANOVA test
			I (n=28)	II (n=25)	III (n=27)	
CIC, general, un. wh. space	M±SD	288.08±26.9	398.00±28.04 ***	418.92±34.58 ***	583.56±52.02 *** ππ⍓⍓⍓	F=273.90; p<0.001
	95% CI	27.6–299.72	387.12–428.04	404.65–433.19	562.97–604.13	
CIC, large, un. wh. space	M±SD	35.78±5.22	47.04±2.75 ***	49.84±7.65 ***	56.41±12.16 *** ππ⍓	F=29.63; p<0.001
	95% CI	33.52–38.04	45.97–48.10	46.68–52.99	51.59–61.22	
CIC, average, un. wh. space	M±SD	84.30±5.29	90.89±11.91	101.80±11.51 ***◊◊	107.48±12.15 *** ππ	F=29.63; p<0.001
	95% CI	82.01–86.59	86.27 – 95.51	97.05 – 106.55	102.67 – 112.29	
CIC, small, un. wh. space	M±SD	168.00±28.51	262.82±41.39 ***	267.28±36.37 ***	419.67±54.89 *** ππ⍓⍓⍓	F=156.43; p<0.001
	95% CI	155.67–180.32	246.77–278.87	252.27–282.29	397.65–441.38	

Consequently, the clinical presentation of comorbid orthopedic and obstetric-gynecological pathology in high-yielding cows is more severe than that of either condition occurring in isolation. This is evidenced by protein metabolism indicators, the level of acute phase inflammation proteins, the cytokine profile, as well as the number of circulating immune complexes in blood samples of experimental animals.

Conclusion

Currently, the issue of a general fundamental study of comorbidity in veterinary practice is urgently needed. It has been established that the clinical manifestation of comorbid orthopedic and obstetric-gynecological pathology in highly productive animals has a more severe manifestation than in the course of individual diseases. This is evidenced by the immunological screening we conducted. Therefore, the management of animals with comorbid conditions requires an individualized approach. This necessitates a comprehensive evaluation of the clinical presentation of primary, concurrent, and previous diseases, coupled with integrated diagnostic methods and rational therapeutic strategies. In the future, it is necessary to create a universal tool that allows a veterinarian to instantly and easily assess the structure, severity and possible consequences of comorbid diseases in animals, conduct targeted diagnostics, and then prescribe the correct set of therapeutic measures.

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AUTHOR CONTRIBUTIONS
The authors contributed equally to this article.

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DATA ABOUT THE AUTHORS
Vladimir I. Lutsay, Professor of the Department of Veterinary Medicine
Russian Biotechnological University
11, Volokolamsiy Ave., 125808, Moscow, Russian Federation
recaro21@bk.ru
ORCID: https://orcid.org/0009-0003-4668-2545

Pavel A. Rudenko, Professor of the Department of Veterinary Medicine
Russian Biotechnological University; People's Friendship University of Russia
11, Volokolamsiy Ave., 125808, Moscow, Russian Federation; 6, Miklukho-Maklaya Str., Moscow, 117198, Russian Federation
pavelrudenko76@yandex.ru
ORCID: https://orcid.org/0000-0002-0418-9918

Vladimir D. Sibirtsev, Postgraduate Student of the Department of Veterinary Medicine
Russian Biotechnological University

11, Volokolamsiy Ave., 125808, Moscow, Russian Federation
sibircev_vd@mail.ru
ORCID: https://orcid.org/0009-0002-5302-3321

Anton M. Nefedov, Postgraduate Student of the Department of Veterinary Medicine
Russian Biotechnological University
11, Volokolamsiy Ave., 125808, Moscow, Russian Federation
goose322@mail.ru
ORCID: https://orcid.org/0009-0002-6908-2895

Andrei A. Rudenko, Professor of the Department of Veterinary Medicine
Russian Biotechnological University
11, Volokolamsiy Ave., 125808, Moscow, Russian Federation
vetrudek@yandex.ru
ORCID: https://orcid.org/0000-0002-6434-3497

ДАННЫЕ ОБ АВТОРАХ

Луцай Владимир Иванович, профессор кафедры «Ветеринарная медицина»
Российский биотехнологический университет (РОСБИОТЕХ)
Волоколамское ш., 11, г. Москва, 125808, Российская Федерация
recaro21@bk.ru

Руденко Павел Анатольевич, профессор кафедры «Ветеринарная медицина»
Российский биотехнологический университет (РОСБИОТЕХ); Российский университет дружбы народов им. Патриса Лумумбы
Волоколамское ш., 11, г. Москва, 125808, Российская Федерация; ул. Миклухо-Маклая, 6, г. Москва, 117198, Российская Федерация
pavelrudenko76@yandex.ru

Сибирцев Владимир Дмитриевич, аспирант кафедры «Ветеринарная медицина»
Российский биотехнологический университет (РОСБИОТЕХ)
Волоколамское ш., 11, г. Москва, 125808, Российская Федерация
sibircev_vd@mail.ru

Нефедов Антон Максимович, аспирант кафедры «Ветеринарная медицина»
Российский биотехнологический университет (РОСБИОТЕХ)

Волоколамское ш., 11, г. Москва, 125808, Российская Федерация
goose322@mail.ru

Руденко Андрей Анатольевич, профессор кафедры «Ветеринарная медицина»
    Российский биотехнологический университет (РОСБИОТЕХ)
    Волоколамское ш., 11, г. Москва, 125808, Российская Федерация
    vetrudek@yandex.ru