Yavuz Öztürkler[1]
Nurjumanova Zhanat Mekeshovna[1], Muratbayev Dauletbek Manarbekovich[1], Tastemirova Shynar Abdualykyzy[1], Mukatayev Aitbek Muratuli[1], Ahmadieva Ainur Zhomartovna[1], Ahmetzhanova Ayzhan Erkingazyevna[1], Mustafa Reha Coşkun[2].

[3] Kafkas University Veterinary Faculty, Department of Obstetrics and Gynecology, Kars–Türkiye
E-mail: yavuzozturkler@gmail.com

[2] NAO "Shakarim University of Semey", Abay region, Semey, 20A Glinka STR., 071412, Kazakhstan

RELATIONSHIP BETWEEN UTERUS INFECTIONS AND FERTILITY IN CATTLE

Annotation

Uterine infections in cows, particularly postpartum uterine diseases such as endometritis and metritis, are significant contributors to reproductive failure and economic loss in the dairy industry. These infections can lead to prolonged calving-to-conception intervals, increased culling rates, and reduced milk production, ultimately impacting herd profitability and animal welfare (Hossain et al., 2015; Rosales & Ametaj, 2021; Sheldon & Owens, 2017). The postpartum period is critical for the recovery of the uterus and the resumption of ovarian cyclicity, both of which are essential for successful conception. However, the presence of pathogenic bacteria can disrupt these physiological processes, leading to inflammation and impaired fertility (Raliou et al., 2019; LeBlanc, 2010). The etiology of uterine infections is multifactorial, often linked to factors such as retained placenta, calving difficulties, and compromised immune status (Onyango et al., 2014; Han et al., 2005). For instance, retained placenta can lead to an increased incidence of endometritis, which is characterized by inflammation of the endometrium and can significantly impair fertility (Han et al., 2005; Negasee et al., 2020). The inflammatory response associated with uterine infections can also alter the uterine environment, affecting the expression of genes related to reproductive function and leading to subclinical endometritis, which often goes undiagnosed but can still adversely affect fertility outcomes (Arias et al., 2018).

Keywords: endometritis, postpartum, the etiology of uterine infections is multifactorial, inflammation

Introduction

Uterine infections in cows, particularly postpartum uterine diseases such as endometritis and metritis, are significant contributors to reproductive failure and economic loss in the dairy industry. These infections can lead to prolonged calving-to-conception intervals, increased culling rates, and reduced milk production, ultimately impacting herd profitability and animal welfare (Hossain et al., 2015; Rosales & Ametaj, 2021; Sheldon & Owens, 2017). The postpartum period is critical for the recovery of the uterus and the resumption of ovarian cyclicity, both of which are essential for successful conception. However, the presence of pathogenic bacteria can disrupt these physiological processes, leading to inflammation and impaired fertility (Raliou et al., 2019; LeBlanc, 2010). The etiology of uterine infections is multifactorial, often linked to factors such as retained placenta, calving difficulties, and compromised immune status (Onyango et al., 2014; Han et al., 2005). For instance, retained placenta can lead to an increased incidence of endometritis, which is characterized by inflammation of the endometrium and can significantly impair fertility (Han et al., 2005; Negasee et al., 2020). The inflammatory response associated with uterine infections can also alter the uterine environment, affecting the expression of genes related to reproductive function and leading to subclinical endometritis, which often goes undiagnosed but can still adversely affect fertility outcomes (Arias et al., 2018). Recent studies have highlighted the role of the uterine microbiota in reproductive health. Dysbiosis, or an imbalance in the microbial community within the uterus, has been associated with increased incidences of uterine infections and subsequent fertility issues. For example, cows diagnosed with clinical endometritis exhibited reduced microbial diversity and an overrepresentation of pathogenic bacteria such as Trueperella pyogenes (Webb, 2023). This shift in the microbiota can disrupt the normal immune response and hormonal regulation necessary for successful reproduction (Ong et al., 2021). Moreover, systemic inflammation resulting from uterine infections can affect ovarian function. Inflammatory cytokines released during uterine infections can interfere with the normal

hormonal signaling pathways, leading to delayed ovulation and reduced fertility (Cheong et al., 2017). The presence of uterine pathogens has been shown to correlate with altered levels of reproductive hormones, such as oestradiol, which are critical for ovulation and conception (Ong et al., 2021; Yagisawa et al., 2023). In conclusion, uterine infections in cows represent a complex interplay of microbial, immunological, and physiological factors that collectively influence reproductive outcomes. Addressing these infections through improved management practices, timely veterinary intervention, and possibly the use of probiotics to restore microbial balance may enhance fertility and overall herd health (Rosales & Ametaj, 2021; LeBlanc, 2010). Fertility and uterine infections in cows are critical issues in the dairy industry, significantly impacting productivity and economic viability. The relationship between milk production and fertility is well-documented, with studies indicating that high milk yield can negatively affect reproductive performance. For instance, Aungier et al. found that increased milk yield was associated with a decreased likelihood of detecting estrous behavior, suggesting that high-producing cows may experience reproductive challenges due to physiological stressors related to lactation (Aungier et al., 2012). This antagonistic relationship is further supported by Walsh et al (2011). who noted that the rise in milk production over the past decades has coincided with a decline in fertility rates among dairy cows, attributing this to a complex interplay of genetic, physiological, nutritional, and management factors. Uterine infections, such as metritis and endometritis, are significant contributors to infertility in cows. Ribeiro et al. highlighted that postpartum inflammatory diseases can adversely affect uterine health and subsequent fertility, indicating that cows suffering from such conditions are less likely to conceive (Ribeiro et al., 2016). Similarly, Dutta et al. reported that a substantial percentage of repeat breeder cows exhibited mucopurulent vaginal discharge, a clinical sign of uterine infection, which was prevalent in 62.5% of the cases studied (Dutta et al., 2019). The presence of such infections can lead to prolonged intervals between calving and subsequent estrus, ultimately reducing the overall reproductive efficiency of the herd. In addition to direct infections, systemic diseases such as leptospirosis have been linked to reproductive failures. Erregger et al. found that seropositive cows for leptospirosis experienced a significant drop in fertility, which could be attributed to the pathogen's presence in the reproductive tract (Erregger et al., 2020). This finding aligns with the observations of Chebel et al.(2018) who noted that postpartum health issues, including infections, could delay the resumption of ovarian cycles and reduce pregnancy rates following artificial insemination. Furthermore, metabolic disorders, often exacerbated by negative energy balance, can also impair reproductive performance, as highlighted by Leroy et al (2018)., who emphasized the importance of managing cow health to optimize fertility outcomes (Vieira, 2023). The role of pathogens in reproductive health extends beyond direct infections. For instance, the presence of Ureaplasma diversum has been associated with reproductive problems in cows, with studies indicating that vulvar lesions and reproductive disorders were significantly more common in cows infected with this bacterium (Azevedo et al., 2016). Additionally, mycoplasma infections have been implicated in various reproductive disorders, including infertility, underscoring the need for effective diagnostic and management strategies to mitigate these risks (Parker et al., 2018). In summary, the interplay between fertility and uterine infections in cows is multifaceted, involving factors such as milk production, systemic health, and the presence of infectious agents. Addressing these issues requires a comprehensive approach that includes monitoring reproductive health, managing nutrition and metabolic status, and implementing effective disease prevention strategies.

Research results

Uterine infections in cows, particularly postpartum uterine diseases such as endometritis and metritis, are significant contributors to reproductive failure and economic loss in the dairy industry. These infections can lead to prolonged calving-to-conception intervals, increased culling rates, and reduced milk production, ultimately impacting herd profitability and animal welfare (Piersanti et al., 2019; Bromfield et al., 2015; Paiano et al., 2023). The postpartum period is critical for the recovery of the uterus and the resumption of ovarian cyclicity, both of which are essential for successful conception. However, the presence of pathogenic bacteria can disrupt these physiological processes, leading to inflammation and impaired fertility (LeBlanc, 2012). The etiology of uterine infections is multifactorial, often linked to factors such as retained placenta, calving difficulties, and compromised immune status (Kasimanickam et al., 2013). For instance, retained placenta can lead to an increased incidence of endometritis, characterized by inflammation of the endometrium, which can significantly impair fertility (Kasimanickam et al., 2013; Yusuf et al., 2010). The inflammatory response associated with uterine infections can also alter the uterine environment, affecting the expression of genes related

to reproductive function and leading to subclinical endometritis, which often goes undiagnosed but can still adversely affect fertility outcomes (Ong et al., 2021). Recent studies have highlighted the role of the uterine microbiota in reproductive health. Dysbiosis, or an imbalance in the microbial community within the uterus, has been associated with increased incidences of uterine infections and subsequent fertility issues. For example, cows diagnosed with clinical endometritis exhibited reduced microbial diversity and an overrepresentation of pathogenic bacteria such as Trueperella pyogenes (Santos & Bicalho, 2012; Becker et al., 2023). This shift in the microbiota can disrupt the normal immune response and hormonal regulation necessary for successful reproduction (Miranda-CasoLuengo et al., 2019). Moreover, systemic inflammation resulting from uterine infections can affect ovarian function. Inflammatory cytokines released during uterine infections can interfere with the normal hormonal signaling pathways, leading to delayed ovulation and reduced fertility (Wang et al., 2021). In uterine infections, bacterial endotoxin lipopolysaccharide (LPS) detected in follicular fluid negatively affects follicular growth (Sheldon et al. 2002). In cows with endometritis, endotoxins suppress GnRH and LH secretion and dominant follicle ovulation does not occur. In addition, follicle development is very slow in animals with endometritis and blood estradiol levels are low. LPS secreted by Gram-negative bacteria inhibits 17β-hydroxylase/17,20-lyase and P450 aromatase enzymes and thus prevents follicular activity (Magata et al. 2014). Even if ovulation occurs in cows with endometritis, the diameter of the corpus luteum (CL) that forms is small and progesterone production by the CL decreases. In addition, cytokines suppress steroidogenesis in luteal cells. Bacterial LPS can initiate the luteolysis mechanism by stimulating the release of PGF2α and PGE2 from the epithelial layer of the endometrium (Sheldon et al. 2009). The presence of uterine pathogens has been shown to correlate with altered levels of reproductive hormones, such as oestradiol, which are critical for ovulation and conception (Miranda-CasoLuengo et al., 2019; Barański et al., 2013).In conclusion, uterine infections in cows represent a complex interplay of microbial, immunological, and physiological factors that collectively influence reproductive outcomes. Addressing these infections through improved management practices, timely veterinary intervention, and possibly the use of probiotics to restore microbial balance may enhance fertility and overall herd health (Bromfield et al., 2015; Osawa, 2021).

Discussion of scientific results

Types of Metritis Metritis can be classified into several categories based on clinical presentation and severity.

Clinical Metritis This form of metritis is characterized by observable clinical signs, typically occurring within the first three weeks postpartum. Cows with clinical metritis often exhibit symptoms such as fever, a thickened uterine wall, and a malodorous reddish-brown discharge from the vagina (Nazhat et al., 2018; Okawa et al., 2021). The condition is usually associated with significant systemic illness, including pyrexia and reduced milk yield. Clinical metritis is often caused by bacterial infections, with common pathogens including Escherichia coli, Trueperella pyogenes, and Fusobacterium necrophorum (Almughlliq et al., 2017; Okawa et al., 2021).

Subclinical Metritis (SCE) Subklinik endometritis mi In contrast to clinical metritis, subclinical metritis does not present overt clinical signs, making it more challenging to diagnose. It is characterized by an inflammatory response in the endometrium, typically identified through endometrial cytology showing elevated levels of polymorphonuclear leukocytes (PMNs) (Hossain et al., 2015; Okawa et al., 2021). Subclinical metritis can lead to prolonged days open and decreased conception rates, significantly impacting reproductive performance without the animal showing obvious signs of illness (Okawa et al., 2021).

Puerperal Metritis This specific type of metritis occurs shortly after calving and is often associated with retained fetal membranes. Puerperal metritis can lead to severe systemic illness and is characterized by a rapid onset of clinical signs, including fever and foul-smelling uterine discharge (Khair et al., 2018).

Endometritis

While not strictly a type of metritis, endometritis involves inflammation of the endometrium and can occur as a sequela to metritis. It may be classified as either clinical or subclinical based on the presence of symptoms and can significantly affect fertility (Williams, 2013; Okawa et al., 2021). In summary, metritis in cattle can be categorized into clinical metritis, subclinical metritis, puerperal metritis, and endometritis. Each type has distinct clinical presentations and implications for reproductive performance. Effective management and early detection are crucial to mitigate the impact of these conditions on cattle health and productivity.

4.5. Particular Role of Subclinical Endometritis on Fertility in Cattle

Subclinical endometritis (SCE) is a prevalent reproductive disorder in dairy cattle that significantly impacts fertility. Unlike clinical endometritis, which presents with overt symptoms such as purulent discharge, SCE often goes unnoticed, yet it can lead to substantial reproductive inefficiencies. The condition is characterized by an inflammatory response in the endometrium, typically indicated by an elevated percentage of polymorphonuclear leukocytes (PMNs) in the uterine cytology (Becker et al., 2023; Miranda-CasoLuengo et al., 2019). Research indicates that SCE can lead to prolonged open days and decreased conception rates. For instance, Vallejo et al. reported that cows diagnosed with SCE had an average of 161 open days, which is significantly higher than that of healthy cows, thereby reducing overall reproductive efficiency (Becker et al., 2023). Similarly, Madoz et al. found that cows with SCE experienced a 16% reduction in pregnancy rates and took approximately 30 days longer to conceive compared to their healthy counterparts (Miranda-CasoLuengo et al., 2019). This delay in conception is critical, as it can lead to extended calving intervals and increased costs for dairy producers. The underlying mechanisms by which SCE affects fertility are multifaceted. The inflammatory environment created by the presence of PMNs and cytokines can disrupt normal uterine function, impairing embryo implantation and development (Wang et al., 2021; Barański et al., 2013). For example, the secretion of prostaglandins and leukotrienes in response to inflammation can alter the uterine environment, making it less conducive for successful embryo attachment (Wang et al., 2021). Furthermore, the presence of inflammatory mediators can lead to changes in the endometrial gene expression profile, affecting uterine receptivity and embryo viability (Barański et al., 2013). The economic implications of SCE are substantial. Herds with a high prevalence of SCE can experience significant financial losses due to decreased reproductive performance, including lower pregnancy rates at first insemination and increased median days open (Nazhat et al., 2018; Okawa et al., 2021). The cumulative effect of these reproductive inefficiencies can lead to increased culling rates and reduced milk production, further impacting the profitability of dairy operations (Nazhat et al., 2018). Effective management strategies are essential to mitigate the effects of SCE on fertility. Early detection through endometrial cytology and appropriate treatment can help restore uterine health and improve reproductive outcomes (Almughlliq et al., 2017; Hossain et al.,2015). Additionally, understanding the risk factors associated with SCE, such as metabolic disorders and calving difficulties, can aid in developing preventive measures to enhance overall herd fertility (Miranda-CasoLuengo et al., 2019; Nazhat et al., 2018). In conclusion, subclinical endometritis plays a significant role in reducing fertility in cattle. Its impact on reproductive performance is characterized by prolonged open days, decreased conception rates, and substantial economic losses for dairy producers. Addressing this condition through early detection and management is crucial for improving reproductive efficiency in cattle herds. Intrauterine infusions of hypertonic solutions, such as dextrose, have been proposed as a therapeutic alternative. These infusions may help reduce bacterial growth in the uterus, increase uterine tone, and provide energy to the natural uterine defenses, such as macrophages and neutrophils (Brick et al., 2012). This approach aims to create a more favorable environment for recovery and improve the chances of successful conception following treatment.

Probiotics The use of probiotics has emerged as a promising alternative therapy for managing uterine infections. Probiotics can help restore the natural microbial balance in the uterus, potentially reducing the incidence of infections and improving reproductive performance (Adnane, 2024). Research indicates that the administration of probiotics may enhance the immune response and promote a healthy uterine environment, which is critical for successful embryo implantation and overall fertility (Adnane, 2024).

Hydroxytyrosol Recent studies have investigated the protective effects of hydroxytyrosol, a phenolic compound found in olive oil, against inflammation and oxidative stress in bovine endometrial cells. Gugliandolo et al. reported that hydroxytyrosol could mitigate lipopolysaccharide (LPS)-induced inflammation, suggesting its potential as a therapeutic agent for managing uterine infections and promoting uterine health (Gugliandolo et al., 2020). This compound may offer a novel approach to reducing inflammation associated with uterine infections.

Silver Nanoparticles Innovative treatments, such as the use of silver nanoparticles, have been explored for their antimicrobial properties. Hussein and Hussein assessed the efficiency of silver nanoparticles in treating endometritis in Iraqi breed cows, finding promising results in reducing bacterial load and improving reproductive performance (Hussein & Hussein, 2022). This approach represents a novel therapeutic avenue that may complement traditional antibiotic treatments.

Management Practices In addition to pharmacological interventions, effective management practices play a crucial role in preventing and treating uterine infections. Uddin et al. emphasized the importance

of good management systems in minimizing the occurrence of uterine infections (Hossain et al., 2015). Implementing strategies such as proper nutrition, minimizing stress during calving, and ensuring optimal hygiene can significantly reduce the incidence of postpartum uterine diseases.

Other Theraphy Alternatives Since antimicrobial resistance is a major problem in the treatment of animals, new and more advantageous treatment methods are being developed instead of antibiotics. Ozone treatment of metritis is one of them (Durrani et al., 2017). Durrani et al showed that intrauterine infusion of ozone was more effective (38/50, 76%) as compared to gentamicin sulphate (37/50,74%) in cross bred dairy cows with bacterial infections. On the other hand, in a study conducted by Kaçar et al. (2007a), the rate of endometritis in cows was determined to be 22% in the control group and 2% in the group administered intramuscular levamisole. In addition, Kacar et al. Showed that Theranekron can be used in the postpartum period to reduce pathological vaginal discharge and accelerate uterine involution (2007b). On the other hand, it has been shown that intrauterine carvacrol infusion applied after artificial insemination can increase pregnancy rates in repeat breeder cows with mild, possibly subclinical endometritis (Lehimcioğlu et al., 2019). In addition, research on intrauterine chitosan infusions, which has been a subject of interest in recent years, has also attracted attention. Intrauterine chitosan applications have also begun to be tested for the prevention and treatment of metritis (Daetz et al., 2016)

Conclusion

It is seen that uterine infections have a large share in the economic losses in cattle breeding. In order to prevent this, protection and treatment from uterine infections are very important. In particular, the development of protection methods is of great importance. In the postpartum period, cows need to return their uterine environment to normal in a short time and prepare optimum conditions for the next pregnancy. If the external and internal factors causing uterine infections are eliminated in advance, it is possible to minimize metritis cases. Therefore, it is essential to diagnose metritis types well and take precautions accordingly. Among the types of metritis, subclinical endometritis has a very important place among the factors causing repeat breeder cases in cattle. Therefore, great care should be taken in the approach to the prevention, diagnosis and treatment of subclinical endometritis. Since proper herd health and fertility management will largely prevent uterine infections, importance should be given to the careful and correct implementation of herd management principles. Priority should be given to the development of protection methods such as vaccination and improvement of management conditions rather than developing treatment alternatives. When choosing treatment methods, the types of absolute metritis should be well diagnosed and, if possible, a method other than antibiotics should be chosen.

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Явуз Өзтүріклер[1]*, Нұржұманова Жанат Мекешқызы [1], Мұратбаев Дәулетбек Манарбекұлы [1], Тастемірова Шынар Әбдуалықызы [1], Мұқатаев Айтбек Мұратұлы[1], Ахмадиева Айнұр Жомартқызы[1], Ахметжанова Айжан Еркінғазықызы[1], Мұстафа Реха Коскун[2], Джихан Качар[3],

Кафкас университетінің Ветеринарлық факультеті, Акушерлік және гинекология кафедрасы, Карс-Түркия E-mail: <url> yavuzozturkler@gmail.com

"Семей қаласының Шәкәрім атындағы университеті" КЕАҚ, Абай облысы, Семей қ., Глинка к-сі 20а, 071412, Қазақстан

ЖАТЫРДЫҢ ИНФЕКЦИЯСЫ МЕН ІРІ ҚАРА МАЛДЫҢ ҚҰНАРЛЫЛЫҒЫ АРАСЫНДАҒЫ БАЙЛАНЫС

Аннотация

Сиырлардағы жатыр инфекциялары, әсіресе эндометрит және метрит сияқты босанғаннан кейінгі жатыр аурулары сүт өнеркәсібіндегі репродуктивті бұзылулар мен экономикалық шығындардың айтарлықтай себебі болып табылады. Бұл инфекциялар төлдеуден тұжырымдамаға дейінгі аралықтардың ұзаруына, жою көрсеткіштерінің жоғарылауына және сүт өндірісінің төмендеуіне әкелуі мүмкін, бұл сайып келгенде табынның рентабельділігі мен жануарлардың әл-ауқатына әсер етеді (Хоссейн және басқалар., 2015; Розалес Және Аметадж, 2021; Шелдон Және Оуэнс, 2017). Босанғаннан кейінгі кезең жатырдың қалпына келуі және аналық бездердің циклділігін қалпына келтіру үшін өте маңызды, олардың екеуі де сәтті тұжырымдама үшін өте маңызды. Дегенмен, патогендік бактериялардың болуы бұл физиологиялық процестерді бұзып, қабынуға және құнарлылықтың бұзылуына әкелуі мүмкін (Raliou et al., 2019; Леблан, 2010). Жатыр инфекцияларының этиологиясы көп факторлы болып табылады, көбінесе плацентаның сақталуы, төлдеудегі қиындықтар және иммундық статустың әлсіреуі сияқты факторлармен байланысты (Онянго және басқалар., 2014; Хан және басқалар., 2005). Жатыр инфекцияларының этиологиясы көп факторлы болып табылады, көбінесе плацентаның сақталуы, төлдеудегі қиындықтар және иммундық статустың бұзылуы сияқты факторлармен байланысты (Онянго және басқалар., 2014; Хан және басқалар., 2005). Мысалы, плацентаның сақталуы эндометриттің жоғарылауына әкелуі мүмкін, ол эндометрияның қабынуымен сипатталады және құнарлылықты айтарлықтай нашарлатуы мүмкін (Хан және басқалар., 2005; Негази және басқалар., 2020). Жатыр инфекцияларымен байланысты қабыну реакциясы сонымен қатар жатырдың ортасын өзгертіп, репродуктивті функцияға байланысты гендердің экспрессиясына әсер етіп, субклиникалық эндометритке әкелуі мүмкін, ол жиі диагноз қойылмайды, бірақ әлі де құнарлылық нәтижелеріне теріс әсер етуі мүмкін (Ариас және басқалар., 2018).

Түйін сөздер: *эндометрит, босанғаннан кейінгі, жатыр инфекцияларының этиологиясы көп факторлы, қабыну*

*** Явуз Озтюрклер [1], Нуржуманова Жанат Мекешовна [1], Муратбаев Даулетбек Манарбекович [1], Тастемирова Шынар Абдуалыкызы [1], Мукатаев Айтбек Муратұлы[1], Ахмадиева Айнур Жомартқызы[1], Ахметжанова Айжан Еркынгазызы[1], Мустафа Рекха Коскун[2], Джихан Качар[3]**

Ветеринарный факультет Университета Кафкас, кафедра акушерства и гинекологии, Карс–Турция E-mail: <url> yavuzozturkler@gmail.com

НАО" Университет имени Шакарима г. Семей", Абайская область, г. Семей, Ул. Глинки 20а, 071412, Казахстан

Инфекции матки у коров, особенно послеродовые заболевания матки, такие как эндометрит и метрит, являются значительной причиной репродуктивных нарушений и экономических потерь в молочной промышленности. Эти инфекции могут привести к удлинению интервалов от отела до зачатия, увеличению показателей выведения и снижению производства молока, что в конечном итоге повлияет на прибыльность стада и благополучие животных (Hossein et al., 2015; Розалес И Аметадж, 2021; Шелдон И Оуэнс, 2017). Послеродовой период необходим для восстановления матки и восстановления цикличности яичников, оба из которых имеют решающее значение для успешного зачатия. Однако присутствие патогенных бактерий может нарушить эти физиологические процессы и привести к воспалению и нарушению фертильности (Raliou et al., 2019; Леблан, 2010). Этиология инфекций матки многофакторна и часто связана с такими факторами, как

задержка плаценты, трудности с отелом и ослабление иммунного статуса (Onyanggo et al., 2014; Хан и др., 2005). Этиология инфекций матки многофакторна и часто связана с такими факторами, как задержка плаценты, трудности с отелом и нарушения иммунного статуса (Onyanggo et al., 2014; Хан и др., 2005). Например, задержка плаценты может привести к усилению эндометрита, который характеризуется воспалением эндометрия и может значительно ухудшить фертильность (Khan et al., 2005; Негази и др., 2020). Воспалительная реакция, связанная с инфекциями матки, также может изменить среду матки и повлиять на экспрессию генов, связанных с репродуктивной функцией, что приведет к субклиническому эндометриту, который часто не диагностируется, но все же может негативно повлиять на результаты фертильности (Arias et al.

Ключевые слова: *эндометрит, послеродовой, этиология инфекций матки многофакторная, воспаление*

Information about the authors

Yavuz Öztürkler the main author, Kafkas University Veterinary Faculty, Department of Reproduction and Artificial Inseminaton, Kars –Türkiye *Corresponadance author: Yavuz Öztürkler E-mail: yavuzozturkler@gmail.com
Nurjumanova Zhanat Mekeshovna, Candidate of Veterinary Sciences, NJSC Shakarim University of Semey, Shugaev 159, 071400 Kazakhstan, zhanat1970s@mail.ru
Muratbayev Dauletbek Manarbekovich, Doctor PhD, https://orcid.org/0000-0003-0007-3421 NJSC Shakarim University of Semey, Shugaev 159, 071400, Kazakhstan, mdm_semey@mail.ru
Tastemirova Shynar Abdualykyzy, Master of Veterinary Medicine NJSC Shakarim University of Semey, Shugaev 159, 071400 Kazakhstan
Mukatayev Aitbek Muratuli, doctoral student of Veterinary Medicine NJSC Shakarim University of Semey, Shugaev 159, 071400 Kazakhstan
Ahmadieva Ainur Zhomartovna, , doctoral student of Veterinary Medicine NJSC Shakarim University of Semey, Shugaev 159, 071400 Kazakhstan
Ahmetzhanova Ayzhan Erkingazyevna, Doctor PhD, NJSC Shakarim University of Semey, Shugaev 159, 071400, Kazakhstan, aijankara_88@mail.ru
Mustafa Reha Coşkun, Kafkas University Veterinary Faculty Department of Microbiology, Kars - Türkiye

Сведение об авторах

Явуз Озтюрклер, основной автор, Ветеринарный факультет Кахкского университета, кафедра воспроизводства и искусственного осеменения, Карс – Турция yavuzozturkler@gmail.com
Нуржуманова Жанат Мекешовна, кандидат ветеринарных наук**,** НАО Университет имени Шакарима города Семей, Шугаева 159, 071400, Республика Казахстан, zhanat1970s@mail.ru

Муратбаев Даулетбек Манарбекович, PhD, и.о. ассоц.профессора, НАО «Университет имени Шакарима города Семей», г.Семей, ул.Глинки 20А, 071412, Республика Казахстан, mdm_semey@mail.ru
Тастемирова Шынар Абдуалиевна, магистр ветеринарной науки НАО "Университет Шакарима", Семей, ул. Шугаева 159, 071400 Казахстан
Мукатаев Айтбек Муратович, докторант ветеринарной науки НАО "Университет Шакарима", Семей, ул. Шугаева 159, 071400 Казахстан
Ахмадиева Айнур Жомартовна, докторант ветеринарной науки НАО "Университет Шакарима", Семей, ул. Шугаева 159, 071400 Казахстан
Ахметжанова Айжан Еркингазыевна, доктор PhD, НАО Университет имени Шакарима города Семей, Шугаева 159, 071400, Республика Казахстан, aijankara_88@mail.ru
Мустафа Реха Кошкун, ветеринарный факультет Университета Кафкас, кафедра микробиологии, Карс –Турция

Авторлар туралы мәлімет

Явуз Өзтүрклер, негізгі автор, Кавказ университетінің Ветеринарлық факультеті, көбею және жасанды ұрықтандыру кафедрасы, Карс-Түркия yavuzozturkler@gmail.com
Нұржұманова Жанат Мекешқызы, ветеринария ғылымдарының кандидаты, Семей қаласының Шәкәрім атындағы университеті КЕАҚ, Шұғаев 159, 071400, Қазақстан Республикасы zhanat1970s@mail.ru
Муратбаев Даулетбек Манарбекұлы, PhD, қауымдастырылған профессор м.а, "Семей қаласының Шәкәрім атындағы университеті" КЕАҚ, Семей қ., Глинка к-сі 20а, 071412, Қазақстан Республикасы, mdm_semey@mail.ru
Тастемирова Шынар Абдуалиқызы, "Шәкәрім университеті" КЕАҚ Ветеринария ғылымының магистрі, Семей, Шұғаев көшесі, 159, 071400 Қазақстан
Мукатаев Айтбек Муратұлы, "Шәкәрім университеті" КЕАҚ Ветеринария ғылымының докторанты, Семей, Шұғаев көшесі, 159, 071400 Қазақстан
Ахмадиева Айнур Жомартқызы, "Шәкәрім университеті" КЕАҚ Ветеринария ғылымының докторанты, Семей, Шұғаев көшесі, 159, 071400 Қазақстан
Ахметжанова Айжан Еркінқызы, PhD, қауымдастырылған профессор м.а, "Семей қаласының Шәкәрім атындағы университеті" КЕАҚ, Семей қ., Глинка к-сі 20а, 071412, Қазақстан Республикасы, aijankara_88@mail.ru
Мұстафа Реха Кошкун, Кафкас университетінің Ветеринарлық факультеті, микробиология кафедрасы, Карс-Түркия