Med Discoveries
An open access journal of science and medicine

Article Type: Review Article
Volume 3, Issue 1
Received: Dec 11, 2023
Accepted: Jan 16, 2024
Published Online: Jan 23, 2024

Postpartum Uterine Diseases; Diagnostic Approaches and Management in Farm Animals: A Review

Natinael Dawit Kalacho*

Jinka University, School of Veterinary Medicine, Jinka, Ethiopia.

***Corresponding Author:** Natinael Dawit Kalacho*

Email: natnael1985@yahoo.com

Abstract

Postpartum uterine infections results from uterine contamination with bacteria during parturition. The postpartum environment of the uterine lumen supports the growth of a variety of aerobic and anaerobic bacteria. There are a number of risk factors for post-partum uterine disease in dairy cattle; cows having dystocia, retained placenta, twins or stillbirths and various metabolic disorders are more likely to develop uterine disease. Inflammation of the uterus slows down the process of involution in the uterus and delays the onset of activities of the ovaries leading to economic loss due to systemic illness, loss of milk and meat production and marked drop in fertility. Pyometra, metritis, clinical and subclinical endometritis are some of the most important illnesses during the postpartum period. A variety of methods such as uterine palpation, ultrasonographic features of the uterus, vaginoscopy, endometrial cytology, uterine culture, and uterine biopsy has been reported to identify postpartum diseases. Prevention of postpartum uterine disease would be better than cure, for both the animals and the economy. Thus, early diagnosis or predictions of uterine infections are important for effective postpartum management.

Keywords: Diagnosis; Farm animals; Postpartum; Treatment; Uterine infection.

Abbreviations: RP: Retained Placenta; RFM: Retained Fetal Membrane; DMI: Dry-Matter Intake; NEFA: Non-Esterified Fatty Acids; AI: Artificial Insemination; PAM: Pathogen Associated Molecule; E coli: Escherichia coli; PMN: Polymorphonuclear; GnRH: Gonadotropin Releasing Hormone; NSAIDS: Nonsteroidal Anti-Inflammatory Drugs.

Introduction

Postpartum period is defined as the period after parturition and lasts until reproductive function is restored so that another pregnancy can occur [1]. This period is the most critical stage in the reproductive cycle of farm animals [2]. In cattle, the postpartum period is associated with uterine tissue remodeling, restoration of immunological homeostasis and resumption of ovarian cyclicity necessary for subsequent fertility [3]. There are four major events during this period which include: myometrial contractions and expulsion of secundus, endometrial repair, resumed ovarian function and elimination of bacterial contamination in the reproductive tract [4]. Postpartum uterine infection is extremely important in dairy cattle. It is both common and detrimental to reproductive performance [5]. A healthy or slightly inflamed uterus will clear pathogenic bacteria and keep its normal state by means of defense mechanisms during the first four to six weeks after parturition [6]. Clearance of bacteria depends on various factors, such as uterine involution, uterine contractions, innate and adaptive immunity, and regeneration rate of the endometrium [7].

Uterine infections are common disorders affecting dairy cows during the postpartum period, when these protective barriers of uterus are breached [8]. The majority of postpartum inflammatory conditions of the uterus begin with bacterial contamination of the uterine lumen [9]. Relaxation of the vulva and cervical dilation during parturition allow for the entrance of bacteria into the uterus, therefore, bacterial contamination of the uterus postpartum is common [10]. Uterine health and the expression of clinical uterine infection in the postpartum period depends on balance between factors such as the animal, immunity, the number and pathogenicity of the microbes, and the uterine environment [6,11].

Postpartum uterine diseases are important for animal welfare and economic reasons, causing cow discomfort, elimina-

Citation: Kalacho ND. Postpartum Uterine Diseases; Diagnostic Approaches and Management in Farm Animals: A Review. Med Discoveries. 2024; 3(1): 1103.

tion from the herd and impaired reproductive performance [12]. Inflammation of the uterus slows down the process of involution in the uterus and delays the onset of activities of the ovaries leading to economic loss due to systemic illness, loss of milk and meat production and marked drop in fertility [13,14]. Postpartum uterine infections can also delay the regeneration of endometrium and disrupt the resumption of cyclic ovarian function which leads to the postponement of first insemination (AI), increase in number of inseminations per conception and thus calving interval is prolonged [15]. These complications are also responsible for slower uterine involution, reduced reproductive rate, prolonged inter conception and calving interval, cost of medication, drop in milk production, reduced calf drop, and early depreciation of potentially useful cows [5,16]. The financial losses associated with uterine infection are dependent on the cost of treatment, reduced milk yield, and infertility [6].

Therefore; the aims of this review are assessing different postpartum uterine diseases; their causes, consequences, and to highlight update on different diagnostic and therapeutic measures in farm animals.

Major risk factors for postpartum uterine diseases

There are several risk factors that contribute to postpartum uterine contamination or physical damage of the uterine tissue; among them the major factors, such as retained placenta (RP), calving abnormalities (dystocia, twins, and stillbirth), angle of the vulva, and parity [12]; and also various metabolic disorders are more likely to develop uterine disease in animals [17,18].

Retained placenta: Retained placenta (RP) is a uterine disease that occurs in the postpartum period and affects cows more frequently than other animal species [19]. Retained placenta is a direct risk factor for postpartum reproductive and metabolic disorders [20]. Negative consequences related to RP are: delayed uterine involution, increased time to first insemination, increased number of services per pregnancy, decreased pregnancy rates and increased days open. Furthermore, RP has been associated with a significantly increased risk to suffer from clinical diseases like metritis, endometritis, ketosis and even mastitis [21].

Dystocia: Dystocia can be defined as the incapability of the cow to expel neonates through the birth canal from the uterus. This condition occurs because of problems with the maternal or fetal [22]. Dystocia is a risk factor that significantly increased the overall incidence of clinical metritis and endometritis after calving [14,23]. Tissue trauma caused by dystocia most likely facilitates adhesion and invasion of the germs [21].

Nutritional and metabolic factors: Metabolic pressure after calving, negative energy balance and metabolic diseases such as ketosis increase the incidence of uterine disease [24]. Regarding the metabolic challenge, the transition period is characterized by a state of negative energy, mineral, and vitamin balance in which there is a decrease in dry-matter intake (DMI), leading to a sharp decrease in glucose, minerals (e.g. calcium, selenium) and vitamins (e.g. A and E) right after parturition, and an increase in body fat mobilization in the form of non-esterified fatty acids (NEFA; this state of negative energy, mineral, and vitamin balance leads to immunosuppression [25]. Decreased postpartum levels of blood minerals are associated with uterine diseases, and hypocalcaemia after parturition was associated with higher incidences of metritis and clinical endometritis [12].

Other managemental factors: Management factors and complications at parturition can increase the incidence of uterine disease [24]. General farm hygiene, especially on beddings and maternity stalls, have been reported as affecting the incidence of postpartum uterine infections [26]. Management factors and complications at parturition such as calving assistance can increase the incidence of uterine disease and have been identified as risk factors for clinical and subclinical endometritis [27].

Major pathogenic bacterial infection of the postpartum uterus: The postpartum environment of the uterine lumen supports the growth of a variety of aerobic and anaerobic bacteria [9,13]. The bacterial agents commonly isolated from postpartum uterus include: Escherichia coli, Arcanobacterium pyogenes, Fusobacterium necrophorum, Bacteroides species, Staphylococcus species, Mannheimia haemolytica, Pasteurella species, Haemophilus somnus, Pseudomonas aeruginosa, Clostridium species and Streptococcus species. Among these, Arcanobacterium pyogenes, coliforms and the Gram-negative anaerobes, Fusobacterium and Bacteroides species are commonly encountered [7,10,13,18].

There is no doubt that uterine pathogens may negatively affect reproduction both by causing direct endometrial damage and by producing toxins. Bacterial colonization or growth within the uterine tissue releases endotoxins called pathogen associated molecules (PAM) [24]. Endotoxins, lipopolysaccharide component of gram-negative bacteria such as E coli, are released into the circulation during bacterial disintegration and induce fever, lethargy, tachycardia, and tachypnea [28].

Common post-partum uterine disorders

Pyometra: Pyometra is characterized by the accumulation of purulent or muco-purulent material within the uterine lumen and distension of the uterus, in the presence of an active corpus luteum on ovary [4,9,29]. Pyometra can happen if ovulation occurs too early in the post-partum period and corpus luteum is formed during uterine infection [22]. A closed cervix is common in most cows; however, in few cases, closure of the cervical lumen is not fully completed, and therefore, purulent discharge can be seen come out from the vagina when the cow lies down, urinates, or defecates [30].

Metritis: Metritis is a severe inflammatory response that occurs within all the layers of the uterus including the endometrium, sub mucosa, myometrium and perimetrium [4]. It is most commonly occurs in the postpartum period of dairy cattle within 10-14 days after parturition [31]. Postpartum metritis usually associated with uterine inertia, twin births, RFM, prolonged manipulations and injuries to the vulva and/ or birth canal [12,13,32].

Puerperal metritis is an acute systemic illness due to infection of the uterus with bacteria, usually within 10 days after parturition [9]. Puerperal metritis is characterized by the following clinical signs: a fetid red-brown watery uterine discharge and, usually, pyrexia; in severe cases, reduced milk yield, dullness, inappetance or anorexia, elevated heart rate, and apparent dehydration may also be present. Toxic puerperal metritis (i.e. acute septic metritis) is characterized by increased rectal temperature, depression, anorexia, fetid watery vulvar discharge. Toxic puerperal metritis can be a severe problem and uterine infections that are life-threatening [33,34].

Endometritis: Endometritis is inflammation of the functional lining of the uterus, called the endometrium [14]. It is defined as inflammation of the endometrium after 21 days postpartum without systemic signs of illness, and can be considered the chronic stage of uterine inflammation. Endometritis has been classified as clinical or subclinical [12].

Clinical endometritis: Clinical endometritis has been defined as local inflammation of the endometrium, and commonly associated with presence of purulent or muco-purulent material, containing >50% pus, in the vagina at or more than 21 days after calving [7,33,35]. There are risk factors related to clinical endometritis in dairy cows such as hygiene of the perineum at the time of calving, peripartum metabolic status, parity, retained fetal membranes, delivery of twins and dystocia [32].

Sub-clinical endometritis: Subclinical endometritis is a uterine disease that does not present clinical signs and cannot be easily diagnosed on farm site. But as a form of uterine disease, it is producing deleterious effects on reproduction in dairy cows [24]. Subclinical endometritis has also been described as 'cytological endometritis' and is defined as "an increased proportion of PMN in endometrial cytology samples obtained by endometrial cytobrush or low-volume uterine lavage [14,27,36,37].

General diagnostic approaches to postpartum uterine diseases

Rectal palpation: Among commonly used diagnostic tools, rectal palpation is probably the most common method for diagnosing uterine infections [14]. The purpose of the trans-rectal palpation is to detect pathological changes in the uterus consistent with endometritis, such as a general enlargement, fluctuating contents and a hardened uterine wall [38].

Examination of vagina and vaginal discharges: Vaginal discharge can be scored and used as an indicator of uterine infection [39]. In practice, the examination of the contents of the vagina for the presence of pus is the most useful procedure for diagnosis of uterine infection [8]. The diagnosis of metritis and clinical endometritis should include an inspection of the contents of the female genital tract by speculum or insertion of a clean-gloved-hand into the vagina [40]. Vaginoscopy has been considered as more sensitive method than simple external inspection for detection of purulent discharge [23].

Ultrasonography: Ultrasonography has become an important diagnostic tool for evaluating the female reproductive system [23]. The use of trans-rectal ultrasonography permits more objective measurement of the diameter of the uterine horns and cervix, and visualization of mucus and pus within the uterine lumen [9]. The Ultrasonographic appearance of abnormal uterine fluid can vary from anechoic fluid with floating particles (referred to as 'snowy specks') to homogenous, purulent exudates that can appear similar to the echogenicity of the surrounding uterus [41].

Cytology: Uterine cytology is the collection and counting of cells obtained from the uterus, and has become the standard to which other techniques are compared. Uterine cytology makes it possible to quantify inflammatory cells [36]. The proportion of neutrophils is counted and then used to assess the degree of uterine inflammation. Cytological samples can be collected either with uterine lavage or a cytobrush. The cytobrush gives an in situ sample wich may represent the inflammatory status of the endometrium [38].

Uterine biopsy: Endometrial biopsy is highly diagnostic for pathology and has potential to generate extensive quantitative data on physiologic or immune mechanisms in cows if genomic and proteomic data can be obtained from the same biopsy material [42]. Biopsy provides detailed information about uterine health status [43]. When biopsy technique is used, pieces of endometrial tissue are taken by using biopsy forceps; all these techniques require laboratory work for evaluation of the uterine samples [5].

Bacterial culture: A uterine culture is an essential tool to determine the etiology of uterine infection. A swab is the most accurate means of obtaining samples for identification of the specific and non-specific bacteria that cause infection. A true uterine culture should be taken from the uterus without contamination by extraneous bacteria [34]. Uterine fluids can be swabbed and cultured to characterize the anaerobic and aerobic bacterial populations during the postpartum period [39].

Management and treatment measures for postpartum uterine diseases

An effective control of post-partum contamination of the uterus provides the chance to improve both fertility and general health condition of dairy herds. Since postpartum uterine diseases are very costly [44]. Prevention and early treatment of postpartum uterine infections are more economical than treatment at a later stage when diseases get established [45]. Thus, early diagnosis or predictions of uterine infections are important for effective postpartum management [46,47].

Management practices: The occurrence of uterine infections can be reduced by minimizing the need for assistance at calving through prenatal knowledge of twin birth, calf sex and oversized calves. Calving assistance should only be carried out when necessary and appropriate hygiene should be used to decrease the incidence of uterine infections [48]. Generally it is believed that disinfection of calving equipment's, frequent replacement of beddings and general hygiene of the calving environment can help minimize cases of uterine infections [26].

Nutrient supplementation: Prevention of uterine disease requires appropriate nutritional management during the transition period and after calving [33]. Trace mineral and vitamin deficiency early postpartum, particularly selenium and vitamin E have long been identified as a cause of uterine disease, and because of the importance of energy balance on the incidence of uterine disease, nutritional supplements that prevent ketosis may be an important component for the prevention of uterine diseases [25].

Hormonal treatments: Drug compounds, such as estrogens, luteolytic prostaglandins, and gonadotropin releasing hormone (GnRH) have been used in the postpartum period alone or in conjunction with other agents to treat retained fetal membranes (RFM), metritis, and Pyometra [47,49]. The effect of these compounds on uterine motility and defense mechanisms makes them useful treatment alternatives to antimicrobial agents. PGF2α is not only luteolytic but also appears to have pro-inflammatory actions that might enhance neutrophil function. The treatment of choice of pyometra in cows is administration of prostaglandin F2a or its analogues at normal luteolytic doses [50].

Estrogen may stimulate uterine tone to evacuate abnormal uterine contents, increase production of mucus that contains host defense compounds and induce estrus, thereby reduce

progesterone levels markedly stimulate neutrophil phagocytosis and resistance of the uterus to infection [48].

Anti-inflammatory drugs: Studies have shown that NSAIDs provide therapeutic effects such as analgesia, ovarian function recovery, and prevention and treatment of uterine inflammation [25,51]. Treatment of postpartum inflammation with non-steroidal anti-inflammatory drugs (NSAIDS) has had varying success due to differences in efficacy with drug choice, mode of action (i.e., cyclooxygenase or prostaglandin-endoperoxide synthase 1 or 2 inhibition), as well as timing and duration of treatment [52].

Antibiotic therapy: The success of uterine infection treatment depends on evacuation of the uterine fluids, response of the infectious agents to the used drug, concentration and frequency of drug use and the exposure of the entire endometrium to the treatments [53].

Systemic and local treatments have been used to treat uterine diseases [24]. The systemic antimicrobial therapy must be used to treat the cases of RFM, metritis and pyometra while intrauterine treatment is preferred treatment of choice for endometritis as it is local inflammation and does not result in systemic illness [41]. Antibiotics commonly used for the treatment of puerperal metritis include penicillin, third-generation cephalosporins, or a combination of ampicillin with Oxytetracycline or cloxacillin [31,50,54]

Alternatives for the treatment of endometritis caused by Gram negatives that are resistant to gentamicin include amikacin sulfate, polymyxin B, neomycin sulfate, ampicillin, carbenicillin, and kanamycin sulfate. The broad-spectrum antibiotics ceftiofur and ticarcillin, with or without clavulanic acid, are also commonly used in mares [55].

Intrauterine treatment: In contrast to systemic administration, intrauterine administration achieves higher drug concentration in the endometrium, but little penetration to deeper layers of the uterus or other genital tissues [56]. Local treatment involving intrauterine antibiotic infusion aims to produce an even distribution of an active drug throughout all layers of the uterus, limited systemic absorption, low tissue irritation, and high antibacterial activity within the uterine environment [57. Antiseptic agents, such as iodine, chlorhexidine, and saline, have been infused into the uterus, but there have been few studies to determine the efficacy of these compounds on postpartum metritis [47]. Intrauterine infusion of a 50% dextrose solution has proven to be effective in treating uterine diseases [1,58].

Conclusion

Uterine infection is one of the commonest causes of poor fertility. They are also responsible for, economic loss due to systemic illness, loss of milk and meat production, cost of medication and poor welfare. There are complex multifactorial causes and a wide range of factors contributes to their diseases occurrence. The main risk factors for uterine diseases are primiparity (for metritis only), dystocia, male offspring, twins, stillbirth, abortion, prolapsed uterus, retained placenta (RP). Antibiotics, hormonal treatment with estrogens, PGF2a, and GnRH, NSAIDS and intrauterine medications are commonly used in treating uterine infections. Good peripartum management and accurate diagnosis are critical to facilitate the use of the most effective treatment and limit the negative impact of postpartum uterine disease on fertility. Thus Prevention and early treatment of postpartum uterine infections are more economical than treatment at a later stage when diseases get established.

Declarations

Acknowledgement: Special thanks to School of Veterinary Medicine, Jinka University, Ethiopia.

Conflict of interest: The author declares no conflict of interest.

Author's contributions

Natinael dawit kalacho: Conceptualization; Organization of manuscript and writing-original draft.

References

1. A Sharma, M Singh, P Kumar, P Sood, A Sharma, A Thakur. Postpartum subclinical endometritis, its diagnosis and impact on early reproductive parameters in dairy cows. Vet. 2022; 92: 233-242. DOI: 10.24099/vet. arhiv.1303.

2. Amal H. Ali and Wahid M. Ahmed.Impact of Post-Partum Due Care on Fertility in Farm Animals. Global Veterinaria. 2015; 15(2): 169-174. DOI: 10.5829/idosi.gv.2015.15.02.

3. Raliou M, Dembe´le´ D, Du¨vel A, Bolifraud P, Aubert J, Mary-Huard T. Subclinical endometritis in dairy cattle is associated with distinct mRNA expression patterns in blood and endometrium. PLoS ONE. 2019; 14(8): 0220244. https://doi.org/10.1371/journal.pone.0220244.

4. Akshay Sharma, Madhumeet Singh, Pravesh Kumar, Amit Sharma, Neelam, Aaqib Majid Jan and Pranshu Sharma Postpartum Uterine Infections in Cows and Factors Affecting it– A Review. Int.J.Curr.Microbiol.App.Sci. 2017; 6(9): 1020-1028. https://doi.org/10.20546/ijcmas.2017.609.123.

5. Hossain MK, Uddin AHMM, Yasmin N, Hossain MM, Lucky NS, Haque MM, Aktaruzzaman M and Alam S. Risk factors of postpartum uterine infection and its subsequent effect on fertility of crossbred dairy cows in Bangladesh. International Journal of Natural Sciences. 2015; 5(2): 107-111.

6. I. Martin Sheldon, Erin J. Williams, Aleisha N.A. Miller, Deborah M. Nash, Shan Herath Uterine diseases in cattle after parturition. The Veterinary Journal. 2008; 176:115-121. doi:10.1016/j.tvjl.2007.12.031.

7. Rosales EB, Ametaj BN. Reproductive Tract Infections in Dairy Cows: Can Probiotics Curb Down the Incidence Rate? Dairy. 2021; 2: 40-64. https://doi.org/10.3390/ dairy2010004.

8. Vidya VK, Niyas E, Shibu S, Gayathri P, Vinayak B. and Revathy MM. Early diagnosis and management of bovine pyometra- A case report. Haryana Vet. 2022; 61(SI): 133-135.

9. I. Martin Sheldon, Gregory S. Lewis, Stephen LeBlanc, Robert O. Gilbert Defining postpartum uterine disease in cattle. Theriogenology. 2006; 65:1516-1530

10. Farhad Ghasemi Characterization of endometritis in postpartum dairy cows. MSc thesis. Western College of Veterinary Medicine, University of Saskatchewan Saskatoon, Saskatchewan. 2011.

11. DA Vallejo-Timaran, J Reyes, 2 RO. Gilbert RC, Lefebvre LG. Palacio-Baena, and J G. Maldonado-Estrada Incidence, clinical patterns, and risk factors of postpartum uterine diseases in dairy cows from high-altitude tropical herds. J. Dairy Sci. 2021; 104: 9016-9026 https://doi.org/10.3168/jds.2020-18692.

12. Vinicius Silva Machado New insights into postpartum uterine diseases of dairy cows. PhD Thesis. A Dissertation Presented to the Faculty of the Graduate School of Cornell University. In Par-

tial Fulfillment of the Requirements for the Degree of Doctor of Philosophy. 2015.

13. S. Deori and Arundhati Phookan Bovine Postpartum Metritis and its Therapeutics: A Review. Indian Journal of Science and Technology. 2015; 8(23). DOI: 10.17485/ijst/2015/v8i23/52386.

14. Negasee KA Clinical metritis and endometritis in dairy cattle: A review. Vet Med Open J. 2020; 5(2): 51-56. doi: 10.17140/VMOJ-5-149.

15. Akshay Sharma, Madhumeet Singh, Pravesh Kumar, Amit Sharma, Aaqib Majid Jan, Aanchal Sharma, Amit Kashyap, Anupama Thakur, Pinki Saini, Shriya Gupta Pyometra in a jersey crossbred cow - diagnosis and treatment. Explor Anim Med Res. 2018; 8(1): Pp. 97-99.

16. Bilal Ahmad Ganaie, Faheem Sultan, Rouf Rashid Dar, Firdous Ahmad Baba and Susheel Kumar (2018): Uterine infection in dairy animals and its ameliorative measures: A review. Journal of Pharmacognosy and Phytochemistry 2018; 7(1): 194-199.

17. EJ Williams Drivers of Post-partum Uterine Disease in Dairy Cattle. Reprod Dom Anim. 2013; 48(1): 53-58. Doi: 10.1111/rda.12205

18. Rachel L. Piersanti and John J. Bromfield The Consequence of Postpartum Uterine Disease on Dairy Cow Fertility. 2022. UF/IFAS Extension. website https://edis.ifas.ufl.edu.

19. Estevão Vieira Rezende, Igor José Reis, Carla Cristian Campos, Ricarda Maria Santos Influence of gestation length, seasonality, and calf sex on birth weight and placental retention in crossbred dairy cows. Cienc. anim. Bras. 2020; 21: 52881. DOI: 10.1590/1809-6891v21e-52881.

20. Yeon-Kyung Han, Ill-Hwa Kim Risk factors for retained placenta and the effect of retained placenta on the occurrence of postpartum diseases and subsequent reproductive performance in dairy cows. J. Vet. Sci. 2005; 6(1): 53-59.

21. Geert Opsomer Metritis and endometritis in high yielding dairy cows. Rev. Bras. Reprod. Anim., Belo Horizonte. 2015; 39(1): 164-172. www.cbra.org.br.

22. Galma Boneya Arero Major Reproductive Health Disorders in Dairy Cows. J Anim Biol Vet Sci. 2022; 2: 1-11.

23. Devender Kumar, Satish and Purohit, G.N. A Discussion on Risk Factors, Therapeutic Approach of Endometritis and Metritis in Cattle. Int.J.Curr. Microbiol. App. Sci. 2019; 8(05): 403-421. doi: https://doi.org/10.20546/ijcmas.2019.805.04.

24. Roger Molina-Coto, Matthew C. Lucy Uterine inflammation affects the reproductive performance of dairy cows: A review. Agron. Mesoam. 2018. doi:10.15517/ma.v29i2.29852.

25. K.N. Galvão Uterine diseases in dairy cows: understanding the causes and seeking solutions. Anim. Reprod., 2013; 10 (3): 228-238.

26. Joshua Onyango Cow postpartum uterine infection: A review of risk factors, prevention and the overall impact. Veterinary Research International. 2014; 2(2): 18-32.

27. A.I. Damarany Impact of Oxytetracycline and prostaglandin f2α during puerperium period on uterine recovery and post-parturient reproductive characteristics in baladi cows. Egyptian J. Anim. Prod. 2022; 59(3): 97-109.

28. Ragnvi Hagman Pyometra in Small Animals. Vet Clin Small Anim. 2022; (52): 631-657. https://doi.org/10.1016/j.cvsm.2022.01.004.

29. K.N. Galvão Postpartum uterine diseases in dairy cows. Anim Reprod. 2012; 9(3): 290-296.

30. Amin YA, Ali RA, Fouad SS, Ibrahim RM The deleterious effect of postpartum pyometra on the reproductive indices, the metabolic profile, and oxidant/ antioxidant parameters of dairy cows, Veterinary World. 2021; 14(2): 329-338. Doi: www.doi.org/10.14202/vetworld.2021.329-338.

31. Audaisabah Asker, Ammar Rahem Mansoor, A.A. Omar, A.F. Majeed Treatment of Postpartum Metritis in Dairy Cattle. Medicolegal Update. 2021; 21(1).

32. Mohammad Rahim Ahmadi, Asghar Mogheiseh, Abdolah Mirzaei, Saeed Nazifi, Eisa Fallah. Treatment of cows with clinical endometritis as cows affected by pyometra—Non antibiotic treatment of severe clinical endometritis. Asian Pac J Reprod. 2018; 7(4): 185-190. doi: 10.4103/2305-0500.237057.

33. I Martin Sheldon, James Cronin, Leopold Goetze, Gaetano Donofrio, and Hans-Joachim Schuberth Defining Postpartum Uterine Disease and the Mechanisms of Infection and Immunity in the Female Reproductive Tract in Cattle. Biology of reproduction. 2009; 81: 1025-1032. DOI 10.1095/biolreprod.109.077370.

34. O.I. Azawi Postpartum uterine infection in cattle. Animal Reproduction Science. 2008; 105: 3-4. https://doi.org/10.1016/j.anireprosci.2008.01.010.

35. Fabio Lima New Advances in the Management of Uterine Diseases. WCDS Advances in Dairy Technology. 2018; 30: 283-295.

36. Nicola Priest The effect of a non-steroidal anti-inflammatory drug on subclinical endometritis in dairy cows and the identification of at-risk cows. MSC thesis submitted in partial fulfillment of the requirements for the Degree of Master of Agricultural Science at Lincoln University. 2013.

37. Moges N Diagnosis of subclinical endometritis during postpartum period on subsequent pregnancy in small, medium and large scale dairy farms in and around Gondar, North West Ethiopia. Online J. Anim. Feed Res. 2018; 8(6): 158-163. www.ojafr.ir.

38. Linda Hulling Uterine health in the postparturient period of the dairy cow. Online publication. 2020. https://stud.epsilon.slu.se.

39. Gregory S. Lewis Health problems of the postpartum cow symposium. J Dairy Sci. 1997; 80: 984-994.

40. Iain Martin Sheldon, Sian E Owens Postpartum uterine infection and endometritis in dairy cattle Proceedings of the 33rd Annual Scientific Meeting of the European Embryo Transfer Association (AETE); Bath, United Kingdom, September 8th and 9th. 2017. DOI: 10.21451/1984-3143-AR1006.

41. Mrigank Honparkhe, Bilawal Singh, Amarjeet BIsha, Parkash Singh Brar, Shahaji Phand. Reproductive Management of Dairy Animals [E-book]. Hyderabad: National Institute of Agricultural Extension Management (MANAGE) & SAU - Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana. 2021.

42. Chapwanya a, KG Meade bF, Narciandi aP. Stanley c, J F. Mee d, M L. Doherty c, J J. Callanan c, C O'Farrelly Endometrial biopsy: a valuable clinical and research tool in bovine reproduction. Theriogenology. 2010; 73: 988-994. https://doi.org/10.1016/j.theriogenology.2009.11.015.

43. LV Madoz, MJ Giuliodori, AL. Migliorisi M, Jaureguiberry RL. de la Sota. Endometrial cytology, biopsy, and bacteriology for the diagnosis of subclinical endometritis in grazing dairy cows. Journal of Dairy Science. 2014; 97 (1): 195-201. https://doi.org/10.3168/jds.2013-6836.

44. Billy I. Smith Therapeutic and Management options for Postpartum Metritis in Dairy Cattle. 2009. http://www.vetlearn.com/Media/PublicationsArticle/PV_24_10_S92.pdf.

45. R Dolezel, T Palenik, S Cech, L Kohoutova, M Vyskocil. Bacterial

contamination of the uterus in cows with various clinical types of metritis and endometritis and use of hydrogen peroxide for intrauterine treatment. Veterinarni Medicina. 2010; 55(10): 504-511.

46. Manimaran A, Kumaresan A, Jeyakumar S, Mohanty TK, Sejian V, Kumar N, Sreela L, Prakash MA, Mooventhan P, Anantharaj A, Das DN. Potential of acute phase proteins as predictor of postpartum uterine infections during transition period and its regulatory mechanism in dairy cattle, Veterinary World. 2016; 9(1): 91-100. doi: 10.14202/vetworld.2016.91-100.

47. Todd Bilby, Ralph Bruno, Kevin Lager, and Ellen Jordan Postpartum uterine diseases in dairy cows. The Texas A&M Agri-Life Extension. 2009. http://texasdairymatters.org.

48. H.H. El-Khadrawy, Wahid M. Ahmed, Zaabal, M.M. and Emtenan M. Hanafi. Strategies for Diagnosis and Treatment of Uterine Infection in Bovines. Global Veterinaria. 2015; 15(1): 98-105. DOI: 10.5829/idosi.gv.2015.15.01.9660.

49. Jerry D, Olson MS, Leslie Ball MS, Robert G. Mortimer. Therapy of Postpartum Uterine Infections. The bovine proceedings-no. 1985; 17.

50. Susan E. Aiello. The Merck veterinary manual. Eleventh edition. Merck & co., Inc. Kenilworth, NJ, USA. 2016.

51. Luying Cui, Yang Qu, Hele Cai, Heng Wang, Junsheng Dong, Jun Li, Chen Qian, and Jianji Li Meloxicam Inhibited the Proliferation of LPS-Stimulated Bovine Endometrial Epithelial Cells Through Wnt/β-Catenin and PI3K/AKT Pathways. Front Vet Sci. 2021; 8: 637707. doi: 10.3389/fvets.2021.637707.

52. MA Crookenden, AVR. Lake, CR. Burke CVC, Phyn JR, Roche A. Heiser. Effect of nonsteroidal anti-inflammatory drugs on the inflammatory response of bovine endometrial epithelial cells in vitro. J. Dairy Sci. 2023; 106: 2651-2666. https://doi.org/10.3168/jds.2021-21742.

53. Mohamed A Gohar, Mohammed A Elmetwally, Abdelmonem Montaser, Samy M. Zaabel. Effect of Oxytetracycline Treatment on Postpartum Reproductive Performance in Dairy Buffalo-Cows with Retained Placenta in Egypt. Journal of Veterinary Healthcare. 2018; 1(3): 45-53. https://doi.org/10.14302/issn.2575-1212.jvhc-18-2146.

54. P Haimerl, S Arlt, S Borchardt, and W Heuwieser. Antibiotic treatment of metritis in dairy cows. A meta-analysis. J. Dairy Sci. 2016; 100: 3783-3795. https://doi.org/10.3168/jds.2016-11834.

55. Pyörälä S, Taponen J, Katila T. Use of antimicrobials in the treatment of reproductive diseases in cattle and horses. 2014; DOI: 10.1111/rda.12324. https://www.researchgate.net/publication/265647501.

56. Stephen J. LeBlanc. Postpartum uterine disease and dairy herd reproductive performance: A review. The Veterinary Journal. 2008; 176: 102-114. https://doi.org/10.1016/j.tvjl.2007.12.019.

57. H Mattice, E Jimenez, E Hovingh, S Bas, M Martinez, AA Barragan. Postpartum intrauterine dextrose infusion: Effects on uterine health, metabolic stress, systemic inflammation, and daily milk yield in clinically healthy dairy cows. JDS Communications. 2023; 4(2): 121-126. https://doi.org/10.3168/jdsc.2022-0310.

58. I Martin Sheldon, James Cronin, Leopold Goetze, Gaetano Donofrio, and HansJoachim Schuberth. Defining Postpartum Uterine Disease and the Mechanisms of Infection and Immunity in the Female Reproductive Tract in Cattle, Biol Reprod. 2010.