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Endometritis in Cattle: A Review of Current Understanding and Practical Causes of Repeat Breeding

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Abstract

One of the most prevalent reproductive illnesses that significantly reduce the livestock industry's profitability is endometritis. Endometritis is an inflammation that occurs in the uterine mucosa (endometrium), which is the inner layer of the uterine wall. *Trueperella pyogenes* is the most common organism linked to endometritis in cattle. Endometritis is a reproductive condition characterized by signs of repeated breeding. It is evident that there is a correlation between the season of delivery and the occurrence of endometritis, with a higher frequency of endometritis occurring during autumnal deliveries. Although endometritis primarily affects cattle, it can also affect sheep, goats, pigs, horses, and camels. The primary clinical signs of endometritis include an enlarged uterus and an expanded cervical diameter, as well as purulent vaginal discharge. Endometritis is frequently diagnosed using the traditional method based on clinical signs and rectal examination. Cattle can contract endometritis from a variety of sources, including retained fetal membranes, assisted birthing procedures, contamination from dead calves, microbes entering the uterus during delivery, and immunological dysfunction in the genital tract of cows that have recently suffered from dystocia. The standard treatment for endometritis consists of a mix of hormones, such as uterotonics, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), and antibiotics. Important strategies to lower endometritis include the following management practices: Prevention of postpartum metabolic disorders, early detection and treatment of postpartum uterine diseases, and close monitoring and support during delivery.

Keywords: Cattle, Endometritis, Sexually transmitted disease, *T. pyogenes*, Uterus

Introduction

The effectiveness of livestock production is largely dependent on reproduction. Uterine infections that result in reproductive abnormalities can prolong the time between calving and pregnancy, which can result in large financial losses for dairy farms [1]. One of the prevalent reproductive illnesses that significantly reduces the livestock industry's profitability is endometritis [2]. Endometritis is an inflammation that occurs in the uterine mucosa (endometrium), which is the inner layer of the uterine wall [3]. Most cases of endometritis occur due to bacterial contamination of the uterine lumen after 3 weeks of delivery, depending on the balance between microbes, host immunity, and environmental factors [4]. *Escherichia coli*, *Fusobacterium necrophorum*, *Arcanobacterium pyogenes*, *Trueperella pyogenes*, and *Prevotella melaninogenicus* are the most pertinent pathogenic bacteria involved [5-9].

A pathogenic bacterial infection enters through the vagina, passes through the cervix, and contaminates the uterus in endometritis instances. Livestock reproductive performance can be negatively impacted by endometritis, which can result in either transient (infertile) or permanent (fertile) reproductive abnormalities [10]. There are 2 types of endometritis in cattle: Subclinical endometritis (SCE) and clinical endometritis (CE). Subclinical endometritis is characterized by an elevated percentage of polymorphonuclear (PMN) cells in the endometrium without clinical disease, while clinical endometritis is defined as the presence of purulent or mucopurulent vaginal discharge identified 3 weeks or more postpartum [11]. Cattle that are affected do not exhibit any outward signs. Endometritis is often transient and goes away on its own when a cow's uterus is exposed to a range of bacterial contaminants in the 1st 2 weeks, following calving [12].

The primary clinical signs of endometritis include an enlarged uterus and an expanded cervical diameter, as well as purulent vaginal discharge [13]. Histologically, this disorder is typified by many surface epithelial defects, inflammatory cell infiltration, vascular congestion and stromal edema, and variable levels of lymphocyte and plasma cell accumulation [14]. Endometritis continues to be a leading cause of repeat breeding and is responsible for 46 % of reproductive problems in cattle [15]. A number of reproductive problems, including anestrus and cystic ovarian disease, are associated with endometritis. It is one of the major reasons for decreased fertility in cows, along with retained placenta, puerperal metritis, pyometra, and other non-specific uterine infections [16].

As endometritis is a complex condition, identifying the contributing components has enormous potential as a source of knowledge that needs to be taken into account for both prevention and therapy. Previous research has found a number of parameters, including the time of calving, lactation, dystocia, nutrition, stillbirth, hypocalcemia, abortion, mastitis, retained placenta, metritis, twinning, negative energy balance, and delayed ovarian cycle [17]. The sensitivity of the diagnostic technique and the postpartum period at which the examination is conducted determine the occurrence of endometritis. In veterinary medicine, vaginoscopic examination and rectal palpation are frequently employed for examination [18]. It is advised to treat endometritis as soon as possible because it may produce pyometra or have other negative consequences for the animal's future fertility [19].

The performance of the global dairy business is negatively impacted by endometritis; financial losses are linked to the disease's treatment expenses, lower milk output, delayed ovarian activity resumption, and increased number of services per conception [20]. So far, there have been few reviews regarding endometritis in cattle. The purpose of writing this review is to explain the etiology, epidemiology, repeat breeding case, host range, pathogenesis, immune response, clinical symptoms, diagnosis, transmission, risk factors, treatment, and control of endometritis. Knowing specifics about this reproductive condition is crucial for choosing the best course of action for prevention and therapy in order to identify endometritis early on.

Etiology

T. pyogenes is the most common organism linked to endometritis in cattle [21]. Various degrees of endometritis are also believed to be caused by other bacteria, including *Streptococcus*, *Arcanobacterium pyogenes*, *Staphylococcus*, and *Escherichia coli*, and then by anaerobic bacteria, including *Prevotella* spp., *Fusobacterium necrophorum*, and *Fusobacterium nucleatum* [22]. The cause of endometritis is also the bovine herpes virus 4 (BoHV-4) [23]. The distinction between the uterine and vaginal microbiomes may be delayed in cows suffering from endometritis. Occasionally, opportunistic infections from the environment or the typical vaginal flora can enter the uterus [24]. The infection can be momentarily eradicated in cows with a strong immune response, but persistent endometritis can develop in cows with a weak immune system [10].

Bacterial contamination of the environment during labor can infect the uterus [25]. Endometritis can occur as a result of environmental bacterial contamination brought on by mastitis [26]. Hypocalcemia results from insufficient calcium mobilization around the time of birth. Since calcium is necessary for the process of uterine involution, any lack of it will cause the process to be delayed. It is also regarded as a risk factor for fetal membrane retention and may affect the occurrence and severity of endometritis [27].

Epidemiology

Numerous bacteria and viruses, categorized based on their toxicity and isolation frequency, cause both clinical and subclinical endometritis [28]. It is evident that there is a correlation between the season of delivery and the occurrence of endometritis, with a higher frequency of endometritis occurring during autumnal deliveries. The incidence is comparable in the spring and winter. Summertime deliveries were associated with the lowest prevalence of endometritis [29].

While the prevalence of endometritis in cows varies from 2.6 to 4.5 % in Spain [30], 6.25 % in Denmark [31], and 47.6 % in Korea [32], it varies from 5.6 to 10.9 % in Australia [33], 10.3 % in the USA [2], and 10.1 % in the UK [34]. In the US, cytology methods for diagnosing uterine bacterial infection, bacterial products, or uterine disease reveal a 53 % prevalence rate of endometritis in dairy cows, which delays uterine involution and compromises fertility [35]. In cattle in India, the frequency of endometritis varies from 3 to 25 %. In Gujarat’s dairy agricultural regions, the prevalence of endometritis is 8.90 % in cattle and 10.38 % in buffalo. In the meantime, 48.79 % of buffaloes in the dairy producing region of Dudhsagar [36].

Repeat breeding case

Repeated mating occurs when a female cow that has previously given birth and has a normal estrus cycle is mated twice or more times but does not become pregnant [15]. Endometritis is a reproductive condition characterized by signs of repeated breeding. A healthy uterine environment promotes embryo implantation and development [37]. The genital system’s physiological defenses weaken following delivery. Opportunistic microorganisms get into the uterus and cause infections [38]. These pathogens form a biofilm that shields and allows them to thrive indefinitely in the uterus [39]. Endometritis is caused by the long-term persistence of possible pathogens in a cow’s uterus or reproductive tract, which leads to repeated breeding [40].

Endometritis is an infection of the uterus that can cause repeat breeding incidents of 12.5 % in cows [15]. Endometritis disrupts the healthy uterine environment, following delivery [41]. In addition to endometritis, other causes that might cause repeated breeding in cows include failure to fertilize, early embryonic mortality, hormone deficit, lack of estrus detection, improper timing of artificial insemination, and increased microorganisms in the uterus [42]. Microbes in the uterus can be discovered in the mucus produced when a cow is in heat or in estrus [43]. Crossbred cattle are more likely to have repeat breeding syndrome than other breeds [44].

Host range

Although endometritis primarily affects cattle, it can also affect sheep, goats, pigs, horses, and camels [45]. Treatment is typically impractical and antemortem diagnosis is uncommon in commercial sheep and goat herds. Macerated fetal remnants should be regarded as a sign of a chronic infection in animals that have continuous uterine discharge [46]. Goats may develop endometritis or chronic metritis during the breeding season or after giving birth. Goats that are affected often eat and do not have a high temperature, although they do have vaginal discharge [47]. Bacterial contamination during culture or postpartum metritis can also result in chronic illness. In these situations, the preferred course of treatment is systemic antimicrobials and prostaglandins. Endometritis in camels is mainly treated empirically based on treatment for cattle and horses. One of the main causes of infertility in horses is endometritis, which is typically brought on by an overreaction to semen and a nonspecific infection [48]. In pigs, a variant of endometritis marked by profuse vaginal discharge at the commencement of estrus has been discovered in Europe and other regions [49]. The disease seems to be spread via mating or artificial insemination, and the causal agent is typically *Staphylococcus hyicus* or *E. coli*.

Pathogenesis

Postpartum bacterial infection of the uterus is thought to be inevitable. This contamination, removal, and recontamination process is intricate and not well understood [50]. The fact that the pregnant uterus is not sterile, as was long believed, but can be colonized by a variety of bacterial species, including strains like *T. pyogenes*, further complicates this idea [51]. These results raise fresh questions about the pathogenic pathways of the bacteria, or the circumstances in which the infection has a negative impact on conception and pregnancy, as well as the long-term repercussions of uterine infections. Additionally, there are some indications that germs, such as those from the colon, can enter the uterus through the blood [52]. The quantity and toxicity of the bacteria, as well as the cow's immunological condition, determine whether the majority of the invasive bacteria are eliminated by natural defensive mechanisms or whether clinical illness develops [53]. Therefore, the type of bacterium that invades is not the only factor that contributes to endometritis. The development of future prevention and intervention techniques may benefit greatly from an understanding of these interactions and shifts in the bacterial make-up of the uterine microbiota prior to the beginning of clinical indications of disease [54].

Endometritis may result from a persistent bacterial infection of the uterus. Common intrauterine pathogens include *E. coli*, *T. pyogenes*, *Fusobacterium necrophorum*, and *Prevotella* spp. [55]. However, little is known about the precise processes of bacterial pathogenicity and the virulence factors that contribute to uterine pathology [22]. The consequences of an *E. coli* uterine infection and the lipopolysaccharide (LPS) endotoxin produced by the bacteria have, however, previously been thoroughly investigated and documented [56]. It has been demonstrated that LPS, a part of bacterial membranes, affects the endometrium negatively and interferes with ovarian and uterine function. It also contributes to the innate immune response. One process is the binding of LPS by endometrial cells' Toll-like receptors (TLRs), which results in the release of cytokines and chemokines. To get rid of microorganisms, chemokines draw in neutrophils and macrophages. There is proof that the main cause of metritis is a particular strain of *E. coli* called Enteropathogenic *Escherichia coli* (EnPEC) [35].

T. pyogenes is believed to be the cause of endometritis later in the puerperium, whereas *E. coli* is one of the primary bacteria linked to early postpartum metritis [57]. It used to be thought that having already contracted *E. coli* might help a future *T. pyogenes* infection endure [58]. This theory is not supported by recent research, though [59]. However, *Streptococcus uberis* was found to be positively correlated with subsequent *T. pyogenes* infection on postpartum day 3, which is consistent with other studies that found α-hemolytic Streptococci to be associated with a higher risk of purulent vaginal discharge [60]. Additionally, it was demonstrated that some *S. uberis* subtypes were linked to the postpartum dairy cow uterus's health [10].

According to a study by Amos *et al*. [61], the primary virulence component of *T. pyogenes* is the exotoxin pyolysin (PLO). It is interesting to note that endometrial stromal cells are more vulnerable than epithelial cells to PLO-mediated cytolysis. Therefore, the endometrial damage caused by *T. pyogenes* seems to happen when the epithelial layer is disturbed following delivery. However, recombinant PLO by itself does not trigger an inflammatory response in the host, and the PLO gene is found in all strains of *T. pyogenes*. Therefore, more research should clarify if other virulence factors of *T. pyogenes* or other co-occurring intrauterine bacterial species induce the cellular responses that are typically linked to bacterial infections [22].

Immune response

The host has several defenses against endometrial infection and uterine microbial contamination. The vulva, vagina, and cervix offer an anatomical barrier to rising infection, with the exception of parturition, even though the animal's surroundings are highly contaminated with germs [62]. It is still up for debate whether vaginal pH or vaginal flora can also compete with pathogens to minimize illness. Nonetheless, the uterus, cervix, and vagina contain a variety of antimicrobial peptides, glycoproteins, and mucins that prevent bacterial growth and combat bacterial infection [63]. Attention is paid to microbial invasion of the female vaginal tract. Increased antibody abundance demonstrated an adaptive immune response, which is consistent with the capacity to vaccinate against uterine infections [64].

The function of innate immunity in female animals' genital tracts has been the subject of recent discoveries. The process by which pathogen-associated molecular patterns from microorganisms attach to host cell pattern recognition receptors is the basis for innate immunity [65]. The cytoplasm or plasma membrane of mammalian hematopoietic cells contains a variety of pattern recognition receptors. The 2 most widely investigated families of pattern recognition receptors are the Toll-like receptors and inflammasome components [66]. Bacterial components, including lipopolysaccharides, lipopeptides, and nucleotides, are bound by toll-like receptors and result in the generation of inflammatory mediators, typically interleukin (IL)-6 and IL-8 [67]. Similarly, the inflammasome is activated by pathogen-associated chemicals that enter the intracellular compartment. However, a number of general cellular disturbances, such as ion fluxes linked to pore-forming toxins released by bacteria can also activate the inflammasome [68]. The mature version of IL-1β is secreted and pro-IL-1β is usually cleaved upon inflammasome activation. Both stromal and epithelial endometrial cells, as well as hematopoietic cells from cows, have the Toll-like receptor system [69]. However, hematopoietic cells may have more inflammasome activity since endometrial cells secrete less IL-1β protein.

The innate immune system reacts quickly and nonspecifically to injury and infections. However, innate immunity must be carefully balanced because excessive inflammation might result in immunopathology or septic shock [70]. A number of checks and balances are in place to boost inflammation to meet the level of pathogenic threat, and to limit inflammation when the infection disappears. The function of STAT3 in controlling the release of IL-6 and IL-8 in stromal cells is 1 instance in the bovine endometrium [71]. Another illustration is the apical release of IL-6 and IL-8 by bovine endometrial epithelial cells, which is directed away from underlying stromal cells and toward invasive pathogens in the uterine lumen [69].

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Along with microbial identification, tissue damage is another characteristic of infection, and in the endometrium, this is frequently brought on by *T. pyogenes* secreting pyolysin [72]. Damaged cells release chemicals that are often not found in the extracellular compartment, such as cytoplasmic and nuclear compounds [73]. An inflammatory response is triggered by a number of pattern recognition receptors that detect molecular patterns linked to injury, especially on hematopoietic cells. After being primed with LPS, damaged endometrial tissue cells release IL-1α, a damage-associated molecular pattern that is typically kept in the cytoplasm of healthy cells [74]. Additionally, endometrial stromal cells have IL-1 receptors and respond to IL-1α by producing an inflammatory response that includes increased IL-6 production [75].

Given that innate immunity is an old and intricate system that has evolved throughout time, its integration with other metabolic processes and cellular homeostasis is not surprising [76]. Following calving, dairy cows undergo metabolic stress, which results in decreased nutritional concentrations and modifications to metabolic hormones such as decreased levels of glucose, glutamine, and insulin-like growth factor 1 [77]. Chronic endometritis can result from negative energy balance, which can also affect the inflammatory response and endometrial bacterial clearance [78], [79]. One notable example is when rats administered LPS consume more than 1 kg of glucose in the 1st 12 h. Moreover, endometrial tissue's *in vitro* inflammatory response is decreased when essential cellular resources like glucose or glutamine are depleted [80]. Chronic inflammation and infection persistence may arise if metabolic stress impairs an animal's capacity to react to infections. This impairs key processes like antigen presentation and antibody production, reducing the immune system's ability to clear infections and leading to prolonged inflammation and tissue damage (**Figure 1**).

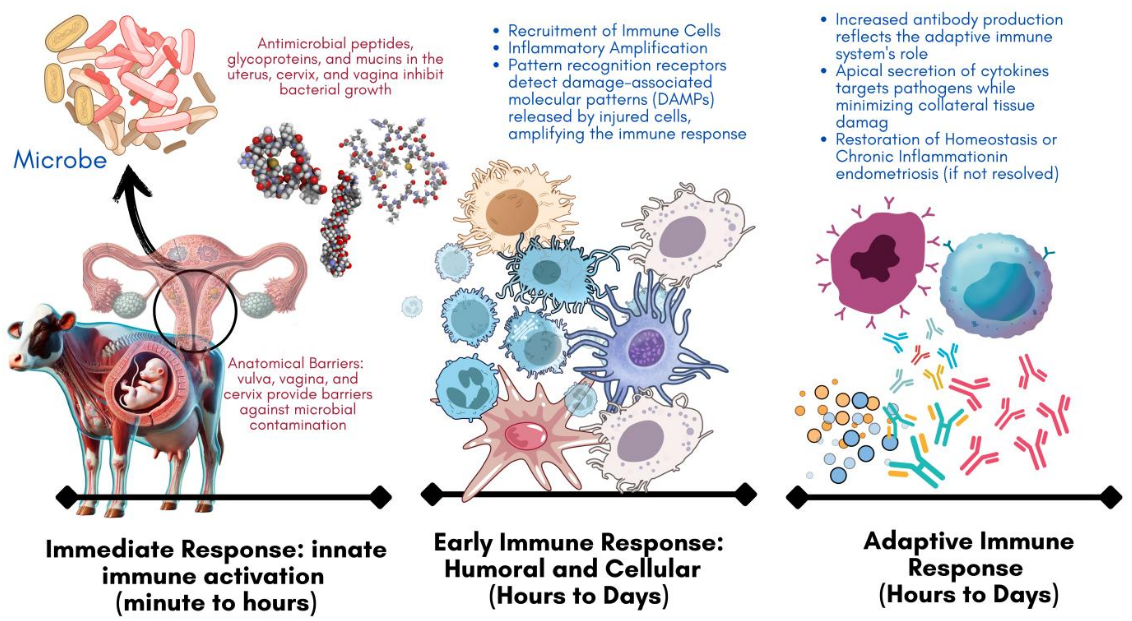

Figure 1 Progression of innate and adaptive immunity in response to endometrial pathogens.

Clinical symptoms

Fertility is impacted by endometritis in 2 ways. First, endometritis is linked to delayed ovulation following calving, extended intervals between ovulations once cows enter estrus, and the lack of estrus behavior. Second, because the diseased uterus is a poor environment for growing embryos, cows with endometritis are less likely to conceive even when they do have estrus cycles [81]. In particular, endometritis lowers cows' reproductive efficiency by increasing the number of inseminations per conception, increasing the culling rate, and lengthening the time between calving and conception [82]. It has been demonstrated that endometritis, both cytological and clinical, is strongly linked to poorer reproductive outcomes [83].

The primary clinical signs of endometritis include an enlarged uterus and an expanded cervical diameter, as well as purulent vaginal discharge [1]. After 3 weeks postpartum, cows with clinical endometritis have purulent (>50 %) or mucopurulent (roughly 50 % pus and 50 % mucus) fluid in the vagina without any systemic symptoms [25]. Since the pus found in the vagina sometimes comes from the cervix or vagina rather than the uterus, the term clinical endometritis is still debatable, and purulent vaginal discharge is the suggested alternative word [2]. The presence of threshold PMNs on cytological examination, which indicates inflammation of the uterine endometrium, without purulent material in the vagina, is a characteristic of subclinical endometritis in cattle.

Histologically, vascular congestion, edema, and leukocyte infiltration indicate a disruption of the uterine endothelium [84]. According to studies, cows with endometritis typically had a 15-day increase in open [18]. Pregnancy rates have been demonstrated to drop by 16 % and the chance of pregnancy up to 150 days in milk by 31 % [85]. The significance of a properly maintained immune system was demonstrated in the example of cytological endometritis, where it was found that cows with no neutrophils on uterine cytology were just as likely to not conceive as cows with high neutrophil counts (>15 %) [86].

Diagnosis

Endometritis is frequently diagnosed using the traditional method based on clinical signs and rectal examination [87]. Although uterine biopsy and culture have been employed as diagnostic techniques, their application in the field is restricted due to their impracticality [45]. Ultrasonography and new diagnostic instruments (Metricheck) are adequate for the precise diagnosis of endometritis [88]. In clinical practice, rectal palpation is the most often used diagnostic method for endometritis, although vaginoscopy is a diagnostic procedure that is rarely employed [87].

The combination of rectal palpation with vaginoscopy has been demonstrated to be a more accurate procedure [89]. The cervical diameter was greater than 7.5 cm, the uterine wall was thickened, there was palpable fluid, and asymmetrical uterine horns were discovered on rectal palpation. Histologically, it is distinguished by a degree of surface epithelial rupture, inflammatory cell infiltration, vascular congestion, stromal edema, and variable levels of lymphocyte and plasma cell accumulation [90].

The degree of inflammatory alterations in the endometrium has been demonstrated to be strongly correlated with the presence of Gram-negative anaerobic bacteria and *T. pyogenes*. After the cervix is constricted per rectum, a catheter is placed into it and subsequently into the body of the uterus. The swab is exposed to the endometrium by pushing the catheter's inner shaft forward, rotating it against the uterine wall, and then pulling it back into the catheter. The smears are incubated for 48 h at 37 °C after being promptly cultivated on MacConkey agar and sheep blood agar. For up to 7 days, the identical colony are incubated anaerobically on sheep blood agar. To identify and isolate, standard biochemical assays are employed [91].

Cytological assessment of uterine fluid obtained by aspiration of uterine contents or uterine lavage using a cytobrush or Foley catheter is a legitimate alternative diagnostic technique for identifying uterine infections in cattle and buffaloes [92]. Cows with endometritis had a considerably higher percentage of polymorphonuclear cells (45.62 %) and neutrophils. Because of the broad changes in cell proportions in postpartum days, the uterine cell proportions in cows are insufficient for diagnosing endometritis, making such procedures practically useless. As a result, veterinarians have not adopted this technique.

The Whiteside test, which involves collecting cervical mucus from repeat breeding cows, adding the same amount of NaOH, boiling it, and then watching for color changes, is a useful method for diagnosing subclinical endometritis [93]. According to the interpretation, mucus that is hazy or colorless is normal, whereas light yellow, yellow, or dark yellow mucus denote mild, moderate, and severe endometritis, respectively. Furthermore, a previously developed diagnostic technique has been employed in the form of a Metricheck device, which is implanted into the vagina and evaluates the correlation between the Metricheck clinical score 35 days before to the onset of reproduction [94]. The Metricheck gadget is used to assess cows having a history of peripartum illness. A clinical score for endometritis can be obtained by scoring vaginal mucous as follows: 0 - Clear or translucent mucus, 1 - Clear or translucent mucus with white pus flakes, 2 - <50 mL exudate with <50 % white or cream pus, and 3 - >50 mL exudate with >50 % white, cream, or bloody pus with an unpleasant odor. Endometritis can also be diagnosed by the evaluation of endometrial cytology in which the proportion of polymorphonuclear cells (%PMN) are assessed and compared with a pre-set threshold [95].

Transmission

Cattle can contract endometritis from a variety of sources, including retained fetal membranes, assisted birthing procedures, contamination from dead calves, microbes entering the uterus during delivery, and immunological dysfunction in the genital tract of cows that have recently suffered from dystocia [4]. Additionally, both natural mating with infected bulls and artificial insemination can result in bacterial endometritis [96]. As many as 90 % of germs in recently delivered cows remain in the uterus for one to 10 days [25]. Poor sanitation might lead to a rise in the microbial load.

Risk factors

Numerous factors have been identified as contributing to the development of endometritis. These include milk production, metabolic disorders, bacterial contamination of the uterus, twins, induction of labor, retention of fetal membranes and restoration of ovarian cycle activity, and dystocia [1]. One significant risk factor for endometritis is retained placental membranes [28]. The preserved placental membrane is an ideal environment for the growth of bacteria. Cow dystocia is frequently linked to a number of postpartum issues, including delayed uterine involution and retained fetal membranes, both of which surely promote the development of endometritis [81].

Endometritis risk factors also include metabolic diseases like milk fever and ketosis, as well as birth issues including stillbirth and multiple births [17]. Endometritis has debilitating impact on dairy cows' reproductive function, as seen by the longer time between 1st calvings and conception, as well as the frequency of 1st calvings per conception when endometritis group were compared to non-endometritis group in a previous report [32]. However, it was observed that the endometritis animal group had a lower percentage of first-time conceptions than the non-endometritis animal group. The most common conditions linked to negative energy balance (NEB) are delayed uterine involution, and severe protracted uterine inflammation. NEB promotes the development of numerous metabolic diseases, especially ketosis, which can raise endometritis risk factors by 6.1 to 9.5 times, especially retained placenta and endometritis [28].

Treatment

Although treating clinical and subclinical endometritis is not a medical emergency, it is essential for enhancing the reproductive ability of cows. It is crucial to remember that if estrus is successful in clearing the uterus, endometritis may heal on its own. On the other side, systemic treatment for endometritis could be necessary to get the cow back to normal. The standard treatment for endometritis consists of a mix of hormones, such as uterotonics, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), and antibiotics [97]. Antibiotics that are most frequently used include tetracycline, ampicillin, amoxicillin, and sulfonamides; trimethoprim, cefadroxime, ceftiofur, and procaine benzylpenicillin [1]. Legal limitations, efficacy against Gram-negative anaerobes, the type and severity of the illness, and non-antibiotic alternatives must all be taken into account when choosing which antibiotic agents to use in a treatment plan.

Due to the toxicity and adverse effects of allopathic medications, the use of herbal medicine is becoming more and more common. As a result, this approach may be an alternate treatment for uterine infections by employing immunomodulators and phytotherapy actions to activate the natural defense mechanisms of cow's uterus [98]. A number of plant products have been employed as medicinal agents and are now being studied by scientists [99]. In recent years, the use of numerous medicinal herbs to treat infertility has been acknowledged. Numerous herbs, including neem, turmeric, ashwagandha, garlic, and tulsi, have been successfully used to treat endometritis in cows [100].

The most widely used NSAIDs include carprofen, meloxicam, ketoprofen, and flunixin meglumine [101]. Oxytocin is one of the uterotonic hormones and medications that can be utilized within the 1st few hours (up to 72 h) following delivery [102]. Prostaglandin F2α can then be used starting on the 3rd day after delivery. The advantage of PGF2α is thought to be the induction of estrus due to the presence of a corpus luteum that responds to PGF2α after ovarian activity is resumed during involution [103]. Estrus encourages the removal of inflammation-causing substances and germs. The choice between systemic (antibiotic) and intrauterine treatment is still up for debate. The intrauterine administration of cephapirin, chlortetracycline, and dextrose has shown some encouraging outcomes [104]. Furthermore, a novel and exciting field of study for the prevention or treatment of endometritis is the use of probiotics.

Control

Encouraging and supporting the innate immune system is the foundation for endometritis prevention. Uterine infections are more common in cows that have hypocalcemia, dystocia, stillbirth, twins, or retained placenta in the time before parturition than in cows that give birth properly [105]. In order to prevent or lessen the occurrence of these risk factors (particularly dystocia), it is imperative that cleanliness, nutrition, population density, and stress be perfectly managed [83]. Important strategies to lower endometritis include the following management practices: Prevention of postpartum metabolic disorders, early detection and treatment of postpartum uterine diseases, and close monitoring and support during delivery [106]. Clinical endometritis may be avoided with regular systemic or intrauterine ceftiofur treatment [107]. Provision of appropriate and hygienic resting areas to ensure that the reproductive tracts of recently calved cows are not overly contaminated.

Even within the same herd, some cows may be more prone in developing and maintaining endometritis than others due to a combination of intrinsic variables that are unique to each individual cow and extrinsic factors that are related to herd conditions [108]. Therefore, in order to prevent and cure afflicted cows, the most significant risk factors should be determined. Then, each cow's treatment should be customized based on the clinical analysis of the discovered intrinsic and extrinsic risk factors. This could lead to improved endometritis management and a decrease in the related financial losses.

Conclusions

In conclusion, endometritis significantly affects livestock reproduction, leading to financial losses due to its association with various reproductive issues. Early identification and effective management strategies are crucial in mitigating its impacts on dairy farm profitability. Understanding its etiology and clinical signs are essential in the prevention and treatment of endometritis.

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