Metritis in Dairy Cattle: Diagnostic Challenges, Economic Impacts, and Emerging Insights

Abstract

Metritis, an inflammatory uterine disorder occurring within 21 days postpartum, poses significant global challenges to dairy herd management. This review comprehensively examines the incidence, diagnostic criteria, clinical manifestations, economic implications, and emerging management strategies for metritis in dairy animals. The classification of metritis, distinguishing between puerperal metritis and delayed uterine involution, is discussed alongside diagnostic approaches such as vaginal discharge scoring, cytology, and rectal temperature evaluation. Metritis incidence varies widely, ranging from 10% to 36%, with early postpartum diagnosis being critical to minimizing its impact. The economic burden of metritis is profound, with affected cows experiencing reduced milk yield, impaired reproductive performance, extended calving intervals, and increased culling rates. Despite its clinical significance, diagnosing metritis remains challenging due to inconsistent presentation of fever and subjective assessment of clinical signs. Non-invasive diagnostic techniques, such as infrared thermography (IRT), are highlighted as promising tools for early detection, offering a stress-free and practical approach to monitoring rectal temperature and systemic health. Recent advances in molecular research have uncovered genetic variants and regulatory pathways, such as cholesterol metabolism and the PI3k-Akt signalling pathway, associated with disease susceptibility and progression. These insights provide potential therapeutic targets and opportunities for precision management strategies. The present review accentuates the critical need for standardized diagnostic criteria, innovative non-invasive technologies, and integrative management approaches to address metritis effectively. Continued research and the application of cutting-edge technologies are essential to mitigate the economic and welfare impacts of metritis, ultimately improving herd health, productivity, and sustainability in the dairy industry.

Keywords: metritis, dairy animals, diagnosis, temperature

Introduction

Metritis is a significant postpartum uterine disorder in dairy cows, typically occurring within 10 to 21 days after calving, characterized by uterine inflammation often accompanied by systemic illness, with or without fever. The condition exerts considerable negative effects on dairy production systems globally, impairing milk yield, reproductive performance, and cow welfare while increasing the risk of early culling (Ribeiro et al., 2013; Stojkov et al., 2015; Dubuc et al., 2011). The economic burden associated with metritis is substantial, stemming from reduced milk production—up to 5 kg/day—prolonged calving-to-conception intervals, increased treatment costs, and higher culling rates (Giuliodori et al., 2013; Daetz et al., 2016; Barragan et al., 2018). Additionally, metritis has been closely linked to poor animal welfare outcomes, emphasizing the need for early and effective management strategies (Neave et al., 2018).

Despite its global prevalence, ranging between 10% and 36% of dairy cows (Sheldon et al., 2006; De Oliveira et al., 2020), metritis diagnosis remains inconsistent. Traditional diagnostic criteria often categorize puerperal metritis based on an abnormally enlarged uterus, fetid uterine discharge, and systemic signs like fever. However, variations in disease presentation complicate this approach, as many cows with fetid discharge do not exhibit fever, and some cases involve delayed uterine involution without systemic symptoms (Sheldon et al., 2006; Martinez et al., 2012). Garzon et al. (2022) emphasise in their study for an urgent need for a unified framework and robust diagnostic protocols to address these discrepancies.

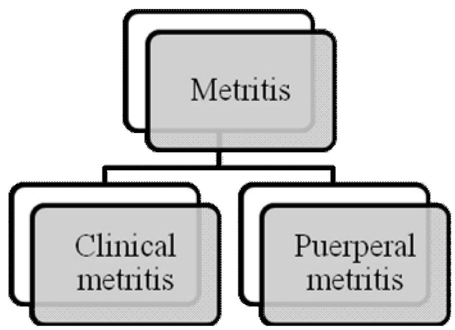
Conventional diagnostic methods, such as vaginal discharge scoring and cytological evaluations, have been widely used but are limited by subjective interpretation and labor-intensive procedures (Jeon et al., 2016). Advanced laboratory techniques, including microbiology and polymerase chain reaction (PCR), offer precision but are time-consuming, expensive, and reliant on specialized facilities, restricting their utility in field conditions (Garzon et al., 2022). In this context, the development of portable, non-invasive diagnostic tools represents a paradigm shift in metritis detection and management.

Emerging technologies like the Metrisor device (Risvanli et al., 2024) and infrared thermography (IRT) (Macmillan et al., 2019) exemplify this shift. The Metrisor utilizes gas sensors to detect intrauterine gases, providing a rapid, accurate, and portable diagnostic solution tailored for field use. Similarly, IRT offers a non-invasive method to identify early postpartum illnesses through surface temperature variations, enhancing disease detection without the need for invasive procedures. These tools hold promise for addressing the limitations of current methods, enabling real-time, scalable diagnostics directly on farms.

This review aims to bridge the existing gaps in metritis detection and management by critically evaluating its definitions, classifications, prevalence, and economic impacts. In doing so, it synthesizes insights from emerging technologies and recent research to propose novel, field-adaptable diagnostic frameworks. By emphasizing the practical feasibility and transformative potential of these advancements, this review seeks to support the development of comprehensive strategies to improve herd health, productivity, and animal welfare while mitigating the economic burden of metritis on the dairy industry.

Metritis- definition and classification

Fig 1: Classification of Metritis



(Sheldon et al., 2006)

Metritis is a significant postpartum uterine disorder characterized by an abnormally enlarged uterus and the presence of fetid, watery, reddish-brown uterine discharge, typically occurring within the first 21 days after parturition (Sheldon et al., 2006; Stojkov et al., 2015). Its prevalence peaks within the first ten days postpartum, making it a critical concern for dairy herd management. Depending on clinical presentation and severity, metritis is classified into clinical metritis and puerperal metritis (PM), with severity ranging from subclinical to life-threatening toxemic conditions.

Clinical Presentation and Challenges in Definition: The characteristic features of metritis include an enlarged, flaccid uterus and discharge varying from watery red-brown to viscous purulent with a distinct fetid odour (Sheldon et al., 2006). However, a unified definition of metritis remains elusive due to variations in clinical signs and diagnostic criteria among studies. PM, a severe form of metritis, involves inflammation of all uterine layers, systemic illness, and fetid discharge. Systemic symptoms often include pyrexia (>39.5°C), inappetence, dullness, and decreased milk production, typically manifesting between 7 to 14 days postpartum (Olson et al., 1986; Sheldon et al., 2006, 2009).

The lack of standardization in diagnostic criteria poses challenges for clinical and research applications. For instance, fever thresholds for PM diagnosis vary across studies, ranging from 39.2°C to 39.7°C (Drillich et al., 2001; Sheldon et al., 2006). Moreover, disparities in describing vaginal discharge—using terms such as red-brown, chocolate, or yellow for color and fetid or putrid for odor—highlight the subjective nature of these evaluations (Garzon et al., 2022). Such inconsistencies can lead to discrepancies in diagnosis, treatment recommendations, and antimicrobial use, underscoring the need for a standardized framework.

Microbial Etiology and Disease Complexity: Metritis is a multifactorial disease predominantly caused by polymicrobial infections. Key pathogens implicated in postpartum uterine infections include *Escherichia coli*, *Trueperella pyogenes*, *Fusobacterium necrophorum*, and *Bacteroides* spp., which often interact synergistically with other bacteria such as *Helcococcus, Filifactor, Porphyromonas, Peptoniphilus, Peptostreptococcus, Campylobacter,* and *Prevotella* to exacerbate disease severity (Jeon et al., 2015). Also, Cunha et al. (2018) reported that metagenomic studies question the traditional focus on *Escherichia coli* and *Trueperella pyogenes* as primary pathogens in metritis. Instead, they highlight the importance of *Fusobacterium necrophorum*, *Prevotella melaninogenica*, and emerging pathogens such as *Bacteroides pyogenes*, *Porphyromonas levii,* and *Helcococcus ovis* in the disease's etiology. The disease's progression depends on factors such as pathogen virulence, uterine environment, and immune response, making it a complex and multifaceted condition.

Puerperal Metritis and Disease Complex: Puerperal metritis (PM), also referred to as acute puerperal metritis (APM), occurs within ten days postpartum and is characterized by systemic illness, including fever ≥39.5°C, fetid uterine discharge, and an enlarged uterus (Sheldon et al., 2006; Machado et al., 2014). The systemic manifestations of PM, such as toxaemia, depression, and reduced productivity, make it a significant health concern. Toxic puerperal metritis (TPM), a severe subtype of PM, presents with increased rectal temperature, fetid vulvar discharge, and uterine atony, requiring immediate intervention to prevent septicemia and mortality (Smith et al., 1998).

Fever in Metritis: Mechanisms, Implications, and Immunological Responses

The treatment protocol for metritis remains consistent irrespective of the presence or absence of pyrexia (McLaughlin et al., 2012). However, metritis-associated fever introduces unique physiological and clinical implications. Both febrile and afebrile metritic cows exhibit reductions in milk production and an increased likelihood of developing clinical endometritis (Benzaquen et al., 2007). However, a significant decline in reproductive performance is observed primarily in metritic cows with fever, potentially due to the systemic inflammatory burden (Giuliodori et al., 2013). Recovery rates for febrile metritic cows are notably lower compared to their afebrile counterparts, which may be attributed to variations in uterine microbiota that influence the response to antibiotic therapy (Lima et al., 2014).

Fever in metritic cows arises from the activation of innate immune pathways triggered by uterine bacterial infections. The inflammatory response is mediated by the induction and release of endogenous cytokines such as tumor necrosis factor-alpha (TNFα), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), along with chemokines like RANTES and MCP-1. These mediators activate polymorphonuclear and mononuclear leukocytes, culminating in the synthesis of prostaglandin E (PGE), which triggers fever via the central nervous system (Netea et al., 2000). Among bacterial components, lipopolysaccharides (LPS) from Gram-negative bacteria serve as the most potent fever-inducing agents, though peptidoglycans from Gram-positive bacteria can also elicit febrile responses (Tavares et al., 2005).

In metritis, fever is commonly associated with uterine infections dominated by Gram-negative bacteria such as *Fusobacterium* spp. and *Bacteroidetes* spp., known for their ability to stimulate robust inflammatory responses (Jeon et al., 2015). Similarly, neutrophils play a pivotal role in propagating inflammation and clearing bacterial infections during uterine infections (Sheldon et al., 2009). However, compromised neutrophil function has been observed in dairy cows during the periparturient period, extending from one week before to three weeks after calving, which predisposes cows to metritis (Hammon et al., 2006; Jeon et al., 2015; Bromfield et al., 2015).

Immunosuppression during the transition period creates a window of vulnerability, allowing bacterial infections to establish. However, not all cows exposed to pathogenic bacteria develop metritis, suggesting that bacterial load and virulence are primary determinants of disease severity and febrile response (Jeon et al., 2015, 2016). These findings underscore the complexity of metritis pathogenesis and highlight the need for targeted therapeutic strategies to mitigate the systemic effects of febrile metritis and improve recovery outcomes.

Incidence and Prevalence of Metritis

Puerperal metritis continues to be a major health concern in postpartum dairy cows, with prevalence rates ranging from 5% to 20% within herds worldwide (LeBlanc, 2014) and metritis in the range of 8 % to 40% (Silva et al., 2024). Despite a global focus on the condition, there is still a lack of extensive research in some regions, such as India. Benzaquen et al. (2007) conducted a study on a commercial dairy farm with 1,000 lactating cows in northeast Florida, finding a 21% incidence of puerperal metritis. The study also revealed seasonal effects, with primiparous cows calving during the warm season having lower odds of developing metritis compared to those calving during the colder months. A more recent study by Torres et al. (2020) in northern Mexico found a 16% prevalence of metritis among 2,500 Holstein cows, with 11.3% of cows showing clinical endometritis following retained fetal membranes (RFM).

Globally, the prevalence of metritis varies across different regions. For example, Kasimanickam et al. (2004) reported a high incidence of 45% in the United States (Kasimanickam et al., 2004), while studies from Canada (13.5%) (Dubuc et al., 2010), Argentina (38%) (Plontzke et al., 2010), New Zealand (29%) (McDougall et al., 2011) and Belgium (27.8%) (Bogado et al., 2016) also show significant variation. In Argentina, Giuliodori et al. (2013) found a 29.7% incidence of puerperal metritis and a 9.6% incidence of clinical metritis in a study of 303 Holstein-Friesian cows. The study highlighted those multiparous cows had lower odds of developing metritis compared to primiparous cows. Factors such as abnormal calving, high pre-partum non-esterified fatty acids (NEFA) levels, and lower pre-partum insulin-like growth factor-1 (IGF-1) were associated with increased risk. Zwald et al. (2004) documented a 21% incidence of metritis, including RFM, from a large dataset involving 97,318 cow records in the United States. Gaddis et al. (2012) reported that the incidence of metritis ranged from 2% to 36% in US Holsteins, with an average of 13%.

More recent studies have focused on identifying key risk factors. Kaniyamattam et al. (2020) observed a consistent 28% incidence of metritis across both first and subsequent lactations in US dairies. De Vries (2017) proposed that retaining a greater proportion of calves could help reduce metritis incidence by increasing the annual cull rate. McCarthy and Overton (2018) found that mild metritis occurred in 24.7% of cases, with severe metritis found in 3.5%, in a study involving a Holstein herd with a one-year calving interval. Misclassification bias is believed to underestimate the true association between metritis and its economic impact, as well as its effects on milk production (Gaddis et al., 2012; McArt et al., 2015; Liang et al., 2017). Newer research continues to refine our understanding of the complex interactions between environmental, physiological, and management factors influencing metritis prevalence. The need for more standardized diagnostic criteria across regions is critical in improving the accuracy of prevalence reports and in mitigating the disease's economic impact in the dairy industry.

Production and economic loss due to metritis

Metritis is a major cause of economic loss in dairy farming due to various factors such as treatment costs, milk withdrawal leading to lost milk production, reduced reproductive performance, and increased premature culling (Heikkilä et al., 2012; Lima et al., 2019). The economic burden of metritis is influenced by several variables, including the milk yield, milk price, and the duration of milk withdrawal during treatment. Puerperal metritis, or early metritis, significantly decreases milk yield and feed intake (Huzzey et al., 2007), while also negatively impacting reproductive efficiency (Melendez et al., 2004). The average cost per metritis case has been reported at approximately $350 (Overton and Fetrow, 2008), with more recent estimates suggesting costs of $511 per case in U.S. dairy herds (Pérez-Báez et al., 2021). This increase highlights the escalating financial burden of metritis and the need for more effective management strategies to mitigate these costs. Beyond direct treatment costs, metritis affects the dairy industry by reducing milk production, impairing reproductive performance, and increasing culling rates, further compounding the financial losses (Lima et al., 2019; Machado et al., 2020). Despite variations in estimations across studies, the economic toll of metritis is clear, emphasizing the importance of continued research to evaluate its impact across diverse dairy farming systems (Mahnani et al., 2015).

Metritis also incurs additional costs related to treatment, which typically range from $46 to $101 per case, depending on factors like cow parity and the choice of antibiotic (Lima et al., 2019). Previous studies reported varying cost estimates, with Bartlett et al. (1986) estimating a total cost per case of $106. More recent studies have found cost ranges between $329 and $386 per case (Overton and Fetrow, 2008). These discrepancies reflect different treatment approaches, disease management practices, and farm conditions, suggesting the need for more comprehensive studies that consider these factors across various farm settings to accurately quantify the economic burden of metritis in the dairy industry. The detrimental effects of metritis on milk production and fertility are well documented. Cows suffering from metritis generally experience decreased milk production and poorer fertility, and they are more likely to be culled (Stangaferro et al., 2016). Lima et al. (2019) estimated that economic losses per metritis case ranged from $267 to $410 due to the combined effects of antibiotic treatment and the adverse impacts on milk production, reproduction, and culling. Drillich et al. (2001) similarly calculated a loss of $380 per affected cow.

Machado et al. (2020) assessed how cow-related factors influence the cure rate and associated economic outcomes of metritis. They found that cows with higher levels of haptoglobin (Hp >0.54 mg/mL), which is a marker of inflammation, produced less milk in the early stages of lactation. Specifically, metritic cows that were not treated with ceftiofur had significantly reduced milk production compared to non-metritic cows. Additionally, metritis negatively affects reproductive efficiency, increasing the number of days between calving and first service (Fourichon et al., 2000), and requiring more resources to induce pregnancy.

Culling decisions on dairy farms are influenced by an animal's reproductive health, with metritis increasing the risk of premature culling, particularly among multiparous cows (Gröhn et al., 2003). Wittrock et al. (2011) found that multiparous cows with metritis ate less during the first three weeks after calving, resulting in reduced milk production and an increased likelihood of culling by 305 days. This long-term reduction in milk production may be partly attributed to a decline in feed intake, which limits the energy available for milk synthesis (Bell and Roberts, 2007; Huzzey et al., 2007). Interestingly, primiparous cows with metritis were found to have a faster immune response to infection and recovered more quickly than multiparous cows (Waldron et al., 2006). Giuliodori et al. (2013) reported that cows with metritis (both clinical and puerperal) produced less milk than healthy cows during early lactation but more milk during late lactation. However, by 90 days in milk (DIM), healthy cows consistently outperformed metritic cows in terms of milk yield.

Clinical and puerperal metritis both have significant adverse effects on peak milk yield, especially during early lactation, with puerperal metritis having a more pronounced impact on production than clinical metritis (Dubuc et al., 2011). Fourichon et al. (2000) emphasized the detrimental effect of metritis on fertility, including delayed return to cyclicity, disruption of the uterine environment, and impaired embryo development (Sheldon et al., 2002; Sheldon and Dobson, 2004; Soto et al., 2003). To reduce the economic burden of metritis, it is essential for dairy farms to implement health-monitoring programs that detect and treat cows with metritis promptly, thereby minimizing its adverse effects on productivity and reproductive performance.

Factors causing metritis

Metritis, an inflammatory condition of the uterus, is influenced by a variety of factors, many of which are linked to parturition and the early post-partum period. Factors such as parity, calving month, infectious disease presence, particularly metritis, and abnormalities during parturition play significant roles in its development. Wenz et al. (2011) found that primiparous cows and those diagnosed with contagious diseases like metritis exhibited higher rectal temperatures (RT), with peak RT occurring on the third day post-partum. These findings align with the fact that normal post-partum RT may be higher during warm summer months compared to typical values (Wenz et al., 2011).

The development of metritis is predisposed by several physical and environmental factors. These include dystocia, twin births, retained fetal membranes (retained placenta), stillbirths, hygiene deficiencies, and metabolic imbalances around parturition, such as low dry matter intake (DMI) and high prepartum serum non-esterified fatty acid (NEFA) concentrations (Ospina et al., 2010). Common pathogens associated with metritis include *Arcanobacterium* (Actinomyces) *pyogenes*, *Trueperella pyogenes*, coliform bacteria, and anaerobic species such as *Fusobacterium necrophorum*, *Prevotella spp.*, and *Bacteroides spp.* (Sheldon and Dobson, 2004; Williams et al., 2005). These bacteria necessitate antibacterial treatment to manage the condition. Historically, it was believed that the uterus was sterile before calving, and that post-partum metritis in dairy cows was caused by the introduction of *Escherichia coli* (*E. coli*) into the uterus during or after parturition. This theory suggested that *E. coli* facilitated secondary bacterial growth, contributing to metritis (Sheldon et al., 2009). However, more recent studies have challenged this belief, showing that both healthy and metritic cows share most bacterial genera at the time of parturition and on day six post-partum, with significant differences primarily in the abundance of certain species (Jeon et al., 2015). The uterine microbiota predominantly comprises

Bacteroidetes, *Fusobacteria*, *Proteobacteria*, *Tenericutes*, and *Firmicutes*, irrespective of infection status (Santos and Bicalho, 2012; Jeon et al., 2015). Shifts in the growth of specific bacteria, such as *Bacteroides, Porphyromonas*, and *Fusobacterium*, have been linked to the onset of metritis (Jeon et al., 2015; Bicalho et al., 2017a). Notably, *E. coli* presence in metritic cows is low (less than 1%), and its role in metritis is only significant in the presence of virulent strains carrying the fimH factor (Bicalho et al., 2012; Jeon et al., 2015, 2016).

Primiparous cows, those experiencing abnormal calving (e.g., dystocia), and those with poor energy balance prepartum, as evidenced by elevated NEFA and low IGF-1 levels, face a higher risk of metritis (Giuliodori et al., 2013). This aligns with findings by Kaneene and Miller (1995) and Dubuc et al. (2011), who found that primiparous cows are at a higher risk due to the increased likelihood of requiring calving assistance, which increases the risk of uterine contamination and lesions (Ghavi Hossein-Zadeh and Ardalan, 2011). Studies have identified specific NEFA thresholds for predicting metritis; Ospina et al. (2010) suggested a threshold of 300 µM, while Dubuc et al. (2011) reported a threshold of 600 µM. Giuliodori et al. (2013) proposed a prepartum NEFA cut-off of 431 µM. In addition to elevated NEFA levels, other metabolic imbalances are significant predictors of metritis. For instance, Torres et al. (2020) found that cows with β-hydroxybutyrate (BHBA) concentrations ≥ 0.8 mmol L^-1 were 2.2 times more likely to develop metritis and 4.4 times more likely to develop clinical endometritis (CE). Elevated serum BHBA levels indicate poor adaptation to the demands of lactation and negative energy balance, which impair immune function (Zarrin et al., 2014). The optimal BHBA cut-off for predicting puerperal metritis was found to be 1.2 mmol L^-1. Furthermore, cows with serum creatinine concentrations ≥ 2.0 mg dL^-1 were at higher risk for metritis and CE due to prolonged tissue protein catabolism impairing immune responses (Titgemeyer and Loest, 2001). Higher serum total protein (TP) levels (≥ 5.0 mg dL^-1) were also associated with increased odds of metritis, suggesting an activated immune response post-infection (Cray et al., 2009).

Additional factors, such as body condition score (BCS), play a role in metritis risk. A BCS of ≤ 3.2 should be avoided to prevent endometritis (Galvão et al., 2009). Cows experiencing significant metabolic, physiological, and immunological changes during early lactation are also more susceptible to diseases like metritis and endometritis (Bicalho et al., 2017b). High plasma glucose levels during early lactation have been associated with an increased risk of post-partum diseases, including metritis. Furthermore, excessive loss of body energy reserves post-calving impairs immune function, making cows more vulnerable to disease, especially under high ambient temperatures (Thompson et al., 2014). Finally, cows diagnosed with metritis are at higher risk for developing clinical and cytological endometritis (Galvão et al., 2009; Martinez et al., 2012). The severity of the immune response in metritic cows is more closely correlated with disease severity than the intrauterine microbiome itself (Jeon et al., 2016). Factors such as parity, retained placenta, calving abnormalities (e.g., dystocia, twins, vulvovaginal lacerations), and elevated metabolic markers (NEFA, BHBA) have been identified as risk factors for metritis and may have predictive value for cure (Lima et al., 2014; Vergara et al., 2014; Vieira-Neto et al., 2016). The circulating concentration of haptoglobin (Hp), an acute phase protein, has also been linked to metritis severity, suggesting its potential role as an indicator of the likelihood of cure (Huzzey et al., 2009). Thus, metritis development is influenced by a combination of cow-related factors, metabolic imbalances, and infectious agents. Early identification and management of these risk factors are crucial for preventing metritis and mitigating its consequences on dairy cattle health and productivity.

Temperature change monitoring during metritis

Rectal temperature (RT) is a critical parameter in diagnosing and monitoring the progression of metritis in dairy cows. Smith et al. (1998) defined a rectal temperature exceeding 39.2°C as indicative of fever in the context of metritis. Several studies have employed different RT thresholds to assess metritis, with values ranging from 39.2°C (Smith et al., 1998) to 39.7°C (Sheldon et al., 2004) depending on the study context. Drillich et al. (2001) used a threshold of 39.5°C, while Kristula et al. (2001) recommended 39.4°C for primiparous cows and 39.7°C for multiparous cows. These variations reflect differences in study design, cow parity, and other influencing factors. A meta-analysis by Garzon et al. (2022) found that the most commonly used rectal temperature threshold for diagnosing metritis was ≥39.5°C, used in 56.8% of studies, followed by ≥39.2°C, which was used in 2.8% of the studies. This highlights the widespread consensus on the ≥39.5°C threshold for identifying fever associated with metritis. Additionally, Garzon et al. (2022) reported variations in the methods used for evaluating vaginal discharge, with rectal palpation being the most frequently used approach (37.3%), followed by intravaginal exploration with a gloved hand (18.4%), Metricheck (9.8%), and speculum examination (5.7%).

In 28.7% of the studies, diagnostic tools used for evaluating vaginal discharge were not specified.

The RT of cows diagnosed with infectious post-partum diseases, including metritis, tends to fluctuate significantly during the first ten days in milk (DIM). Burfeind et al. (2010) confirmed that repeatable and accurate RT measurements are crucial for diagnosing metritis, and noted that thermometer type and depth of insertion into the rectum can influence individual RT measurements. In their study, Wenz et al. (2011) suggested an optimal RT measurement depth of 11 cm. The study also observed that primiparous cows were more likely to develop metritis or co-infections with other infectious diseases during the first 10 DIM compared to multiparous cows ($P = 0.004$; $P = 0.021$). Furthermore, Wenz et al. (2011) reported that cows with metritis had a peak RT of 39.6 ± 0.1°C on the day of diagnosis, which was 0.8°C higher than that of healthy parity-matched cows ($P = 0.001$). This elevated RT persisted for at least four days before and after the diagnosis of metritis, providing valuable insight into the temporal dynamics of RT changes in infected cows. The fever associated with metritis is primarily driven by the inflammatory response triggered by the uterine microbiome. Leukocyte activation and the release of endogenous cytokines and chemokines induce prostaglandin E synthesis, which in turn leads to fever by affecting the central nervous system (Netea et al., 2000). Both Gram-negative and Gram-positive bacteria can contribute to fever, with lipopolysaccharides (LPS) from Gram-negative bacteria being the most potent fever-inducing agents (Tavares et al., 2005). In metritis cases characterized by an overrepresentation of *Bacteroidetes* and *Fusobacteria*, Gram-negative bacteria are often implicated in the fever response (Jeon et al., 2015).

Despite its utility, RT alone is not always a reliable diagnostic tool for metritis due to its overlap with other infectious diseases like mastitis. However, it remains an important parameter when used alongside other diagnostic criteria (Sheldon et al., 2006). Studies have proposed RT thresholds ranging from 39.2°C to 39.7°C for diagnosing metritis. For example, Giuliodori et al. (2013) found a receiver operating characteristic (ROC) area of 0.604 for RT at the time of metritis diagnosis, with a threshold of 39.2°C showing reasonable sensitivity and specificity. Thus, RT changes over time can provide valuable insights into disease severity and the effectiveness of treatment (Machado et al., 2020). In addition to RT, factors such as plasma haptoglobin levels, dystocia history, and milk yield can also influence temperature readings and help refine the diagnosis (Machado et al., 2020). For example, cows with a history of dystocia may exhibit higher RT due to uterine trauma, which could contribute to a more severe inflammatory response. Moreover, cows with higher milk yields might show distinct RT patterns due to increased metabolic demands post-calving, which could potentially exacerbate the risk of metritis.

Metritis is not unique to dairy cattle. In other livestock species, such as goats, metritis is often associated with retained placenta or uterine trauma and can result in infertility if not managed appropriately. In dogs and cats, metritis commonly follows prolonged labor and retained fetal tissues, with symptoms including fever, lethargy, and vulvar discharge. Mares are particularly susceptible to septic metritis, a life-threatening condition that requires prompt intervention, especially in larger draft breeds. Similar to dairy cows, these species benefit from early detection and temperature monitoring as part of a comprehensive diagnostic approach. A promising new method for monitoring RT in dairy cows is infrared thermography (IRT), which offers a non-invasive and remote way to detect elevated RT. IRT has shown potential for early detection of metritis, enabling proactive management and improving herd health (Skliarov et al., 2023). By using RT alongside other clinical parameters, such as body condition score (BCS), leukocyte counts, and metabolic markers, dairy farmers can better manage metritis and mitigate its impact on cow health and productivity.

Diagnostic methods for metritis

Metritis remains one of the most inconsistently diagnosed and documented diseases in commercial dairy farming (Sannmann et al., 2012). Diagnostic challenges include variability in definitions, inconsistent approaches by herd personnel, and differences in the timing of disease evaluation (Espadamala et al., 2016). These inconsistencies can lead to underdiagnosis or misclassification, which introduces bias and underestimates the association between disease and performance outcomes (Johnson et al., 2014). Accurate and consistent diagnostic methods are critical for advancing our understanding of metritis' impact on productivity and improving herd health management practices.

Clinical Examination and Vaginal Discharge Evaluation: The diagnosis of metritis typically relies on clinical examination, focusing on uterine enlargement and the characteristics of vaginal discharge. Common clinical signs include a fetid, watery discharge, systemic symptoms such as fever, depression, anorexia, and dehydration, and an enlarged uterus

(Benzaquen et al., 2007; Risco and Melendez Retamal, 2011). Espadamala et al. (2018) reported significant variability in diagnostic practices across dairy farms, with discrepancies in how systemic illness and discharge characteristics were evaluated. This lack of standardization underscores the need for universally accepted diagnostic protocols to reduce the risk of underdiagnosis and ensure accurate identification.

Vaginal discharge scoring systems have been used to categorize discharge characteristics on scales such as the modified Vaginal Discharge (VD) scoring system (Oliveira et al., 2020), which ranges from 1 (normal) to 5 (fetid discharge indicative of metritis). Metricheck, a widely used tool, facilitates easy collection of vaginal discharge samples and has shown higher sensitivity but lower specificity compared to other methods (McDougall et al., 2011). Garzon et al. (2022), in their meta-analysis, highlighted the variability in descriptors for vaginal discharge color, odor, and viscosity across studies, further complicating consensus in metritis diagnosis. Terms like "fetid," "putrid," and "purulent" were commonly used but lacked consistent definitions, emphasizing the need for standardized terminology.

Rectal temperature (RT) is a key diagnostic parameter for detecting puerperal metritis (PM). Studies have used different RT thresholds for diagnosis, with ≥39.5°C being the most commonly cited cut-off (Garzon et al., 2022; Benzaquen et al., 2007). Daily RT monitoring is critical, as fever typically precedes clinical signs. For example, cows diagnosed with PM exhibit linear increases in RT starting 48 hours before diagnosis, peaking at ≥39.6°C (Benzaquen et al., 2007; Wittrock et al., 2011). Despite its utility, RT alone may not be reliable due to overlapping symptoms with other diseases such as mastitis. Kristula et al. (2001) noted that 48% of cows with normal calving showed transient RT spikes (>39.1°C), compared to higher rates in cows with retained placenta, mastitis, PM, and dystocia. This suggests that a comprehensive health monitoring strategy combining RT measurements with other diagnostic tools is essential.

Systemic and Automated Monitoring Tools: Emerging technologies such as automated activity and rumination monitors show promise in metritis detection. Stangaferro et al. (2016) demonstrated that metritic cows exhibit altered rumination and activity patterns during the first week postpartum. These changes can be captured using automated health monitoring systems, which provide real-time data on cow behaviour and health index scores. While promising, further research is needed to validate their efficacy in commercial farm settings. Blood biomarkers like haptoglobin (Hp), an acute-phase protein, also show potential as diagnostic tools. Elevated Hp levels at 3 and 7 days in milk (DIM) have been associated with metritis severity, poor reproductive outcomes, and reduced milk yield (Pohl et al., 2015; Barragan et al., 2018). However, Hp concentrations are also elevated in other conditions, such as dystocia and retained placenta, limiting their specificity for metritis diagnosis (Huzzey et al., 2009).

Advances in Molecular and Genetic Diagnostics: Molecular diagnostics, such as multiplex PCR, offer high sensitivity and specificity for detecting uterine pathogens, including *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus cereus* (Wei et al., 2024). This method enables simultaneous detection of multiple pathogens, reducing diagnostic time and cost compared to conventional PCR. Additionally, Sanchez et al. (2024) identified genetic factors associated with metritis susceptibility, including genes involved in cholesterol metabolism and autophagic processes, offering potential targets for genetic selection and disease management. In addition, metabolomics offers valuable insights into the uterine environment at the time of metritis diagnosis, identifying key metabolites that are strongly correlated with the overgrowth of opportunistic pathogenic bacteria, tissue damage, and immune dysregulation, thereby providing potential targets for future interventions to mitigate metritis in dairy cows (Casaro et al., 2024).

Despite advancements, diagnostic inconsistencies persist. Garzon et al. (2022) emphasized the lack of consensus in PM criteria across studies, with 40.2% of reviewed articles providing no reference for PM definitions. Standardizing diagnostic protocols, including unified scoring systems for vaginal discharge and thresholds for RT, is essential to improve the accuracy and reliability of metritis diagnosis.

Future Prospects

The future of metritis diagnosis and management in dairy herds lies in the integration of advanced technologies, precision farming practices, and holistic approaches to herd health. Emerging diagnostic tools, such as automated activity and rumination monitors, infrared thermography, and non-invasive biomarker assays, hold promise for early and accurate detection of metritis, enabling timely interventions. Molecular techniques like multiplex PCR and genetic profiling offer opportunities to identify pathogen-specific and host susceptibility factors, paving the way for targeted therapies and genetic selection for disease resistance. Additionally, developing probiotics, vaccines, and non-antibiotic therapeutics can address antimicrobial resistance concerns while improving reproductive outcomes. Standardizing diagnostic criteria and protocols globally is essential to bridge the gaps in clinical practice and research, ensuring consistency in disease management across dairy operations. Future research should focus on validating these innovative tools and approaches in real-world settings, alongside exploring the economic feasibility of implementing such technologies to improve productivity, animal welfare, and sustainability in the dairy industry.

Conclusion

Metritis remains a multifaceted challenge in dairy herd management, significantly impacting milk production, reproductive efficiency, and the economic sustainability of dairy operations. Despite advancements in diagnostic methodologies and management strategies, the complexity of metritis requires ongoing innovation and research to address persistent gaps in understanding and control. Future efforts must prioritize the development and adoption of standardized diagnostic criteria, particularly integrating non-invasive technologies. Infrared thermography and automated health monitoring systems offer promising avenues for routine, cow-side detection of rectal temperature changes and other early indicators of metritis, enhancing the accuracy and timeliness of diagnosis while minimizing stress on animals. However, unravelling the molecular and genetic underpinnings of metritis remains a critical frontier. Identifying key pathways, such as those related to cholesterol metabolism and the PI3k-Akt pathway, will provide novel therapeutic targets and support the development of precision interventions. These advancements, combined with the refinement of management practices and exploration of innovative therapeutics like probiotics and vaccines, hold the potential to transform metritis control, improving herd health, productivity, and overall dairy industry sustainability. Through interdisciplinary research and the integration of cutting-edge technologies, the dairy sector can overcome the challenges posed by metritis, ensuring a future of enhanced animal welfare and economic viability.

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Conflict of Interest

The authors have no conflict of interest.

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