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Endometritis in bovine: Prevalence, etiopathogenesis, diagnosis and therapeutic approaches

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Abstract
This scientific study provides a review of the literature on the various endometritis diagnostic and therapy approaches in bovines.

Keywords: Cytology, endometritis, subclinical endometritis

1. Introduction
The most prevalent cause of infertility in bovine is uterine infections such as endometritis, subclinical endometritis which results in delayed uterine involution, a longer period before the first oestrus, a higher number of services per conception, and longer calving to conception interval. Endometritis is a superficial inflammation of the endometrium characterized by inflammatory cell infiltration with or without epithelial disruption and extending no deeper than the stratum spongiosum with vascular congestion and stromal edema, as well as varying degrees of lymphocyte and plasma cell grouping in the superficial layers (Meira *et al.,* 2012; Bogado *et al.,* 2016) [13, 2]. Clinical endometritis (CE) is characterized as endometrial inflammation accompanied by purulent (>50% pus) or mucopurulent (50% pus and 50% mucus) vaginal discharge detected more than 21 days after parturition (Sheldon *et al.,* 2006) [21, 22]. There are no systemic symptoms associated with it (LeBlanc *et al.,* 2002) [11]. Similarly, Subclinical endometritis (SE) is defined as the inflammation of the endometrium without clinical signs, that commonly develops around 3 to 8 weeks after parturition. It is characterized by the increased infiltration of polymorphonuclear cells (PMN) in the endometrium (predominantly neutrophils) which impairs the subsequent reproductive performance (Sheldon *et al.,* 2009) [20]. On dairy farms, uterine disorders result in significant financial losses, owing to the costs of treating the afflicted animals.

2. Prevalence of Endometritis
Because microbial infection of the vagina and other external reproductive organs may occur while wallowing, buffalo had a greater frequency of uterine infection than cows (Azawi, 2010) [1]. The frequency of buffaloes with endometritis varied from 20.0 to 47.9%. (Ghanem *et al.,* 2002) [7]. Clinical endometritis is the most frequent periparturient condition, accounting for around 15% of all periparturient diseases. In dairy cows, a wide range of prevalence of SE following parturition has been documented, ranging from 5% to 68 percent of the herd. (Cheong *et al.,* 2011; Pascottini *et al.,* 2017) [5, 15]. In beef cows, SE was reported to range from 2 to 31% (Ricci *et al.,* 2015; Pfeifer *et al.,* 2018) [17].

3. Etiopathogenesis
The most common bacteria obtained from the bovine uterine lumen are *Trueperella pyogenes, Escherichia coli, Fusobacterium necrophorum, and Prevotella melaninogenica.* After 24-48 hr of parturition, vaginal discharge of animal was found to have significant levels of lipopolysaccharides (LPS), which are membrane components of Gram-negative bacteria causing uterine inflammation. As LPS concentrations in the peripheral blood rise, the incidence of systemic inflammation increases. Increased LPS level in the uterine lumen decreased the pre-ovulatory LH surge, resulting in unsuccessful ovulation and ovarian follicular cyst development. The development of endometritis induces the production and release of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6, and IL-8) which promote increased phagocytosis and bacterial elimination (Brodzki *et al.,* 2015; Shao *et al.,* 2017) [3, 19].

In case of endometritis, neutrophils dominate at the endometrial epithelium and in the uterine lumen (Bogado *et al.,* 2016) [2]. The marked neutrophil cellular reaction infiltrating into and around the endometrial glands due to the increased concentrations of pro-inflammatory cytokines (e.g., IL-1b, IL-6 and TNF-α and IL 8) associated with the development of clinical and/or subclinical characteristics of endometritis.

4. Diagnosis

For the diagnosis of endometritis, cytology is the most trustworthy approach, which is more accurate than ultrasonography and vaginoscopy. In cytobrush cytology, the ratio of PMN leucocytes to epithelial cells in healthy animals was1:180, and in uterine fluid cytology, it was 1:93. The ratio of PMN leucocytes to epithelial cells in SE-affected animals was 1:14 in cytobrush cytology and 1:6.4 in uterine fluid cytology (Gahlot *et al.,* 2017) [6]. The threshold value for polymorphonuclear cells (PMN) as diagnostic for subclinical endometritis depends on the postpartum time and varies from 5 to 18% (Sheldon *et al.,* 2009) [20]. The effectiveness of the white side test for detecting subclinical endometritis was determined by boiling point, and the intensity of colour changes after cooling was evaluated as normal (no color), mild infection or subclinical endometritis (light yellow color), moderate or clinical endometritis (yellow color) and serious infection or chronic endometritis (dark yellow color) (Kumar *et al.,* 2015) [10]. The quantity of leukocytes in normal discharge is insufficient to induce any colour change, however in subclinical cases of endometritis, the number of leukocytes in the discharge is elevated, resulting in a colour response (Pateria and Rawal, 1990) [16]. According to Gupta *et al*. (2011) [8], the colour response is caused by ribonucleic acid contained inside the nucleus of leukocytes reacting with 5% NaOH. A prior investigation in cattle with endometritis found an increase in pH in vaginal secretions greater than 7.8 (Singla *et al.,* 2004) [23]. This might be due to bacterial contamination in the uterine fluids, causing an elevation in pH that is unfavorable for spermatozoa and embryo survival in the uterus (Sheldon *et al.,* 2006) [21, 22]. Furthermore, the levels of the pro-inflammatory cytokines IL-8 and TNF- α were found to be many times higher in cows with subclinical endometritis, indicating that IL-8 and TNF- α both valid diagnostic indicators for subclinical endometritis (Loyi *et al.,* 2013; Kalyaan *et al.,* 2016) [12, 9]. Ultrasonographic examination can be a rapid and effective way to detect fluid in the uterus as a sign of an inflammatory condition. Following the detection of less than 2 mm of fluid in the uterine lumen using ultrasonographic vision, cytobrush samples are collected and microscopic analyses are performed to estimate the proportion of polymorphonuclear cells.

5. Therapeutic Approaches to Treat Endometritis

Intrauterine infusion of cephapirin or systemic administration of PGF2α has improved pregnancy rates of cows with clinical endometritis (Brodzki *et al.,* 2018) [4]. Intrauterine infusion of polyvinylpyrrolidone-iodine (PVP-I) improves fertility and promotes endometrial epithelial cell regeneration, suggesting that PVP-I could be a good alternative to antibiotics (Osawa, 2021) [14]. Intrauterine infusion of immunomodulators, such as E. coli lipopolysaccharides (endotoxin), infusion with serum, plasma or hyperimmune serum or leukotriene B4 has been widely reported. Antioxidants, such as vitamins C and E, are modulators of oxidative stress and reduce endometrial damage at both the biochemical and histological levels. In animals, the uterus appears to have a significant ability for spontaneous regeneration and hence does not require any therapy, especially because certain therapies are ineffective and may even do more harm than benefit.

6. Conclusion

Early diagnosis of post-partum infection is essential to minimize the economic loss and for improving the reproductive performance and productivity of herds.

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