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Retained placenta in bovines: Current understanding and future directions

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Abstract
Retained placenta (RP) is a condition in which foetal membranes are seen at vulva or are present in uterus even after more than 24 hours post-partum. The cases present with symptoms like pyrexia, inappetence, sudden weight loss and udder inflammation with reduced milk yield few days post-partum. Treatment included uterine lavage, antibiotic therapy, and supportive care. It is a significant reproductive disorder in dairy cattle, associated with substantial economic losses. This review study discusses current understanding of RP aetiology, diagnosis, treatment, and its complications including metritis, mastitis, and tetanus. This article highlights the complexity of RP and the importance of prompt, comprehensive treatment strategies. It also discusses recent advances in understanding RP pathophysiology, and emphasizes the need for improved prevention and management protocols.

Keywords: Retained placenta, bovines, metritis, management

Introduction
Retained placenta (RP) or retained foetal membranes (RFM), defined as the failure to expel foetal membranes within 24 hours post-partum, is a common periparturient disorder in dairy cattle (Beagley *et al*., 2010) [1]. RFMs usually affect 5–10% of normal calvings, making them a common anomaly in dairy cows. It is considered as primary contributor to reproductive problems in the puerperal and post-puerperal stages, which result in substantial financial losses at the level of the herd (Shenavai *et al*., 2010) [2]. Durrani *et al*. (2009) [3] reported the incidence of retained placenta in buffaloes to be 22.8 percent and in dairy cows' 19.44 percent. A number of issues arise because of this, including the possibility of an open cow the following year, inflammation, fever, weight loss, decreased milk yield, and longer calving intervals due to microorganisms growing inside the uterus or animal may die if the severity of infection is very high (Le Blanc, 2008) [4]. The condition predisposes animals to various postpartum complications including metritis, endometritis, and mastitis, leading to reduced fertility and milk production (Li *et al*., 2022) [5]. The economic impact of RP is substantial, with estimates ranging from $600 million annually in the US dairy industry (Bansal and Gupta, 2009) to significant per-cow costs for treatment and lost production. Given these impacts, effective management strategies are crucial for maintaining herd health and productivity.
This study aims to contribute to the current body of knowledge by presenting a detailed account of RP diagnosis and treatment in a clinical setting, while reviewing recent advances in understanding RP pathophysiology and management.

Aetiology
The aetiology of RP is multifactorial, involving complex interactions between physiological, environmental, and management factors. Nutritional deficiencies include calcium, selenium, carotene and vitamin E deficiency (Patel and Parmar, 2016) [6]. Pontes *et al*. (2015) [7] demonstrated the effectiveness of pre-partum supplementation of injectable α-tocopherol in decreasing incidence of retained placenta and improving reproductive efficiency. Hormonal imbalances also play a key role in postpartum retention of placenta. Prostaglandin F2α levels were found to be 30% lower in affected cows. Oxytocin receptor expression was reduced by 40% in placental tissues of affected animals (Gupta *et al*., 2009) [8].

Infectious diseases like brucellosis, leptospirosis, bovine viral diarrhoea, listeriosis, trichomoniasis, vibriosis lead to retention of foetal membranes (Laven and Peters, 1996) [9]. Environmental factors have also been found associated with RP. Maximum incidence of retained placenta was found in summer and spring seasons (27.72 and 29.20% respectively) while minimum was observed in autumn season (20.94%) (Sharma *et al*., 2017) [10]. Poor sanitation: 2.5 times higher risk in farms with suboptimal hygiene (Patel and Parmar, 2016) [6]. Genetic predisposition: Jersey crossbreeds showed 1.5 times higher risk compared to local breeds. Obstetrical issues: incidence of retained placenta is more in pluriparous animals in comparison to primiparous animals. Furthermore, dystocia, twin births and premature births increase the chances of retained placenta. The incidence rates of twin calving, stillbirths, and abortions increased the risk of RP to 25.9, 16.4, and 43.8%, respectively. Retained placenta can be caused by management factors such as stress, genetics, inbreeding, and obesity (Joosten *et al*., 1991) [11]. Recent research has elucidated the critical role of immune function in the pathogenesis of RP. Studies conducted in dairy cattle by Kimura *et al*. (2002) [12] demonstrated that, neutrophil function is a decisive factor in the development of RP. Additionally, in cows developing RP, decreased IL-8 production could be a factor impacting neutrophil function. Pomeroy *et al*. (2017) [13] have demonstrated associations between pre-partum immune cell populations, particularly neutrophils and monocyte subsets, and the subsequent development of RP and related infections. These findings suggest potential avenues for early prediction and prevention of RP.

Case Presentation

Cases present few days post-partum with complaint of inappetence, pyrexia, and recumbency, calving with/without assistance but foetal membranes retained even after 24 hours of calving. Clinical examination reflects increased body temperature, congested mucus membranes due to septicaemia, dehydration with depressed demeanour, reduced ruminal movements, foetal membranes hanging from vulva, straining, foetid smell from the placenta etc. Udder examination may reveal mastitic changes or if, the infection is severe, there can be severe inflammation with gangrenous changes in the quarters. Per-rectal palpation elicits purulent, blood-tinged discharge from the vagina upon uterine manipulation.

Complications of RP

Metritis and endometritis, decreased milk production, delayed uterine involution, reduced fertility (increased calving interval, reduced conception rate, increased risk of pyometra, endometritis), increased risk of metabolic disorders (higher risk of ketosis and milk fever) (Haxhiaj *et al*., 2022) [14], tetanus (due to contamination with soil), economic losses (the direct costs-treatment, labour, reduction of milk production and milk discharge during the treatment period and indirect costs-increase in the service period, increase in the number of semen doses and increase of the risk of disposal). For primiparous and multiparous cows, the average monetary losses linked with RP were estimated to be US$ 350.4 and US$ 481.2 per incidence, respectively. Decline in milk production (38.5% of total loss) and reduced fertility (28.5% of total loss) contributed most to the financial losses incurred by RP in primiparous and multiparous cows, respectively (Mahnani *et al*., 2021) [15].

Treatment

- Manual removal of placenta though debatable is practised but there is risk of uterine trauma if performed too early or aggressively. Treatment of retained foetal membranes without intrauterine manipulation and parenteral treatment can be as effective as conventional treatment (Skuja, S., & Antane, V., 2017) [16].
- Uterine lavage-0.9% NaCl solution, followed by systemic and intrauterine administration of antibiotics. Intrauterine infusion of oxytetracycline effectively improves reproductive performance in dairy buffalo-cows with retained foetal membranes (Gohar *et al*., 2018) [17]. Intrauterine tetracycline boluses and ozone foam both effectively treat retained foetal membranes in cattle, with ozone foam showing greater effectiveness in reducing fever and reducing escape therapies (Imhof *et al*., 2019) [18].
- Sheldon *et al*. (2014) [19] compared minimum inhibitory concentrations of different antibiotics against bacteria causing uterine infections in cattle and found cefquinome and enrofloxacin had lowest MIC90 and MIC50 values for *E. coli*. Oxytetracycline had highest MIC values while cephalosporins have lowest MIC values for *Arcanobacterium pyogenes* and anaerobic bacteria. Ceftiofur hydrochloride administered at 2.2 mg of CE/kg, SC or IM, once daily for 5 days effectively treats acute postpartum metritis in dairy cows (Chenault *et al*., 2004) [20].
- Pyrogenium 200C, a homeopathic remedy, is an effective, economical, and non-technical treatment for retained foetal membranes in ruminants (Dabbir *et al*., 2021) [21].
- Hormonal treatments- Prostaglandins and oxytocin are the most often used hormonal agents in the treatment of RFM. These hormones are involved in uterine contraction and can also be useful in treating retention of the foetal membranes (Patel and Parmar, 2016). PGF2 treatment at 22.5mg/i.m. effectively expelled retained foetal membranes in dairy cows, with 100% efficacy, followed by 100i.u. of oxytocin and 72% for other treatments (Asker& Dakheel, 2015) [22] . Oxytocin injections in cows with retained foetal membranes resulted in 66.67 (4/6) percent placental expulsion within 12 hours, improving postpartum reproductive efficiency (Shah *et al*., 2019) [23].
- Supportive care- Fluid therapy, NSAIDs, Calcium borogluconate, selenium and vitamin E injection, vitamin C injection (Bourne *et al.* 2007) [24].
- Recent treatment approaches- An innovative method for treating RFM involves injecting bacterial collagenase obtained from Clostridium histolyticum into the umbilical arteries of retained foetal membranes. Its superiority over standard treatments may stem from the fact that it addresses the issue of lack of cotyledon proteolysis particularly. Ozone foam can also be injected intrauterine for desired outcome but at the same time they are quiet costly too (Ganaie *et al*., 2018) [25].
- Traditional remedies including fenugreek seed paste, neem leaf decoction, feeding radish tubers along with lady's finger are few practices that are being carried out to treat cases of retained placenta.

Discussion

This review study exemplifies the complex nature of RP and its associated complications. The observed clinical signs and progression align with previous reports in the literature (Beagley *et al*., 2010[1]; Li *et al*., 2022[5]). The development of metritis and mastitis following RP is consistent with the increased susceptibility to infectious diseases in the postpartum period, as

described by Pomeroy *et al*. (2017) [13].

Managing RP effectively requires a comprehensive strategy. This includes uterine cleansing, antibiotic administration, hormone therapy, and general supportive care. The treatment approach employed should be focused on addressing both the primary condition (RP) and its sequelae. Uterine lavage aims to reduce bacterial load and inflammatory mediators, while systemic antibiotic therapy targets potential systemic infection. The use of anti-inflammatory drugs is supported by evidence of their efficacy in managing pain and inflammation associated with RP and its complications (Risco and Hernandez, 2003) [26]. Emerging treatments, such as using specific bacterial enzymes, show potential for improving outcome.

It is noteworthy that despite the pre-partal administration of oxytocin, RP can still occur. This observation is consistent with findings by Youngquist and Threlfall (2007) [27] who reported no significant benefit of routine oxytocin administration for RP prevention. This underscores the complex aetiology of RP and the limitations of single-intervention approaches to prevention.

Recent research has highlighted the role of immune dysfunction in RP pathogenesis. Kimura *et al*. (2002) [12] demonstrated impaired neutrophil function in cows that developed RP, while Pomeroy *et al*. (2017) [13] found associations between pre-partum monocyte subset populations and postpartum disease occurrence. These findings suggest potential for developing predictive biomarkers and targeted interventions for RP.

The economic impact of RP, as outlined by Bansal and Gupta (2009) [8], emphasizes the need for effective prevention and treatment strategies. Prevention approaches need to receive more attention than curative ones since the non-infectious causes of placental retention are complex and challenging to identify. In order to minimize the chance of acquiring RFM, the genetic component should be considered while selecting animals for future breeding. More focus needs to be paid on the complex interactions between immune function, metabolic status, and environmental factors in RP development. This could lead to more targeted prevention strategies and improved treatment protocols.

Conclusion

The complexity of RP aetiology, involving immune dysfunction and various risk factors, necessitates a multifaceted approach to prevention, management and resulting financial strain on dairy operations. The management of risk factors needs to be the main priority to lessen the risk of retained placenta. Livestock owners must thus be made aware of the risk factors for RP as well as available preventative and control methods. The occurrence of retained placenta can also be decreased by keeping animals' condition and nutrition under control throughout the dry period and preventing them from getting overweight. Future research directions should include further investigation of immunological biomarkers for early prediction of RP risk and development of targeted interventions to modulate immune function (neutrophil activity and pre-birth immune cell composition) in the periparturient period. Hence, improved understanding of RP pathophysiology will be crucial for developing more effective prevention and treatment strategies in dairy herds.

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