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Review Article

Clinical and Sub-Clinical Endometritis and its Impact in Reproductive Performance of Cattle: A Review

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Abstract

Reproductive health problems are one of the most important problems that affect the reproduction and productivity of dairy cows. Among the major reproductive problems, abortion, dystocia, retained fetal membrane (RFM), pyometra, metritis, endometritis, anestrus, repeat breeding have a direct impact on reproductive performance and results in considerable economic loss to the dairy industry. Endometritis in cattle is defined as inflammation of the uterine endometrium more than 21 days post-partum and not associated with systemic signs of illness. There are different risk factors like intrinsic which includes calving season, and nutrition. There are also extrinsic factors like dystocia, retained placenta, negative energy balance, and milk yield. Economic losses due to endometritis include reduced reproductive rate, prolonged inter-conception and calving interval, negative effect on fertility, increased cost of medication, drop in milk production, reduced calf crop, and early depreciation of potentially useful cows resulting in reduces farm profitability on dairy farms. Consequently, to avoid its adverse effects every dairy farm implement endometritis monitoring program and employ management practices that limit the occurrence. Besides determining all the factors that enhance its risk of occurrence is more important than treating the diseases.

Introduction

Cattle production has been considered as the main component of agricultural development in most parts of Sub-Saharan Africa. The overall cost of keeping cattle in terms of costs associated with health care, nutrition, and management, however, has not matched their contribution to the livelihood and the economics of the people in the region. As in many countries, livestock, particularly cattle play multiple roles in Ethiopia being a source of milk, meat, hides [1]. The productivity of indigenous cattle breeds is low due to many constraints including diseases and parasites, nutrition, poor management systems, poor reproductive performance, and large socioeconomic factors by decreasing reproductive efficiency, shortening the expected length of productive life, and lowering milk production. Reproductive problems are the most common which occur in lactating dairy cows and can dramatically affect the reproductive potential of the dairy herd. Poor reproductive performance is a major cause of involuntary culling and therefore reduces the opportunity for voluntary culling and has a negative influence on the subsequent productivity of a dairy herd [2]. Reproductive health problems result in considerable economic losses to the dairy industry and are the main causes of poor productive performance of smallholder dairy farms [3]. Among the major problems that have a direct impact on the reproductive performance of dairy cows, RFM and the subsequent endometritis and pyometra have been reported to be the most common clinical and economic problems [4,5]. These have been implicated to cause a considerable economic loss to the dairy industry due to slower uterine involution, reduced reproductive rate, prolonged inter-conception period and calving interval, high cost of medication, drop in milk production, reduced calf crop and early depreciation of potentially useful cows. It has also been shown that low reproductive efficiency hinders genetic improvement in zebu (*Bos indicus*) cattle and causes direct economic losses [2,6,7].

In Ethiopia, dairy cattle are kept under different production systems and these greatly affect the occurrence of reproductive health problems. Therefore, reproductive disorders are one of the most important problems that affect the reproduction and productivity of dairy cows [8]. In the absence of regular breeding and calving at the appropriate time, the enterprise will not be profitable. The main goal of dairy reproduction is to obtain a healthy calf from each dairy cow every year. through improving the reproductive efficiency of the cow. Successful reproduction encompasses the ability to mate, the capacity to conceive, nourish the embryo, and deliver the viable young ones at the end of a normal gestation period [9]. However, endometritis is one of the reproductive problems that may be defined as inflammation of the uterine endometrium that persists over 21 days post-partum and not associated with systemic signs of illness. Moreover, It may have negatively affected the performance of the dairy industry; economic losses are related to delay in the resumption of ovarian activity, increased number of services per conception, decreased milk yield, and costs of treatment of the disease [10-12]. Endometritis is considered to be a multifactorial disease with many factors having a direct or indirect, determining, or predisposing influence [13]. Thus, the aim of this article is organized to highlight the impact of endometritis on the reproductive performance of cattle.

Causes of Endometritis

The possible causes involved in the development of endometritis are retentions of fetal membrane, injury to the reproductive tract due to the difficult in calving or excessive force used to assist at calving or injury at the time of breeding or uterine treatment contamination of the reproductive tract at calving, over conditioning which may predispose cows' to many health problems at the time of parturition [14]. The causes of endometritis are multifactorial and extensive. During the last 2 weeks of pregnancy and the first 3 weeks postpartum, the immune function of the dairy cow is suppressed. Immediately post-calving there is bacterial contamination of the uterus which normally persists for 2 to 3 weeks. This is an inevitable and natural occurrence as the cervix dilates and the vestibule and vagina relax, resulting in the natural barriers and bacterial defenses being temporarily impaired [15]. Different factors contribute predisposes the uterus for various infections and this compromises the ability of the dairy cow to effectively clean the uterine environment. As a result of these factors, it is a common finding that cows begin to mobilize body reserves to support their genetic predilection for milk production. This results in elevated non-esterified fatty acids (NEFA). Increased circulating NEFA contributes to the risk of fatty liver and ketosis, this is in turn associated with an impaired function, in particular neutrophils [16,17].

Immediately post-calving, neutrophils play an important role in the detachment of the placenta, clearance of bacteria, and lochia. There is evidence however that an excessive inflammatory response in the first and second week postpartum is associated with a higher incidence of endometritis. The most common bacteria that cause postpartum endometritis in cattle are *Escherichia coli*, *Trueperella pyogenes*, and anaerobic bacteria such as Prevotella species and Fusobacterium necrophorum. The virus most consistently associated with postpartum uterine disease in cattle is *Bovine Herpesvirus 4* (BoHV-4) [15,18,19]. Besides, several specific diseases are associated with endometritis. These include brucellosis, leptospirosis, campylobacteriosis, and trichomoniasis in cattle, a bacterial infection of the uterus affects almost all animals after parturition and does not mean they will get the disease. Beef cattle rarely have disease unless they have a predisposing factor such as retained placenta or difficult parturition. However, the uterine disease is common in dairy cattle-particularly high-milk-yield cows such as *Holstein-Friesian*cows [20,21].

Impact of Endometritis on Fertility and Economic Losses

It has been shown that there is a strong association between endometritis and reduction in reproductive performance [18]. Histologically the endometrial endothelium is disrupted with infiltration of leukocytes and vascular congestion and edema [15]. According to Gilbert [14], low-grade uterine infection in dairy cattle is the most important cause of depressed conception rate. The diseases occurring at parturition and the length of the postpartum interval before breeding is of greater importance in determining fertility. Cows having postpartum diseases had longer calving intervals and required more services per conception. Fertility is reduced in cows with endometritis. The percentage of first service conception is lower than normal cows. While [21] examined cows between 28 to 35 days postpartum for uterine infections using uterine cultures and endometrial biopsy and found that animals diagnosed to be suffering from endometritis required a significantly higher number of services per conception [12]. The calving to conception interval are longer in cows with endometritis and failure to conceive. Animals that suffered from puerperal endometritis, the conception rate is lower and the interval from calving to conception 7 to 12 days longer as compared to normal cows. It is also reported that the interval from calving to first estrus, calving to conception, and the number of services per conception increased in animals that suffered from postpartum endometritis as compared to normal cows [12,22].

According to a study, the impact of endometritis on reproductive performance as a decrease in 20 percent for conception at fist service, an increase in additional 19 days open, and a 6 percent decrease in overall pregnancy rate (Table 1). Cows with clinical endometritis have 1.6 times as likely to be removed from herd as cows without clinical endometritis. Cows with clinical endometritis had 1.7 times more chance than normal cows to be culled for reproductive failure [12,18]. Besides, based on a study on the effect of endometritis on reproductive performance in dairy cows, cows with endometritis were less likely to become pregnant compared to those with no endometritis [23].

Risk Factors for Endometritis

Importantly, the characteristics of the dairy herd can directly or indirectly affect the prevalence of endometritis. The farm is also considered as a risk factor for endometritis [21,24].

Table 1: The prevalence of endometritis in a different part of Ethiopia.

Study Area	Prevalence (%)	Source
Asella	2.6	(Yohannes and Alemu [83])
HorroGuduru, Wollega Zone	7	(Wagari and Shiferaw [82])
Kombolcha	18.7	(Ebrahim [78])
Alage dairy farm	28.5	(Amene [74])
	6.36	(Gebremeskel et al. [79])
Southern Ethiopia	4.93	(Berhanu et al. [76])
Central Ethiopia	8.7	(Hadush et al. [80])
In and around Jimma town	4.81	(Argaw et al. [75])
In and around Fitche town	5.4	(Dufera [77])

Extrinsic factors

Calving season: According to different research findings, calving occurring between November and April that predispose and dramatically increased the incidence of infection of the uterus during the first month of postpartum. This relationship may be explained by the fact that during these seasons, the general health of cows decreases, making them more vulnerable to uterine infections [25,26]. According to a study on 57,301 dairy cows, there is a direct association between season (winter) of the calving and clinical metritis [27]. Metritis is considered to be one of the most important risk factors for endometritis [28].

Nutrition: The quantity and quality of proteins included in the food ration play a key role in the efficiency of the immune system. Cellular immunity is also affected by protein quantity in food rations; protein deficiency dramatically reduces cellular phagocytosis [29]. Noteworthy also is that excess protein intake induces high serum ammonia, which reduces lymphocyte production and favors the development of endometritis. Many vitamins are involved in the functioning of the immune system, including vitamins B and C, which have a role in antibody synthesis, and vitamin C, which ensures the integrity of immune cell membranes and protects them from free radicals [30,31].

A is important for epithelial tissue development and cell differentiation, which are very important in the early postpartum stage. Vitamin A also has immunological functions by increasing the early inflammatory phase through enhancing the number of macrophages at the site of a wound, which improves localization and stimulation of the immune response in the case of uterine infection. A variety of minerals are involved in the uterine defense mechanisms. Calcium acts as complement-activator and calcium deficiency delays uterine involution and prolongs uterine infection. Calcium deficiency may be induced by excessive intake of phosphorus [32,33]. Magnesium is involved in opsonization mechanisms. Selenium is involved in neutrophil function and its deficiency disrupts the reproductive performance of the cow and increases the risk of endometritis. Copper, zinc, and iron intervene in lysosome production and their deficiency dramatically reduces phagocytosis and favors the growth of bacteria and development of endometritis [33,34].

Intrinsic factors

Body condition Score: There are practically very few reports on the relationship between body condition score at the time of calving and incidence of postpartum endometritis in dairy cows. In the study on the diagnosis of endometritis based on cytology, all cows appeared healthy and were of body condition score greater than 2.5 and that none had conspicuous genital tract exudates [20,35]. On the other hand, there is no significant effect of body condition score on the incidence of postpartum endometritis [36].

Age and parity of the cow: Younger cows are more susceptible to a higher incidence of post parturient uterine diseases whereas the incidence of endometritis decreased with an increase in parity. Further, the risk of puerperal metritis was highest following first calving and lowest in second parity cows [37,38]. It appears clear that the duration of endometritis is related to the severity of initial uterine lesions. Older cows have reduced uterine elasticity and uterine involution is slower than in younger cows, which presumably increases the vulnerability of older cows to persistent uterine infection and endometritis. Balancing this effect, though, is the fact that in older cows there will have been more episodes of uterine bacterial contamination, with the potential for some immunological resistance against uterine infection. In cases of bacterial contamination, older cows may efficiently and rapidly eliminate bacteria from the uterus while younger cows may have limited prior exposure, which delays the immune response, resulting in more severe and prolonged endometritis [16,39].

Dystocia: In cows, dystocia is often associated with multiple postpartum complications, for example retained fetal membranes and delayed uterine involution, both of which no doubt favors the development of endometritis [40,41]. Dystocia is a risk factor that increased the overall incidence of endometritis during the first month after calving. Furthermore, dystocia indirectly increases the opportunity for the development of endometritis by increasing the probability of metritis. Abnormal calving and dystocia can induce trauma of the endometrium and calving assistance favors the introduction of bacteria into the uterus and increases the potential for endometritis todevelop [25,27].

Calving assistance encountered in the case of dystocia significantly increases the incidence of endometritis [9,21]. Calving assistance is a risk factor for endometritis. Interestingly, the birth of a male calf, which is often larger than a female, may increase the risk of dystocia and thereby the risk of endometritis. It is reported that the birth of a male calf was a risk factor for endometritis. It is also suggested that in the studied herd the prevalence of endometritis could be reduced by 60% of all calves born were female. The high incidence in male calves is related to their size, both increasing the risk of dystocia

and the subsequent need for calving assistance [17,20,42].

Milk yield: In cows with postpartum endometritis, the milk yield for standard 305 days lactation was almost identical to that of healthy cows whereas cows which yielded less milk in the period before drying off compared to their higher-yielding counterparts had a greater tendency to develop postpartum endometritis after second calving [29,37]. High producing cows had a higher incidence of postpartum reproductive disorders including metritis than medium or low producing cows [42,43].

Retained placenta: An increased incidence of puerperal uterine infections following RFM in dairy cattle. RFM was found to be a single greatest factor contributing to the incidence of postpartum metritis in dairy cattle [44]. In his studies, RFM was observed in 17 out of 153 cows and all the animals with RFM exhibited the evidence postpartum endometritis between 15 to 20 days postpartum. Retained placental tissue represents the main risk factor for endometritis in dairy cows [12].

Residual tissue encountered in the case of a retained placenta represents a favorable medium for the growth of bacteria in the uterus and necrotic tissue delays uterine involution and the repair of the endometrium. Furthermore, residual tissues may result in the cervix being held open and an increase in bacterial contamination of the endometrium [45,46]. Cows affected by endometritis have a very high concentration of bacterial lipopolysaccharide (LPS) and immune-depressant products that decrease the recruitment of leukocytes into the uterus to clear bacteria [17,37]. A positive correlation between a retained placenta and endometritis seems to be due to the impairment of neutrophil function [6]. Indirectly, pregnancy length, induced calving, twins, and stillbirth increase the prevalence of endometritis by favoring the retention of fetal membranes. A study conducted on 2017 calving distributed throughout 1 year concluded that primiparous cows with prolonged gestation (>270 days) had a greater risk of developing endometritis than those with a normal length of gestation [37,45]. Furthermore, multiparous cows with short gestation were more vulnerable to the most important risk factor for endometritis, a retained placenta, than those with normal gestation [47,48]. Cows with short gestations (<270 days) were four times more likely to experience a retained placenta than cows with a normal length of gestation (270-280 days) [27]. Induced calving, directly and indirectly, affects the incidence of endometritis by increasing the risk for metritis, metabolic disorders, retained placenta, and stillbirth. The induction of calving using dexamethasone negatively affects phagocytosis activities, and, as a result, disengagement of cotyledons is reduced and retained placenta is favored, which increases the risk of developing endometritis [3,48].

The birth of twins has often been considered a risk factor for uterine infection as it can indirectly increase endometritis by favoring the development of other uterine diseases known as potential risk factors for endometritis. It seems that the incidence of retained placenta was higher in cows with twins than those with a single calf (35.7% vs. 7.7%, respectively) [39]. This observation and declared that the birth of twins was highly correlated with retained fetal membranes. Cows with twins had a six times greater chance of developing metritis and a three times greater chance of developing a retained placenta than cows with singletons [27,45]. Twins were associated with endometritis. The birth of twins, dystocia, and the trauma associated with them enhance bacterial contamination of the uterus and increase the risk of developing a retained placenta, metritis, and endometritis [37,45]. A relationship between stillbirth and subsequent uterine infection and proposed that cows with stillbirths are often exposed to a retained placenta and metritis. Indirectly, stillbirth increases the risk of endometritis by increasing the incidence of metritis [6,27]. Placental immaturity associated with the shortened length of pregnancy seen in the case of stillbirth may also be part of the cause of a retained placenta, metritis, and endometritis [48,49].

Metritis: Until relatively recently, metritis and endometritis were not considered to be two separate clinical conditions. Currently, however, it would be inexcusable not to distinguish between these two uterine conditions [24,25]. Almost all cows develop metritis without any systemic signs after parturition. There is then divergence some cows return to normal while others develop puerperal metritis with systemic signs and those cows that continue to have a contaminated uterus after the third week postpartum develop endometritis [13,17].

Cows that developed metritis soon after calving had a greater chance of developing endometritis[28]. Metritis is a risk factor for endometritis. It seems that there is a positive correlation between the degree of the clinical signs of metritis and the risk of developing endometritis [50]. Since the relationship between metritis and endometritis appears strong, any risk factor that favors the development of metritis soon after calving increases the risk of developing endometritis. dystocia, stillbirth, retained placenta, twins, primiparity, calving during winter, and male calves significantly affected the risk of developing metritis [27].

Hypocalcemia: Failure of adequate calcium mobilization around the time of calving results in hypocalcemia. Since calcium is an important element in the process of uterine involution, any deficiency delays this process and is considered a risk factor for retained fetal membranes and it may affect the incidence of metritis and endometritis and the severity of endometritis [27].

Metabolic disorders including hypocalcemia may significantly affect the incidence of endometritis. Other authors confirmed that hypocalcemia reduces uterine contractions, causes dystocia, prolongs gestation, and increases the risk of occurrence of retained placenta and endometritis [51,52]. Moreover, hypocalcemia decreases rumen motility, leading to reduced feed intake, which increases the risk of ketosis, and since hypocalcemia can affect rumen motility, it can indirectly increase the risk of developing a displaced abomasum [53]. However, the effects of a displaced abomasum on the incidence of endometritis are not yet well understood. Metabolic disorders (displaced abomasum, hypocalcemia, ketosis) increase the incidence of endometritis and significantly increases the prevalence of endometritis in dairy cows [54].

Mastitis: Mastitis represents a source of bacterial contamination within the environment that may favor the development of endometritis. Often, isolated bacteria in the case of uterine infections are nonspecific, often environmental bacteria that contaminate the uterus during parturition [55]. Indirectly, the risk factors for mastitis are sometimes considered to be risk factors for endometritis. Among these factors are retained placenta, milk fever, and calving during winter [27]. Subclinical mastitis can directly influence the prevalence of endometritis at 30 days postpartum and 60 days postpartum [37,46].

Negative energy balance: A negative energy balance (NEB) is often linked with severe and prolonged uterine inflammation and delayed uterine involution, which appears to be associated with a lack of bacterial killing after ingestion by phagocytes [18,23]. NEB favors the development of many metabolic disorders, especially ketosis, which can increase the main important risk factors for endometritis, namely retained placenta and metritis, by 6.1 to 9.5 times [56].

Subclinical ketosis was considered as a gateway condition for many metabolic disorders such as clinical ketosis and displaced abomasum, and infectious problems like metritis and mastitis [57]. At the start of lactation, dairy cows require a significant amount of glucose to produce lactose, and these requirements are maximal after the third week of postpartum. During this period, dairy cows have an insufficient appetite to consume the required energy. Energy deficiency results in lipid mobilization and ketone accumulation that can reach toxic concentrations and reduce immune functions and increase the risk of endometritis [58]. *In vitro* studies showed that high plasma ketone concentrations negatively and significantly reduced the efficiency of the ovine nonspecific immune system including phagocytosis and neutrophil. Metabolic disorders including ketosis affect the prevalence of endometritis. Ketosis was a risk factor for subclinical endometritis [7,37,57]. Lipid mobilization induces an accumulation of non-esterified fatty acid (NEFA), which increases the potential for endometritis in 80% of cases and contributes directly to a strong inflammatory reaction by binding to Toll-like receptor 4 (TLR4) and starting an inflammatory cascade [18,36].

Moreover, high postpartum NEFA levels increased the risk of clinical endometritis [39,59]. The elevation of circulating plasma NEFA induces hepatic steatosis (fatty liver) and impairs polymorphonuclear function, notably phagocytosis [32]. The diminution of feed intake capacity, NEB, and lipid mobilization contribute actively to poor immune function from 2 weeks before calving to 3 weeks after calving [12]. High-yielding dairy cows are more exposed to the effects of the NEB and are more likely to develop endometritis [50]. Since the postpartum period is characterized by low food ingestion capacity, NEB, and lipid mobilization, metabolic disorders and fatty liver are common, and both reduce the efficiency of the immune system [18]. Cows with very high or very low BCS may suffer prolonged pregnancy, dystocia, retained fetal membranes, persistent uterine infection, and endometritis [59]. According to a study, cows with clinical endometritis have lower BCS than normal cows at all weeks before and after calving. Moreover, the loss of 1 to 1.5 points of BCS between 30 days before calving to 30 days after calving is often associated with a high prevalence of clinical endometritis. This effect may have been associated with hepatic steatosis further to lipid mobilization [60].

These observations also confirmed for subclinical endometritis and found that cows with a low BCS (≤2.5) at 30 days postpartum have a higher prevalence of subclinical endometritis [24,59]. Because NEB is inevitable around calving, to prevent a decrease of BCS many farmers increase the amount of concentrate fed, which increases the risk of acidosis [18]. The fall of rumen pH favors the growth of pathogenic bacteria and the production of bacterial endotoxins which occurs at the same time as the immune system is negatively affected by decreasing food intake [18,60].

Cyclicity: Clinical and subclinical endometritis are common causes of delayed resumption of ovarian activity after parturition, and importantly the onset time of

the resumption of the ovarian activity itself affects the process of uterine involution and consequently the potential for the development of endometritis. Dairy cows that have an early resumption of ovarian activity are less predisposed to endometritis at 30 days postpartum compared with cows that resume cyclicity later [17]. In the case of endometritis induced by gram-negative bacteria such as *Escherichia coli* inhibits the secretion of gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH). It also suppresses the sensitivity of the pituitary gland to GnRH. As a result, follicular waves develop but the dominant follicle does not ovulate, or when ovulation does occur, the resultant corpus luteum persists due to inadequate synthesis of uterine PGF2α. In the latter case, the continuous secretion of progesterone delays the recruitment of phagocytic cells, and the efficiency of the immune system is then decreased [6,13].

Cyclic cows had less than 30% chance of developing metritis compared with less than 50% chance for non-cyclic cows. Delayed resumption of ovarian activity represents a risk factor for spontaneous recovery from uterine infection due to improved immune function and phagocyte recruitment and function induced by estrogen. Furthermore, estrogen results in the significant secretion of cervical mucus which is considered to be a physical barrier that prevents bacterial entrance into the uterus [26,37].

Diagnosis of Endometritis

History and Physical evidence

The bacteriological data from uterine swabs of 101 cross breed cows with subacute/chronic endometritis reported that externally visible discharge on tail, vulva, or perineum was present only in 43 percent of cows [61]. The incidence of chronic postpartum metritis as 20.3 percent based on a history of mucopurulent discharge noticed by the animal attendant. Further, in 34.38 percent of these animals mucopurulent or purulent discharge was observed on the perineum, tail and external genitals but was not reported by the animal attendant [62]. The prevalence of clinical endometritis at days 50 postpartum as 20 percent based on purulent discharge detected by farm personnel by visual inspection of the perineum, vulva, tail, and confirmed by trans-rectal palpation of uterus and the vaginal canal [63,64].

Vaginoscopy

In the field, the diagnosis of postpartum endometritis is generally based on the identification of pus mixed with the vaginal mucous on vaginoscopy [22]. A diagnosis of endometritis was based on vaginal speculum examination. Vaginoscopic examination is described to be more sensitive to detect abnormal vaginal discharge [22,65]. The bacteriological data from uterine swabs of 101 cross breed cows with subacute/chronic endometritis concluded that vaginoscopic examination was a good tool for the diagnosis of subacute/chronic endometritis [61]. Vaginoscopic examination revealed discharge with flakes of pus in 20 percent of cows, mucopurulent discharge in 45 percent, purulent discharge in 29 percent, and hemorrhagic/foul-smelling discharge in 7 percent of cows. The incidence of postpartum endometritis as 24 percent based on the presence of mucopurulent or purulent mucous in the vagina. Vaginoscopy correctly predicted uterine infection in 59 to 82 percent of cases [61,63]. A diagnosis of postpartum endometritis based on the identification of mucopurulent discharge in the vagina and reported that only 20.31 percent had the history of mucopurulent discharge observed by the attendee and 34.4 percent exhibited the presence of mucopurulent discharges on the external surface of genitalia [62].

Rectal palpation

Rectal palpation of the cow help to diagnosis different reproductive anomalies such as a large fetus, metritis, pyometra, endometritis and dead fetus [42,66]. Rectal palpation could identify uterine infection only up to 22 percent of cows predicted to have a uterine infection, in comparison with identification by uterine culture. Using rectal palpation technique to diagnose postpartum endometritis, uterus was normal and involuting in 28 animals (43.75 percent), moderately enlarged, flabby and with palpable fluids in the uterus in 14 animals (21.87 percent) and considerably enlarged and filled with a large quantity of exudates in remaining 22 animals (34.37 percent) [37,65].

Treatment of Endometritis

Early handling of endometritis leads to better conception rates and shorter calving intervals in herds that suffer from the condition. Treatment success rates are higher for mild cases compared to more severe cases and those with a foul-smelling odor. For Intra-uterine infection antibiotics are a common treatment for the condition. If intra-uterine antimicrobials are to be used it should be considered that at less than 30 days post-partum, penicillin may be rendered ineffective due to the presence of bacteria that produce penicillinase [17,67]. Both oxytetracycline and cephalosporins are broad-spectrum antibiotics and effective in the uterine environment and should be considered as the drugs of choice [13]. Use of Cephapirin in cows with endometritis 3-6 weeks before breeding has been shown to improve fertility [68]. Alternatively, uterine infusions with 2% povidone-iodine have shown to be an effective non-antibiotic alternative [37,69].In some cases, prostaglandin (PGF) injections may prove useful. The effectiveness of PGF improves if there is a corpus luteum present and, although it may help in cases without a corpus luteum due to its direct effect on the myometrium, there may be some later impacts on pregnancy rate [70,71]. There appears to be no advantage to using intra-uterine cephalosporin rather than prostaglandin in terms of subsequent reproductive performance [67].

Gentle flushing of large quantities (several liters) of warmed saline into the uterus and subsequent siphoning may help remove some of the uterine content, although this has not been extensively validated [17,31]. Administration of a variety of antiseptic solutions has been reported, although the success is not well documented and may be counterproductive in some cases [13]. There appears to be no clear protocol for the treatment of endometritisand treatment should probably be assessed on an individual basis by the farm's veterinary surgeon and reserved for those cows with more severe clinical signs more than 4 weeks after calving [71].

Prevention

Prevention of endometritis is based around the promotion and support of the innate immune system. Management of nutrition in the early post-calving period is critical to minimizing the negative energy balance and circulating NEFA concentration that inhibits PMN function. Proposed management practices include provision of bunk space for ease of feed consumption, provision of suitable; clean rest area so that fresh in milk cows can lie without excessive contamination of the reproductive tract. Regulate temperature so cows are comfortable and manage monitor methods and targets so that problems can be identified and managed. Early Management of risk factors will also decrease the prevalence of endometritis such as retained placenta and all its underlying factors as well as the early resolution of dystocia and twinning [18,72]. To minimize infection calving pens should be kept as clean as possible with fresh bedding. Also, if calving assistance is needed this should be carried out hygienically. The control of post-partum infection focuses on the main causes of the condition. Controlling the incidence of the retained placenta will have a direct effect on the levels of endometritis. Improved hygiene in calving boxes and calving assistance are also likely to reduce the occurrence of endometritis- especially in herds where hygiene has been poor. Equally important risk factors for endometritis are hypocalcemia, RFM, high NEFA, therefore, ensuring correct nutritional management both pre and post-calving is important [31,73]. Ensure cows are not over fat at the time of calving and that excessive weight isn't lost in the pre- or post-calving period [70].

Conclusion and Recommendations

Endometritis is a multifactorial disease and determining its risk factors has great potential as a source of information that must be considered for the treatment and prevention of endometritis. Many risk factors and details about endometritis are as of yet unknown and only a few extrinsic risk factors such as calving season and nutrition and intrinsic factors such as parity, dystocia, retained placenta, metritis, hypocalcemia, mastitis, NEB, and cyclicity have been identified and studied. There are interactions between the risk factors themselves; for example, a variety of nutritional imbalances, high or low BCS, and high milk yield may all predispose to endometritis [74-83]. The prevalence and severity of endometritis are related to the conditions of the livestock as extrinsic factors but also to intrinsic factors specific to each cow, which means that even in the same herd some cows may be more susceptible to developing and sustaining endometritis than other cows. For these reasons, for prevention and besides treating affected cows, the most important risk factors must be identified and treatment should be adapted specifically to each cow according to the clinical examination of the intrinsic and extrinsic risk factors identified. This results in better management of endometritis and thus will reduce the associated economic losses. In conclusion, the owners should be responsible to keep the sanitation of dairy cows through improved housing system & nutrition to reduce bacterial exposure of cows at parturition and increase the rate of pregnancy of cows after calving. Besides, gloves should be worn appropriately to reduce endometritis during pregnancy diagnosis. Proper attention to sanitation & periparturient hygiene should be given during assisted calving. Proper diagnosing & treatment measures should be taken to minimize the economic impact of endometritis.

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