INTRODUCTION

Parturition is a period of high risk for mother and offspring in all species, and cattle are not exceptional. The risks of physical damage during the birth process or failure to release the placenta after parturition and there is often an upsurge of microbial infections in the cow. Some animals acquire infections of the uterus or mammary gland during late gestation, which may lead to premature parturition, or compromise fetal or calf health. However, the greatest impact on health and productivity is associated with microbial contamination of the uterine lumen after parturition. Amongst the mammals, Bos Taurus, and particularly dairy cattle farmed in intensive systems, commonly acquires microbial contamination of the uterus. Indeed 80–100% of animals have bacteria in their uterine lumen within the first 2 weeks after calving. Although immune responses progressively eliminate the microbes, up to 40% of animals still have a bacterial infection 3 weeks after calving.[1]

The normal uterus is a sterile environment compared to vagina, which hosts many microorganisms. Opportunistic pathogens from the normal vaginal flora may invade the uterus at different times especially, at mating and parturition.[2] During the Postpartum period, reduction in the size of uterus to its normal non-gravid size is extremely important in order to decrease the susceptibility to the multiplication of infectious agents; this reduction is mostly managed by PGF2α and oestrogen.[3] If the uterus is not returned to normal non-gravid size at proposed period of time and the cleanliness of the calving area is not satisfactory there is the likelihood development of uterine disease.[4] Uterine disease can be classified as puerperal metritis, clinical metritis, clinical endometritis and subclinical endometritis.[4] As pathological entity, endometritis is an inflammation of the endometrial lining of the uterus without systemic signs and is associated with delayed uterine involution[5]; While Subclinical endometritis is defined as an inflammation of the internal lining of uterus (Endometrium) in the absence of clinical signs of endometritis seen externally such as vaginal discharge.[4]

These diseases are highly prevalent in high producing dairy cows and have been associated with decreased pregnancy per artificial insemination, extended interval to pregnancy and increased culling rate.[6][7][8] Subclinical endometritis is the most prevalent of all uterine diseases; it affects approximately 30% of lactating dairy cows.
with the prevalence ranging from 11 to >70% in some herds.\(^7\)^19\(^{10}\)\(^{11}\)\(^{12}\)

A scoring scheme for vaginal discharge ranging from clear or translucent mucus (clinically healthy) to purulent discharge has been suggested.\(^{13}\) Several causes of endometritis have been proposed by many authors, which are generally infectious causes. Most infectious agents gain access to the uterus during postpartum period, which is mostly described as the risky period in reproduction of cattle. Postpartum uterine infection has an adverse effect on reproductive performance and causes economic loss.\(^{14}\)\(^{15}\)\(^{16}\)\(^{14}\)

Uterine infection has a seasonal incidence, being highest during the housed period, presumably because of environmental contamination. A dirty calving environment may increase the risk of endometritis. Recent studies shown that Subclinical endometritis causes significant economic losses because of decreased reproductive performance, increased feed intake per lactation, increased number of services per conception and increased culling rate.\(^7\)

Therefore, the objective of this paper was:

- To highlight risk factors for subclinical endometritis
- To review the diagnostic and treatment options of subclinical endometritis
- To highlight recent information’s on the effect of subclinical endometritis on bovine fertility

POST PARTUM PERIOD IN COW

Post partum period is the time required for the completion of uterine involution that is the interval from parturition to complete uterine involution.\(^{17}\) It takes 3 weeks under normal condition, from size point of view, and functional resumption needs 6 weeks. It has been reported that uterine involution in normal cows largely completed as indicated by the size of the uterus and the condition of the endometrium at about 30 days post partum.\(^9\)\(^{18}\) The complete uterine involution ranges 26 to 52 days after calving, but the changes after 20 to 25 days post calving are generally almost imperceptible. Complete re-epithelialization of the caruncle is complete from 25 days onwards.\(^{19}\)

The postpartum period is divided into three sub periods: puerperal, intermediate and postovulatory periods. The puerperal period was defined as the interval from calving until the pituitary becomes responsive to gonadotropin releasing hormone (GnRH); which is approximately 7-14 days postpartum (PP). The intermediate period is the interval from the time at the pituitary becomes responsive to GnRH to the first PP ovulation. The postovulatory period is the interval from the first ovulation to complete uterine involution.\(^{17}\)

The PP period is crucial in the life of dairy cows, during which the animal should re-establish normal uterine and ovarian activates. During this period, dairy cows are at risk of developing calving related diseases, such as hypocalcaemia, endometritis, metritis, ketosis and displacement of abomasums.\(^{20}\)

During the first few days after delivery, the uterus contracts gradually so that by the fourth day it is approximately one-half that during pregnancy and by day 7-8 it is only one third the size of gravid uterus. By day 14, the uterus has reached its approximate non-pregnant size. Cows may continue to expel uterine fluid and lochia for up to 18 days postpartum; those that continue to discharge beyond this time should be investigated for abnormality. Nevertheless, as long as the discharge does not have a foul odor, it is probably normal.\(^{18}\)

Postpartum Uterine Involution

The physiologic changes that occur in the uterus during the postpartum period when it is returning to its normal non-gravid functional and anatomic state are referred to as PP uterine involution. PP involution in cows is generally complete by 45 to 50 days PP.\(^{18}\)

PGF2α is likely the most contributors to uterine size reduction in the immediate PP period for all domestic species. This can be inferred from the episodes of discomfort that parturient animals undergo during the hours immediately after delivery. The corpus luteum of pregnancy begins to regress prior to parturition and is in advanced stage of degeneration within a few days after calving.\(^{15}\)

Postpartum Ovarian Activity and Utero-Ovarian Relationship

Ovarian activity during the early pueriparum period exerts an important influence on the ability of the uterus to resist or eliminate infections. The uterus of the cow can resist uterine infection during estrus period, but are very susceptible during the luteal phase of the cycle. Since cellular defense mechanisms are potentiated during estrus, it has been generally assumed that a delay in return to cyclical to ovarian activity would predispose cows to endometritis.\(^{21}\)

In addition, it has been seen that a short exposure to luteal or exogenous progesterone will down regulate immune function and in some animals transform the uterus from an organ that is resistant to susceptible to infection.\(^3\)

CAUSES OF ENDOMETRITIS

Endometritis and subclinical endometritis are caused by many numbers of microorganisms, including viruses, bacteria and fungus. The microorganisms commonly enter the vagina during the calving process, parturition and mating process. Manipulation of the calf during the calving process, often referred to as pulling the calf, can also cause additional microorganisms to enter the cow.\(^{22}\) Infectious causes of endometritis are those infectious agents, which are responsible to cause endometritis. Postpartum uterine infection has an adverse effect on
reproductive performance and causes economic loss\textsuperscript{[14]} \textsuperscript{[15]} \textsuperscript{[16]} The majority of postpartum inflammatory conditions of the uterus begin with bacterial contamination of the uterine lumen. One should differentiate between uterine contamination and uterine infection.

The uterus of postpartum cows is usually contaminated with a range of bacteria, but this is not consistently associated with clinical disease. Infection implies adherence of pathogenic organisms to the mucosa, colonization or penetration of the epithelium, and/or release of bacterial toxins that lead to establishment of uterine disease. The development of uterine disease depends on the immune response of the cow, as well as the species and number (load or challenge) of bacteria. The number of pathogenic bacteria in the uterus of postpartum cows may be great enough to overwhelm uterine defense mechanisms and cause life-threatening infections, although these are relatively uncommon.\textsuperscript{[22]}

Indeed, non-life-threatening uterine infections are most common and associated with impaired reproductive performance. Furthermore, inflammation, even in the absence of active bacterial infection, may perturb embryo survival.\textsuperscript{[24]} The most common infectious agents, which cause endometritis, are discussed as follows.

**Campylobacter Fetus**

It is a bacterial disease that was formerly known as *Vibrio fetus*, which is mainly characterized by abortion. Within the uterus, it causes mild endometritis. Endometritis caused by *C. fetus* is diffuse and macroulcerative, characterized by periglandular accumulation of lymphocytes and the collection of exudates in the uterine lumen.\textsuperscript{[26]} The endometritis is a mild type and cannot be identified by rectal palpation.

**Escherichia Coli (E.Coli)**

It is a Bacterial agent, which reaches uterus during stress and cause abortion and mild endometritis, so it causes opportunistic infection to uterus, which leads to reduced productivity of the cow. *E.coli* infections not only cause endometritis but it also predisposes the cows for the *A.pyogenes* infection.\textsuperscript{[26]} Current evidence shows that *E.coli* is particularly prevalent in the first week postpartum and is associated with endometritis. Infection of the endometrium with *E.coli* precedes infection by *A. pyogenes* and possibly *Bovine herpesvirus 4*, and is associated with the severity of clinical disease and impact on fertility.\textsuperscript{[13]}\textsuperscript{[27]}

Recently, it was observed that a specific *E.coli* causes uterine disease, which is different from known diarrheic or extra-intestinal pathogenic *E.coli*. Extra-intestinal pathogenic *E.coli* was found to be more adherent and invasive to endometrial cells and to stimulate greater production of PGF2α and interleukin 8.\textsuperscript{[28]}

**Fusobacterium Necrophorum**

It is a bacterial agent, which is mostly seen to cause a mild type of infection to the uterus and known to cause some degree of abortion and endometritis. *Fusobacterium necrophorum* produces a leukotoxin.\textsuperscript{[29]}

**Arcanobacter Pyogenes**

*A. pyogenes* is a bacterial agent known to cause endometritis in cows postpartum; *A. pyogenes* secretes the exotoxin pyoolysin and based on in vitro and in vivo inoculation with killed bacteria or bacteria-free filtrate, it appears that a heat-labile component. *A. pyogenes* itself may be responsible for inducing uterine inflammation, but that intact endometrium in healthy animals may be protective. Therefore, while *A. pyogenes* are commonly found in cows with metritis and especially with endometritis, it is not clear that there are specific strains or virulence factors of. *A. pyogenes* associated with uterine disease. *A. pyogenes* produces the cholesterol-dependent cytotoxin pyoolysin which facilitates for the growth of *F. necrophorum*.\textsuperscript{[24]}

**Bovine Herpes Virus -4 (BOHV-4)**

*BoHV-4* is a member of the herpes virus causing reproductive disease in cattle in the form of endometritis, vulvovaginitis, and associated abortion. Most of the time *BoHV-4* cause’s subclinical endometritis and cause retained fetal membrane which intern leads to endometritis. *Bovine herpesvirus 4* (*BoHV-4*) is the only virus consistently associated with uterine disease after parturition in cattle, and *BoHV-4* infection is widespread in the endometrium.\textsuperscript{[30]}\textsuperscript{[31]}

**PREDISPOSING FACTORS OF SUBCLINICAL ENDOMETRITIS**

Even if infectious agents mostly contaminate uterus during PP period, the infectious agents are easily removed by the normal immunity of cows, if they are not at the stage of causing endometritis. However, there are many risk factors which makes the uterus favorable for the development of infectious agents and which drops the immunity of dairy cows.\textsuperscript{[15]} Some of the predisposing factors of subclinical endometritis are.

**Retained Fetal Membrane**

Expulsion of fetal membrane is the third stage of labour and usually accomplished within 6 hours of parturition. However, in some cows the fetal membrane remains attached to the uterine caruncules for a variable period after parturition. Placental retention is usually accomplished and followed by delayed involution of uterus.\textsuperscript{[32]}

Retained fetal membrane predispose to impairment of subsequent reproduction performance. The fertility of such cows is often reduced in terms of a delayed calving to first service interval, calving to conception interval and pregnancy rate of first service.\textsuperscript{[40]} RFM services as a favorable media for many infectious agents growth and multiplication, which intern leads to the development of
clinical and subclinical endometritis. Retention of fetal membrane is a condition in which the cow fails to release the placenta 12-24 hrs after calving. Although retention of fetal membrane is not a disease by itself, many researchers have tried to treat this condition because it is the major risk factor for endometritis.\[33\] Clinical Endometritis
Clinical endometritis is defined in cattle as the presence of purulent uterine discharge detectable in the vagina 21 days or more post partum.\[33\] Clinical endometritis can develop quickly or slowly, based on the course of the disease process. Clinical endometritis is further classified as acute and chronic which are discussed as follows.
Acute Clinical Endometritis
Acute clinical endometritis usually follows parturition, artificial insemination (AI) and invasion of the uterine lumen with infusion solution and instruments. In most cases, acute endometritis is transient and offending, microorganisms are removed within several estrus cycles by the uterine defense mechanisms. It operates within 5-15 hours puerperium period. Clinically there will be some elevation in body temperature, serous foul-smelling discharge from the uterus and vulva with systemic disturbance. The most presenting sign of acute endometritis is white or whitish yellow discharge from the vulva, which is variable in amount.\[36\]

Chronic Clinical Endometritis
Chronic endometritis is also referred as clinical endometritis is characterized by the presence of mucopurulent or purulent discharge from the vagina three weeks or more after parturition and it is not associated with elevated temperature depressed general attitude. Chronic endometritis is identified based on its histopathology. It is a chronic inflammatory process of endometrium manifested by plasma cell infiltration.\[32\][33]

Subclinical Endometritis
Subclinical endometritis is defined as an inflammation of the internal lining of uterus (endometrium) in the absence of clinical signs of endometritis seen externally such as vaginal discharge.\[31\] Subclinical endometritis have negative impact on subsequent reproductive performance of dairy cattle.\[9\][7][12]

Subclinical endometritis usually occurs over a long period of time rather than progressing quickly. The pus discharge from the vagina may be present under speculum examination. The prevalence of subclinical endometritis varies depending the parity the cows; of 82 cross breed dairy cows the prevalence of subclinical endometritis were 100%, 52.4% and 71.4% in pregnant heifer, primiparous and multiparous cows respectively.\[37\]

In the absence of clinical endometritis, subclinical endometritis is defined by the presence of >18% PMN in uterine cytology samples collected between 22 and 33 days postpartum and >10% PMN between 34 and 47 days postpartum.\[1\]

Dystocia
Dystocia may be defined as difficult birth as opposed to normal birth, which is delivery of fetus without difficulty under normal physiological process. Causes of dystocia are generally classified as fetal and maternal causes. Dystocia predisposers to endometritis by several reasons. Firstly, there is a higher than normal incidence of RFM in animals that suffered dystocia. Secondly, there is often damage to maternal tissues causing deviation. Thirdly, the obstetrical intervention to correct the dystocia increases the load of pathogens with uterus.\[22\]

Management Factors
Uterine infection has a seasonal incidence, being highest during the housed period, presumably because of environmental contamination. A dirty calving environment may increase the risk of endometritis.\[19\]

Described two hygienically contrasting farms: one with a relatively clean environment the incidence of endometritis was 2-3 percent, compared with an incidence of 15 per cent for one with dirty environment. Problem in management includes the improper feeding of cows with excess or deficiency of nutrients during the dry period; which may lead to metabolic disease such as hypocalcaemia, ketosis and over feeding, which intern predispose to endometritis.

Decreased dry matter intake (DMI) prior to parturition is associated with mobilization of lipids, which are released as non-esterified fatty acids (NEFA) from adipose tissue. Decreased DMI and increased NEFA levels are associated with periparturient suppression of the immune function, resulting in a greater susceptibility of cows to infection.\[34\]

CLASSIFICATION OF ENDOMETRITIS
As pathological entity, endometritis is an inflammation of the endometrial lining of the uterus without systemic signs and is associated with delayed uterine involution. Endometritis as superficial inflammation of the endometrium only, extends no deeper than stratum spongium; they characterize endometritis by some disruption of surface epithelium, infiltration with inflammatory cells, vascular congestion and stromal edema and by varying degree of lymphocyte and plasma cell accumulation in the superficial layer.\[3\] More often endometritis is the result of non-specific infection by opportunistic pathogens that have a significant effect on fertility of dairy cows.\[3\] Endometritis in bovine is classified as clinical and subclinical which are discussed as follows.

Cyclic Endometritis
Clinical endometritis is defined in cattle as the presence of purulent uterine discharge detectable in the vagina 21 days or more post partum. Clinical endometritis can develop quickly or slowly, based on the course of the disease process. Clinical endometritis is further classified as acute and chronic which are discussed as follows.
EFFECT OF SUBCLINICAL ENDOMETRITIS ON FERTILITY OF DAIRY CATTLE

Inflammation of the uterus due to SCE has an effect on reproductive performance. Irritation of the endometrium may cause premature release of prostaglandin and lysis of the corpus luteum resulting in a short inter estrus interval. Subclinical endometritis is inflammation of the uterine endometrium without external indicators of apparent clinical signs; such as vaginal discharge. Subclinical endometritis affected cows have prolonged days to first service and days to pregnancy. Subclinical endometritis causes significant economic losses because of decreased reproductive performance, increased feed intake per lactation, reduced milk yield and increased culling rate. The economic cost of subclinical endometritis depends on the detrimental effect on fertility, increased culling rate and, to a lesser extent to the cost of treatment.

Up to 50% of cows, 40-60 days after calving had neutrophils in the uterine lumen or endometrium, concomitant with inflammation of the tissues, and subclinical endometritis reduces conception rates. Cows with genital tract microbial infections have slower growth of dominant follicles, lower peripheral plasma oestradiol or progesterone concentrations and are less likely to ovulate.

A mean of 2.4 services per conception was required for cows that were positive for SCE at the 4th week postpartum where as 1.7 services per conception was required for cows negative for SCE. For those cows that were positive for SCE at the 8th week PP a mean of 2.7 services per conception was required compared to 1.7 NSPC for normal cows. At both 4th and around 8th weeks postpartum, the presence of SCE has a significant effect on the number of services on conception indicating that cows with subclinical endometritis required more services per conception. The median calving to first service interval for cows with subclinical endometritis at the 4th and 8th weeks postpartum were 96 and 100 days, compared to 80 and 82 days for cows without SCE respectively.

DIAGNOSTIC OPTIONS OF SUBCLINICAL ENDOMETRITIS

Although, many methods are used for the diagnosis of endometritis few of them may be of use in practice, especially in diagnosis of subclinical endometritis. Subclinical endometritis can be diagnosed accurately by either cytologically (cytobrush and uterine lavage technique) or histologically (biopsy). Some practitioners frequently use biopsy method, use of this procedure is practically questionable; because this method is invasive, expensive and time consuming.

Furthermore, biopsy may be associated with delayed conception because of induced damage of uterine tissue. Cytobrush technique might cause irritation to the endometrium. Furthermore, this technique was reliable, easy and not time consuming. Subclinical endometritis in bovine is one of the most difficult portions due to the lack of golden diagnostic standard. Although it is difficult, different researches used different diagnostic techniques, which are summarized as follows.

Ultrasoundography

As it is the popular diagnostic method in bovine reproductive tract and as a non-invasive method, it is used to visualize small amount of fluid in the uterine lumen. False positive findings may result from clear mucus in the uterus appearing during estrus. Therefore, the ovaries should be scanned as well to define the stage of estrus cycle.

Nonetheless, this method was found to be less sensitive than endometrial cytology. The use of trans-rectal ultra-sonography permits more objective measurement of the diameter of the uterine horns and cervix, and visualization of mucus and pus within the uterine lumen. At present, there is little evidence that ultra-sonography provides more information about clinical endometritis than examination of the contents of the vagina. Although, there is limited information on the relationship between ultrasonographic findings and clinical or subclinical endometritis, this is likely to be a fruitful area for research.

Endometrial Cytology

Collection of endometrial and inflammatory cells can be performed by flushing the uterus, uterine biopsy, guraded cotton swabs and a cytobrush from the endometrium. On the basis of relative number of neutrophils from endometrial cytology it is possible to diagnose and define subclinical endometritis. The percentage of polymorphonuclear (PMN) in the cytological preparation provides information on the presence of subclinical endometritis. The optimum value for PMN varies among different authors between 5 to 30 percent. A technique that yields well-preserved cells representative of a large uterine surface area without causing harm to the reproductive tract is required for consistent and reliable cytological results. Some of the cytological techniques are described as follows.

Lavage Technique

The uterine body is lavaged by infusing 60ml of 0.9% sodium chloride solution in to the uterine body with 60ml syringe attached to 52cm disposable plastic infusion rod. The uterus was massaged and then retracted to recover the fluid. As much fluid as possible was recovered by negative pressure aspiration into the syringe and transferred to a 50 ml modified polystyrene centrifuge tube without preservatives. Uterine lavage samples were brought to the laboratory within 2 hours and centrifuged at 500 revolutions per minute for 5 minutes. A drop of sediment was streaked on to a clean microscopic slide and air-dried. All slides were fixed with methanol and stained with gimesa stain and
examined under a microscope at 400x magnification by counting 80-100 cells to determine the percentage of neutrophils. Initially the whole slide was assessed and a representative area was selected to determine the percent of PMNs. If greater than 5% of the cells are neutrophils per 400x microscope power field, it was categorized as subclinical endometritis. [7][16]

Cytobrush Technique
Cytobrush is a less harmful technique for the endometrium than the uterine lavage, since the fluid in uterine lavage produces endometrial irritation. The normal cytobrush handle was cut to approximately 3 cm in length, threaded on to a 65 cm solid stainless steel rod, and placed in a stainless steel tube 50 cm on length and 5 mm in diameter for passage through the cervix. The vulva was cleaned with wet paper towel, after which the covered lubricated instrument was passed through the vagina to the external cervical orifice; the sanitary sleeve was punctured and the instrument was advanced through the cervix in to the base of the larger horn, at which point the stainless steel tube was retracted for enough to expose the cytobrush. [12]

Endometrial cytology samples were collected by rotating the cytobrush in a clockwise direction while in contact with the uterine wall. The cytobrush was retracted in to the stainless steel tube prior to removal from uterus. Slides were prepared by rolling the cytobrush on to a clean glass microscopic slide and fixing the sample with cytofixative. Slides were brought to laboratory within 2 hours and stained with modified Giemsa stain. [12]

The cytobrush technique yield an in situ sample which might represent the inflammatory nature of the endometrium, compared with the uterine lavage technique, which yielded diluted sample of luminal contents. The cytobrush technique is a more consistent and reliable method than the lavage method to obtain endometrial cytology samples from postpartum dairy cows. [12]

Guarded Swaps
Guarded swap method is essentially the same as cytobrush technique. The only difference is on solid stainless steel rod cotton swaps are placed instead of cytobrush. [32]

Endometrial Biopsy
Endometrial biopsy for cytological examination is obtained using biopsy instrument. The instrument has a window of cutting edge on the tip that is screwed on to the 65 cm stainless steel, which contains a thin rod that pushes endometrial tissue against the cutting edge. The instrument is guided through the cervix in to the uterine horn. The endometrial wall is rectally pushed in to the window a cutting edge before the thin rod is advanced through a stainless steel and passed in to the cutting tip. Then the instrument is withdrawn and the cutting tip is unscrewed to collect the endometrial tissue for cytology. [32]

Vaginoscopy
The evaluation of vaginal discharge is commonly used for the diagnosis of clinical endometritis and sometimes for the diagnosis of subclinical endometritis in cows. Vagina should be inspected by vaginoscopy for the presence of pus. The character of vaginal mucus can be scored to produce a clinical endometritis score. Vaginal discharge score is based on the color and volume of pus. If the vaginal discharge shows clear translucent mucus character, the score is 0 and when it shows clear mucus containing flecks of white pus character, the score is 1 and it contains ≤50% white or yellow white pus character, the score is 2 and when it contains ≥50% white, yellow white or bloody pus character, score is 3. [11]

The absence of uterine discharge by vaginoscopy examination is not truly indicative of uterine infection. [12]

TREATMENT OPTIONS OF SUBCLINICAL ENDOMETRITIS
For veterinarians in dairy practice, treatment decision should consider the use gained after treatment of the animal and the cost of treatment. In addition, veterinarians should be aware of a growing public concern about a possible association between the use of antibiotics and multidrug resistance of infectious agents in humans. Subclinical endometritis can be treated with a prostaglandin by intra muscular injection (cloprostenol 500 mg) or an intrauterine antibiotic therapy (cephapirin) at 20–33 days PP to improve the reproductive performance. Due to different types of infectious agents involved in uterine infections, a set recommendation of drugs is impossible. Ideally, identification of the infectious agent and drug sensitivity is done. Subsequent treatment with an approved drug is the most practical, economical and efficient approach. However, there are no recommended doses on most drug labels for intrauterine therapy. [14]

The goal of reproduction management is to have cows become pregnant at a biologically optimal time and at an economically profitable interval after calving. The timing of examination of animals after parturition should allow for the normal process of involution, yet also provide sufficient time for treatment and response prior to the start of the breeding period. The aims of uterine disease treatments are to reverse inflammatory changes that impair fertility, whilst enhancing uterine defense and repair. [11] The following are some of the treatment options of subclinical endometritis.

Antibiotic Treatment
Although there is no approved antibiotic treatment for subclinical endometritis, metircure was found to improve reproductive performance of cows with SCE. [16] There is consistent evidence that cows with PP period have improved reproductive performance when treated with a single intra-uterine infusion of cepapirin approximately
one month before first insemination, relative to receiving no treatment.[10]

A formulation containing 125 mg of ceftifur hydrochloride in 10 ml of oil-based sterile suspension labeled for treatment of clinical mastitis was shown to reduce the bacterial contamination of dairy cows with clinical and subclinical endometritis; however, it did not improve fertility.[10]

**Injection of Prostaglandin**
The beneficial effects of PGF2α administration could be associated with the presence of a responsive CL that leads to the induction of estrus and subsequent physical removal of contaminant from the uterus. Treatment with PGF2α did not affect time to first AI. PGF2α treatment decreases the proportion of cows with SCE, increases the first service pregnancy per AI in cows and decreased time to pregnancy in cows with low BCS. The administration of PGF2α induces estrus in cows with a responsive CL, and might help to cleanse contaminates from the uterus and improve fertility.[34] In endometric cows with no palpable CL, prostaglandin treatment was ineffective.[42]

The role of PGF2α in the therapy of uterine infections are elimination of CL by improvement of contractility, elimination of immune suppressive effect of progesterone and direct stimulation the function of immune cells in endometrium.[43]

But a large clinical trial found that PGF2α did not improve fertility in cows with clinical endometritis.[44] PGF2α is not only luteolytic but also appears to have pro-inflammatory actions that might enhance neutrophil function.[45] Because there is increased concern about bacterial acquisition of antibiotic resistance, PGF2α would provide an efficacious method of treatment of endometritis. Nonetheless, later studies found no beneficial effect of PGF2α for treatment of subclinical endometritis.[44] [45] Therefore, the combined literature suggests that PGF2α is not an efficacious method to treat subclinical endometritis, but still it needs more research.

**CONCLUSIONS & RECOMMENDATIONS**
Infectious agents that could invade the uterus during parturition may contaminate the maternal reproductive tract and lead to uterine disease; therefore, it needs to have maximum care at the time of calving, for the cleanliness of the calving area and at the time of helping the cow at dystocia through caesarian section strict sanitation measures should be taken. There are many factors, which will contribute for the inability of dairy cows to have maximum productivity. From these uterine abnormalities such as delayed uterine involution, and endometritis can result in increased calving to conception interval in dairy cows by prolonging luteal phase. Recent studies have also showed that subclinical form of endometritis has an impact on reproductive performance. It causes significant economic losses because of decreased reproductive performance, increased feed intake per lactation, reduced milk yield, increases NSPC and increased culling rate. Therefore, it needs modified diagnostic and treatment options to reduce the economical impact of subclinical endometritis on dairy cows.

Based on the above conclusions the following recommendations were given.

- Proper attention to sanitation and periparturient hygiene should be given especially during assisted calving.
- The owners should be responsible to keep sanitation of dairy cows through improved housing system and nutrition to reduce bacterial exposure of cows at parturition and increase the pregnancy of cows after calving.
- Proper diagnosing and treatment measures should be taken to minimize the economic impact of subclinical endometritis.

**REFERENCES**


