Effect of uterine infection on milk production and reproductive performance in dairy animals - A review

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Abstract
A healthy uterine environment is believed to be the main determinant of good fertility as any sort of insult to endometrium can disrupt the normal reproductive functions leading to infertility. The development of uterine infection is governed by the immune status and execution of the same against the infectious agents, bacterial load/ number and its virulence. Post-partum uterine infection results in persistent inflammatory responses in the endometrium and subsequent infertility. Uterine infection may delay the time of uterine involution, compromises ovarian follicular growth, luteal dysfunction by altering the luteal cell activity, postpartum resumption of ovarian activity, number of services per conception, number of days open and subsequently prolongs the inter-calving interval. Further at the hypothalamic and pituitary level, the estradiol-induced preovulatory LH surge is blunted with intravenous infusion of bacterial endotoxin or administration into the uterus. Uterine infection incurs a huge economic loss to the dairy farmers. Uterine infection not only affects milk production but also have a negative impact on the ovarian follicular development and steroid production, expression of estrus and ultimately the conception rate. Keeping in view all the above-mentioned facts, the following review will try to enlight the impact of uterine infection on milk production and reproductive performance in dairy animals.

Keywords: infertility, uterine infection, endometrium, ovary

Introduction
In dairy animals the uterus is thought to be apparently sterile or at least clear of pathogens for the most part of reproductive cycle, still the uterus is readily contaminated with microbes during coitus and around the time of parturition [1]. Uterine bacterial contamination is a dynamic condition wherein dairy animals have regular contamination of uterine lumen with a wide spectrum of microorganisms during the early postpartum period, clearance of same and spontaneous re-contamination rather than just a contamination. During first few weeks of parturition, uterine lumen supports the growth of a variety of aerobic and anaerobic bacteria which affect about 80 to 100 percent of dairy cattle [2]. Although immune responses progressively eliminate the microbes, still 40 percent of animals fail to clear the uterus off the bacterial infection even after 3 weeks following calving resulting in a persistent inflammatory response of the endometrium and are often infertile. [1,3]. Following parturition bacterial infection of the uterus causes endometritis and infertility in cattle [4]. Uterine infection reduces the rate of uterine involution and ovarian follicular development during the early postpartum, which may prolong the interval from calving to estrus and artificial insemination (AI) [5] It has been reported that dairy cows that were having endometritis had a decline in conception rate by a factor of 20, median calving to conception interval longer by 30 days and 3 percent more animals were culled than their normal counterparts.

In India, the most common reproductive tract infection in the buffalo has been observed through coitus by communal/local bulls used for breeding purposes, apart from inflammation of endometrium occurring during estrus, AI or in postpartum period [7]. Cows that were having dystocia, retained placenta, twins or stillbirths, and various other metabolic disorders are more likely to develop metritis than their counterparts. Aberrant immune function before and after calving seems to predispose cows to severe uterine infections. Although only a few cows use to die from uterine infections but are more likely to be culled for poor reproductive performance [8]. In India, it has been reported that about 18-40 percent of cattle and buffaloes are culled mainly due to infertility [6]. Dairy cows with endometritis are 1.7 times more likely to be culled for reproductive failure than those without endometritis [9]. The estimated financial losses in the European Union due to postpartum uterine infections vary between €160 and €420 per animal [10].
Taking conservative incidence rate of metritis around 20 percent, the annual costs of uterine disease are estimated to be €1.4 billion within the European Union and $650 million in the United States [11].

Numerous studies have demonstrated both direct and indirect negative impacts of uterine diseases on overall dairy herd performance and profitability [12]. Lactation yield and 305 days milk yield are adversely affected by abnormal calving in the buffaloes [13]. California researchers found that cows with metritis averaged 4.9 lb/d less milk over the first 120 d of lactation compared to normal herdmates [14]. Kumari et al. (2016) [15] has reported in buffaloes that milk yield decreased by 239 kg for retained fetal membranes, 181 kg for stillbirth, 173 kg for dystocia and 98 kg for metritis during a single lactation. Thus in general, uterine infection in cattle and buffaloes not only affect the production performance but also have an adverse impact on fertility parameters such as days open, number of AI/conception and calving interval. Losses are also incurred due to veterinary and insemination costs, withdrawal period associated with antimicrobial therapy and increased culling rate. Therefore, keeping in view all the above-mentioned facts the following review will try to highlight the impact of uterine infection on production and reproductive performance in dairy animals.

Effect on uterine function
A healthy endometrium is necessary for the nutrition of the blastocyst and embryo, and for the successful establishment of pregnancy. Therefore a healthy uterine environment is regarded as a key to excellent fertility in dairy animals since any sort of insult to endometrium disrupts the normal reproductive functions leading to infertility. Uterine infection with pathogenic bacteria appears to preclude conception [16]. Moreover, there is embryonic mortality if uterine infection occurs with these bacteria after conception [17]. The effect of pathogen-associated molecules on uterine cells is not limited to inflammation, but also affects endocrine function by altering the uterine milieu. Uterine infection is associated with a delay in uterine involution, extend the time until first postpartum estrus, increases the number of services per conception, increases the number of days open and therefore incurs a huge economic drainage to the dairy industry.

Effect on ovarian function
Suppression of folliculogenesis in the ipsilateral ovary decreases as the postpartum interval advances, concurrent with the disappearance of the corpus luteum of previous pregnancy, uterine involution and elimination of the ubiquitous uterine bacterial contamination after parturition [18]. A large healthy estrogenic follicle at the time of ovulation is important for the establishment of a successful pregnancy [19]. Reports have shown that uterine infection causes luteal dysfunction by alteration of luteal cell function, uterine infection also perturbs ovarian follicle growth and function in cows and buffaloes [20]. In animals with uterine infection ovarian follicular waves arise during first few weeks post-calving as follicle stimulating hormone (FSH) concentrations remain unaffected in such animals [21]. However, Karsch et al. (2002) [22] has reported in sheep, that E. coli derived LPS (endotoxin) suppress GnRH and LH release from hypothalamus and pituitary gland respectively, and the sensitivity of the pituitary to the gonadotropin-releasing hormone (GnRH), thereby reducing the ability of dominant follicle to ovulate. Peter et al. (1989) [23] has reported a similar finding from dairy cattle on post administration of LPS, Indeed, LPS or various intermediary cytokines such as interleukin (IL)-1 or tumour necrosis factor (TNFα) blocks GnRH secretion and the pituitary responsiveness to GnRH pulses [24]. Williams et al. (2008) [25] demonstrated that the dominant follicle formed during LPS or TNF α treatment was less likely to ovulate than the control animal. Sheldon and Bromfield, (2011) [20] reported that LPS treated granulosa cells failed to produce estradiol and down-regulated the mRNA of aromatase enzyme, which catalyzes the conversion of androstenedione to estradiol. Cows with uterine diseases have smaller ovarian follicles and lower peripheral plasma estradiol concentrations.

Conclusion
Postpartum uterine infections have a negative impact not only at the ovarian level but also interfere with the functioning of hypothalamus/ pituitary. Animals that are having a uterine infection have slower growth of the dominant follicle, lower plasma circulating level of estrogen, lesser expression of normal heat signs, the lesser sensitivity of pituitary towards positive feedback control of estrogen and are subsequently less likely to ovulate. Further, there is lesser circulating level of progesterone if the affected animals somehow manage to ovulate. Moreover, normal luteolytic activity is disrupted by bacterial agents as they manage to shift endometrial epithelial cell secretion of prostaglandins from F series to E series. In addition, multiple uterine infections are believed to deplete the ovarian follicular reserve. Thus, in general uterine infection incurs a huge economic loss to the dairy farmers by diminishing profitability and sustainability of dairy operations. Therefore, the necessary adaptive measures should be taken so as to mitigate the losses associated with uterine infection.

Conflict of interest
The authors declare that they have competing interests.

References
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