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Review Paper

Features of Uterine Involution in Dairy Animals: A Review

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ABSTRACT

Uterine involution is the process of resumption of pregnant uterus to non pregnant state along with restoration of ovarian function which occurs during puerperium/post-partum period. Estrogen and progesterone hormones are responsible for changes in shape and size of uterus during pregnancy whereas, release of fetus, reduced oxytocin and increased $PGF_{2\alpha}$ help uterus to resume normal state. Fast involution of uterus is essential in order to make cow receptive and conceive again. Though rectal palpation is most commonly used technique for assessing uterine involution in cows but it is less accurate than trans-rectal ultrasonography. Annual incidence of uterine infection in herd has been recorded by different scientists to the extent of 10-50% in cows and 20-75% in buffaloes whereas an anatomical, physiological and phagocytic barriers prevents the uterus from getting infection. Purulent discharge and its odour indicate severity of infection due to pathogenic bacteria under field condition. pH of secretions act as first line defense preventing infection through tract. Poor and delayed uterine involution contributes to poor reproductive efficiency in dairy cattle and it is affected by age, nutritional status, suckling by calves and milk yield of the individual cows, respectively. Rate of uterine involution can be accelerated by using $PGF_{2\alpha}$, methylergometrine maleate, Vitamin E, selenium and cloprostenol injection, respectively. Intrauterine lactobacilli application puts a very positive effect of on involution.

Keywords: Cyclicity, Gravid uterus, Post-partum, Ovarian activity

Process of resumption of pregnant uterus to non pregnant state along with restoration of ovarian function is known as uterine involution which occurs during puerperium/post-partum period. Uterine system though never fully resume to pre-gravid condition especially in primiparous cows (Mutevelic *et al.*, 2003).

The uterus increases in weight and size during pregnancy due to hormones estrogen, progesterone and constant stretching on myometrium due to developing fetus. Even after parturition dam experience regular well coordinated contractions in uterus similar to labour. Uterine contractions decreases slowly after parturition lead to discharge of debris, fluids and compression of vasculature which ultimately resume its shape, size and biometry.

Early necrotic change in septal mass of caruncle leads to constriction of caruncle blood vessels and starts sloughing of necrotic material followed by release of small blood vessels on surface of caruncle. Sloughing of uterus is complete by 2-3 weeks of parturition. Release of fetus, reduced oxytocin and increased $PGF_{2\alpha}$ help uterus to resume normal state. Fast involution of uterus is essential in order to make cow receptive and conceive again.

A phase of sexual serenity of variable length is also observed in cow after parturition which further elongates in suckling or intensively milking

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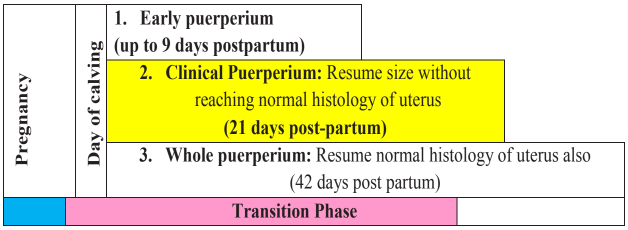
animals. This acyclic period is commonly described as "postpartum anoestrus" which has massive influence on subsequent fertility.

Barriers of uterine infection: Common barriers of uterine infection include: Anatomical barriers like vulva, vagina, vestibule and cervix. Example of physiological barrier is mucus which discharged during the estrus time. Phagocytic barrier composed mainly of neutrophils and non specific inflammatory barrier include acute phase proteins and lactoferrin (Zerbe *et al.*, 2000; Sheldon *et al.*, 2002).

Puerperium: Puerperium is period between calving to complete uterine involution approximately 40 days post-partum in cows. Parturition in cow followed by crucial events like expulsion of fetal membrane, uterine involution, endometrial regeneration, return of ovarian cyclicity and elimination of bacteria (Sheldon, 2004; Sheldon *et al.*, 2008). During this period microorganisms of ambience, skin and faeces are known to infect uterine lumen (Sheldon and Dobson, 2004) while other route of infections are ascension from vagina and blood. Rate of infection increases during first week of postpartum (Griffin *et al.*, 1974), however after a few weeks there is significant reduction in infection and animals get back from infection using their own defense system (Grunert *et al.*, 2005). It is reported that infection reduces to 9% during 46-60 days post partum as compared to 93% on 15th days of post-partum (Elliot *et al.*, 1968). Additionally dystocia, metabolic diseases, retention of fetal membrane etc., is supposed to aggravates the situation (Fonseca *et al.*, 1983). On the basis of endocrine status the puerperium is divided into three stages: 1. Puerperal period (10-12 days postpartum), 2. Intermediate or pre-ovulatory period (12-30 days post-partum) and 3. Post-ovulatory period (30-45 days post-partum).



Uterine involution *vis-a-vis* age, milk yield and nutritional status: Aged cow take more time in involution of uterus as compared to the young primiparous animals (Elmetwally *et al.*, 2016), however, study also reported that age did not affect uterine involution (Moller, 1970).

High milk production delays uterine involution in cows (Izaike *et al.*, 1989) however, milk yield not affect uterine involution was also reported (Fonseca *et al.*, 1983).

Inadequate nutrition before parturition negatively affects post-partum estrus, the effect is pronounced more in heifers as compared to cow (Gutierrez *et al.*, 1997). High fat (Gordon, 1996) and protein in diet leads to over-conditioning in animal which adversely affect the reproduction and uterine status.

Echography of uterine involution

Precise relationship exists between uterine involution and resumption of ovarian activity and puerperal fertility (Aslan *et al.*, 2002).

It is reported that ovarian activity returned to function several days postpartum, while the first follicular wave observed 7-10 days postpartum followed by ovulation of dominant follicle 21-30 days if estradiol concentration is sufficient to trigger LH surge (Beam and Butler, 1999; Crowe, 2008).

Transrectal colour sonography showed definite alteration in uterine blood flow during first four day of calving (Heppelmann *et al.*, 2013). Doppler sonography is supposed to be an ideal non-invasive technique for the objective assessment of uterine involution in cattle. Hajurka *et al.* (2005) reported duration of uterine involution as 23 and 27 days in primiparous and multiparous cows respectively. Similar ultrasongraphic study of postpartum Ongole cows suggest that uterine involution was faster in primiparous as compared to multiparous animals (37.33±1.15 vs. 38.67±1.15 days); moreover, average time of first ovulation was also less in primiparous as compared to multiparous cows (27.67±1.15 vs. 28.33±1.15). Clear cut estrus sign was observed in second postpartum estrus (Sukareksi *et al.*, 2019). Postpartum insemination after three follicular waves tended to have greater pregnancy as compared to two follicular waves (Sakaguchi *et al.*, 2004).

Uterine contractility: The uterine contractility is the process of corrugation of wall of uterus after parturition in order to expel uterine contents like fetal membrane and lochia. Under field condition still drugs like oxytocin and prostaglandins are routinely used for improving uterine contractility in cows.

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Cow possess bicornuate type uterus. As per transmission electron microscopy bovine placenta is epitheliochorial during early pregnancy which progressively modified to sinepitheliochorial at beginning of second trimester (Santos *et al.*, 2017). This type of placenta having six tissues layers between dam and fetus. On the basis of distribution of allantochorionic villi the placenta in cow is classified as cotyledonary type (Noakes *et al.*, 2001a). The allantochorionic membrane makes connection with wall of uterus through villi called cotyledons. These villi interdigitate with crypts of specialized areas of uterine endometrium called caruncles. Cotyledon and caruncle together called placentomes in pregnant uterus. The intercarancular endometrium is not attached actually it is only opposed to the inter-cotyledonary part of fetal membranes therefore separation of fetal parts of placenta only takes place within the placentomes (Bjorkman and Sollen, 1960) due to lose connection and related enzymatic process (Eiler and Hopkins, 1992; Gross and Williams, 1985).

Although uterine contractibility is related with uterine involution, however increased level of uterine activity is also observed in case of retained fetal membrane (Traverne *et al.*, 1979) which suggest strong clue that decrease contractility of uterus is probably not a causal factor for retention of fetal membrane. Additional factors of importance include plasma calcium level which helps in fiber contraction.

Uterine contractility is recorded by electrodes implantation (Gajewski *et al.*, 1999), ballon catheters, telemetric methods and ultrasonography (Cross and Ginther, 1988).

Reduced uterine involution contributes to poor reproductive efficiency in dairy animals. Frequency, duration and strength of uterine contraction during post-partum period hasten involution. Intravenous application of oxytocin provokes strong uterine contraction; $PGF_{2\alpha}$ stimulates uterine activity during early puerperium and ergometrine showed variable responses. Oxytocin and $PGF_{2\alpha}$ are common ecbolic utilized to improve uterine involution though it showed no significant effect on involution and endometritis when applied within 24 hours of parturition in normal cows (Stephen *et al.*, 2019).

Nitric oxide (NO) concentration: Nitric oxide concentration was higher on day of calving in cows (Islam and Kumar, 2015) which suggest its active physiological role in parturition. Nitric oxide supposed to play role in uterine quiescence or reduce contractility during pregnancy (Yallampalli *et al.*, 1998).

Course and characteristics of uterine involution: Uterine involution can be measured by decrease in horn diameter and thickness of wall. Normal cows take 26-52 days to complete the involution (Noakes *et al.*, 2001b; Elmetwally *et al.*, 2016) and cows with abnormal puerperium require more time to complete the process (Cengic *et al.*, 2012).

It was reported that gravid horn after calving reduces in size to halved by days 5 and length halved by 15 days of calving (Roberts, 1986); moreover, weight of uterus decreased from 9.0 kg at the time of parturition to 1.0 kg at 30 days of calving (Gier and Marion, 1968). As far as rate of involution is concerned, it was faster for first three days followed by a decrease during 4-9 days thereafter accelerated changes between 10-14 days and further gradual decrease there after (Morrow, 1986).

Duration of changes during postpartum	**Changes in uterus** (Arthur *et al.*, 1996)
Up to 45 hours	Necrotic changes in septal mass of caruncle of uterus and occlusion of caruncular blood vessels
	↓
Up to 5 days	Sloughing of lochia (necrotic tissues loaded with leucocytes), reddening of discharge due to release of blood from protruding arterioles of caruncle
	↓
Up to 10 days	Sloughing of necrotic tissues continued and liquefaction of discharge observed
	↓
Up to 15 days	Sloughing completed though the surface of bed is rough due to leftover blood vessel
	↓
Up to 19 days	Smooth uterine bed

Dynamics of uterine microbiota *vis-à-vis* involution: Microbiota of Phylum Bacteroidetes and Fusobacteria (*Trueperella pyogenes*) were more prevalent in cows suffering with clinical enodometritis as compared to sub-clinical endometritis and healthy cows (Pascottini *et al.*, 2020).

Increase in count of Bacteroides, Porphyromonas and Fusarium and loss of diversification were associated with endometritis and purulent discharge from genitalia (Bicalho *et al.*, 2017a; Bicalho *et al.*, 2017b).

Postpartum voluntary waiting period (VWP): It is time period between parturition and time at which cow is eligible for insemination, though the farmers decide not to breed cows even if estrus occurs. This period varies from herd to herd but typically lasts for about 50 days. Most important reason for altering the voluntary waiting period is post partum health (50%) followed by effect of season and milk yield (Dejarnette *et al.*, 2007). VWP longer than 6 weeks puts farm under economic debt (Inchaisri *et al.*, 2011). Selecting VWP for cows is supposed to increase conception rate (Tenhagen *et al.*, 2003). Use of VWP along with synchronized breeding and timed artificial insemination leads to improvement in dairy herd (Miller *et al.*, 2007).

Uterine discharge and its scoring: Health status of uterus in field condition is evaluated on the basis of vaginal discharge. Purulent secretion and its odour indicate severity of infection due to pathogenic bacteria (Williams *et al.*, 2005).

Concept of discharge scoring was given by Sheldon *et al.*, 2006.

Vaginal discharge score	Description
1.0	Clear or translucent mucus
2.0	Mucus containing white or nearly white pus
3.0	Discharge contains <50% purulent material
4.0	Discharge contains ≥50% purulent material
5.0	Score 4.0 along with strong unpleasant smell

Endometritis score: Cervical mucus is scored for character and odour as per description. Two scored are summed to give the overall endometritis score.

Discharge	Description	Score
Cervical mucus character	Clear or translucent	0
	Clear or translucent mucus with flecks of white pus	1
	<50 ml exudates with <50% white cream pus	2
	>50 ml exudates containing ≥50% white, cream or bloody pus	3
Mucus odor	No unpleasant odour	0
	Fetid odour	3

Uterine discharge score and *uterine D-index* was also given by Gorzecka *et al.*, (2011). They reported that uterine index was delayed in cows with high D-index.

Uterine involution was significantly delayed in the high-D-index group of cows.

Discharge features	Score				
	0	1.0	2.0	3.0	4.0
Proportion of pus	No	Flecks	≤50%	>50%	—
Amount	No	<1 handful	1 handful	>1 handful	—
Consistency	No	Watery	Semi-viscous	Mucus like	Dense
Smell	No	Yes	—	—	—
Colour	No	Pink	Red	Brown	Black

Tract pH: The pH of secretions has been recognized as primary defense mechanism preventing infection through tract (Granato, 2003). Variation in vaginal pH may act as predisposing factor for infection like bovine necrotic vulvo-vaginitis (Blum *et al.*, 2008).

Cows in second parity and above showed more acidic (7.35) vaginal pH as compared to primiparous cows (7.48) and heifers (7.58) and this difference supposed to increase susceptibility of heifers to tract infection (Beckwith-Cohen *et al.*, 2012). High vaginal pH value and lowest level of progesterone occurred during estrus might be used for timed AI in small ruminants (Sitaresmi *et al.*, 2018).

Rectal palpation to evaluate status of uterine involution: Though rectal palpation is most commonly used technique for assessing uterine involution in cow, it is less accurate than trans-rectal ultrasonography due to its high level of individual variation (Usmani and Lewis, 1984; Wishy and Ghoneim, 1995; Sheldon and Dobson, 2000; Ramoun *et al.*, 2019). Prerequisite of rectal palpation include palpation by same examiner beginning on at least third day post-partum. Uterine involution considered complete when diameter of base of two uterine horns is nearly symmetrical and no further change in horn diameter could be detected during two successive palpation of uterus (Kask *et al.*, 2000); Moreover, cervix narrowed quickly and restrict hand insertion 10-12 hours and permits just two fingers by 96 hours of calving (Arthur *et al.*, 1996).

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During the process of involution diameter of cervix was 15 cm on 2nd day, 7-8 cm on 30th day, 5-6 cm on 60th day and completely involuted when cervical diameter 3.0 cm anterior to external OS (Okano and Tomizuka, 1987).

Effect of nutrition and cow body condition score (BCS) on uterine status: Body condition of animals can give a clue to energy reserve available to the animals for future use (Edmonson, 1989). As the cow enters into transition phase (21 days before to 21 days after parturition) she undergoes a physiological shift marked by increased energy demand to meet milk production and fetal development associated with reduced feed intake which leads to negative energy balance (Paiano *et al.*, 2018), depressed immune system and metabolic disease ultimately affecting reproductive efficiency in animals.

During post-partum period there is an increase in nutrient requirements with three folds for glucose and two folds for amino acids, this increase comes at a time of weakest ingestion ability and as a result negative energy balance is common during early lactation (Salat, 2005) which forces to mobilize body reserves (Drackley *et al*., 2001).

Cow with metabolic diseases spends more time in uterine involution as compared to normal healthy animals (Paiano *et al.,* 2019). Increased body condition at parturition using grain feeding improves reproductive traits like uterine involution, pregnancy rate and ovarian follicle status (Laflamme and Connor, 1992). Weight gain in cows is related to combination of body condition at calving and good management condition during postpartum period (Richards *et al*., 1986).

Cows with lower BCS at parturition showed significantly ($p<0.05$) high serum phosphorus (88.015 vs. 63.757 mg/l) and creatinine (15.415 vs. 9.797mg/l) as compared to the cow with high BCS level. High level of phosphorus in lean cow is supposed to be a protective adaptation in cow to ensure smooth uterine involution (Bouhroum *et al.,* 2013). Similarly Jilek *et al*. 2008 reported a significant effect of BCS at calving on reproductive performance, whereas, Waltner *et al*. (1993), Gillund *et al*. (2001) and Buckley *et al*. (2003) reported absence of any remarkable effect.

Effect of supplementation of dietary minerals and vitamins: During post-partum period immune suppression commonly seen in cows which noticeably affect dairy industry with respect to its economics due to slower uterine involution along with production loss (Resum *et al.,* 2017). Vitamin E is commonly used cellular antioxidant which interacts with Glutathione peroxidase of selenium and prevents the oxidative breakdown of tissue membranes.

Uterine involution was faster (28.78±1.40 vs. 34.22±2.17 days) in Murrah buffaloes supplemented with vitamin E and minerals (Khan *et al.,* 2015). Positive effect of vitamin E supplementation of uterine involution was also reported by Gamit (2014) in Surti buffaloes.

Endocrine aspects of involution of uterus

During the period of postpartum involution of uterus occur together with release of $PGF_{2\alpha}$, moreover, the duration of its release are negatively correlated with uterine involution (Kindahl *et al.,* 2007).

Uterine involution vs. fertility

Uterine involution act as barriers of fertility up to 5-6 weeks postpartum in cows (Kiracofe, 1980).

Quantification of uterine dimension during involution: Diameter of uterine horn reduces after parturition as per table (Morrow *et al.,* 1986).

Days of postpartum	Diameter of uterine horn (cm)
4-9 days	12.0 -14.0
by day 14	7.0
by day 25	2.0 - 4.0

The mean size of horn and cervix of buffaloes on day 27 (4.09±0.09 and 3.56±0.08 cm) decreased significantly as compared to day 6 postpartum (9.07±0.74 and 8.58±0.00 cm). Follicles in 50% of the buffaloes ovulated within 24 to 54 days post-partum and remaining 50 percent of animals ovulated after 65 days postpartum (Lohan *et al.,* 2004).

Normal vs. abnormal uterine involution: Cows with usual puerperium completed involution 38-45 days and with abnormal puerperium require more time to complete it or require additional therapy for the purpose (Cengic *et al.,* 2012).

Uterine infection and endometritis affect involution: Annual incidence of uterine infection in herd is 10-50% in cows and 20-75% in buffaloes (Lewis, 1997; Usmani *et al.*, 2001). Uterine infection reduces reproductive efficiency of livestock (Lewis, 1997). Initial colonizing bacteria in uterus were not known specifically, though some common bacteria were isolated from infected uterus such as *Arcanobacterium pyogenes* and *Escherichia coli* (Griffin *et al.*, 1974). Bovine herpes virus-4 is common virus infecting and causing cytopathic effect in endometrial cells. Elimination of pathogen by innate immune system is possible by recognizing receptors binding pathogen associated molecules. Toll-like receptor-4 on uterine epithelium and stromal cells binds with *E. coli* lipopolysaccaride (Sheldon *et al.*, 2008).

Eicosanoids like $PGF_{2\alpha}$ and leukotriene-B4 (LTB_4) are associated with improved uterine immune response. $PGF_{2\alpha}$ is a pro-inflammatory agent which stimulates the production of various cytokines and leukotriene-B_4 (LTB_4) in order to enhance phagocytosis and lymphocyte functions (Lewis, 2003).

Immunology of uterine infection: Immune function of the endometrium of cow after parturition is influenced by the metabolism and serum progesterone level. During post-partum period neutrophil is first cell to enter in uterine lumen defense. Increased level of triacylglycerols and metabolic disease in cow leads to reduced cytotoxic activity of neutrophils predisposing the uterus to infection (Zerbe *et al.*, 2000). High progesterone level reduces $PGF_{2\alpha}$ and lymphocyte proliferation which suppresses immune response making uterus susceptible to infection (Lewis, 2003).

Pyometra: Abnormal parturition like twin-birth, dystocia, premature birth, retained placenta etc. culminates into pyometra. Uterine walls appear thicker on palpation in case of pyometra. Uterus is doughy, allantochorion membrane not show sleeping feels along with absence of caruncle and fremitus. Pyometra is common type of uterine infection characterized by accumulation of purulent or muco-purulent content in lumen in presence of corpus luteum (CL), interruption of estrous cycle and associated with reduced reproductive efficiency in cattle (Lewis, 1997). Bacteria reaches uterus and resides there without increasing number until luteal phase down regulates immune function of cow and infection usually persist unless luteolyis. Post service pyometra is also reported in cows due to infection of flagellate protozoan (*Trichomonas foetus*) which colonizes in uterus and leads to early embryonic mortality (Praveen *et al.*, 2015).

Types of pyometra: (1) Open pyometra: Discharge of pus from vulva due to open cervix, this condition is easier and safer to treat. (2) Close pyometra: In this condition cervix is fully closed, discharge is totally absent from vulva.

Uterine stimulant and Ecbolic therapy: Poor uterine involution contributes to poor reproductive efficiency in dairy cattle (Salasel and Mokhtari, 2011; Thatcher *et al.*, 2006). Stimulants and therapy which increases the frequency, strength and duration of uterine contraction during postpartum period believed to enhance uterine involution (Barrett *et al.*, 2009). However, combination of oxytocin and $PGF_{2\alpha}$ not at all showed significant effect on uterine involution when used during first week of postpartum (Stephen *et al.*, 2019).

Use of NSAID in addition to antibiotics did not improve inflammatory parameters or elimination of bacteria and ultimately the clinical cure in case of cow with puerperal and clinical metritis (Jeremejeva *et al.*, 2012).

Rate of uterine involution is accelerated by using $PGF_{2\alpha}$ by 6-13 days (Kindahl *et al.*, 1982); moreover, uterine health in terms of tonicity of uterus, reduced incidence of endometritis and reduced time of conception in cows can be promoted by weekly postpartum (Three i/m injection on 7, 14, 21d postpartum), $PGF_{2\alpha}$ protocol (Yu *et al.*, 2016). By improving dose rate twice of normal luteolysis showed positive effect on involution of uterus and reduced repeat breeding syndrome (Salasel and Mokhtari, 2011). Similar finding was also reported by (Melendez *et al.*, 2004). Administration of $PGF_{2\alpha}$ during fresh period has been shown to have favourable effect on fertility including uterine health. Similarly Patel *et al.* (2016) used $PGF_{2\alpha}$ after calving in cows resume ovarian activity and induced postpartum estrus earlier due to its luteolytic effect.

Some of the researchers were not able to get significant effect of treatment of $PGF_{2\alpha}$ and oxytocin (Stephen *et al.*, 2019).

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Use of Methylergometrine maleate and Cloprostenol

Alagar *et al.* (2016) used methylergometrine maleate during post-partum period effectively hastened the uterine involution rate in HF cross bred cow. Uterine involution was significantly faster in crossbred cows injected with vitamin E, selenium and cloprostenol as compared to control (Resum *et al.*, 2018).

Subclinical endometritis

Uterine health of cow is compromised due to infections in lumen due to bacteria which lead to sub-fertility related with disturbed hypothalamus, pituitary and ovary. Bacterial components in uterus prevent LH surge, ovulation and postpartum dominant follicle has a slower growth rate. Examination of vaginal secretion and its scoring is helpful in detection of endometritis (Sheldon and Dobson, 2004).

Subclinical endometritis associated with distinct mRNA expression i.e., transcript immune factors C3, C2, LTF, PF4 and TRAPPC13 were up regulated in suffering cows 445-55 days after calving in both blood and endometrium (Raliou *et al*., 2019).

Uterine involution affects hormonal and blood biochemical profile: The values of glucose (61.15±3.70 vs. 41.54±3.90 g/L) and triglyceride (97.64±6.50 vs. 68.49±8.40 mg/L) were higher (P=0.057) in pregnant as compared to non pregnant Egyptian buffaloes. Estrogen and progesterone level was also higher in pregnant as compared to non-pregnant buffaloes though it was not significantly different (Hussein *et al.*, 2013). Total cholesterol concentration (138.78±9.73 vs. 76.47±4.82 mg/dL) along with progesterone, estrogen, T3 and T4 hormones were significantly higher ($P<0.05$) in normal buffaloes with proper involution of uterus as compared to anestrus buffaloes (Hafez, 2019).

Uterine involution vs. serum mineral profile

Serum phosphorus and zinc was significantly higher in normal buffaloes with proper involution of uterus as compared to anestrus buffaloes (Hafez, 2019).

Placentophagia affect uterine involution

Placentophagia, is a unique maternal and ingestive behavior in cow where cow use to eat not only placenta and cord but amniotic fluid as well. Placentophagia produces beneficial effect with respect to mother young interaction, reproductive competence, protection against predators, and immunological protection to mother or young (Kristal, 1980).

Advantages of placentophagia

(i) It is essential behaviour in cow to create hygienic environment.

(ii) Reduces the odour; which, attracts predators (Lehrman, 1961).

(iii) Replenishes nutrient loss during pregnancy.

(iv) Help dam to acquire additional hormones.

(v) It increases the dam-calf contact, bonding and caretaking behaviour (Kristal, 2009).

(vi) Boosts endogenous opioid production to improve maternal behaviour and alleviate labour pain.

Proteolytic enzyme and furazone on uterine involution: Proteolytic enzyme infusion intrauterine (trypsin, chymotrypsin and papain in 20 ml normal saline) reduced inflammation and days in non pregnancy in subclinical endometritic buffaloes (Singh *et al.*, 2020). Nitrofurazone combined with proteolytic enzyme had better effect on involution of uterus (Homan, 1967).

Suckling stimulus on uterine involution: Postpartum cyclicity and ovulation are delayed in suckling animals and conception is also delayed (Usmani *et al.*, 1985), said effect is pronounced in high yielders (Rao *et al.*, 1997). Suckling noticeably lengthens involution of uterus particularly in undernourished animals with poor body condition (Jolly *et al.*, 1995).

Administration of lactobacilli intrauterine: Administration of lactobacilli intrauterine post-partum improved reproductive performance in cow (Peter *et al.*, 2018); moreover, it is also reported that pre-calving intra-vaginal administration of lactic acid bacteria reduces metritis and also regulates blood neutrophil gene expression after calving (Genis *et al.*, 2018).

Conscientious study of topic conclude that resumption of ovarian activity has positive effect on uterine involution which decreases days open and service per conception. Post-partum description may provide a good predictor of fertility status in dairy animals accordingly management steps may be planned to improve herd health.

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