Fetal Membranes and Associated Complications in Dairy Animals: A Review

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ABSTRACT

Fetal membrane is temporary organ that feeds the fetus intrauterine. It also permits transfer of oxygen and nutrients from mother to fetus and release of carbon dioxide and waste products from fetus. Placenta is partly maternal and partly embryonic in origin. Actual mixing of maternal and fetal blood is not possible due to placental membrane. After conception uterine contraction and tonicity decreases to retain blastocyst *in situ* position in uterus. Protein factors like blastokinin, trophoblastin has role in maternal recognition of pregnancy (MRP). Placenta of dairy animals is polycotyledonary and non-deciduate type. Prevention of RFM includes reducing stress, improving comfort and balance ration during transition period. Proper exercise, Vitamins (Vitamin A, E and Selenium), minerals along with infection control are common factors which control post-parturient problems including retention of placenta. Use of ecbolic, collagenase, antibiotics, herbal preparation and hormones are common practice used by farmers and farms with very positive effect i.e., reducing infertility.

Keywords: Conceptus, Feeding, Infertility, Placenta, Retention

A flattened circular temporary vascular organ comprised of veins and tissues in uterus of pregnant eutharian mammals associated with the developing and nourishing fetus in other words temporary organ that feeds the fetus intrauterine. Blending of fetal membrane to uterine endometrium in order to permit transfer oxygen and nutrients from mother to fetus and also permitting release of carbon dioxide and waste product from fetus. Placenta is partly maternal and partly embryonic in origin. There is no actual mixing of maternal and fetal blood as placental membrane separates maternal and fetal blood. Both nutrients and gases like CO_2 and O_2 some viruses, drugs and RBC antigens can pass across membrane through diffusion to reach conceptus. Actually fetal and maternal blood never mix within placenta actually exchange of nutrients and essential gases.

The placenta function as feto-maternal organ with two components i.e., fetal part of placenta is "chorion frondosum" develops from same blastocyst that forms the fetus and the maternal component of placenta is "decidua basalis" develops from maternal uterine tissues.

The four extra-embryonic layers which form the fetal membrane is amnion, chorion, allantois and yolk sac. Amnion and chorion together form amniotic sac which surround and protects the

fetus. Amniotic sac formed by extra-embryonic mesoderm and two layers of trophoblast that surrounds the embryo and other membranes. Innermost layer surrounding the fetus is called amnion. The allantois is the middle layer of the placenta (derived from embryonic hindgut); blood vessels originating from the umbilicus traverse this membrane.

The chorionic villi present on outer surface of chorion; invade the endometrium and accordingly allow the transfer of nutrients from maternal to fetal blood. Chorion composed of two layers of cells inner cytotrophoblast and outer syncytiotrophoblast. The chorion and allantois fuse to form the chorioallantoic membrane.

The allantois becomes the urachus which connects the fetal bladder to yolk sac. The urachus removes nitrogenous waste from the fetal bladder.

Yolk sac responsible for initial circulation and in-charge of delivering nutrients via primitive aorta to the developing embryo through a process called vitteline circulation.

Changes before implantation/attachment of fetus

Following changes are reported for the development of conceptus and maintenance of pregnancy:

- ❒ Decrease uterine contraction and tonicity, which retain blastocyst *in situ* position in uterus.

- ❒ Increase blood supply to the uterus to ensure nutrition of conceptus

- ❒ Increase in amino acid and protein concentration for nutrition.

- ❒ Degradation of high molecular weight substance like carbohydrate and protein into low molecular

weight substance in uterus. The material along with cellular debris and extravagated leukocytes in the uterine lumen form histotroph i.e., uterine milk to provide nutrition.

- ❒ Production of certain protein fraction i.e., blastokinin or utero-globulin or trophoblastin which has role in maternal recognition of pregnancy (MRP).

Implantation/attachment

Implantation in dairy animals is superficial, non-invasive type which involves apposition and adhesion phases of trophoblast and uterine epithelial cells. The cleaved zygote passes through the fallopian tube into the uterus, after short period of free life it begins to adhere to the uterine endometrium. This is followed by attachment and formation of placental connection from mixing of fetal-maternal tissues. There is close attachment between embryonic membranes and the endometrium overlying caruncle at the age of 5 weeks in cattle followed by development of placenta shortly. Fetus and fetal placenta together form conceptus (Eurell and Frapier, 2006). The formation of attachment of the fetal membrane to the endometrium is known as placentation. During the period of development, conceptus is nourished by its own yolk substrate, oviductal fluid and uterine milk. After synthesis of placenta, maintenance and growth of embryo takes place through it. Term implantation is more appropriate in those species in which embryo becomes buried in wall of uterus like rodent and primates.

Development of placenta

Placenta was epitheliochorial type in early pregnancy, becoming progressively

Species	Maternal recognition of pregnancy (MRP)	Beginning of attachment	Attachment completes	Gross form of placenta	Histological type of placenta	Separation type
Cattle	16-17 days	28-32 days	40-45 days	Cotyledonary	Epitheliochorial type	Semi-deciduate

sinepitheliochorial at the beginning of second trimester. At the end of pregnancy there were clear cut signs of cell degeneration in both trophoblast and uterine epithelium. Interdigitation between surface of trophoblast and the uterine epithelium is common throughout pregnancy; however, at the end interdigitation disappear favouring parturition and detachment of fetal membranes (Santos *et al.,* 2017). Placental size and quantity of fetal fluid increase throughout the pregnancy but not in constant proportion. The fetal fluid averages about 5 litres at 5 months and 20 litres at end of pregnancy. Sharp rise in volume was observed during 40-65 days (allantoic growth) followed by 3-4 (amniotic growth) and finally on 6.5-7.5 months (allantoic growth). The allantoic fluid is watery or like urine throughout the gestation; however, amniotic fluid is become mucoid during last one third of pregnancy. This changes during last one third of pregnancy in fluid of amnion helps in lubricating tract and fetus at the time of parturition (Noakes *et al.*, 2001a). At the time of parturition the allantoic sac forms the first and the amnion the second water bag. Allantochorion is comparatively thicker and tougher as compared to transparent amnion.

Placentome of cattle provided with stalk during development where as placentome of buffaloes is sessile dome shaped with simple, slightly conical villi branching less than cattle (Schmidt, 2006). Placental estrogen and progesterone control caruncular growth along with its differentiation and functions (Hoffmann and Schuler, 2002).

Vascular supply to the Placenta

Release of blood to the placenta is a direct result of angiogenesis that take place, which facilitates the placenta to perform through gestation. During second half of gestation, when 75% of total fetal growth takes place, there is an exponential increase in umbilical blood flow. Uterine blood flow increases 4.5 fold (2.92-13.181/min) and umbilical blood flow increases 21-fold (0.28-5.861/min) during the last half of

pregnancy in cow (Meschia, 1983; Reynolds *et al.,* 1986).

Uterine artery and anastomoses from ovarian and vaginal arteries supply oxygenated blood to placenta. The arteries are enlarged and modified during the course of pregnancy and their capillaries have a diffuse or localized distribution or lose their endothelium to form blood spaces. The uterine placenta drained by satellite veins (Eurell and Frapier, 2006). The allantoic placenta gets blood from paired umbilical arteries, from caudal part of aorta, and returns oxygenated blood through the umbilical veins. The left umbilical vein carries blood to the heart via the liver; the right vein undergoes involution within the fetus.

Vascular supply of placenta- potential therapeutic target

Placental blood flow and vascular development are essential components of normal placental function along with fetal growth. If fetal or placental growth or both are impaired, utero-placental blood flow are reduced. Treatments which increase potential blood flow (nitric oxide, arginine and citrulline) can rescue fetal growth that was reduced due to low maternal dietary intake (Reynolds *et al.,* 2006). Heat stress causes decrease in uterine blood flow, reducing supply of nutrients required for development of gravid uterine tissue may also be manipulated using therapeutic agents (Reynolds *et al.,* 1985).

Maternal nutrition restriction influences the capillary vascularity, angiogenic profile and vascular function of the placenta in cattle therapy augment placental nutrient transport capacity and improve performance of offspring, hormone *indolamines* supplementation during the time of nutrient restriction may improve placental activity (Vonnahme and Lemley, 2011).

Gross Anatomy of placenta

Placenta of dairy animals are polycotyledonary

i.e., numerous smaller placentae. Placentation in dairy animals described in terms of:

Cotyledon: The fetal part of placenta

Caruncle: The maternal part of placenta

Placentome: A cotyledon and caruncle together.

Caruncle is oval or round thickening in uterine mucosa resulting from proliferation of sub-epithelial connective tissues. Moreover, these are the actual site in uterus to form connection with fetal membranes. Patches of chorioallantoic membrane become cotyledons by developing villi that extend into the crypts of caruncular epithelium. Placentomes are round, ovid or irregular shape and arranged in four rows along the center of uterine horn. Distribution of placentome near tip is irregular. Most advanced placentome is placed near center of pregnanat uterine horn. Placentomes are sessile in buffaloes and stalked in cattle, dome shaped maternal or uterine caruncle come in contact with the corresponding fetal cotyledon. Cattles have a single fetus located in one horn or the other, the large chorioallantois fills both uterine horns and placentomes are present throughout the uterus.

Placenta of Dairy animals

In viviparous animals the fetal membranes become apposed to uterine tissues forming placenta, which function as organ of exchange. The distribution of villi on fetal chorion grouped into multiple circumscribed areas called cotyledonary type. Placenta can also be classified on the basis of degree of proximity of the maternal and fetal blood circulations (Grossers, 1909). Said classification is based on phagocytic property of trophoblast or chorionic epithelium that may be exerted on tissues with which it comes in contact. Placenta of cow in this system is _syndepithelialchorial_ type (Wooding, 1992). Just after embryonic attachment a syncytium is formed on the maternal side of the placentome by the fusion of binucleated cells derived from the trophectoderm and the endometrium.

Morphological features of fetal membranes

Weight (Kg)	Length (cm)	Width (cm)	No. of cotyledons	Time of expulsion of fetal membrane (min.)	Animal types	References
3.47	172	31	115	242	Swamp buffaloes	Bhuyan _et al._ 2016
4.6	146	43	114	228	Swamp buffaloes	Das _et al._ 2008
—	—	—	80-120	Within 720	Cattle	Bowen, 2000

*Similar morphological features were also reported in riverine (Bhosrekar and Sharma, 1972; Sharma _et al_., 1979) and swamp buffaloes (Tulloh and Holmes, 1992) at different places. In yak morphological features of placenta include weight 1.6 kg, total number of cotyledon 72 and total area of cotyledon 1494 cm^2 (Mohanty _et al.,_ 2002).

Microscopic structure of placenta

Common feature of placenta of dairy animals include presence of large number of bi-nucleate cells. These cells arise as part of the fetal trophoblast from cells; fail to go through cytokinesis following nuclear division. Cells again fuse with caruncular epithelial cells to form small syncytia. Binucleate cells secrete the hormone placental lactogen. Placenta of cattle and buffaloes is actually epitheliochorial type. However, due to the modification of uterine epithelium by incursion and fusion of binucleate cells, its structure is referred to as synepitheliochorial. Before detailed study of placenta, it was believed that maternal epithelium was eroded away, leaving trophoblast in contact with maternal connective tissue. Term syndesmochorial was used to describe this apparent structure and is used in old literature discussing the placenta of ruminants.

Functions of Placenta

1. Fetal gut: It helps in exchange nutrients between maternal and fetal unit.

2. Fetal lung provide gas exchange for fetus with O_2 coming in and CO_2 going out.

3. Fetal kidney: Work in order to removes waste.

4. Fetal liver: Serve as detoxification system and also filter channel for the fetus.

5. Endocrine function: Different hormones especially progesterone are produced from placenta in order to maintain pregnancy.

6. Temperature regulation: It maintains a temperature slightly above dam's internal temperature.

7. Protection: The fluid contained within placenta work as a protective surrounding for the delicate and growing fetus.

Mechanism of placental detachment in cattle

During calving there is considerable loosening of the cotyledonary villi from caruncles and placentome generally expands laterally. After calving there is loss of fetal circulation to the cotyledons, accordingly capillaries within the villi collapse, leading to decrease in their size. The uterus contract and caruncle shrink, which further enhances separation of cotyledon and caruncles. As there is no significant loss of maternal tissues during the parturition time, the placentation in dairy animal is considered as non-deciduate type (Bowen, 2000).

Placenta of dairy animals is cotyledonary type formed by fetal cotyledon and maternal caruncle to form placentomes. Placental estrogen and progesterone are important factors controlling caruncular function, growth and its differentiation (Hoffman and Schuller, 2002). Collagens are enriched at the connecting sites, which plays a very crucial role for separation of caruncle and cotyledon at the time of expulsion of fetal membrane (Eiler and Hopkins, 1993).

Declining progesterone due to luteolysis and high concentration of relaxin results in increased collagenase activity ultimately leads to softening of cervix, relaxation of pelvic ligaments and detachment of cotyledon and caruncle (Maj and Kankofer, 1997). Increased collagenase activity is also preconditioned by:

1. Increase leucocyte and cytokines reactivity to chemotactic stimuli as a result of development or maternal immunological recognition of fetal MHC (Major histocompatibility complex) class-1 molecules helps in fetal membrane separation and calving, these molecules are absent during early pregnancy. Blood leukocytes and neutrophils of cows with retained placenta are less reactive to chemotactic stimuli as compared to cows with normal placental separation.

2. Maturation of fetal MAO (Monamine oxydase) enzyme system leads to decreased serotonin level (Fecteau and Eiler, 2001).

Placental transport

Placenta of dairy animals like cattle and buffaloes are unique in the sense that immunoglobulins are not transported across the placenta from the mother to the fetus, therefore calves are born without circulating antibodies in their blood. Therefore colostrums which rich in antibody required to be fed in calf as early possible in order to develop passive immunity in calf.

Placental endocrinology

The major hormones of cattle and buffaloes placentae are progesterone and other progestins, estrogens and placental lactogens. Luteal progesterone is essential throughout the gestation in cattles and buffaloes because their placentae secrete smaller quantities of progesterone. Placental lactogen is detected in maternal serum at about 4 months of gestation and remain low through parturition (Bowen, 2000). Hormone progesterone remains high level during the whole pregnancy originating and released from corpus luteum, maternal adrenal and placenta. Oestrone sulphate show elevated

level from mid pregnancy until expulsion of fetal membrane. For onset of normal parturition, change of hormone progesterone to oestrone sulphate is crucial. Increasing level of oestrone are time related to increasing synthesis of prostaglandins (PGF2α) causing prepartum luteolysis followed by action of several hormones involved in labour process such as cortisol and oxytocin. The level of pregnancy associated glycoproteins (PAGs) originating from the trophoblast binucleate cells increasing during last ten days before parturition is very good indication of normal parturition in cattle (Kindahl *et al.* 2002).

Placentophagia

Placentophagia is commonly seen in cow to remove smell to avoid predators towards her and very young vulnerable calf under natural settings. Placentophagia is due to natural instinct of cow. Placentophagia is positive and good with respect to maintaining balance in hormone concentration of dam; however, many farmers discourage it due to fear of choking. Placenta is calcium dense food that is difficult for the cow to digest. Placentophagia sometimes related to severe indigestion in newly calved cows.

Umbilical cord

It is connecting stalk between fetus and placenta. It consists of two umbilical arteries, two umbilical veins, the urachus and vestige of yolk sac. Amnion is reflected on the surface of the umbilical cord. In cattle and buffaloes the cord is short and breaks as the calf enter into the birth canal. Length of umbilical cord in cow at the time of birth is 30-40 cm (Mc Geady *et al.,* 2006). Ruptured umbilical arteries retract within the abdomen due to recoil of elastic fiber in the wall of their lamina thus preventing the hemorrhage; however umbilical vein remain open for some time as they lack elastic tissues in their wall. Open vein sometimes allow entry of bacteria leading to joint ill cases in calf.

Retention of fetal membrane (RFM)

Normal time of expulsion of fetal membrane is 0.5 to 8 hours after parturition in cattle and buffaloes (Roberts, 1982). RFM is defined as failure to expel fetal membrane within 24 hours of parturition (Takagi *et al.,* 2002); normally expulsion of fetal membrane occurs within 3-8 hours after calving. Placental detachment rather than uterine motility is responsible for retention of fetal membrane. Lack of uterine motility plays little or no role in incidence of RFM. Moreover, cows with RFM have normal or increased uterine activity in the days after calving (Frazer, 2005).

Types of RFM (Patel and Parmar, 2016):

1. **Primary retention:** Primary retention of fetal membrane results from lack of detachment from the maternal caruncles.

2. **Secondary retention:** It is related to mechanical difficulty in expelling fetal membrane which detached normally.

Retention of fetal membrane affects health, milk production and reproductive efficiency in herd (Sundals *et al.*, 1979). RFM significantly increases post partum first estrus, services per conception, days open and calving interval as compared to cows with normal placental release (Hossain *et al.*, 2015).

Incidence

The incidence of RFM generally varies from 4.0 to 16.0%. If rate of RFM incidence is more than 10% in herd, we need to cautiously look into the problem. Incidence up to 30% is also reported associated with under nutrition (Gupta *et al.*, 1999). Under natural mating incidence of post-partum reproductive disorder was lower as compared to artificial insemination system and buffaloes are more prone as compared to crossbred cow with respect to postpartum reproductive disorders (Khan *et al.,* 2012).

Signs of RFM

Common sign of RFM include fetal membrane hanging from vulva, decreased appetite, arched back with straining, dysurea, decreased milk production (Noakes *et al.*, 2001b), Sign of secondary infection including fever, inappetance, depression and foul smelling discharge from vagina. Large pieces of tissues coming from placenta, profuse bleeding and continuous pain are pertinent indication.

Retention of fetal membrane may sometimes lead to "clinical metritis" characterized by fever, foul fetid vulvar discharge, uterus with excess fluid and lacking tone along with prostration and off fed condition. Clinical metritis is commonly seen during first ten days post-calving.

Etiology of RFM

1. Mechanical factors: Male calf due to large size, Dystocia, abortion (Joosten *et al.* 1987), twin parturition, fetotomy, still birth, Lengthening or shortening gestation length (Muller and Owens, 1974), uterine torsion, induction of parturition using steroids, PGF2α etc.

2. Nutritional factors: Mineral and vitamin deficiency especially Vitamin E (Bourne *et al.* 2007), Higher risk of RFM in cows was observed due to lower circulating Vitamin E concentration in blood (Le Blanc *et al.,* 2004). Selenium and Vitamin A, Low level of calcium in blood. Staples *et al.* (2005) reported that Vitamin A (@ 110 IU/Kg body weight) and Vitamin E (1.6 IU and 0.8 IU/Kg body weight pre and post partum cow respectively) may improve the immune status of transition cows there by reduce incidence of mastitis and retained fetal membrane, which in turn may increase pregnancy rates, where plasma concentration of α-tocopherol are < 3.0 to 3.5 ug/ml.

3. Managemental factors: Managemental factors include Stress and obesity in animals. Stressful situation should strictly be avoided during the close up period such as pen movement, change in diet, noise and overcrowding. It is essential to provide cool, comfortable environment especially during transition period or as per necessary requirement.

4. Infectious disease: Brucellosis, leptospirosis, vibriosis, listeriosis, IBR, BVD etc.

5. Hormone imbalance and immunity: Decreased leucocytes number and activity especially neutrophil (Kimura *et al.* 2002), decreased estrogen level and SOD, use of NSAID.

Incidence of RFM was more in crossbred as compared to local cows (Hossain *et al.*, 2015). Sharma *et al.* (2017) reported that the incidence of RFM increases with increase in parity and age of animals; moreover, the retention of placenta was higher during spring (29.20%) and summer (27.72%) as compared to autumn season (20.94%).

Body condition scoring (BCS)

Changes in BCS should be minimized. Excess gain in body weight during dry period is common; therefore energy intake should be monitored in order to avoid excess gain in body condition. Moreover, during the close up period, the drop in feed intake may result in undesirable loss in body condition. Therefore easy access to fresh, palatable food is imperative. Le Blanc *et al.* (2004) reported that cows with a greater degree of negative energy balance indicated by higher plasma NEFA concentration were 80% more likely to suffer from RFM. Rasby *et al.* (1990) reported that cow with low or thin BCS had greater cotyledonary weight as compared to cow with moderate BCS; however, cow with low BCS produces more placental hormones.

Quality of feed and fodders

Feed and fodders contaminated with molds and fungal toxins impair the cow's immune system.

Spoiled materials should strictly be discarded and never fed to cows. During summer season, close-up cows should be fed at least two times a day to avoid TMR heating at feed bunk.

Histopathological changes in RFM

Histological section of retained placenta show coagulative necrosis in fetal membrane, infiltration and proliferation of macrophages and binucleated cells, desquamation of syncytiotrophoblast. Section of RFM also revealed dystrophic calfication along with fatty infiltration (Al-Kennany *et al.* 2010).

Manual handling of RFM

In case of RFM manual removal of placenta is common practice in field condition though manual removal of fetal membrane is not advised. If it is essential, manual removal of retained fetal membrane should be practiced under prior use of sedatives and analgesics.

During early postpartum, the uterine wall are thin and fragile, therefore manipulation of uterus may cause harm to the cows. Trimming out fetal membranes may decrease dirt caught by fetal membrane from beddings of calving pen; conversely, the pulling force of the fetal membranes will be reduced which may further enhance the chances of fetal membrane retention (Silva del Rio, 2010).

The cows should not be treated if she is not sick, as fetal membranes normally drop within a week by putrefactive degradation of bacteria.

Blood profiles and oxidative stress

Blood picture of buffalo with RFM showed anaemia along with leucocytosis, lymphopenia and monocytosis. Oxidative stress is a contributory factor to disease susceptibility in cow (Miller *et al.* 1993). As demand of metabolites during transition phase rises to increase reactive oxygen species i.e., ROS (Sordillo, 2005). RFM was observed to be associated with oxidative stress in dairy cows (Kankofer, 2005). Oxidative stress was also commonly associated with increase in plasma malondialdehyde (2.27 ± 0.44 vs. 0.98 ± 0.09 mmol/ml) and nitric oxide (22.29 ± 2.17 vs. 15.55 ± 1.58 μmol/L) and decrease of catalase (0.88 ± 0.15 vs. 2.28 ± 0.04 U/ml), superoxide dismutase (271 ± 17.39 vs. 338.16 ± 7.11 U/ml), ascorbic acid (84.84 ± 4.25 vs. 132.17±5.12 U/ml), reduced glutathione (1.67 ± 0.07 vs. 6.38 ± 0.11mmol/L) and total antioxidant capacity (0.45 ± 0.05 vs. 1.43 ± 0.08 mmol/L) values with low zinc, copper, iron and selenium concentration (Ahmed *et al.* 2009).

Hormonal assay of dam affected with RFM

Blood progesterone concentration was lower (1.20 ± 0.14 vs. 0.51 ± 0.11 ng/ml in follicular and 2.87 ± 0.39 luteal phase) in buffaloes with RFM as compared to normal (Ahmed *et al.* 2009).

TREATMENT OF RFM

Use of antibiotics: Antimicrobial therapy of RFM has conflicting consequences (Bolinder *et al.*, 1988). Use of intrauterine antibiotics could control bacterial growth in uterus; however, this bacteriolytic activity of antibiotics actually interferes with necrotizing process required for release of retained fetal membranes. Tetracycline commonly used in intrauterine treatment, though it inhibit normal placental detachment by inhibiting matrix metalloproteinase (Eiler and Hopkins, 1993).

It is reported that administration of Penbiotic (Procaine penicillin + Benzyl Penicillin + Streptomycin) and oxytocin 8 hours post-partum encourage the expulsion of fetal membranes and early resumption of estrus cycle in buffaloes (Kunbhar *et al.*, 2011).

Herbal treatment: Herbal therapy is very effective alternative to overcome retention of fetal membrane. Cui *et al.* (2014) reported that use of a herbal preparation (Herbal leonuri, Angelicae sinensis radix, Flos carthami, Myrrha,

Rhizoma cyperi by percolation with 70% ethanol to a concentration of 0.5g crude herb/ml) in 48 dairy cows with retained placenta facilitate expulsion of retained placenta and significantly improve days at first service (70 vs. 102.5 days) and days open (76 vs. 134 days) in herbal as compared to chemical treatment with oxytetracyclin intrauterine. Similarly while working with 14 cows with retained featal membrane, Umadevi *et al.* (2016) reported that efficacy of herbal treatment (powdered Abrus precatorius seed mixed with boiled and minced Solanum melongena) was 80%.

Use of collagenase enzyme: In case of retained fetal membrane collagenase injected (1 litre saline containing 200,000 IU of bacterial collagenase) into umbilical arteries of retained placenta overcome placentome proteolysis deficiency of cow in order to enhance placental release (Beagley, 2010). Collagenase treatment is more effective as compared to traditional therapy (Eiler and Hopkins, 1993), the authors also reported that umbilical injection of bacterial collagenase was more effective in the treatment of retained fetal membrane as compared to jugular vein injection..

Hormones: Common hormones used in treatment of RFM include prostaglandins and oxytocin. These hormones are choice of drug in uterine atony. Uterine atony is not a common cause of RFM, therefore their use as a general treatment should be restricted (Drillich *et al.*, 2005).

PGF2α treatment: PGF2α and its analogues provide effective alternatives to antibacterial therapy using antibiotics for most post-partum disorder (Paisley *et al.*, 1986).

GnRH treatment: As per the report of El-Malky (2010) GnRH had significantly (P<0.05) reduced calving interval and days open by 10.41 and 28.33% respectively; moreover, services per conception also declined from 3.5 to 2.6. Milk production and blood profiles also improved by GnRH treatment in RFM case.

UTERINE INVOLUTION

Involution of uterus after parturition includes restoration of endometrium, resumption of ovarian activity and elimination of bacterial contamination of female tract. Retained placenta delayed involution of uterus which leads to long days open and calving interval due to anoestrus (Abdelhameed *et al.*, 2009).

PROGNOSIS OF RFM

Prognosis is generally good, particularly if there are no secondary infections. Conversely, RFM delay uterine involution and predispose to endometritis, which leads to sub-fertility and cause systemic illness and caries a guarded to poor prognosis. Culling of animals is essential when the RFM is associated with uterine fibrosis.

CONCLUSION

Prevention of RFM includes reducing stress, improving comfort, balance ration during transition period. Parity of dam, sex and weight of calf has pronounced effect on incidence of RFM. Lacks of exercise, low Vitamins (Vitamin A, E, Selenium), minerals along with infections are aggravating factors. Ecbolic and collagenase injection may be used in suffering animals with very positive effect. Antibiotics may be used intrauterine but some time it may delay putrefaction and release of retained fetal membranes. Umbilical injection of bacterial collagenase was more effective in the treatment of retained fetal membrane as compared to jugular injection.

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