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POSSIBLE CAUSES AND RISK FACTORS OF ANESTRUS IN CATTLE : A REVIEW

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Abstract

The reproduction is an essential process for species survival, the lack of detected estrus in cattle herds is still a major factor contributing to low fertility. Anestrus (AE) is absence of estrus behavior in female animals which occurs physiologically and pathologically in heifers before reach puberty and in postpartum cows. During AE period, normal follicular waves may occur but the standing estrus and ovulation may not occur. Therefore, visual observation for behavioral signs of estrus or hormonal treatment of AE is classical, time consuming, low sensitive and inefficient method requires more advanced technique to support detection and successful correction. Worldwide, Researchers were classified AE broadly into different categories based on multiple animal and management-related factors. Hence, the basic understanding of AE causes and further improvement of estrus detection can clearly increase the effectiveness of reproduction and support the management schemes. To our knowledge, it seems that the present study is the first detailed investigation for the causes and risk factors of AE in heifers/cows in Iraq.

Key words: Anestrus, Cattle, Cause, Risk factor, Iraq.

Introduction

Reproductive efficiency is an effective highly important factor in both dairy and beef herds. The proper detection of estrus early in breeding season and timing of insemination play a vital role in improving efficient and profitable reproductive performance, as well as high milk production (Howley *et al*., 2012; Galvão *et al*., 2013). The greater losses occur as a result of female cattle lack the ability to get gestation (Looney *et al*., 2006). Anestrus (AE) occurs physiologically in heifers before reach puberty and in cows between estrus periods for variable time after parturition (postpartum AE) or during lactation and during pregnancy. Whereas pathologically, AE can result from disruption of the reproductive axis and typically involves the absence of both the behavioral signs of estrus and the underlying normal ovarian events associated with cyclic activity though the follicular waves still occur. Mainly, there are two categories of animals with persistent AE, primary AE refers to females that have never cycled and secondary AE applies to females that have previously cycles but no longer are (Short *et al*., 1990; Peter *et al*., 2009a).

In several countries, visual observation of individual cows is a major routine method used to identify of estrual cows based on external estrus signs. This method is not practical within the available time of herd management and is often inefficient particularly in large herds (Diskin and Sreenan, 2000; Roelofs *et al*., 2010). In addition, the high variability in duration and intensity of the expressed estrous signs among individuals and great influence a number of various factors, participate actively in failure detection of estrus (Roelofs *et al*., 2005). By now, a number of fully automated sensor-based technologies of highly and different advantages are available recently. These systems are most practical and can support herd manager in determining the onset of estrus (Reith and Hoy, 2018). In addition, the history and physical examination findings determine the nature of any additional diagnostic tests performed (Farin and Estill, 1993; Bon Durant, 2005). In order achieve efficient management

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strategies; this review article presents a brief overview for most probable causes and risk factors associated with AE in cattle in Iraq.

Causes and Risk Factors

Management factors

Silent estrus (SE)*:* In some herds, a few open cycling cows may contribute to the problem of SE, absence the signs of estrusal behavior, though the reproductive system undergoes a normally cyclicity. In SE that counted to be occurs in 10%-40% of different herds, a cow lack the known symptoms as it acting nervous and excitable, standing to be mounted and licking or sniffing (Finn and Gee, 1994). The failure of owner to detect of cow in estrus and characterization estrus behavior by visual observation with absence of accurate reproductive information doesn't properly provided a valid data about duration and intensity of estrus (Lopez *et al*., 2004a). However, bulls have the ability to know a SH cow that can still become pregnant. Therefore, vasectomised bull (teaser) can be used for detect of SH cow even it appeared without behavioral signs of estrus (Dawuda *et al*., 1989; Gordon, 2011). Moocal HEAT is a developed estrus tool that having the natural capability of bull to identify SE cows and sending the information straightly to owner phone about which cow is in heat and how strong it is (Kulatunga *et al*., 2017).

Lameness: The increased vulnerability of crossbred cows to certain diseases including lameness has been one of main reasons for decreasing of reproductive performance, production potential and increased culling rate of the affected cows (Sood *et al*., 2009; Olechnowicz and Jaskowski, 2011). Garbarino *et al*., (2004) reported that delay in ovarian activity in earlier postpartum is correlated with lameness; whereas, Alawneh *et al*., (2011) detected the lame cows took 12 days longer to get pregnant compared with their non-lame counterparts. However, Morris *et al*., (2011) reported that there was a graded effect ranged from 21% lame cows failed to express estrus and 29% with absence of ovarian activity. These findings suggested that intrinsic changes and husbandry practices can affect on periparturient animals (Blowey, 2005). Reduced animal management is of importance as it having marked impacts on animal reproduction. Very slippery surface may cause gait's abnormality due to the vascular stasis and poor horn damage. Webster, (2002) confirmed that the sole hemorrhage increased significantly in heifers transferred into cubicles before calving. To enhance infertility and estrus expression, adequate loafing areas may of great support (Leonard *et al*., 1996).

Milk production: Expression of estrus can be altered obviously during the period of high milk yielding due to totally an unknown mechanism. Lopez *et al*., (2004b) detected that there a negative association the period and duration of estrus expression and milk productivity. López-Gatius *et al*., (2008) showed that the previous AE and late stage of lactation in dairy cows can have negative and positive effects, respectively, on the response of clinical AE to specific treatment. Based on walking activity and milk progesterone profiles, Ranasinghe *et al*., (2010) determined that the high milk yields were associated with the incidence of silent ovulation and impaired reproductive performance.

Endocrine hormones: Many studies suggested that the endocrine balances are required to support the normal estrus and to re-establishment of fertility after calving (Bridges *et al*., 2010). In cattle, estrus expression stimulated by sufficient secretion of endogenous estradiol can provoke the standing response. It was found that the high concentration of estradiol at the end of pregnancy may make a cow refractory or fail to display estrus in the subsequent normal ovulation and hypothesized that progesterone treatment prior to the first postpartum ovulation can re-sensitize the brain and allow for estrus to be expressed (Woody *et al*., 1967; Edwards *et al*., 1968). Nonetheless, Kyle *et al*., (1992) reported that the administration of progesterone early postpartum did not increase the proportion of cows expressing estrus at the first ovulation. Concerning to other hormones, the using of gonadotropin releasing hormone (GnRH) can cause leuteal hormone (LH) releasing in an estrus range cows and treatment with 1,000 or 2,000 IU pregnant mare serum gonadotropin (PMSG) can initiate the ovarian activity (Wettemann *et al*., 1982). Although the secretion of LH can be inhibited by estradiol it reported that the increased number of pulses of small amounts of LH alone is sufficient to induce follicular maturation in AE, resulting in ovulation and formation of a corpus luteum with normal function and an inadequate frequency of the pulsatile release of LH causes failure of normal preovulatory follicular development in AE animals (McNeilly *et al*., 1982; Imakawa *et al*., 1986). Therapeutic protocols using progesterone/progestogen (P4) releasing devices associated with estradiol benzoate can increase the pregnancy rates in AE postpartum cows (Baruselli *et al*., 2004).

Changes in metabolic hormones correspond to the time from calving to resumption of cyclicity are of importance. To date, two hormones have been analyzed, growth hormone (GH) and insulin-like growth factor-I (IGF-1), (Crowe, 2008). Many studies indicated that maintenance of cattle on lower levels of energy intake increases the levels of GH and suppresses levels of IGF-I (Haspolat *et al*., 2007). Thus, the chronic restriction of energy intake affects GH and IGF-I in apposite fashions. It was of interest to determine whether the levels of these hormones would be useful indicators of when cows would resume cycling. Under the control of GH, synthesis of IGF-I have been modulated (Schneider *et al*., 2010). Analysis revealed that postpartum interval was negatively associated with IGF-I for cows maintained on the lowest levels of energy. In simplistic terms, when energy intake is low, cows with high levels of IGF-I will likely resume cycling sooner than most of the cows with low levels of IGF-I (Roberts *et al*., 1993). However, other studies demonstrated that the levels of IGF-I are not as consistent for predicting postpartum intervals as high levels are. Hence, measuring of circulating IGF-I levels is probably not acceptable as a management tool for predicting the length of postpartum interval and incidence of anestrus (Zurek *et al*., 1995; Chagas *et al*., 2006).

Congenital factors

Congenital abnormality is one of the most economic burdens to the herd's owner because the birth of congenital calf is usually accompanied by dystocia and it may causes severe damage for internal and external genitalia during parturition. Furthermore, every abnormal calf is one less replacement for cows that leave the herd and is mostly infertile (Purohit and Mehta, 2006). It is assumed that all congenital abnormalities are not genetically initiated and they attributed to other causes including the interaction of genes and the environment, environment factors alone, vitamin deficiency, poisons and diseases (Herschler *et al*., 1962; Berglund, 2008). There a definite association of certain types of abnormalities with specific breeds, between sire and number of abnormal animals born, abnormal gestation length and twining were demonstrated (Mulvihill, 1972; Gentile and Testoni, 2006). However, congenital abnormalities may affect a particular part of the body like the skeletal system, skin and hair, head and thorax, udder and teat and reproductive system, or compromised more one (Leipold *et al*., 1993; Agerholm *et al*., 2001). Among reproductive system, there many congenital abnormalities are described in female cattle such as:

Freemartinisim: It's abnormality intersexual form among cattle herds. Freemartin is a XX/XY chimeras result from fusion of the chorioallantoic circulation of twin male and female fetuses, with subsequent interchange of leukocytes and masculinization of the female twin (Ladds, 1993). Typically, freemartin female has an extreme ovarian hypoplasia and nearly complete absence of the tubal genitalia but the external genitalia seem to be normal or slightly differed (Palmieri *et al*., 2011; Esteves *et al*., 2012). It is assumed that 11 out of 12 such co-twins to males are freemartins (Agarwal *et al*., 2005). In cattle, female calf born twin to a male is considered to be sterile and must be detected earlier in order to culling it. Nonetheless, some freemartins born singleton may identify as a normal calves because its co-twin has been dead in uterus (Horton *et al*., 1980; Esteves *et al*., 2012).

Ovarian hypoplasia: It's a rare condition characterized by incomplete ovarian development wherein the affected ovary or part of the ovary completely lacks follicles (Akkoyunlu *et al*., 2014). Based on their morphology, three types of ovarian hypoplasia described are total, partial and transitional (Settergren, 1997). A number of etiologies have been suggested for ovarian hypoplasia include autosomal dominant genes, autosomal recessive genes resulting in different types of XX gonadal dysgenesis and X chromosomal abnormalities (Simpson and Rajkovic, 1999).

Nutritional factors

Body condition: There strongly correlates between the state of body condition and the reproductive events that greatly affect net income in calf/cow operation, which include calving difficulty and survival, weaning weight, milk production, calving interval, services per conception and postpartum interval (Wiltbank and Remmenga, 1982; Sanz *et al*., 2004). The early resumption of estrus cycles following calving is meaningful for high reproductive efficiency in both year round and seasonally calving herds (Rhodes *et al*., 2003). In pastured cows, high level of body's condition is significantly reduces of estrus/ovulation intervals and resuming estrus cycles before the breeding season (Reist *et al*., 2000). In the last trimester of pregnancy and in early lactation, balanced diet to beef heifers/cows is critical due to the great increases of nutritional demands (Freetly *et al*., 2000). Obviously, pregnancy rate in cattle influences by state of body condition at calving and level of feeding particularly during the first 20 days postpartum (Rae *et al*., 1993; Buckley *et al*., 2003).

Energy: Many studies confirmed that the reduced energy in forage is a primary cause of delayed cattle puberty, suppressed estrus and ovulation and low conception (Schillo, 1992; Abeygunawardena and Dematawewa, 2004; Pradhan and Nakagoshi, 2008). Balanced energy can reflect on the variation between the consumed energy and that consumed for milk production and maintenance. In many studies, it confirmed that the negative energy balance increases the interval to first ovulation after calving (Beam and

Butler, 1999; Butler, 2000). Practically, the accurate measurement of balanced energy is not possible; however, the better signals can be reflected in depending on the physiological indicators of metabolic status (Brosh *et al*., 2002).

Protein: In many instances with warm or cool-season perennial forages, there is inadequate crude protein (Griffin *et al*., 1980; Moore *et al*., 2004). In forage having a crude protein below 7%, dry mater intake may decline rapidly due to a reduction of rumen nitrogen and depression of microbial activity (Funston, 2008). Silent estrus, weak offspring, premature parturition, fetal re-absorption and low conception are the main consequences of low protein intake (Bearden and Fuquay, 1992). Nitrogen is the building block of proteins in feeds and forages, which receives more attention as a component of nutrient plans on cattle herds and potential ammonia emissions (Chaturvedi, 2005). Sinclair *et al*., (2000) reported that there were interactions between the nitrogen metabolism and fertility in cattle and the development of oocystes recovered from heifers offered diets differing in their rate of nitrogen release in the rumen. Before or after calving, feeding excessive amounts of nutrients must bewared because the excess body condition can reduce the performance of reproductive organs and calving in these animals is more difficult than those with moderate body condition (Beever, 2006). During early gestation and breeding season, suppressed fertility can occur in animals receiving inadequate supply of energy though there is sufficient amount of protien (Elrod and Butler, 1993; Rajala-Schultz *et al*., 2001). As documented in dairy literature, it is well known that the overfeeding protein can negatively affect on rumen activity and reproduction (Santos *et al*., 2011).

Minerals: The normal metabolic processes in animal depend on different elements and their deficiency cause hypothalamic-pituitary-ovarian, oogenesis and follicular genesis disorders ultimately extend the postpartum anestrus period in cows (Ali *et al*., 2014). These elements play a direct and indirect relationship with production and reproduction, normal growth, overall metabolism (Nocek *et al*., 2006). Requirement for these components is very low in amount, so that, deleterious effects in health may be seen due to imbalance supplementation of these elements (Ahuja and Parmar, 2017). During periparturient period, mineral imbalance of minerals either have negative impacts on subsequent fertility, or solely associated with milk fever, metabolic disorders, vulval discharges, weak calf syndrome, abortion, dystocia and retention of fetal membranes (Husband *et al*., 2006; Overton and Yasui, 2014; Yasothai, 2014). Calcium (Ca), phosphorus (P), potassium (K), sodium (Na), magnesium (Mg), copper (Cu), manganese (Mn), selenium (S) and zinc (Zn) are of variable importance for reproductive performance (Siciliano-Jones *et al*., 2008).

In dairy herds, sub-clinical and clinical incidence of hypocalcaemia can associate with many disorders of varied degree according to severity of losses (Kelly and Whitaker, 2001). Muscle contraction is one of the main functions of Ca. Chronic reduction in serum Ca can result in decrease of rumen functions, ketosis, impaired uterine involution and poor fertility (Esslemont and Peeler, 1993; Wilde, 2006). In the body, P considers as the second most abundant mineral, which required for normal growth and efficient use of feed by the rumen microorganisms. In dairy cows, impairment sexual behavior, failure of estrus, silent or irregular estrus in heifers, delayed onset of puberty, delayed sexual maturity and inactive ovaries and low conception rates are the most common sequelaes related to the reproductive performance (Lopez *et al*., 2004a; Tallam *et al*., 2005). Excess K and Na in diets may lead to a slight alkalinity of blood which reduce the activity of parathyroid hormone that responsible on controlling of Ca absorption from the diet or resorption from bone, as well as stimulate the vitamin D production from the kidney (Horst *et al*., 1994; Silver *et al*., 1999). Furthermore, the potential roles of parathyroid hormone in modulation and supporting of normal bovine sexual behavior have been demonstrated (Stewart *et al*., 1993). Mg deficiency can reduce the responsiveness of kidney to parathyroid hormone. Also, physiological signs of estrus in cows do not appear unless there is an optimal level of this hormone (Fontenot *et al*., 1989; Goff, 2008). Deficiency of Cu is found to be associated with decrease conception rate and anestrus, low fertility with delayed or depressed estrus, early embryonic death, increase chance of retained and necrosis of placenta (Muehlenbein *et al*., 20001; Ahola *et al*., 2004; Griffiths *et al*., 2007). Zn has a significant role in early return of postpartum estrus, speeding return to normal reproductive function and in the repair and maintenance of reproductive functions (Green *et al*., 1998). Whilst, Zn deficiency can result in failure of implantation reduction in litter size, lower conception rate and delayed puberty (Boland *et al*., 2003). A positive correlation has been found for Cu and Zn with the reproductive hormones particularly estradiol and progesterone (Akhtar *et al*., 2009; Formigoni *et al*., 2011). The organic and inorganic forms of Cu, Mn, Se and Zn have a significant role in increasing the conception rates and days to first service, as well as improving of fertility in the months prior to insemination during lactation (Ballantine *et al*., 2002). In sufficient cobalt levels, there may be a sub-optimal conditioning of the offspring, reduced fertility, irregular estrous cycle, decreased conception rate, delayed uterine involution and increased the early calf mortality (Heinrichs, 1996; Arthington, 2002).

Vitamins: C, D, E and B are the most important vitamins that either being available in common feeds or synthesized by the body (Schwab *et al*., 2006). Under natural condition, the levels of these vitamins in normally maintained. Deficiency of vitamin A occurs naturally in cows consuming low quality forages and crop residues, or grazing dry winter range (McDowell, 1996; Weiss, 1998). The role of vitamin A in reproduction and embryo development has been reviewed previously (Clagett-Dame and DeLuca, 2002) whereas, supplementation of this vitamin in pre and postpartum period can increase the conception rate (Hess, 2000). Also, the rate of estrus detection following prostaglandin treatment was about twice as high for the high vitamin A group as for the control group (Tharnish and Larson, 1992). Vitamin D is involved with Ca and P homeostasis and immunity. Although cattle that fed hay/sun-dried forages and exposed to sunlight can synthesize appreciable quantities of vitamin D, requirements are not defined for adult cows (Batajoo and Shaver, 1994; Weiss, 1998). However, total confinement of cows that limited exposure to sunlight and increased reliance on silage may reduce the amount of vitamin D that is synthesized by the cows and consumed in the basal diet (Hurley and Doane, 1989; Fox and Tylutki, 1998).

Vitamin E deficiency during peripartum period impairs immune function in dairy cows. It plays an important role in birth process of females, maintaining reproductive performance and plummeting periparturient disorders in cattle (Khan *et al*., 2014). Prepartum vitamin E supplementation has been depicted to decrease the incidence the postpartum anestrus, metritis and retained fetal placenta (Arechiga *et al*., 1994). In general, vitamin E and Se (E-Se) can enhance of cell viability, immune response and muscular contraction leading to early involution of uterus (Baldi, 2005). Oral administration of E-Se to anestrus animal is more beneficial in decreases of lipid peroxidation and increasing of antioxidant status (Nayyar and Jindal, 2010). Injection of E-Se can increase the fertility in cattle that did not become pregnant at first service (Aréchiga *et al*., 1998). Feeding supra-nutritional levels of E-Zn could be a better nutritional strategy for improving of fertility (Wilde, 2006). Maintaining adequate vitamin B_{12} status benefits both the dam and offspring (Balamurugan *et al*., 2017). It is well known that ruminal bacteria can synthesize B vitamins including folic acid and B_{12}. In many previous studies, the findings have been shown that the supplementation of folic acid and vitamin B_{12} together improved energy balance in postpartum cows (Gagnon *et al*., 2015; Li *et al*., 2016). Also, a higher percentage of easy calving and an earlier first breeding date were observed in multiparous cows receiving additional amounts of both vitamin B_{12} and folic acid (Balamurugan *et al*., 2017).

Pathologic factors

Pyometra: It is an acute condition characterized by presence of pus in uterus as a result of either persistent existence of corpus luteum on ovary and interruption of the estrus cyclein a cow, or transmission of infection form infected bull by bacterial or parasitic pathogens to a cow during insemination (Földi *et al*., 2006; Sheldon *et al*., 2006). Actually, there is a relationship between uterine infection and failure to ovulate and prolonged luteal phases (Sheldon *et al*., 2008). Generally, the drug of choice is administration of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) or its analogues at normal luteolytic doses for once. Expulsion of exudates and bacteriologic clearance of the uterus follows in about 80% of treated cases and most treated cows may be expected to conceive within 3-4 inseminations. In approximately 20% of first-non respond cases, $PGF_2\alpha$ may need to be repeated (Galvão *et al*., 2009; Larson, 2016; Ahmadi *et al*., 2018). Intrauterine treatment with 500mg cephapirin can improve reproductive performance of cows in particularly those that had a history of retained fetal placenta, dead calf and vulval discharges (McDougall, 2001). However, the best strategy for treatment of bovine pyometra is the administration of both $PGF_2\alpha$ and intrauterine or injection of antibiotic (Metronidazole, oxytetracycline, cephalexin), (Stephens and Slee, 1987; Bhat and Bhattacharyya, 2012).

Mummy: It is an uncommon gestational accident in most domestic species due to intra-uterine death of fetus commonly at fourth, fifth, or sixth month of gestation (Jana and Ghosh, 2014). Bovine fetal mummification (BFM) has an incidence of less than 2%. Although, the exact outcome for occurrence of early BFM is unpredictable, it may influence by many factors such as the number of fetuses, stage of gestation at fetal death, differences in pregnancy between species and fetal mortality (Lefebvre *et al*., 2015). In cows experienced a similar events in a previous gestation, there is an increased risk for frequent incidence of condition (Roberts, 1986). Also, BFM occur usually post the 70s day of gestation, particularly from the third to eighth month, without any concomitant symptoms for opening of cervix and luteolysis of corpus luteum (Lefebvre, 2015). BFM can be suspected when the owner observe that the pregnant cow is having a less unusually abdomen at the given stage of pregnancy, with absence of systemic or other type of illness (Azizunnesa *et al*., 2009; Lefebvre *et al*., 2009). Trans-rectal palpation and ultrasonography can be applied to detect the mummified fetus as a compact, firm, immobile mass without placental fluid or placentomes (Kumar *et al*., 2017). Injection of prostaglandins such as $PGF_2\alpha$ are the primary and most effective drug for BFM; however, the treated cow should be assessed at the 5th day post injection to evaluate the existance of corpus luteum, dilation of cervix and mummy in vagina (Krishan, 2015; Parmar *et al*., 2016). Surgical intervention may be advised when the injection of prostaglandin fails to expel of the mummified fetus (DESAI *et al*., 2017).

Anovulatory defects: Typically, ovulation occurs normally in cows 10-12 hours post the end of estrusal behavior and 18-26 hours post the ovulatory luteinizing hormone peak. During periods of estrus and diestrus, though a number of follicles are developed, only one or rarely two is ovulate (Cavalieri *et al*., 1997; Esterman, 2010). The consequences of anovulatory defects are either the oocyte is not liberated too late so that the fertilization is failed (delayed ovulation), or else the oocyte has aged and is not capable of normal development (anovulation). However, endocrine deficiency or imbalance and mechanical factors are the main causes of ovulatory defects (Veiga-Lopez *et al*., 2006; Abraham, 2017). In delayed ovulation, the hormone that plays a big role in failure of fertilization and for delayed ovulation is luteinizing hormone. This condition cannot be detected easily since the ovaries must be palpated sequentially (Viker *et al*., 1989). Anovulation is a state characterized by lack of ovulation leading to either cystic ovarian disease or true anestrus (Wiltbank *et al*., 2002). Trans-rectal palpation and ultrasonography can be used to detect follicles persistence longer than suspected. Treatment can be directed towards ensuring that ovulation occurs at the next estrus and GnRH hormone that indicated for delayed ovulation (Fricke *et al*., 1989; Hanzen *et al*., 2000).

Cystic ovary: Ovarian cysts are defined as follicular structures of greater than 2.5cm in diameter and persist for at least 10 days in the absence of a corpus luteum (Peter, 2004). Ovarian dysfunction such as cysts occurs mostly in earlier period of postpartum when there is a transition from the non cyclic condition during pregnancy to the establishment of regular cyclicity (Smith, 2014; Abraham, 2017). Generally, these dysfunctions are developed as a result of disturbances in hypothalamic pituitary ovarian axis due to multiple factorial causes, in which, environmental, phenotypic and genetic factors are involved (Garverick, 1997; Peter, 2004). Based on their types, ovarian cysts are classified to follicular and luteal cysts. Follicular cysts defined as a follicular structures found on ovary with absence of luteal tissue, contain fluid of many components (insulin, progesterone and estradiol) and affects on estrus cycle of the animal (Kesler *et al*., 1980; Youngquist and Threlfall, 2007). As long as the cysts existed, most cows remains anestrus (Vanholder *et al*., 2006). Luteal type is defined as an enlarged ovary with one or more cysts that contain a high level of progesterone. The incidence of luteal ovarian cyst that associated with infertility and mucometra, increases with age and most often affects cows with high milk production (Peter *et al*., 2009b).

Repeat breeder: This term describes a normal cyclic cow without clinical abnormalities but failures to be fertilized post 3-4 inseminations. Multiple factors, which varied from animal to animal and from herd to herd, are responsible on this condition such as infectious, managemental, anatomical and hormonal factors (Jagir *et al*., 2009). Therefore, diagnosis can be implemented by vagnial examination, rectal palpation, ultrasonography and history data of cow (Stevenson *et al*., 1990). Uterine lavage with administration of $PGF_2\alpha$ is the best preferable method for treatment of repeat breeder. Conception rate in repeat breeder cows can be significantly increased by administration of Gonadotropin-releasing hormone (GnRH) (Meethal and Atwood, 2005).

Conclusions and Recommendations

AE is a multi-factorial reproductive condition affects on large and small domestic animals resulting in effective losses particularly in dairy herds. Mainly, AE is classified as primary and secondary when occurs in heifers and postpartum cows, respectively. Following some hormonal therapy, reproductive performance of AE cows can equivalent to these cows that have resumed estrous cycles in herds with greater estrous detection rates. Response to any therapeutic strategy was appeared to be based on those factors that influence depth of estrus. Accurate evaluation for the causes and risk factors of AE will require further studies. For a better management, there a number of steps that must be followed in order to prevent further economic losses are the early and active diagnosis with following a suitable therapeutic system.

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