Ovarian Cyst and its Economic Impact in Dairy Farms: A Review

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Abstract: Ovarian cyst is one of the major causes of reproductive failure and economic loss in the dairy industry. The objectives of this paper were to give general overview about cystic ovarian disease and its economic impact in dairy cattle. By rectal palpation, ovarian cysts are characterized as structures greater than minimum diameter of 17mm persisting for more than 6 days. Major categories of cysts include follicular cysts, luteinized follicular cysts and cystic corpora lutea. Follicular cysts result from failure of ovulation and luteinization. Luteinized cysts apparently fail to ovulate, but some luteinization occurs. Because of the varying degree of luteinization, luteinized cysts are firmer to touch than follicular cysts though not as solid as corpus luteum. Cystic corpora lutea are corpus luteum with a fluid filled center. Various risk factors related to development of ovarian cysts in individual cows have been identified, although the actual cause of cystic ovarian disease is unknown. The basic pathophysiology of cystic ovarian disease involves a neuroendocrine dysfunction of the hypothalamic-pituitary-ovarian axis resulting in ovulation failure. An abnormal pattern of estrous behavior is the most noticeable sign of cystic ovarian disease. A cow with an ovarian cyst might exhibit "constant" estrus (nymphomania), no estrus (anestrus) or anerratic combination of estrus and anestrus. Accurate diagnosis currently employs a combination of transrectal palpation, transrectal ultrasonography and plasma progesterone assay. During earlier times, the manual rupture of ovarian cysts was advocated, yet during the past several years single or combinations human chorionic Gonadotrophin, Gonadotrophin releasing hormone, progesterone and prostaglandins have been frequent in clinical practice. The success of therapy is governed by many confounding variables such as persistence of the cystic follicles and initiation of therapy as pathological alterations that occur following ovarian cysts persistence require some time for spontaneous recovery. Generally all of these risk factors should be thoroughly considered and based on the knowledge of their existence, measures should be taken to prevent increased incidence of ovarian cysts COD.

Key words: Ovarian cysts · Follicular cysts · Luteinized follicular cysts · Cystic corpora lutea · Nymphomania · Dairy cattle

INTRODUCTION

Ovarian Cyst (OC) is an important ovarian dysfunction and a major cause of reproductive failure in dairy cattle [1]. Over the past few decades, milk yield per dairy cow has increased considerably due to continuing genetic selection and improvement of nutrition and herd management. Simultaneously with this selection for production characteristics, dairy cow fertility has declined significantly [2]. The reduced fertility, observed in modern high yielding dairy cows is most likely due to alterations at several consecutive steps in the reproductive process.

One of the known causes of reduced fertility in dairy cow is ovarian dysfunction. Formation of a cyst following ovulation failure is the most common ovarian dysfunctions during the postpartum period [3].

In the past ovarian cysts were defined as fluid filled or hard structures of 2.5 cm or more in diameter persisting on the ovarian surface for 10 or more days [4]. Over time new definitions have been suggested, however, there is still lack of consensus and clarity in the definition. Silvia *et al.* [5] defined them as follicle like structures, with a minimum diameter of 17 mm and persisting for more than 6 days in the absence of a corpus luteum and clearly

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interfering with normal ovarian cyclicity. It has been reported that up to 60% of cows develop cysts before the first postpartum ovulation. Cysts arise as a result of anovulation of Graafian follicle. Under normal circumstances, anovulation is followed by either atresia or luteinisation, after which the follicle undergoes regression. In cystic ovarian disease the follicle increases in size and persists for several days. There is degeneration of the granulosa cell layer, which results in an alteration of the normal cyclical activity of the cow andbecomes either acyclic or nymphomaniacal [6].

Lack or inappropriate release of hypothalamic gonadotropin-releasing hormone at the time of estrus appears to be an important pathological factor in development of ovarian cysts [7]. Although, the exact cause of ovarian cysts is not certain various risk factors related to development of ovarian cysts in individual cows have been identified. Some predisposing factors include heredity, cow parity, seasonal variation, high milk production, abnormal puerperium, uterine infection and nutrition [8]. Cystic Ovarian Disease (COD) is a common and economically significant condition of dairy cattle and first described in the early 1900's as an important cause of reproductive loss in cattle [9].

Although COD is a very economical important disease, a review on economic impact of the disease in dairy farms of Ethiopia is very scanty. This condition inspires us to review on the cystic ovarian disease and its economic impact in dairy cattle. Therefore, the objective of this paper is to review ovarian cyst and its economic impact in dairy farms.

Classification, Characteristics and Causes of Ovarian Cysts: The most likely cause of COD is a disruption along the pathway from the hypothalamus, a part of the brain that regulates hormones through the pituitary gland to the gonads [10]. There are several types of cysts that can be found on the ovaries of the cow which can have a significant impact on the reproductive efficiency of the animal. The cystic structures that were studied include follicular cysts, luteal cysts and cystic corpora luteum [4].

Follicular Cysts: Ovarian follicular cysts are any follicular structure on the ovary in the absence of luteal tissue, larger than normal follicular size that persists for a significant amount of time and affects the estrus cycle of the animal [4]. From the factors that do predispose cows to develop follicular cysts genetics, hormonal imbalances, or exogenous factors are considered as the primary factors [10]. Disorders that include twinning, retained

placenta, primary metritis and ketoneuria, or a combination of the conditions can also predispose cow to follicular cysts. Cows with abnormal puerperium were found to have about twice as likely to develop new follicular cysts, but the condition was not determined to be a risk factor for late ovarian cysts. According to López-Gatius [11] Older cows were more likely to develop a chronic cyst condition than those in first lactations. All of these risk factors should be thoroughly considered in the management of dairy facilities and based on the knowledge of their existence, measures should be taken to prevent increased incidence of ovarian cysts.

When follicular cyst is compared to other ovarian cystic conditions, it is characterized by thin walls and produce very small amounts of progesterone. Occasionally, a persistent condition can lead to increased testosterone levels, causing some cows to exhibit masculine aggressive and sexual behavior. However, most cystic cows will remain in anestrous as long as the condition persists [12]. The fluid in follicular cysts contains many components including hormones like estradiol, progesterone and insulin. Anti-Müllerian hormone, a hormone strongly linked with polycystic ovarian syndrome in humans, is also present in follicular cysts [13].

Luteal Cysts: The Merck Veterinary Manual, Kahn [14] describes luteal cystic ovary disease as being characterized by enlarged ovaries with one or more cysts, the walls of which are thicker than those of follicular cysts because of a lining of luteal tissue. Ball and Peters [12] call these cysts; luteinized cystic follicles and define them as cysts with thicker walls that produce high levels of progesterone. In appearance, they are smooth and rounded, with a spherical cavity that is lined by a layer of fibrous tissue surrounded by the luteinized cells [15]. Luteal cysts are considered anovulatory cysts and are associated with infertility and mucometra in cattle. When compared to follicular cysts, luteinized cysts are more likely to persist over long periods of time and can lead to nymphomania in some animals [12].

Luteal cysts develop when ovulation fails to occur and the theca undergoes luteinization [15]. They are also often considered to be the later form of ovarian follicular cysts and therefore the causes pertaining to follicular cysts can also be considered the original causes of luteal cysts [16]. The luteal cyst occurs when the cells of the follicular cyst (granulose and theca) become luteinized and start producing progesterone. Luteal cyst incidence increases with age and most often affects cows with high milk production [17].

Cystic Corpora Luteal: A cystic corpus luteum in a cow is defined as luteal tissue initiating from a corpus hemorrhagicum and containing fluid in a central cavity greater than 7 mm in diameter. The terms for cystic corpus luteum (CL) can often be confused with those for luteal cysts, though the first is a normally functional structure and the latter a pathological condition. Because of this, the contemporary term 'corpus luteum with a cavity' has been suggested to replace the classical term cystic corpus luteum [18].

Incidence of cystic CLs ranges from 25.2% to 78.8% during diestrus and decreases with progression of the estrous cycle. Because cystic corpora lutea are found in cows that are normally cycling or pregnant, they are considered to be a normal stage or variation of CL development. Cystic CL have a soft, mushy core area, due to presence of fluid from a degenerating blood clot, compared with the homogeneous, liver-like consistency of the base of a typical CL [14]. Although diagnosis is not essential as cystic CLs are not pathological and therefore do not require treatment, the ideal time for detection of the structure is 5-7 day after estrus. At this point in time, the ovarian structure is near the end of the corpus hemmorhagicum stage of development [14].

Factors Affecting Incidence of Cystic Ovarian Disease: There is a clear genetic predisposition for COD. In Sweden, the incidence was reduced from 11% in 1954 to 3% in 1977 as a result of genetic selection. Therefore, although progress through genetic selection will be slow, ignoring the existence of a genetic predisposition for COD will only contribute to an increased incidence of the disease and related economic losses. In addition, COD is more common in cows with greater milk production [19]. A recent study reported a positive genetic correlation between milk production and COD. One report demonstrated that COD incidence tripled when milk yields doubled (9% and 27% incidence for lactations with 6,000 and 12,000 kg of milk, respectively). According to this study, selection based solely on milk production would increase COD incidence by 1.5% for every 500 kg increase in lactation production [20]. The incidence of COD increases with parity, especially after the first lactation the incidence in first lactation cows is 40% to 80% lower than in the general cow population [21].

The seasonal effect on COD incidence is not clear. Some studies were unable to demonstrate any effect, while others described an increased incidence during fall-winter. Cows with abnormal postpartum conditions including retained fetal membranes, metritis, ketosis and lameness are 1.4 to 2.9 times more likely to develop COD than cows having a disease-free postpartum period. Therefore, measures to reduce other postpartum problems should also reduce COD incidence [22].

Pathogenesis of Ovarian Cysts: According to Vanholder *et al*. [23], ovarian dysfunctions like cysts occur most often during the early postpartum period when there is a transition from the noncyclic condition during pregnancy to the establishment of regular cyclicity. It is generally accepted that cystic follicles develop due to a dysfunction of the hypothalamic pituitary-ovarian axis. This dysfunction has a multifactorial etiology, in which genetic, phenotypic and environmental factors are involved.During discussing the pathogenesis of COD, a distinction may be made between a primary defect in the hypothalamus-pituitary and a primary defect at the level of the ovary in the follicle itself. However, COD formation may result from defects in both ovary/follicle and the hypothalamus/pituitary as well [24].

Hypothalamic-Pituitary Dysfunction: In normal cows, increased circulating estradiol concentrations have positive feedback effects on the hypothalamus when circulating progesterone concentrations are low. This results in the release of gonadotropin-releasing hormone (GnRH) that, in turn, stimulates the pituitary to release the preovulatory luteinizing hormone (LH) surge. Cystic ovarian disease develops as a result of the absence of a preovulatory LH surge that is caused by a disturbance in the positive feedback effect of estradiol on the hypothalamus [25]. Unresponsiveness of the hypothalamus, can be because inherent, interference by abnormal circulating progesterone concentration, reduced circulating estradiol concentration, either as a consequence of abnormal follicular production or increased metabolism [26].

The most common cause of COD is hypothalamic unresponsiveness to estradiol. Cows that develop COD do not have a preovulatory LH surge even when the dominant follicle secretes high concentrations of estradiol. Moreover, exogenous estradiol treatment either cannot elicit an LH surge in cows with COD or the surge is delayed. Unresponsiveness to estradiol may be associated with decreased hypothalamic GnRH content and may develop if an LH surge is not followed by ovulation. After an LH surge, exposure to progesterone may be necessary to up-regulate estradiol receptors in the hypothalamus and reestablish responsiveness to estradiol [27].

Abnormal circulating progesterone concentrations interfere with hypothalamic responsiveness to estradiol and result in the formation of cysts. In a recent study, 66% of cows with cysts and no detectable luteal tissue in cyst or ovary, had intermediate circulating progesterone concentrations (0.1-1 ng/ml) and only 10% of the newly-developed follicles ovulated in these cows. Follicles that develop in the presence of cysts producing abnormal amounts of progesterone are likely to become cysts themselves [10]. Hypothalamic-pituitary function and follicular growth/development may be affected by negative energy balance (NEB) through metabolic/hormonal adaptations. In addition, in the situation of NEB, the expression of genetic hereditary factor(s) associated with COD may be promoted or the functional importance may increase, which in turn may affect follicle growth and hypothalamic-pituitary function [24].

Ovarian/Follicular Dysfunction: A FSH surge stimulates the development of a new follicular wave, from which a single dominant follicle is selected at the time of deviation. Through a positive feedback loop oestradiol stimulates GnRH and LH pulsatility, which in turn supports growth and development of the dominant follicle. Upon reaching preovulatory size, follicular steroidogenic activity reaches a peak and produces a preovulatory oestradiol surge. If this surge either fails to elicit a GnRH and subsequent LH surge or the GnRH/LH surge is mistimed (delayed) the dominant follicle does not ovulate but, due to the ongoing LH pulsatility it continues to grow and becomes a cyst [24, 27].

A primary dysfunction at the level of the follicle may disrupt the hypothalamic-pituitary-ovarian axis and cause the formation of OC. First of all, alterations in LH receptor expression and content may cause anovulation of the follicle. The LH surge initiates a complex multi-gene, multistep process in which timing is essential, finally leading to ovulation of the pre-ovulatory follicle. Follicle stimulating Hormone (FSH) and LH receptor numbers in granulosa cells of cysts are decreased when compared to normal follicles [28]. Oestrogen-active cysts show a higher expression of 3β-hydroxysteroid dehydrogenase messenger Ribonucleic Acid (mRNA), a steroidogenic enzyme and cows developing a cyst have increased oestradiol concentrations during the early stages of follicular dominance [29].

Apart from changes in (mRNA) expression for certain receptors and steroidogenic enzymes, cell proliferation and apoptosis in the theca interna cell layers also seem to be altered in cystic follicles [30].

Recently, Imai *et al.* [31] suggested that matrix metalloproteinase's (MMP) could be involved in the formation of cysts: higher proMMP-2 and -9 levels were present in the follicular fluid of cysts than in the follicular fluid of normal dominant follicles. MMP play a role in follicle wall remodeling and rupture at the time of ovulation, but here to the inactive proMMP form needs to be transformed to the active MMP form. This activation is triggered by the LH-surge. Since an aberrant LH-surge causes COF formation, the higher proMMP-2 and -9 levels in the follicular fluid of COF are most likely an indication of the lack of an LH-surge [28]. Figure (1) indicates the pathogenesis of ovarian cysts and the possible pathways involved.
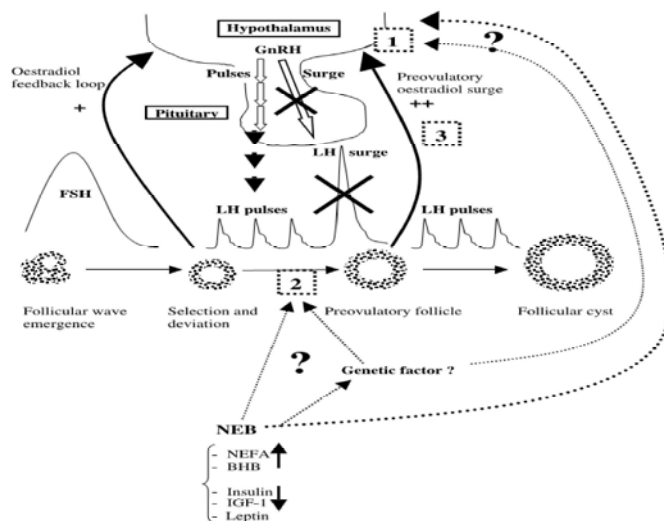

Fig. 1: Schematic representation of the pathogenesis of ovarian cysts and the possible pathways involved according to Vanholder *et al.* [23].

According to Vanholder *et al.* [23], the disruption of the hypothalamic-pituitary-gonadal axis can be caused by:

- Factors affecting the oestradiol feedback mechanism and GnRH/LH release at the hypothalamic-pituitary level.
- An aberrant follicle growth and development with alterations in receptor expression and steroidogenesis.
- Factors leading to an altered oestradiol surge and feedback.

Clinical signs of Cystic ovarian disease

Cystic ovarian disease has been a concern for producers and veterinarians for almost two centuries because a diagnosis of COD usually means the cow is not pregnant. A German scientist in 1831 wrote one of the earliest records of COD noting its relationship to infertility and documented some of the physical conditions associated with COD [32]. These symptoms included: Loss of tone throughout the female genital tract, Relaxation or stretching of the sacrosciatic and sacroiliac ligaments giving the raised tail head appearance, Formation of a cyst or cysts on the ovary or ovaries, Behavioral changes occurred (buller cow) which are characteristic of nymphomania (i.e., excessive mounting, standing and bawling with noticeably deeper tone), Erratic milk production, Most of these symptoms are still recognized in cows. However, with earlier detection, only extreme cases tend to exhibit the relaxed ligaments, bulling and a deepening of the vocalizations. The main symptom observed in modern day dairy cattle is anestrus [6]. Cows with COD may have frequent, irregular, prolonged or continuous signs of estrus (nymphomania), but the majorities are anestrus. Relaxation of the pelvic ligaments, elevated tail-head and development of masculine characteristics may be observed in chronic cases [19].

Diagnosis of Cystic Ovarian Disease: For many years, cysts have been determined by behavioral and palpation criteria. In practice, a veterinarian seldom has the opportunity to recheck a cow in 10 days. Thus, most diagnoses are based on the one time detection of a large fluctuant structure meeting most of the previous criteria and treatment is usually administered at the time of diagnosis. Diagnostic approaches for OC in cows include history and clinical signs, transrectal palpation, ultrasonography and plasma or milk progesterone assays [24]. Ovarian cysts diagnosed after the puerperium had a negative effect on fertility, whereas when cysts are diagnosed during the puerperium they do not affect reproduction [33].

The most likely time of diagnosis is 30-60 days after parturition in high-yielding dairy cows but the detection of anovulatory follicles during the first weeks after calving should not be considered an ovarian impairment. From a practical point of view, an ovarian impairment may be suspected when anovulatory follicles are detected no earlier than 7 weeks after calving, a time when reproductive functions are thought to be restored [34].

Ovarian cysts and normal preovulatory follicles are differentiated on the basis of number and size but mainly on the basis of uterine tonicity. During transrectal palpation, ovarian cysts are identified as multiple follicles that are typically larger than normal ovulatory follicles with an increased overall ovarian diameter along with a flaccid uterus in the absence of a corpus luteum while cows in proestrus have an erect, turgid uterus [35].

Although transrectal palpation has long been the diagnostic approach, follicular cysts cannot be differentiated from luteal cysts solely by palpation. It is difficult to distinguish between follicular and luteinized cysts without using ultrasonography in anoestrous cows. The accuracy of diagnosing ovarian cysts and differentiating follicular and luteal cysts can be increased by combining transrectal palpation of the genital tract to determine that a corpus luteum is absent and the uterus lacks tone; ultrasonography to confirm that a corpus luteum is absent, to determine the size of follicles that are present and to check for luteinization measurement of plasma progesterone concentration is essential [36].

The accuracy of diagnosis can be increased by obtaining information about the reproductive history of the animal, vaginal examination and progesterone determination [37]. Ultrasonography is effective in detecting follicular and luteal cysts with high accuracy. Color Doppler sonography is superior to B-mode sonography for differentiating follicular and luteal cysts and aids in the selection of treatment [38]. Determining the presence of ovarian follicular waves during a 7 to 10 day period with follicles that reach ovulatory size (12 mm) can be used to retrospectively differentiate ovarian cysts from shallow nutritional anestrus with low body condition score(BCS) [36].

In general, luteal cysts are associated with relatively high concentrations of progesterone in the peripheral circulation while follicular cysts are associated with relatively low concentrations of progesterone. Many researchers have used a plasma (Progesterone 4) P4 concentration greater than 1 ng/ml as the minimum P4 concentration for a cyst to be considered luteal. Thus accurate diagnosis of the type of OC requires a

combination of diagnostic approaches such as transrectal palpation, transrectal ultrasonography and plasma progesterone profiles [39].

Treatment of Cystic Ovarian Disease: The OC therapy appears to be simple however, regaining fertility which often requires longer time due to perturbations in endocrinology and uterine pathology that follows in long standing cases seems to be more important. Treatments for OC are numerous and variable and have changed considerably over the years [35]. Economically, the decision to treat an animal is influenced by the costs and the expected treatment benefits, the costs of replacement and the breeding value of the animal [40].

Many endocrine based treatments for cysts have been evaluated including steroids, Gonadotrophin and GnRH. The success of therapy in terms of disappearance of OC with different hormonal treatments is good, yet the establishment of pregnancy requires variable times due to formation of new OC and pathological alterations that occur in the uterus with long term persistence of OC. Many variables such as OC time of diagnosis, OC persistence period, presence of mucometra and milk production determine the outcome of therapy [1].

Gonadotrophin releasing hormone alone; since the distinction between follicular cyst and luteal cyst is not important in practice, the response of both types of cysts to GnRH treatment is similar and usually results in luteinization of the cysts followed by estrous within 4 weeks of treatment. GnRH is most effective for returning cows with anovulatory follicular cysts to a normal cyclic ovarian condition. It induces the release of LH with a maximum plasma LH concentration being reached 90 to 150 minutes after application, which initiates the formation of active luteal tissue, as indicated by increased serum progesterone levels 7 days after treatment onwards. In response to treatment with GnRH, ovulation of the cyst does not occur, but other follicles present at the time of treatment may ovulate [41].

Thus, a single GnRH treatment has been the standard treatment for cows with ovarian cysts. There is presence of a CL approximately 7 days after treatment with GnRH indicating that the CL formed from ovulation of an ovarian follicle and not the existing ovarian cyst [42]. After the GnRH treatment and subsequent luteinization, the cyst becomes responsive to prostaglandin-F2α (PGF2α) because the steroidogenic synthesis pathway has switched from estradiol to progesterone. The newly elevated levels of progesterone are responsible for a restoration of responsiveness to the positive feedback effect of estradiol, resulting in the resumption of normal cyclic ovarian activity after the release of endogenous PGF2α and cyst regression [41].

Gonadotrophin releasing hormone analogs; the epidural administration of lecirelin (a GnRH analogue) promotes the remission of follicular cysts and an improvement of reproductive parameters [43]. A single intramuscular injection of buserelin at a dose of 10 ìg or higher is recommended for the treatment of ovarian follicular cysts in cows. A single injection of 20 µg buserelin and 200 µg fertirelin have equal therapeutic effects in lactating cows having OC. Buserelin, a nanopeptide GnRH analog, is 10 to 20 times more potent than fertirelin acetate in eliciting the release of LH and FSH. In comparative studies, buserelin (a more potent GnRH analogue) or human chorionic gonadotropin (HCG) produced similar effects [41]. A recent study found beneficial effects of a single Intramuscular administration of 0.1 mg lecirelin acetate in the therapy of cows suffering from OC. Since the 1970s HCG and GnRH analogues have been used to treat ovarian cysts and both appear to be equally effective with regards to treatment response and fertility, but the next estrus would occur 5-21 days after treatment [14].

Prostaglandin F2α; has been used for the treatment of luteinized cyst because of its luteolytic activity and estrous symptoms can be observed within 2 or 3 days of treatment. It is the most effective treatment for luteinized cysts and in one study, 75% of the cows were in estrus within 7 days after treatment and pregnancy rates at first estrus were 66% [41].The luteolytic doses of PGF2α as the ideal treatment for luteal cyst, with estrus being evident within 3-5 days [14]. Intervals from treatment to resumption of ovarian activity are affected by the characteristics of ovarian cysts, with a faster recovery for the luteal type [44].

Progesterone and progesterone implants; treatment with progesterone may disrupt the endocrine environment needed to maintain ovarian follicular cysts and thus lead to their regression [45]. At high doses, it exerts a strong negative feedback on LH pulse frequency which reduces LH in cows with cysts and this was followed by development of normal ovulatory follicles. Acute treatment as well as chronic treatment (9-14 days) with progesterone caused a rapid reduction in the size of persistent follicles and restored cyclic ovarian activity. Cows with persistent follicles can be successfully synchronized and time inseminated using progesterone, GnRH and PGF2α, but show a limited response to treatment with GnRH plus PGF2α [11].

Treatments with progesterone releasing intravaginal devices (PRID) in combination with estradiol benzoate for 12 days evidenced therapeutic efficacy in resolving OC in post partum dairy cows [46]. The effects with progesterone treatments were proposed to be mediated by restoration of the ability of hypothalamo-pituitary axis to generate an LH surge in response to an increasing estradiol [47]. Moreover, when progesterone is used for estrus synchronization after embryo collection instead of PGF2α, the proportion of cows developing OC decreased from ~25% to <3% [41].

Gonadotrophin releasing hormone plus controlled internal drug release treatment of cows with OC with controlled internal drug release (CIDR) intra vaginal placement, GnRH followed by PGF2α 7 days later resulted in recruitment of new healthy follicles, synchronization of ovulation and resulted in a marked improvement in pregnancy rate [40]. The CIDR reduces and maintains LH secretion at normal luteal levels, thereby, inducing atresia of estrogen-active cysts and preventing formation of cysts from the newly emerged follicles [48]. Although the use of CIDR may eliminate the need for evaluation of the presence of a corpus luteum at the time of PGF2α treatment [36], the combination of both minimizes the risk of incorrect treatment and provides sufficient reproductive performance [49].

Homeopathic drugs like *homeopathic Apis* (for the right side OC) or *homeopathic Lachesis* (for the left side OC) twice daily for 5 days, with either one being immediately followed by homeopathic *NatrumMur;* twice daily for three days are effective treatments for OC. *Apismellifica* is a common homeopathic medicine made from the female honeybee, while Lachesis is prepared from the fresh venom of the South American bushmaster snake and *NatrumMur* is made simply from sodium chloride, or table salt. If this treatment doesn't work, heat seek, a botanical herb blend typically used to enhance the observable signs of estrus, may be given as 10 tablets orally every other day for twelve doses 24 day treatment [50].

Manual rupture; in the past it had been suggested. But, currently it is not suggested due to potential dangers of hemorrhages and adhesions that may contribute to fertility reduction [41].

Prevention of Cystic Ovarian Disease: Careful genetic choice and eliminating bulls that have sire daughters suffered from cystic ovarian disease is one method of COD prevention. Preferably, cows should not be treated for cystic ovaries and certainly their offspring should not

Table 1: Drug amounts, routes and protocols for treatment of follicular cysts

Drug	Dose	Route
Gonadorelin (GnRH)	100 µg	IM
HCG	10,000 IU	IM
Dinoprost (PGF2α)	25 mg	IM
Cloprostenol (PGF2α)	500 µg	IM
Progesterone	1.9 g	Intravaginal Implant

Treatment Protocols according to Brito and Palmer[41]

(1) GnRH (or HCG) + PGF2α (day 0); PGF2α (day 9 if no estrus)
(2) Ovsynch: GnRH (day 0); PGF2α (day 7); GnRH (day 9); fixed time (Artificial Insemination) AI, 16 h after last GnRH treatment
3 Progesterone implant for 12 days (not for dairy cows).

be used for breeding [51]. Use of GnRH as prophylactic treatment has shown some success in decreasing occurrence of cysts in herds. It has been recommended that all cows should be treated with 100–200 ìg of GnRH 12–14 days postpartum. Minimizing stress and by preparing cows to cope with the stresses they inevitably encounter. Good nutrition is essential, prevention has to begin with condition scoring midway through the previous lactation. Cows should be fed to achieve a score of 3.5 - 3.75 during the last half of lactation at dry off and maintained at this level through to calving. Adequate (but no excessive) body reserves will help to decrease negative energy balance in early lactation. The dry cow feeding program stresses attention to the specific needs of the cow at this stage of her production series. Close-up rations must be designed with the objective of minimizing the occurrence of hypocalcaemia, ketosis, abomasum displacement and other disorders which occur after calving. Trace mineral and vitamin intakes are often insufficient in the dry period when cows are not receiving additional grain. Numerous studies have demonstrated the beneficial effects of supplemental selenium along with vitamin A, vitamin E and beta-carotene in maintaining immune competency against cystic ovary [6].

Economic Impact of Cystic Ovarian Disease: Reduced reproductive performance is the most common cause of economic loss in dairy cattle industry at worldwide level. Cystic ovarian disease is a cause of temporary infertility and one of the most common reproductive disorders in dairy cows with a reported incidence of 6 to 23% [2]. COD is associated with a 6 to 11 day extend in the calving to first service gap and a 20 to 30 day increase in the calving to pregnancy interval above the standard. It is also known to increase the risk of culling. The economic loss resulting from the rate of ovarian cysts are mostly due to the effects on the cost of feed, average growth of calves, labor and medical prices [52].

The culling rate was greater in the ovarian cyst group (21.2%) than in the non-ovarian cyst group (13.4%) beyond 8 weeks postpartum, while its rate was not different between the ovarian cyst group (13.5%) and the non-ovarian cyst group (15.0%) within 8 weeks postpartum. The economic loss associated with the occurrence of ovarian cysts was estimated at approximately 823,996 won ($687) due to the effects on the cost of nutrition, average growth of calves, labor and medical costs and culling in Korea dairy farm [8]. Bartlett *et al*. [53] reported that the economic loss associated with the average lactating cow with ovarian cysts was estimated at approximately $137, resulting from the effects on reproduction, culling and medical and labor expenses in Sweden dairy farm. The different economic losses reported in the two studies might be explained by differences in reproduction, feed costs and items included for calculation of economic loss [8].

Status of Cystic Ovarian Disease in Ethiopia: In Ethiopia, there is no well documented information about cystic ovarian disease and its economic impact. However, there are some data reported by different authors, which indicate the prevalence of the disease in the country. The report of COD prevalence in different areas of the country is summarized in the table below.

Table 2: Prevalence of cystic ovarian disease in some parts of Ethiopia

Study area	Prevalence	References
Hawassa	5.22%	[54]
Bahir Dar	3.5%	[55]
Sululta	3.3%	[56]

CONCLUSION AND RECOMMENDATIONS

Cystic ovarian disease is the most economically important problem of dairy farm which can result in anovulation, delay in reproduction, decreased milk production leading to loose of money and economic crisis for dairy producer. There are three types of ovarian cysts in dairy cattle; follicular cysts, luteal cysts and cystic CL. The most likely causes of COD are the disruption along the pathway of hypothalamus or neuro-endocrine imbalance involving the hyphothalmic-hypophyseal-gonadal axis. The most important clinical symptom to determine ovarian cysts are nymphomania and anoestrus. COD is accurately diagnosed when combination of physical examination, ultrasonography and plasma progesterone testing are applied. The most effective treatment after accurate diagnosis of COD is GnRH followed by PGF2α and prevention is directed against the removal suspected cause (reducing stress and by genetic selection).

Based on above conclusive remarks the following recommendations are forwarded

✓ Improve and enhance the fertility of dairy cows through selective culling of bulls that have sire daughters suffered from COD is recommended.

✓ Since COD significantly reduces the reproductive efficiency as well as the expected output of dairy farm, the dairy producer must be awared of the condition and brought the cow to veterinary clinic while showing an abnormal estrus behavior or nymphomania and fails to conceive twice or more times after insemination.

✓ Since there is no organized information about cystic ovarian disease in Ethiopia, detail national review and upload in national repository system is mandatory.

✓ The information concerning the status and economic impact of the disease in Ethiopia is very scanty, therefore, research focusing on this particular disease is requiring due attention.

✓ Capacity building in animal reproductive health and biotechnology should be promoted to reduce the economic impact of this disease.

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