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Factors affecting first ovulation in postpartum dairy cows under tropical conditions: A review

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Abstract
It is documented that the reproductive performance of postpartum dairy cows is influenced by both internal and external factors. One of the most important reproductive performance indices is the first ovulation postpartum. This review aimed to describe factors affecting first ovulation postpartum in dairy cows, particularly those raised under tropical climates. Negative energy balance and its consequences; metabolic disorders; uterine pathology; udder health; lameness; and heat stress are discussed for their potential effects on the first ovulation postpartum. Understanding the underlying mechanisms of those affecting factors would assist in justifying the treatment and prevention plans in order to optimize the reproductive performance of postpartum dairy cows.
Keywords: Dairy cows, First ovulation, Heat stress, Reproduction, Tropical condition.

Introduction

Reproduction management is an important area for economic success in dairy farming. Many key indices are used to evaluate the reproductive performance of dairy cows, including days open, pregnancy rate, heat detection rate, number of inseminations per pregnancy, etc. Economic impacts were reported to be approximately £2.41 per day of prolonged days open (Esslemont *et al.*, 2001) and $622.40 per cows with failed conception at first ovulation (Kim and Jeong, 2019). To reduce economic losses, a cow has to be maintained in a well condition of nutrition, reproduction, health, and comfort. In particular, two main factors to be considered were the ability of cows to ovulate early postpartum and the pregnancy succession after ovulation. In case of failure to conceive, factors associating with cow; insemination; and heat detection must be considered. Follicular development and ovulation postpartum are stimulated by an appropriate function of gonadotropin-releasing hormone (GnRH) that is closely related to energy status (Garcia-Garcia, 2012).

Under tropical conditions, cows exposed to high temperature and/or high humidity could suffer from heat stress. Thereafter, reduced milk production, poor reproductive performance, and impaired health conditions are observed in heat-stress cows (Tao *et al.*, 2020). To maintain normal thermoregulation, cows would adapt metabolically, endocrinologically and behaviorally to heat stress conditions (Tao *et al.*, 2020). All adaptations to minimize the impact of heat stress could alter energy status (West, 2003) and welfare (Polsky and von Keyserlingk, 2017), resulting in prolonged first ovulation postpartum; thus, creating significant problems in tropical dairy farming. This review aimed to describe factors affecting first ovulation postpartum in dairy cows, particularly those raised under tropical climates. It is essential to understand the underlying mechanisms of those affecting factors prior to justifying the treatment and prevention plan in order that the reproductive performance of postpartum dairy cows could be optimized.

Postpartum reproductive problems

Postpartum reproductive disorders in dairy cows especially under tropical climate are unique in various aspects as compared with other geographical areas. Apart from environmental conditions, tropical areas were dominated by small-holder farming that usually had a greater chance of improper farm management than did the commercial ones (Moran, 2005). In the tropics, a key factor to be considered is heat stress that has several negative effects on milk production, reproductive performance, and health condition.

Failure of reproductive performance in dairy cow postpartum could occur intrinsically by reproductive disorder such as delayed uterine involution, retained placenta, metritis, or cystic ovaries. In addition, extrinsic factors both from negative energy balance

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(NEB) related conditions and from diseases leading to NEB were in concerned. In general, first ovulation was expected to occur within the first month after calving (Cheong *et al.*, 2016). To maintain early ovulation, good management throughout prepartum to postpartum period must be practiced.

Several diseases that occurred during the postpartum period were consequently from failures of prepartum management for example milk fever, dystocia, or fatty liver (Tillard *et al.*, 2007). During postpartum period, appropriate overall management and heat stress prevention, while maintaining proper cow comfort conditions, were the key factors to be considered. Reproductive-related problems including dystocia, metritis, endometritis, delayed uterine involution, cystic ovarian diseases play as postpartum intrinsic factors that delay first ovulation in transition dairy cows (Tillard *et al.*, 2008). Not only reproductive disorders, but other extrinsic factors influencing energy balance conditions or increasing stress and serum cortisol could also delay first ovulation in transition dairy cows (Baruselli *et al.*, 2016).

NEB is a major condition that is unavoidable in dairy cows during the transition period. Failure to minimize NEB leads to a deficiency of energy to activate reproductive activity. When NEB is severe, the cows are prone to ketosis and fatty liver that could impair immune responses and increase the risks of other diseases (Raboisson *et al.*, 2014). On the contrary, postpartum diseases and other health disorders that have negative effects on dry matter intake (DMI) enhance the severity of NEB condition in the transition cows (Suthar *et al.*, 2013). Factors related to cow comforts are improperly practiced by tropical dairy farms especially small-holder ones, for example, increased standing time, lack of routine claw trimming, overcrowding, and lameness.

Tropical condition and its effects on reproductive performance

A dairy cow is an important livestock animal that has ability to adapt to a wide variety of geographical areas. High production of milking cows has been reported ranging from frozen tundra to dessert throughout North America, Europe, Australia, and Asia. Heat stress is a major limitation for maximizing the production of dairy cows in sub-tropical and tropical climates. In dairy cattle, Temperature Humidity Index (THI) calculated from environmental temperature and humidity was the conventional parameter to evaluate heat stress conditions (Bouraoui *et al.*, 2002). When THI exceeds 72, cows would shift their physiological status to maintaining normal core temperature. This adaptation reduces overall production and impairs health conditions.

The first signs of physiological responses to high THI are a decrease in DMI and an increase of respiratory rate. In the condition that cows were offered separate feeding, a dramatic drop in forage intake should be monitored for preventing sub-acute ruminal acidosis (SARA). Behavior changes by increased standing time and reduced lying time are also noted. In dairy cows, a longer standing time together with SARA increase risk of lameness (Polsky and von Keyserlingk, 2017). If heat stress condition is greater than the ability of cattle to cope with all adverse consequences, body temperature would increase, causing a significant reduction in milk production, reproductive performance, and health condition.

In sub-tropical or low humidity-tropical area, water spraying system has been used to keep the cows cool both in the feeding line and holding area. A combination of showering and ventilation system strongly reduces the negative impact of heat stress. In tropical areas, particularly near the equation line, high humidity normally occurs. Methods of heat stress alleviation using water should be carefully practiced with caution on elevating humidity or increasing the risk of mastitis in the cows lying down on wet surfaces. Mismanagement of the cooling system possibly leads to illnesses indirectly result in delayed first ovulation and reduced reproductive performance. Another aspect of heat stress prevention is genetic selection. Heritability estimates of the body temperature and the decline of milk yield during heat stress in Holsteins were 0.17 and 0.19, respectively. According to these numbers, breeding selection to encounter heat stress problems in dairy cows is also possible (Nguyen *et al.*, 2016).

Differences in forage availability between geographic areas are important factors. In the tropics, forages could be available to cultivate year-round. However, the nutrient quality of the forages is relatively low as compared to those forages in the temperate area. Therefore, the stability of the forage quality is considered a constraint in most small-holder farming. At peak production, especially during the hot season, feeding dairy cows to maintain body condition score (BCS) is challenging in tropical area due to the fact that the DMI of the cows is reduced and low-quality forage is fed to the cows. This leads the cows to be prone to NEB condition and, subsequently delaying first ovulation.

Effect of heat stress both short and long term on reproductive performance of dairy cows have been studied extensively by many researchers. Method to study the effect of heat stress has been conducted artificially by climate control chambers or in natural conditions within tropical areas. During pregnancy, heat stress has epigenetic modification effects on offspring via ovarian glucocorticoid responses. This epigenome changes have the potential to have trans-generational effects on reproduction when offspring reach puberty (Huber *et al.*, 2020). During the transition period, many studies found a negative relationship between THI and reproductive disorders in dairy cows. There was a report showed a high dystocia percentage of first calving heifer when THI is above 77 (Mellado *et al.*, 2019). Increased percentage of cows with retained placenta compared between each season in tropical areas were studied (Ahmadi and Mirzaei, 2006). Rather than ovulation, heat stress had significant negative impacts on conception rate, early embryonic death and days open (Wolfenson and Roth, 2019). Some immunocompromisation is also reported in heat stress cows. When exposed to high THI, oxidative stress and cytokine production are altered, which might result in the reduction of immune responses and reproductive performance (Safa *et al.*, 2019).

First ovulation postpartum

Period of calving to first ovulation of post parturient dairy cow is reported to correlate with overall reproductive performance (Smith and Wallace, 1998). Dairy cows ovulating before 21 days post parturition had a better reproductive outcome when compared with cows that ovulate 21–49 days post parturition (Galvão *et al.*, 2010). For a dairy cow to ovulate early after calving, factors related to the hormonal pathway name hypothalamic-pituitary-ovarian (HPO) axis need to be considered. HPO axis starts by secretion of GnRH from the hypothalamus that stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary. FSH and LH are major hormones responding to follicular development and ovulation.

Relationship between metabolic pathway and HPO axis were studied. Leptin was a hormone that involved in the regulation of both metabolic status and reproduction system (Liefers *et al.*, 2005). When cows have adequate energy balance, leptin acts as a hormonal signal of nutritional status that increased secretion of growth hormone and GnRH (Hoya *et al.*, 2015). Delayed first ovulation, first estrous sign and decreased circulatory serum leptin were found in dairy cows enter NEB post parturition (Liefers *et al.*, 2003; Çolakoğlu *et al.*, 2017).

Direct effects of heat stress on HPO axis and other reproductive hormones were also found. When exposed to stress, there are physiological changes in hypothalamus-pituitary-adrenocortical axis result in the alteration of serum cortisol concentrations. However, changes of serum cortisol in responded to heat stress are varied. The variation depends on the stage of stress response; acute stress tends to increase serum cortisol concentration (Chen *et al.*, 2015). In contrast, chronic exposure to stressor demonstrates both high and low serum cortisol concentrations as compared to normal cows. these variations have been suggested to be depended on the degree and type of stressor that affects the dairy cows (Trevisi and Bertoni, 2009). Cortisol from stress conditions including heat stress has negative impacts on reproduction. Thus, it inhibits HPO axis function, reduces GnRH secretion, inhibits LH secretion from the pituitary gland and declines estrogen concentration. Not only hormone secretion, cortisol also has negative effects on estrogen-targeted tissue (Fernandez-Novo *et al.*, 2020).

Suppression of LH pulse and the earlier surge of LH pre-ovulation in dairy cows during the warm season has been reported. For serum FSH, increased serum FSH concentration is suggested to be resulting in decreased ovarian inhibin. Elevation of FSH and suppression of LH in heat stress cow are associated with an increase of anovulatory follicles, cystic ovarian or double ovulations (De Rensis *et al.*, 2017). Prolactin is a hormone causing an extension of post-partum anestrus period. It is noted that serum prolactin concentrations are increased during high temperature climate, which might influence reproductive performance in heat stress dairy cows (Prathap *et al.*, 2017). Alteration of estrogen during heat stress has been reported. Decreased serum estrogen concentrations result in reduced follicular development and oocyte quality in post-partum dairy cows (Wilson *et al.*, 1998). In sub-tropical areas with a wide difference in photoperiod between hot and cool season, the effects of day length on melatonin production that subsequently alters serum insulin-like growth factor-1 (IGF-1) concentrations should be considered (Dahl *et al.*, 2000).

Factors influencing postpartum ovulation

NEB and its consequences

Heat stress has strong effects on the energy balance of dairy cows mainly by reduction of DMI. For transition cows exposed to heat stress conditions, the cows will enter a higher degree of NEB compared to non-heat stress cows. Directly, NEB suppresses HPO axis function resulting in the reduction of follicular development. Indirectly, metabolic consequences of NEB, such as ketosis, fatty liver, also impair follicular development and early ovulation of postpartum cows.

During the NEB stage, lipolysis process in adipose tissues occurs. If non-esterified fatty acid (NEFA) exceeds the capacity of the cows to metabolize to produce energy, these excess NEFA must be further metabolized into other metabolic fuels namely ketone bodies. If ketone bodies are synthesized at a high degree, the cows could enter into sub-clinical or clinical ketosis stage. Cows with sub-clinical ketosis are at increased risk to postpartum diseases and disorders, including metritis, mastitis, displacement abomasum, milk fever, and impaired immune functions. The latter would result in increased risk of infectious disease that consequently delayed ovulation (Seifi *et al.*, 2011; Trevisi *et al.*, 2012). Another NEB-related disease is a fatty liver that also causes an alteration of reproductive hormone. IGF-1 is a reproductive-related hormone produced mainly by the liver in adult cows. In cows with fatty liver disease, there is a decrease in serum IGF-1 concentrations, which impairs reproductive performance (Fenwick *et al.*, 2008). A study in the tropical area demonstrates that multiparous cows in the late ovulation group (greater

than 45 days post-parturition) have significantly lower concentrations of serum IGF-I (Kadivar *et al.*, 2012).
For initiation of follicle waves after calving, a study in tropical climate shows no differences in first follicular development, but longer duration from calving to first ovulation, lower BCS, and higher incidence of lameness in the delayed ovulation cows as compared with the early ovulation cow (Guáqueta *et al.*, 2014). The other study found that the start of folliculogenesis is not in regard to the NEB status; however, the development of the ovary and period of ovulation is decreased when BCS is lower than the appropriate level (Wathes *et al.*, 2007).

Metabolic disorders

Milk fever was an important metabolic disorder to be monitored in tropical small-holder farms. Prevention of hypocalcemia post-partum is failed due to the inability to provide low calcium and negative DCAD diet to pre-parturition cows. Though there is no direct relation between heat stress and milk fever, but there is a high risk of NEB in heat stress cows. NEB cows have dropped in DMI post parturition; then their daily feed intake of calcium and magnesium could be reduced to the levels that lead the NEB cows to develop hypocalcemia (DeGaris and Lean, 2008). In addition, the study in humans found that non-alcoholic fatty liver disease, caused lower serum concentrations of active vitamin D compared to healthy ones. NEB cows suffer from fatty liver disease might have insufficient amounts of the active vitamin-D to prevent hypocalcemia (Mulligan *et al.*, 2006). Study in tropical climate shows that serum calcium negatively correlated with serum NEFA, and positively correlated with serum glucose. Both NEFA and glucose are the indicators of NEB condition (Noorman, 2014). As a consequence, cows with milk fever increase risk of dystocia, abomasum displacement, retained placenta, metritis and uterine prolapse, which could prolong first ovulation after calving.

SARA also a metabolic condition to be concerned in tropical transition cows. Firstly, heat stress cows have a reduction in rumen buffering capacity as a result of hyperpnea, saliva loss, and behavior changes (Shearer, 2005). Moreover, there is an increase in lactate producing bacteria in the rumen of cow exposed to heat stress (Zhao *et al.*, 2019). In separate feeding or total mixed ration system with improper particle size management, forage intake refusal also found in heat stress cows. There is a study demonstrating that the group of cows with SARA have a higher anestrous percentage at 60 days after calving as compared to noon-SARA cows (Vallejo-Timarán *et al.*, 2020).

Uterine pathology

Heat stress has effects on uterine pathology for example delayed uterine involution, retained placenta or metritis. A study shows that during hot period (May to September), incidence rate of retained placenta and postpartum metritis was two times higher compared to the rest of the year (DuBois and Williams, 1980). Accordingly, cows suffered from puerperal metritis have a delayed first ovulation and a higher risk for double dominant follicle at first follicular wave, after the first ovulation (Juodžentis *et al.*, 2020). Other study found that cows with retained placenta have 7 days longer for mean intervals from calving to first service compared to healthy cows (Han and Kim, 2005).

Udder health

Mastitis is an inflammation condition of udder in dairy cows that should be monitored intensively during heat stress (Dahl, 2018). Cows with clinical mastitis have an impairment of reproductive functions. Even with subclinical mastitis, high SCC also has negative effects on follicular development and oocyte quality (Wolfenson *et al.*, 2015). It is possible that cytokines or inflammatory stress from mastitis that occurred during follicular development could suppress pulsatile LH secretion and delay preovulatory LH surge, resulting in a failure of early ovulation (Kumar *et al.*, 2017). An experiment shows that some mastitis cows that have extended the period of estrous to ovulation time have lower estrogen concentration at the onset of estrous as compared to healthy cows (Lavon *et al.*, 2010).

Lameness

From behavior responding to the heat stress, dairy cows exposed to heat stress increase standing time and decrease laying time significantly (Cook *et al.*, 2007). Behavior changes during heat stress would increase the risk of SARA. Together with improper housing design in a small holder farm, high percentage of lame cows is recorded in tropical dairy farms. Previous study shows that lame cows that do not ovulate and fail to express estrus or ovulate a low estrogenic follicle were 29% and 21% during 30–80 days post parturition, respectively (Morris *et al.*, 2011). When classified as lame, lame cows show 3.5 times greater chance of delayed ovulation compared with cows classified as non-lame. Thus, prevention of lameness could reduce delayed ovarian cyclicity in lame cows for 71% (Garbarino *et al.*, 2004). In tropical small holder farm, a study shows a significantly longer calving to first service of lame cows compared to non-lame cows in both high and low lameness prevalence (Ratanapob *et al.*, 2020).

Heat stress

Elevation of THI induces several consequence conditions leading to delayed ovulation including NEB, metabolic disorders, uterine pathology, mastitis, and lameness. It also affects reproductive hormones, stress responses, and antioxidative capacity, resulting in a prolonged period of calving to first ovulation. A study in lower-temperate area found that there are 3.9-time increased risk of ovulation failure postpartum in dairy cows during the hot season compared to cool season (López-Gatius *et al.*, 2005). In contrast, a study from tropical area does not find any effects of climate (mild *vs.* severe heat stress) on calving to first ovulation (Kaewlamun, 2010). Another study also does not find any differences in calving to the onset of ovarian activity interval between cooled-cows kept in evaporative cooling system and un-cooled cows under tropical climate (Suadsong *et al.*, 2008).

Conclusion

First ovulation postpartum in tropical dairy cows is influenced by various factors. Heat stress in combination with low quality forage or disadvantage of small-holder scale farming in tropical area could affect follicular activity directly by alteration of HPO axis function, or indirectly by stress responses and reduced antioxidant capacity. When cows respond to high THI, physiological and behavioral changes increase risk of other diseases and disorders namely NEB, fatty liver, milk fever, metritis, mastitis or lameness that consequently increase severity of delayed ovulation. A key to improving reproductive performance and to reduce calving to the first ovulation period is to alleviate heat stress conditions and the prevention of other consequences condition in tropical dairy production.

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