



## Transition Period in Dairy Cows: Monitoring, Challenges, and Future Perspectives



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### Abstract

THE transition period represents the most critical time, with excessive metabolic stresses, endocrine changes, and impaired immune function. Monitoring dairy cows during the first 15 days in milk (DIM) is necessary for early prediction and intervention with any disease biomarkers during the subclinical stage. Several metabolic disorders have been recorded during the transition time such as, clinical hypocalcemia, subclinical hypocalcemia (SCH), clinical ketosis, subclinical ketosis (hyperketonemia), and fatty liver. The incidence of clinical metabolic disorders has been decreased with the improvement in dietary management of cations and anions during periparturient time, as well as a deeper understanding of transition period physiology. Traditionally, metabolic profile tests, Urine pH, and changes in BCS were used to monitor the transition cows. Inclusive, automated precision technology records any changes in activity and rumination time and alerts dairy staff to potential health issues in dairy herds. Additionally, metabolomics approaches aim to identify any predictive biomarkers for dairy cows suffering from metabolic disorders. Liver activity index (LAI) has been used as a predictor in dairy herds to evaluate the severity of inflammation around periparturient time.

**Keywords:** dairy cows, hypocalcemia, transition period, ketosis, precision technology.

### Introduction

Periparturient time has different physiological challenges for dairy cows. This vulnerable time has more metabolic stresses, significant endocrine changes, and declining immune function, which consequently increase the risk of disorders such as hypocalcemia, ketosis, hepatic lipidosis, laminitis, and abomasum displacement [1,2]. The transition period is a critical stage in the dairy cattle production cycle and has an impact on health and production. Thus, the success of this time phase directly affects the total profitability throughout all lactation seasons [3]. This period is marked by extensive changes in the animal's endocrine condition that are significantly more noticeable than at any other stage in the lactation-gestation cycle because of reduced feed intake, increased nutrient demand for the growing fetus, and lactogenesis [1,4]. During this time, dairy cows have a negative energy balance (NEB) because of the significant increase in energy requirements which caused by milk production [5,6]. Briefly, the NEB occurs when feed intake is too low to meet the energy requirements for body maintenance and milk production [6].

Dietary management has been widely investigated due to the significant changes that dairy cows must make to adapt to the metabolic challenge of high milk supply [7]. Furthermore, the most critical metabolic disorders that affect the performance and production of dairy cows occur at this crucial phase [8]. Dry matter intake drops with a reduction in energy and essential minerals [9]. Also, the coordination of lipid and mineral reserve mobilization is dependent on homeostatic and homeoerotic adjustments [10,11]. Cows that produce a lot of milk require better food and medical care. Inclusive, they must switch from anabolic to catabolic metabolism as the need for energy intake increases from 30% to 50% during the first few weeks of lactation compared to pre-partum energy consumption [12]. The stages of the lactation cycle, starting from the dry period until the whole lactation season, are documented in Figure 1. Hormonal changes during the periparturient time are sudden. Thus, the perfect hormone concentration is critical for maintaining the cow's health and an effortless manner of parturition [13]. Dynamic changes for many hormones, such as progesterone, estrogen, cortisol, and insulin, are associated with the stress of

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parturition and lactogenesis during the transition period.

#### *Monitoring the Transition Dairy Cow*

The ideal stocking density within dairy farms is critical to avoid any health disorders [14]. An increase in stocking density is associated with higher health disorders [15]. Perfect heat regression with clean, dry, and well-constructed stalls is recommended to minimize the detrimental effect of heat stress. [16,17]. Daily cow ration monitoring is recommended to determine whether the feed is being delivered; the fundamental goal of effective transition cow nutrition management is to match the recommended diets for each group of cows. [14]. Completer documentation of the causes of death is necessary to determine the future direction of management [18]. The early lactation milk yield and milk composition analysis can be used to assess the health of transition cows and determine whether peak milk production meets performance and management expectations [19]. Disease development and the high risk of culling from the herd by the first three months in DIM are closely related to decreased milk production during early lactation [20,21]. Inclusive, daily examination of post-parturient cows is critical for detecting disease markers in the subclinical stage [22,23]. Interestingly, tracking disorder incidences during the first few weeks of lactation offers valuable information regarding transition period management efficiency [24].

The metabolic profile is an effective instrument used in dairy herds to identify blood chemistry abnormalities associated with production diseases [25]. Its role has been expanded to measure any body fluids that can reflect pathophysiological changes [26]. The metabolic profile test can be an effective tool for predicting periparturient problems and assessing nutritional status and stress levels [27]. Changes in the body condition score (BCS) can be used to assess the severity of mobilization during periparturient time [28]. Furthermore, body condition scoring provides a quick, convenient, and cost-effective monitoring indicator for evaluating the nutritional status of dairy cows, making you feel efficient and resourceful in your management practices [29].

#### *Metabolic challenges during transition period*

##### *Hypocalcemia*

The average calcium requirement in non-lactating dairy cows for daily body function and activity is approximately 21g [30]. The Holstein cows, which produce 50kg of milk daily, need an additional 55 g of Ca per day to maintain the normal adaptation [31]. The dramatic increase in Ca demand coincides with a 30% drop in feed consumption near parturition, limiting this vital macro-mineral at a critical time. As a result, proper Ca homeostatic regulation is crucial

for sustaining life and productivity [32,33]. The failure of dairy cows to regulate the blood concentration after calving led to clinical hypocalcemia, which affected less than 5% of post-parturient cows [34]. The average calcium concentration ranged from 8.7 to 11 mg/dl in healthy fresh cows [35].

The prevalence of milk fever in dairy cows ranged from 0.60 to 5.0%, while subclinical hypocalcemia affected 14% to 50% of the cows after calving [36]. Hypocalcemia occurs in high-producing multiparous dairy cows [37]. Hypocalcemia has been a problem in the dairy industry for more than 200 years, particularly in clinical cases which, are usually known as milk fever [38]. Through dietary management of cations and anions during the dry phase and early lactation, as well as a deeper understanding of transition period physiology, the incidence of hypocalcemia has been decreased [39]. Hypocalcemia also has been associated with reproduction problems and impaired rumen and abomasum motility [34]. Also, [40] said that mastitis and endometritis are linked to hypocalcemia, which also reduces milk quality and production. Moreover, the dairy industry consequently experiences significant losses. [41] concluded that hypocalcemia increases the risk of abomasum displacement, decreases feed intake, and impairs immune cell functions. [36] mentioned that in modern dairy cattle, the prevalence of clinical cases is low due to the advancements in nutritional and management strategies. Subclinical hypocalcemia may occur in 73% of animals of parity more than two during the first three days in milk [42].

Subclinical hypocalcemia (SCH) is known as low calcium levels without the appearance of clinical symptoms [3]. Several cut-off points have been used to define the SCH, which ranged from 8 to 8.8 mg/dl, depending on the time of evaluation [39,43]. Blood Ca concentrations in healthy dairy cows with normal adaptation reach a nadir at 24 h postpartum [34,44]. [39] mentioned that 50% of high-producing dairy cows suffer from a reduction in Ca concentration immediately after parturition without any symptoms, which is known as subclinical hypocalcemia. The incidence of SCH increases the risk of reduced fertility milk production [33], metritis, hyperketonemia, displaced abomasum, culling, and other adverse health outcomes [44,45]. Subclinical hypocalcemia induction resulted in a decrease in dry matter intake (DMI) compared with normo-calcemic cows. Furthermore, a drop in rumen contractions which has an adverse effect on rumination and passage speed of the feed in cows with induced SCH [46]. The reduction in the digestive capacity which was detected in cows with SCH could explain the decrease in DMI [47].

The transit reduction of Ca concentration after parturition represents a beneficial part of normal adaptation to the start of colostrum production and milk yield expansion. However, the persistence or delayed drop of calcium after calving increases the risk for poor production and reproduction performance and represents a significant metabolic disturbance [47]. A single blood sample taken within 12 hours of calving, which is used to diagnose SCH, does not provide an accurate predictor of increased risk of disease development [48]; It is recommended to monitor the dairy cows and measure the total Ca concentration during the first 4 DIM for perfect prediction of SCH and detection the reduction dynamics [33,43]. In comparison to cows that were only normo-calcemic or hypo-calcemic during the first 1DIM, those that had SCH for the first 3DIM had a higher disease risk and reduced reproductive success [49]. The persistence of SCH after the first day is positively correlated with a greater risk of later disease development and lower milk production [33]. The reduction in Ca concentration immediately after calving does not affect the possibility of diseases or milk production. Furthermore, the persistence of SCH is associated with adverse outcomes and poor performance [49,50].

#### *Hypocalcemia and hypomagnesemia*

The lack of magnesium is a significant risk factor for low calcium levels [31,51]. The metabolism of Calcium (Ca) decreases gradually with any reduction in magnesium (Mg) level due to the reduction of parathyroid hormone secretion (PTH) [44,52]. Thus, postpartum hypocalcemia can be monitored by assessing Mg status to avoid hypomagnesemia [44]. The PTH stimulates the mobilization of the Ca from the skeleton store, improves the absorption of Ca from the intestine, and decreases the Ca loss [52]. Therefore, PTH insufficiency increases the incidence of hypocalcemia. Subclinical hypocalcemia reduces the rumen contractions and, consequently, affects the passage of digesta inside the rumen [46,53]. Also, SCH decreases dry matter intake [46,47]. Any reduction in DMI can have a harmful effect on the blood levels of Ca and Mg because feed represents the primary source for these minerals [31,51].

#### *Ketosis (Hyperketonemia)*

Dairy cows experience a negative energy balance (NEB) around the calving [54]. Additionally, it increases energy requirements to support colostrum and milk production expansion [55]. Ketosis occurs in dairy herds during the first two weeks of lactation, either in clinical or subclinical form [9]. This period is associated with a voluntary reduction in feed intake and start of lactogenesis, which requires glucose to support milk lactose [54,55]. Thus, dairy cows suffer from hypoglycemia during this time. The failure to meet the energy demand for producing milk and colostrum after calving leads to severe

negative energy balance (NEB), which is followed by extreme lipid mobilization, as well as an increase in circulating non-esterified fatty acids (NEFAs) and ketone bodies in tissues, blood, and milk [56,57]. [58] mentioned that severe mobilization leads to higher concentrations of circulating ketone bodies (hyperketonemia). Furthermore, the poor adaptation to NEB with more NEFA overloading in the liver leads to this metabolic disorder [56]. Dairy cattle with ketosis may show clinical signs (clinical form) or may not show signs (subclinical form) during transition period [59,60]. The unsuccessful adaptation to NEB with a severe or prolonged decline in dry matter intake around calving leads to subclinical ketosis (SCK), which is also known as hyperketonemia [59]. The peak incidence of SCK in the first five days in milk. Moreover, 43% of dairy cows suffer from SCK during the first two weeks of lactation [11,59]. Subclinical ketosis can result in significant economic losses due to an increase in postpartum disorders such as displaced abomasum, metritis, and fatty liver [58]. Additionally, the removal of animals from the herd with poor milk production and reproductive problems [61].

Some authors [11] reported that early detection of ketosis allows for prompt treatment, reducing productivity loss. The gold standard for ketosis diagnosis is the measurement of plasma or serum Beta-hydroxybutyrate (BHB) concentration, which is costly and time-consuming to establish an intervention plan [62]. Ketone sensors designed for human use have been monitored and tested over the last decade for use as quick and affordable diagnostic instruments for dairy cows [63]. Recently, the detection of SCK has improved due to technological advancements [11,64]. The determination of blood BHB concentration on the farm by the electronic cow side test has been validated [65], making the detection of SCK reliable, rapid, and accurate. Hyperketonemia detection is currently a challenge for producers in reducing economic losses [66]. There is substantial evidence that assessment of the animal behaviors and activity can be used to detect cows suffering from hyperketonemia [67]. On the other hand, a recent study reported that animal behaviors and activity prior to calving could not predict dairy cows with high BHB or NEFA postpartum [68].

#### *Fatty liver*

Fatty liver is associated with decreased reproductive performance and impaired health status, with 50% of all cows having some accumulation of triacylglycerol in the liver [69]. The adipose tissue fatty acid mobilization is a regular biological event in most lactating cows to support lactation nutrient demands [2]. The excessive concentrations of NEFA in dairy cow blood cause triglyceride accumulation in hepatocytes and impairment of liver function [11]. Fatty liver infiltration is highly relevant in dairy

cows because the liver is also vital for regulating feed intake, reproduction, immunity, and metabolism [70]. The NEFA metabolism must be monitored to reduce fat deposition in the liver during early lactation for effective metabolic health and production [71]. Additionally, reducing the detrimental effects of NEFA toxicity [72].

The transfer of NEFA into the blood supplies energy to tissues throughout the body but in low concentrations because the excess may become harmful and has detrimental effects on health conditions and productivity [72]. The normal function of the liver is impaired by an excessive accumulation of triacylglycerol (TAG), which also increases the risk of fatty liver syndrome development [73,74]. The development of fatty liver reduces the gluconeogenic activity of liver tissue [72].

#### *Future perspectives and precision technology*

Variations in activity and rumination time in dairy cows can be detected by the automated monitoring systems, which send alerts to farm managers. Furthermore, these systems are predictive tools for reducing costs and improving the general health conditions of animals [75]. These systems help veterinarians to focus on animals that need examination and more investigations during the transition phase [75,76]. Precision technology seeks to improve decision-farm productivity and profitability [77]. This technology gives farmers independent methods for monitoring animal behavior and detecting any health issues [78], allowing them to use better management techniques [79]. These technologies could predict which cows are at risk for disorders. For instance, prepartum behaviors are linked with postpartum disorders [80,81], indicating that they can predict transition cow health [82,83].

Many researchers [78,84] reported that daily activity, eating, and ruminating patterns are widely regarded as essential predictors of cow productivity and health, which may aid in understanding the nutritional physiology of dairy cows. Automated systems can predict dairy cows that suffer from clinical hypocalcemia [85,86], metabolic and digestive disorders [87], and metritis and pneumonia [88] before farm owners intervene with the disease. Production producers must investigate the behavioral features of transition cows to develop protocols for treatment, as well as management methods [64,85]. Moreover, the detection of any changes or alterations in the physiological and behavioral conditions is vital to reduce any losses from poor milk production and health costs [78, 87].

Visual observation of rumination time and activity is considered the gold standard method, but it is labor-intensive, time-consuming, and needs more effort, especially in large herds [89]. Recently, more devices have been validated and used to monitor

daily rumination and activity through different algorithms. Such as the Hi-tag rumination monitoring systems (neck collars), which records the mastication sounds with high sensitivity for detecting indigestion, ketosis, and displaced abomasum [64,87,89]. Also, behavior Recorder systems (IGER) measure jaw movements as an indication of rumination [90]. Another system, the Cow Manager Sensor records the ear movements to detect rumination and activity behaviors [91]. The ear tag sensor has been validated and scored high sensitivity compared to the visual observation to detect any reduction in rumination, feeding, and activity [78].

#### *Rumination time (RT) and activity behaviors*

Rumination time, dry matter intake, and activity behaviors can be used to predict possible health disorders [83]. The metabolic state and disease condition of dairy cattle are linked to rumination time around parturition. As a result, rumination monitoring may be helpful in predicting the health status of dairy cows during a critical time such as the transition phase [92]. Rumination time during the first week of lactation is an effective way of identifying cows that have high-risk odds for diseases [93]. The rumination time and activity behaviors were calculated by precision technology as total min/h spent ruminating or being active and reported as the total number of min/d, with rumination or activity presented as a 24-hour interval from 00:00 to 23:59 [43,68]. The early prediction of clinical and subclinical disease using RT and activity declines the economic losses associated with poor production and extends treatment [94].

Approximately 90% of dairy cows with low prepartum RT suffer from clinical disorders and poor production in the first days of lactation [93]. Furthermore, daily rumination time reduction was detected in dairy cows with subclinical diseases and health disorders in the first days of lactation [83]. The differences between animals in rumination time and activity can be used as indicators to detect the different health disorders [95]. Understanding rumination behavior can support the identification of dairy cows in the transition phase who are at risk for metritis, subclinical ketosis, and lameness [81,96]. Several studies reported a strong correlation between rumination behavior and post-partum disorders. For example, cows with postpartum subclinical ketosis (SCK) and metritis are ruminated less than healthy cows [66]. Also, dairy cows with low prepartum DMI and eating time have high odds of developing ketosis postpartum [97]. Also, [98] mentioned that total daily rumination time (TRT) is a valuable predictor of Subclinical ketosis (SCK) during the transition phase. Healthy cows spent more time active than diseased cows during both prepartum and postpartum periods and had more rumination time than sick cows [99]. Cows with metritis during the

transition phase showed different feeding behaviors and consumed less food than healthy cows [96].

#### *Metabolomics approaches*

Metabolomics is the science of detecting and quantifying metabolites and tiny molecules [100,101]. The investigation of metabolites allows the discovery of new predictive biomarkers [102]. Metabolomics has been shown to be a particularly effective platform for investigating the pathophysiology of pregnancy-associated diseases in humans, such as pregnancy-induced diabetes, and identifying predictive biomarkers for those conditions [103]. Metabolomics includes different methods such as, nuclear magnetic resonance, liquid chromatography, gas chromatography, and metabolic chips [104].

Metabolomics could offer a more general and effective instrument for investigating metabolic processes and potential markers for ketosis, shedding light on the pathogenesis of ketosis in dairy cows [101]. For a better understanding of the pathobiology of ketosis and its diagnosis, several metabolomics studies reported different variations in the blood of cows suffering from ketosis [105].

#### *Liver activity index (LAI)*

The liver activity index (LAI) is a significant indicator of the function and severity of inflammation during metabolic diseases [106]; it evaluates and categorizes animals based on the concentration of positive acute phase proteins and negative acute phase proteins [107]. Indeed, The LAI is calculated from negative acute phase proteins as it is stable for a long time in the bloodstream compared to positive acute phase [108]. Briefly, the LAI evaluates the

average blood level at 7, 14, and 28 days in milk (DIM) of albumin, total cholesterol, and retinol. Inclusive, the mean values of the herd population of each plasma parameter are subtracted from each cow value at 7, 14, and 28 DIM and divided by the standard deviation [107]. Consequently, the LAI values represent an estimate of the outcome of an inflammation that occurs around calving time. The different methods used for monitoring and early detection of any disorders during the transition period are documented in Table 1.

#### **Conclusion**

The transition period is a critical stage in the dairy cattle production cycle and has a significant impact on health and production. Monitoring transition cows utilizing practical and easy approaches will increase our ability to predict health issues, such as metabolic disorders, and provide a deeper understanding of the possible causes of transition cow disorders. Utilization of automated precision technology to detect any changes in prepartum behaviors. Indeed, metabolic profile test abnormalities, changes in BCS, urine pH, and metabolomics investigation, as well as LAI, have been associated with postpartum disorders, indicating that they can predict transition cow health.

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Not applicable

#### *Conflict of Interest*

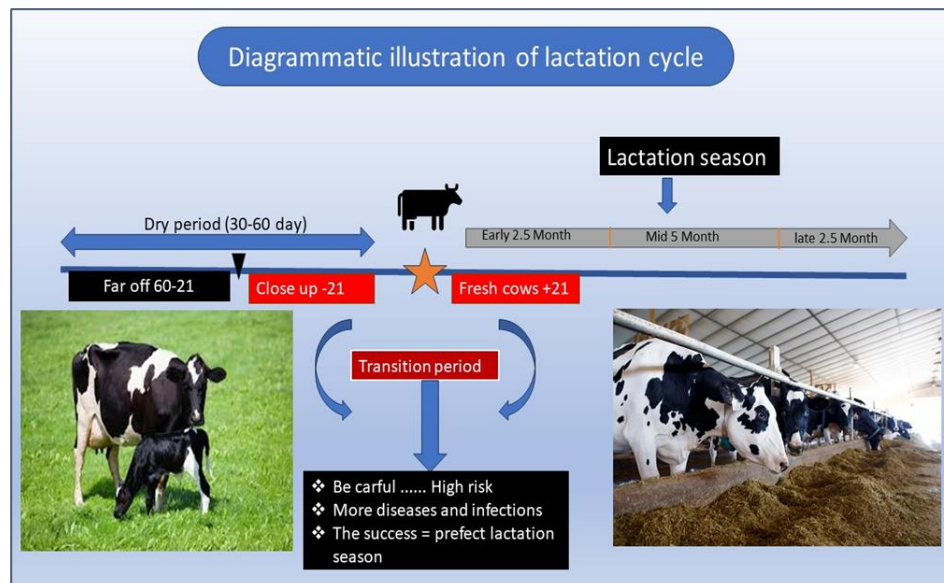
The authors declare no conflict of interest.

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**TABLE 1. Most common methods which are used during monitoring and early detection of disorders during transition period.**

| Methods                                             | Disorders                                        | References  |
|-----------------------------------------------------|--------------------------------------------------|-------------|
| <b>Metabolic profile test</b>                       | Metabolic diseases and stress level              | [25,26]     |
| <b>Body condition score (BCS)</b>                   | Ketosis and fatty liver                          | [28,29]     |
| <b>Hi-tag rumination systems (neck collars)</b>     | Indigestion, ketosis, and displaced abomasum     | [64, 87,89] |
| <b>Behavior Recorder systems (IGER)</b>             | Hypocalcemia, ketosis                            | [90]        |
| <b>Cow manager system (rumination and activity)</b> | Hypocalcemia, ketosis                            | [78, 43]    |
| <b>Urine pH</b>                                     | Subclinical hypocalcemia and subclinical ketosis | [109,110]   |
| <b>Metabolomics</b>                                 | Ketosis and subclinical mastitis                 | [101,111]   |
| <b>Liver activity index (LAI)</b>                   | Metabolic health condition                       | [107,108]   |



**Fig. 1. Diagrammatic illustration of dairy cows season. Dry period ranges from 60-30 days prior to calving with far-off and close up time. The transition period from last 3 weeks prior to calving (close up) until 3 weeks postpartum (fresh time). The lactation season divided into early, mid, and late production.**

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## المرحلة الانتقالية في الأبقار الحلاب: التقييم والتحديات ووجهات النظر المستقبلية

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### الملخص

تمثل الفترة من 3 أسابيع قبل الولادة حتى 3 أسابيع بعد الولادة الفترة الأكثر أهمية خلال موسم الحلابه بأكمله لذلك تعد مراقبة الأبقار الحلاب خلال الخمسة عشر يوماً الأولى في الحليب أمراً ضرورياً للتنبؤ المبكر والتدخل مع أي مؤشرات حيوية للمرض خلال المرحلة تحت الاكلينيكية. تم تسجيل العديد من الاضطرابات الأيضية خلال الفترة الانتقالية مثل نقص كالسيوم الدم الاكلينيكي ، ونقص كالسيوم الدم تحت الإكلينيكي ومشاكل نقص الطاقة، والكبد الدهني. حديثاً انخفض حدوث الاضطرابات الأيضية الاكلينيكية مع تحسن الإدارة الغذائية للكاتبونات والأنيونات خلال الفترة المحيطة بالولادة، بالإضافة إلى فهم أعمق لفسيولوجيا الفترة الانتقالية. داخل المزارع يتم استخدام اختبار التمثيل الغذائي، ودرجة الحموضة في البول، والتغيرات في درجة حالة الجسم لمراقبة الأبقار خلال المرحلة الانتقالية. يتم استخدام التكنولوجيا الدقيقة الآلية والشاملة لتسجيل أي تغييرات في الحركة ووقت الاجترار في الأبقار للتنبؤ المبكر والتدخل إلى المشكلات الصحية المحتملة في قطعان الألبان. بالإضافة إلى ذلك، تهدف مناهج التمثيل الغذائي إلى تحديد أي مؤشرات حيوية تنبؤية لأبقار الألبان التي تعاني من اضطرابات التمثيل الغذائي بالإضافة إلى استخدام نشاط الكبد كمؤشر في قطعان الألبان لتقييم شدة الالتهاب في الفترة المحيطة بالولادة.

**الكلمات الدالة:** الأبقار الحلاب، نقص الكالسيوم، المرحلة الانتقالية، الكيتوزية، التكنولوجيا الدقيقة.