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Role of Nutrition in Preventing Metabolic Disorders in Transition Cows and Improving Postpartum Performance

Farwa Aslam[1], Hammad Ahmad[2], Muhammad Farrukh Naeem[3], Syed Rizwan Ahmad[2*], Muhammad Rizwan[4] and Muhammad Hasnain Javed[5]

[1]University of Veterinary and Animal Sciences, Lahore, Pakistan; [2]Faculty of Animal Husbandry, University of Agriculture, Faisalabad, Pakistan; [3]Faculty of Veterinary Sciences, University of Agriculture, Faisalabad, Pakistan; [4]Department of Clinical Medicine and Surgery, University of Agriculture, Faisalabad, Pakistan; [5]Department of Theriogenology, Faculty of Veterinary science, University of Agriculture, Faisalabad, Pakistan
*Correspondence: zaidirizwan23@gmail.com

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ABSTRACT

The transition phase is the most physiologically demanding phase for a dairy cow which involves nutritional, metabolic, endocrine and immunological adjustments to facilitate lactation. The nutrient demands elevate at this stage, energy needs rise to 300 percent and calcium needs increase to 65 percent to produce colostrum and milk. Despite the advances in dairy management, postpartum disorders are high with over 60 percent of cows getting subclinical disease within 90 days in milk and one out of three cows contracting at least one clinical metabolic or infectious disease. Transition cows are unable to match the nutrient intake by the metabolic demand, leading to a negative energy balance and the increase in non-esterified fatty acids and beta-hydroxybutyrate. These are the metabolic changes linked to ketosis, hypocalcemia, and fatty liver. Besides the metabolic stress, transition cows also experience immune suppression hence the prevalence of diseases like mastitis and metritis. Nutritional strategies such as controlled-energy feeding during the dry phase, optimization of non-fiber carbohydrate, glucogenic supplements with propylene glycol, DCADS, fat supplement, minerals, and using rumen-protected amino acid minimize the transition disorders. In this review, we will explore nutritional and supplementation strategies to counter the problems during the transition period for optimum health and production.

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INTRODUCTION

The transition period for dairy cows involves 3 weeks before calving and 3 weeks after calving. This period is the most challenging period in the life of a dairy cow (Tufarelli et al. 2024). The changes in this stage are sufficiently profound regarding nutritional, metabolic, endocrine, and immunological alterations, which allow the cow to commence lactation and to meet the physiological and nutritional requirements (Trevisi et al. 2025). Throughout this period, the cow would have to adapt promptly to nourishing a growing fetus into producing high amounts of colostrum and milk, which means that a sharp rise in nutrient needs would be experienced (Kalita et al. 2025). The energy demand can rise to 300 percent, whereas calcium needs rise to over 65 percent for colostrum production and mammary gland activity after calving (Zarei 2024). During the onset of lactation, the mammary gland turns into a central source of nutrient that requires enormous amounts of glucose, amino acids, fatty acids, and trace minerals (Biswas et al. 2022). It is estimated that the glucose needs of the lactating mammary gland can increase threefold at approximately four days postpartum compared to the equivalent needs in the gravid uterus at 250 days of gestation and that needs of amino acids and fatty acids increase two-fold and five-fold respectively (Work 2024). Although the dairy management has been improved, transition disorders are still considerable in present dairy herds (Medeiros et al. 2022). This critical period of metabolic maladaptation predisposes cows to a range of both metabolic and infectious diseases which compromise both the health and the productivity of the cows (Kang et al. 2025). As evidenced by commercial dairy cow operations, over 60 percent of dairy cows experience sub-clinical disease during the first 90 days in milk, and about one third of all develop at least one clinical metabolic or an infectious disorder during the initial lactation (Arya 2023). The disorders result in high culling risk, decreasing milk production, and reducing reproductive performance which causes major economic losses to dairy producers (Castro-Montoya et al. 2022).

One of the main metabolic issues in this stage is that there is the risk of negative energy balance (NEB) (Mekuriaw 2023). During gestational periods when the intake of dry matter (DMI) becomes lower in the latter weeks of gestation period, the cows find it difficult to satisfy their increasing energy requirements during the postpartum period (Talley 2025). The resulting energy shortage causes mobilization of body fat stores resulting in the release of non-esterified fatty acids (NEFA) into the bloodstream (Mekuriaw 2023). In case of surpassing the ability of liver to metabolize NEFA, the triglycerides build up in the hepatocytes, and this leads to fatty liver and ketosis (Holzhauer and Valarcher 2024). The other common problem is hypocalcemia due to increased calcium requirement for colostrum production and lactation (Sohrabi et al. 2024). Cows could experience impaired calcium homeostasis without optimum prepartum dietary techniques to promote calcium movement out of the bones and intestinal absorption (Kang et al. 2025). Subclinical hypocalcemia has widespread presence in more than half of the multiparous cows(Berean et al. 2025). Clinical cases present with more apparent neuromuscular dysfunction (Chetan Kumar et al. 2025). A combination of metabolic imbalances results in a condition of immunosuppression and oxidative stress (Bellanti et al. 2025). Higher rate of lipid oxidation and metabolic activity results in the formation of reactive oxygen species (ROS), which under the influence of the absence of antioxidant defense mechanisms can damage the cell structure and aggravate the inflammation process (Masenga et al. 2023). Consequently, cows in the short term postpartum are prone to infectious diseases like metritis and mastitis which again affect health, milk output and reproductive efficiency (Egyedy and Ametaj 2022). Over the past years, research has shown that systemic inflammation and immune activation are the key elements of transition cow maladaptation (Pascottini et al. 2022). The process of inflammation can start as early as before calving that causes tissue damage, dietary alteration, intestinal or reproductive microbial translocation (Bruinjé and LeBlanc 2025). Haptoglobin and acute phase proteins are systemic inflammatory mediators, which are found to increase in cows who proceed to develop either uterine or metabolic disorders, and they demonstrate that metabolic and immune pathways intersect during the transition period (Seminara et al. 2025). Unchecked inflammatory hyperactivity may impair follicular development, slow down ovulation, and disrupt the utility of the uterus, and hence connection between transition health and long-term reproductive success has been made.

Current dairy studies aimed at identifying nutritional and management interventions aimed at promoting metabolic resilience during transition period (Ashar et al. 2026). The most outstanding recommendation is categorizing dry cow diets into Dry-off and close-up periods as this gives the ability to control energy consumption and adapt to metabolism prior to calving (Joshi et al. 2022). Dry-off diets have less energy to avoid overweight body condition whereas close up diets offer moderate energy to support rumen adaptation before lactation (Cunha et al. 2025). Assessment of dietary composition, fermentability and microbial adjustment is thus still outstanding in enhancing the result of transition cows (Yu et al. 2026). Besides macronutrient strategies, specific nutritional treatments, including rumen-protected amino acids, supplemental glucogenic precursors, antioxidants, and minerals have also proven effective in regulating metabolism and immune response (Khan et al. 2023). The objectives of these interventions include promoting the supply of glucose, increasing lipid metabolism, and antioxidant defenses to reduce the severity of NEB and the course of its downstream consequences (Hu et al. 2025). An example is propylene glycol which has been applied successfully in the form of an oral drench to decrease circulating NEFA and BHBA levels and by this way lower the frequency and intensity of ketosis (Song et al. 2025). The complex nature of metabolic adaptation has resulted in the propagation of transition cow disorders despite the development of nutritional science (Kang et al. 2025). In this manuscript we will review the common disorders of transition cows and the field of precision nutrition along with monitoring of metabolic rates that will promise more specific and effective approaches to enhancing health and productivity of dairy herds. The integration of metabolism, immunity and nutritional management can contribute to improving the welfare and performance of transition cows, decreasing the number of diseases and promoting the sustainability of dairy production.

Challenges with Metabolism in Transition Cows

Transition represents a phase for dairy cattle characterized by an abrupt change in the nutritional demand so that the mammary gland must regulate metabolism to provide energy, glucose, amino acids, and Calcium post-calving (Mukherjee et al. 2023). From estimations of the lactating mammary glands demand at 4 days postpartum and the gravid uterus demand at 250 days of gestation for these nutrients and net energy, it appears that glucose demand is increased approximately three-fold, Amino acid demand is doubled, and fatty acid demand is increased approximately five-fold during this period (Murgor 2025). Furthermore, the demand for calcium is increased approximately four-fold on the day of parturition (Murgor 2025).

Negative Energy Balance, Lipolysis, and Ketosis:

The main hallmark of metabolic transition is the phenomenon of Negative Energy Balance (NEB), a condition that occurs when energy requirements of lactation surpass the voluntary consumption of feeds (Mekuriaw 2023). During the closeup period there is a decrease in dry matter consumption and an increase in energy needed to synthesize milk, so, as adipose tissue is mobilized, non-esterified fatty acids (NEFA) and beta-hydroxybutyrate (BHBA) concentrations in circulation rise (de Oliveira Cunha 2024). These metabolites are useful biomarkers of metabolic imbalance and put cows at risk of ketosis and fatty liver (Mondal et al. 2026). Under normal physiological conditions, NEFA released by adipose tissue is either used in energy production in the liver or points out to very-low-density lipoproteins (VLDL) (Holzhauer and Valarcher 2024). In severe NEB though, the liver is overwhelmed in oxidation and lipoprotein assembling processes leading to hepatic triglyceride accumulation which impairs the metabolic activity (Drackley 2025). Increased NEFA and BHBA have a strong relationship with decreased immune responses, lack of gluconeogenesis and increased susceptibility to secondary ailments including displaced abomasum, metritis, and mastitis (Sammad et al. 2022). A brief metabolic illustration has been shown in Figure 1.

Transition cows that had higher pre- and postpartum NEFA levels had higher rates of metabolic disorders, decreased postpartum DM consumption and decreased early milk production when compared to cows that were keeping a more favorable energy balance (Castillo et al. 2026). The studies further point at the multifactorial nature of NEB, which require nutritional management practices that include controlled energy prepartum diets and strategized carbohydrates formulation (Mekuriaw 2023). These strategies are important in regulating the extent of energy shortages and subsequent downstream effects on metabolism (Chaves et al. 2024). The cows accustomed to moderate energy diets prepartum showed slower change in energy status during the postpartum phase restricting excessive lipolysis and facilitating better metabolic resilience (da Silva 2024).

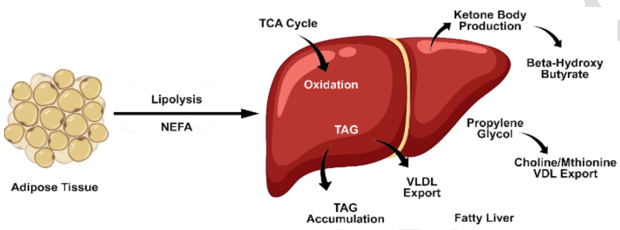

Fig. 1: Production of NEFA through lipolysis and role of liver in metabolism.

To elevate the risk of negative energy balance and ketosis , nutritional strategies are being used that focus on gluconeogenesis (Yogeshpriya et al. 2024). Propylene glycol is one of them that has received extensive research interest and has potential value in the transition cow nutrition (Tan et al. 2024). It has been concluded that propylene glycol as an oral drench or added to pre- and post-calving diets has a consistent effect on reducing the circulating NEFA and BHBA levels and raising the plasma glucose concentrations (Song et al. 2025). Mechanically, propylene glycol act as a substrate for hepatic gluconeogenesis that produces glucose that is required to replace the energy deficit during the crises so that adipose breakdown is minimized (Singh and Singh 2024). Besides enhancing metabolic biomarkers, the propylene glycol supplement consumption has been linked to reduced cases of clinical ketosis, enhanced appetite and increased milk production during early lactation (Tan et al. 2024).

Hypocalcemia

The production of colostrum and onset of lactation result in a very sharp rise in the demand of calcium during the transition period(Pascottini et al. 2022). To aid in the production of colostrum and milk, high amounts of calcium quickly move out of the blood supply into mammary secretions, and this is frequently faster than the cow can replace calcium in the blood stream (Ramtek et al. 2023). Consequently, the cows may develop clinical hypocalcemia (milk fever) or more commonly, subclinical hypocalcemia (Ametaj 2025c). Subclinical hypocalcemia is very common in transition cows with more than half of multiparous animals being infected despite no clinical symptoms being observed (Berean et al. 2025).The condition reduces the feed intake, causes a weakening of the immune and muscle functions, which increases the chances of retained placenta, dystocia, mastitis, and other secondary diseases in the early lactation (Singh and Alam 2025).

Endocrine processes such as parathyroid hormone (PTH), active vitamin D (1,25-dihydroxyvitamin D) and bone calcium mobilization processes play a crucial role in the calcium homeostasis of periparturient dairy cows (Frizzarini 2024). A decrease in blood calcium levels increases secretion of PTH, which helps to promote bone resorption and calcium renal retention, and boosts vitamin D activation to promote calcium intestinal absorption (Akimbekov et al. 2022).

According to recent studies, calcium is more than a promoting factor of neuromuscular activity; it is closely associated with immune competence and in general, transition health (Neves 2023). Calcium ions are important in the immune cell signaling, phagocytic activation, and regulation of the inflammatory pattern (Rocha and Perez 2024). In such a way, hypocalcemia is both a metabolic deficiency and the cause of immune dysfunction, which impairs the effectiveness of neutrophils and macrophages to react to the pathogen (Ametaj 2025b).Further studies state the fact that even subclinical changes in the levels of blood calcium are linked to a coordinated change in mineral balance, energy metabolism, and behavioral parameters, such as rumination behavior change and milk composition, and its systemic character of calcium imbalance (Yadav et al. 2024).

Due to the complex role of calcium in metabolic as well as immune pathways, nutritional strategies that favor calcium mobilization and homeostasis are important in reducing incidence and severity of clinical and subclinical hypocalcemia (Rocha and Perez 2024). These strategies involve manipulation on dietary cation-anion difference (DCAD), to increase tissue sensitivity to PTH, feeding with close-up low-calcium diets to tune homeostatic regulation, and feeding on agents like zeolites that trigger calcium regulation networks (Moore 2025).

An illustration of organ-level metabolic changes along with possible outcomes and mitigating strategies is shown in Figure 2.

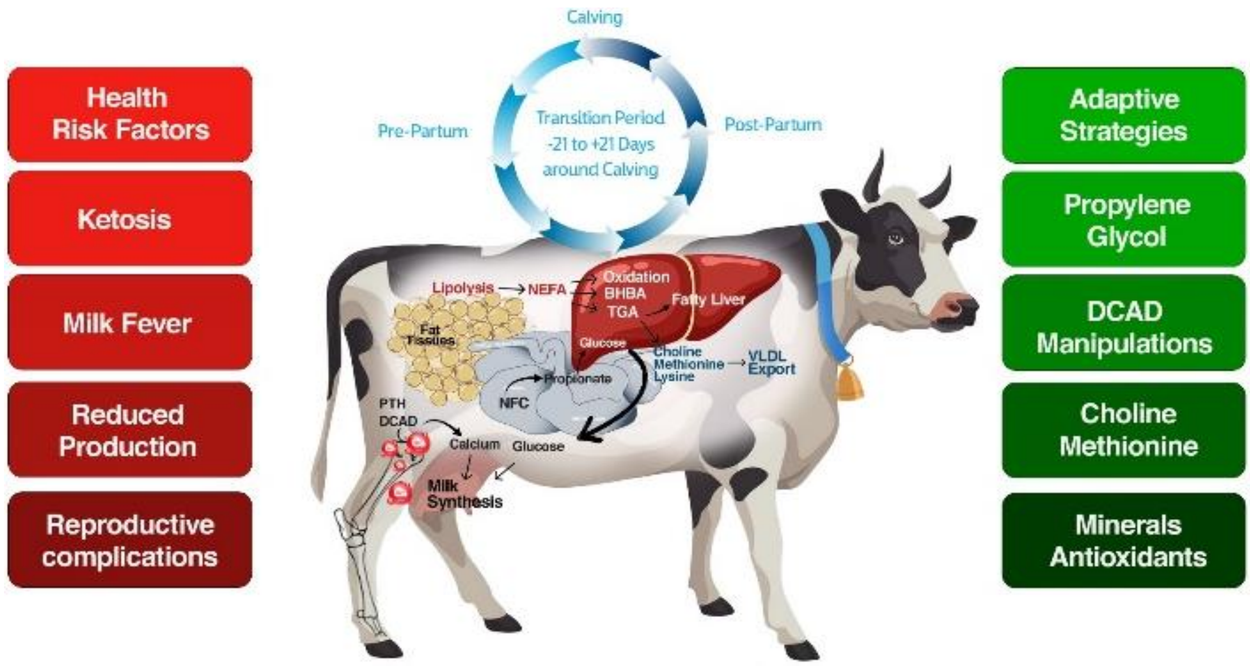

Fig. 2: Metabolic processes and nutritional treatment of energy balance, calcium metabolism, and health in transition dairy cows at the organ level.

Immune suppression and oxidative stress

Transition phase is not only a period of metabolic strain but also shows the severe disturbance of the immune system (Trevisi et al. 2025). During early lactation phase of dairy cows, negative energy balance (NEB), lack of glucose, and need to mobilize fatty acids converge to a state of metabolic stress which directly affects immune competence (de Oliveira Cunha 2024). Low energy also reduces access to glucose, which is an important substrate to cellular immune functions (Habel and Sundrum 2023). The high conversion rate of lipid mobilization raises the production of circulating non-esterified fatty acids (NEFA) and other lipid metabolites capable of disarranging leukocytes (Gnott 2023). Meanwhile, overproduction of lipid oxidation produces a high level of reactive oxygen species (ROS), causing oxidative stress that impairs signaling cascades in cells, damages cellular organelles, and in addition to weakening immune responsiveness (Liu et al. 2025).

Recent immunometabolism studies have emphasized the fact that metabolic stress and immune functioning are both strongly linked via some common signaling pathways and lipid mediators (Garcia et al. 2023). NEFA and other lipid metabolites are produced as ligands that can regulate inflammation and leukocyte activity (Zhang et al. 2025a). The Elevated NEFA in circulation may suppress neutrophil chemotaxis, neutrophil phagocytosis and limit the ability of the innate immune system to react to invading pathogens (Lv et al. 2022). At the same time, lipid oxidation and ROS production leads to disruption of redox homeostasis and stimulates stress recognition routes leading to compromised adaptive immune functions (Manoharan et al. 2024). The impaired immune response also plays a role in the occurrence of reproductive diseases, e.g. mastitis and metritis etc., which are highly linked to both systemic inflammation and metabolic imbalance in transition cows (Bruinjé and LeBlanc 2025). The action of inflammatory cytokines, including tumor necrosis factor-a (TNF-a), interleukin-1b (IL-1b), and interleukin-6 (IL-6) as responses to infection can also influence metabolism by changing insulin signaling and facilitating lipolysis that further increase NEFA flux and ROS generation (Hadid et al. 2024). Research indicates that long-term high concentrations of inflammatory mediators have the potential to shift the immune system to chronic low-grade inflammatory condition, decreasing the effectiveness of immune responses to new pathogenic events (Cifuentes et al. 2024).

Omega-3 and other polyunsaturated fatty acids (PUFA) have been of specific interest in immunometabolism studies due to their ability to regulate the inflammatory signaling (Bodur et al. 2025). The application of omega-3 PUFA supplementation during the transition period has been linked with a lower rate of inflammatory pointers, better neutrophil operation, and a decrease in the rate of uterine infections, proving the hope of targeted nutritional interventions to aid immuno-metabolic resilience (Fabjanowska et al. 2023).

Reproductive Disease

Dairy cows have been associated with close association of transition with metabolic status and reproductive performance (Sammad et al. 2022). In case of inadequate metabolic adaptations, which are required to maintain the production of milk, the efficiency of the reproductive system tends to decrease (Sammad et al. 2022). Some of the most significant metabolic issues with regards to reproduction include negative energy balance (NEB), excessive mobilization of lipids, ketosis, and fatty liver, which are densely distributed in early lactation (Mekuriaw 2023). Although moderate mobilization of fats is also a normal physiological action, the high or the sustained activation of NEFA and BHBA is highly correlated with their hindrance of reproductive functionality (Toralová et al. 2025). It has been established in many studies that cows that are high in NEFAs and BHBs during the early postpartum period take a long time to resume cyclic ovary activities, express estrus, and have low conception rates (Thompson et al. 2022).

The development of fatty liver is one of the most important correlations between metabolic stress and impaired reproduction (Sammad et al. 2022). In case when hepatic uptake of NEFA surpasses the first-degree oxidation or export of NEFA as very-low-density lipoproteins (VLDL), hepatic triglycerides build-up (Melendez and Pinedo 2024). This lipid accumulation of the liver impairs the liver functioning capacity such as gluconeogenesis, hormone metabolism and the production of major metabolite intermediates (Hu et al. 2025). Since the liver is the main component of the regulation of circulating glucose, insulin, and insulin-like growth factor-1 (IGF-1), the fatty liver causes events that indirectly affect endocrine messages that are important in normal ovarian functioning (Campbell and Jialal 2022). Low levels of IGF-1 in the blood during early lactation are always linked with retarded follicular development, late ovulation, and lowered fertility (Wathes 2022).

NEB also impacts directly upon ovarian follicular dynamics (Shahzad et al. 2024). The energy deficiency lowers availability of glucose and other substrates of metabolism needed for the growth of follicles and production of hormones (Mo et al. 2024). Research indicates that cows with severe NEB possess small dominant follicles, and decreased levels of estradiol and lack follicular sensitivity to gonadotropins (Mekuriaw 2023). Therefore, the initial ovulation after parturition is frequently disrupted, and estrus performance can be poor or absent, which makes heat recognition inconvenient that results in failed Inseminations (Triwutanon and Rukkwamsuk 2023). Prolonged anovulation is most prevalent in cows that achieve high postpartum NEFA or BHBA concentrations (Mekuriaw 2023).

In addition to ovulation, there is a negative effect of metabolic stress in early lactation on quality of oocytes and premature embryo development (Zhang et al. 2025b). Such outcomes decrease the oocyte developmental competence and enhance the vulnerability to premature embryonic deaths (Sahu et al. 2025). Also, it has been suggested that ketosis and fatty liver are related to lower levels of progesterone in early pregnancy probably because of slowed down steroid hormone metabolism by hepatocytes and a weakened luteal activity (Sood 2026).

Additional research highlights that metabolic upheavals during the initial two weeks of postpartum may have prolonged effects on reproductive output in later stages of lactation (Mekuriaw 2023). Early NEB and metabolic conditions in cows during the postpartum period are associated with a high number of days open and low pregnancy rates during the initial artificial insemination (Sammad et al. 2022).

Nutrition during the transition phase is hence vital for the protection of reproductive performance (Ding et al. 2024). There are strategies to reduce NEB, increasing the adaptation of the rumen to lactation feeding, and assisting the hepatic lipid metabolism which enhances the post-partum ovarian activity and fertility (Raja et al. 2025).

Nutritional Strategies during Transition Phase

Effective metabolic adaptation by dairy cows is based on energy management of the dry phase and transition period (Yogeshpriya et al. 2024). Cattle having a dry period of about 40 -60 days are traditionally fed on a two-diet system which comprises of a Dry-off and a close-up ration (Serrenho et al. 2022). This strategy is aimed at maintaining the start of lactation and preventing excessive fat mobilization and metabolic stress (Mondal et al. 2026). The diet that is given to the cows usually fed within the first four to five weeks of the dry period is low in energy density and high in fiber content (Schubert et al. 2025). Its chief goal is to maintain body condition score (BCS) and not stimulate excessive energy intake and adipose tissue accumulation (Praveen et al. 2024). The Dry-off stage of over-conditioning has always been linked to the development of more extreme negative energy balance in the postpartum period, higher lipid mobilization and the likelihood of ketosis and fatty liver (Pascottini et al. 2022).

The close-up diet which was initiated in the last two to three weeks prior to calving is characterized by moderate energy density and high NFC as compared to the Dry-off ration (Pineda et al. 2022). The dietary change will be proposed to initiate rumen adaptation and papillae growth ahead of a high-energy lactation diet that is fed immediately after calving (Goselink et al. 2024). Slow accumulation of fermentable carbohydrates in the close-up phase increases ruminal propionate synthesis, helping to sustain hepatic gluconeogenesis and metabolic preparedness to early lactation (Litherland et al. 2025). The close-up diet should, therefore, be formulated properly to decrease the intensity of postpartum negative energy balance and excessive mobilization of body reserves (Gheller 2024).

The sudden switch of the low-energy Dry-off diets to high-energy postpartum diet is a major problem (Haisan 2024). Rapid alterations in diet may upset ruminal microbial communities, disrupt feed consumption and promote the occurrence of ruminal acidosis (Elmhadi et al. 2022).These disturbances suggest the need of the seamless diets changes that can synchronize the rumen activities with the rapidly shifting nutrient requirements (Kamidi et al. 2026).

Recent research studies have given good grounds into creating controlled energy feeding strategies during the dry period as an alternative to the conventional stepped-up energy approaches (Scilacci et al. 2024). Cows in the controlled-energy group adjusted by eating controlled energy diets, a diet formulated by typically high-energy ingredients to meet rather than exceed energy needs, showed better metabolic performance than those in a higher-energy dry cow group (Pineda et al. 2022). The use of controlled-energy feeding decreases BCS at prepartum, regulates postpartum NEFA and BHBA concentrations, and enhance dry matter consumption in early lactation (Sammad et al. 2022).

Cow grouping and management consistency were also considered to be very crucial (Giordano et al. 2022). Feeding and keeping cows in distinct Dry and close-up groups provided more accurate control over the diet and more consistent consumption patterns (Gheller et al. 2024).Nevertheless, without proper balance these manipulations can harm the rumen to adapt to lactation diets, that indicates the importance of maintaining nutrient control and monitoring with utmost precision (Kadim et al. 2024).The application of these nutritional strategies can ensure the reduction of the number of transition-related metabolic disorders significantly as well as lead to better performance at the beginning of lactation (Vidu et al. 2025).

Improving Glucose Supply and Ruminal Absorption

To achieve sufficient absorption of volatile fatty acids (VFA) generated during ruminal fermentation, it is suggested to use prepartum feeding regimens with increased portion of non-fiber carbohydrate (NFC) than the traditional dry cow feed (Li et al. 2025a). The increased NFC intake during the close-up period causes ruminal papillae to grow and ruminal microbial adaptation to carbohydrate-rich lactation diets is promoted (Fukumori et al. 2022).

Increased NFC in prepartum ration results in more propionate, the major glucogenic VFA of ruminants (Ma et al. 2022). Propionate acts as the prime nutrient that facilitates hepatic gluconeogenesis, thus sustaining glucose supply (Pang et al. 2023).An enhanced glucose supply reduces excessive mobilization of adipose tissues as well as reducing the levels of non-esterified fatty acids (NEFA) in circulation (Qiao et al. 2024). Moreover, when more NFC is fed, there is an augmentation in microbial protein production, given that there is enough adequate ruminal degradable protein which guarantees amino acid needs to be met to sustain the body, late pregnancy, and mammary tissue development (Rosmalia et al. 2022).

The mechanisms are supported by evidence of dietary interventions that substitute the crushed maize with steam-flaked corn that enhances NFC fermentability (Sun et al. 2022). Diets in which the proportion of steam-flaked corn made 39 percent of total NFC have been found to elevate the plasma insulin concentrations, enhance prepartum dry matter intake (DMI) and raise postpartum milk production (Haisan 2024). Notably, the less fermentable carbohydrate fed cows recorded high NEFA levels in the prepartum (Chen et al. 2022). This evidence shows that enhancing NFC fermentability, and not merely raising dietary energy density, is a highly important approach to counter negative energy balance (NEB) (Deng et al. 2025).

The studies also demonstrate that carbohydrates-driven metabolic adaptation is essential during the transition period as examined in the framework of recent cohort-based investigations (Thillapudi et al. 2025). Their large-scale observational study has found that those cows which could sustain more stable patterns of prepartum intake demonstrated better adaptation to the supply of fermentable carbohydrates and showed lower postpartum NEFA and BHBA (Yang et al. 2022). Studies have shown that an increased metabolic strength and increased insulin responsiveness during the early lactation stage were linked to better ruminal adaptation prior to calving (Cattaneo et al. 2023). Such cows showed higher early milk production and less occurrence of hyperketonemia, which underscores the economic advantages of strategic carbohydrate feed management in the dry season at the level of the herd (Dorella 2025).

To alleviate the metabolic effects of NEB besides dietary NFC manipulation, direct supplementation with glucogenic precursors has been extensively utilized (Jiang et al. 2025). One of the most studied glucogenic agents is propylene glycol, which is usually used as an oral drench (Ponter et al. 2026). After absorption, propylene glycol is rapidly broken down under hepatic gluconeogenesis into glucose which supplies an instant source of energy during acute glucose deficiency (Tufarelli et al. 2024). Studies show a decrease in the levels of plasma NEFA and beta-hydroxybutyrate (BHBA) by the propylene glycol supplementation, thus leading to a reduction in the intensity and occurrence of clinical and subclinical ketosis (Zhang et al. 2025c).

The cows that received specific metabolic assistance, such as glucogenic supplementation, during transitional phases demonstrated better metabolic adaptations and quicker energy balance restoration (Ashar et al. 2026). The present results indicate that dietary mechanisms that improve ruminal adjustment are complementary to the short-term intervention with glucogenic precursors to enhance the energy metabolism in transitional cows (Rocha Dorella 2025).

Altogether, enhancing NFC supply and fermentability in prepartum diets, as well as the selective application of the glucogenic precursors, should be viewed as a promising nutritional intervention (Gheller 2024). This supplementation will decrease NEFA mobilization and provide glucose availability throughout the transition period (Rocha Dorella 2025).

Dietary Cation–Anion Difference (DCAD) Manipulation

Prepartum nutritional management for calcium balance is a highly vital strategy to avoid hypocalcemia among transition dairy cows (Nikkhah et al. 2023). One method that has been extensively used to stimulate the calcium mobilization mechanisms before the onset of lactation is feeding of low calcium content diets during late gestation (Beiranvand et al. 2025). Nevertheless, recent studies have put more emphasis on the manipulation of the dietary cation-anion difference (DCAD) which is a better and more physiologically oriented method for optimum calcium homeostasis (Ametaj 2025c).

The main goal of manipulation of DCAD is to avoid metabolic alkalosis and rather cause a compensated mild metabolic acidosis during the prepartum period (Melendez and Chelikani 2022). According to the data, dairy cows that feed on diets with large levels of cations, especially sodium and potassium, will develop metabolic alkalosis (Tufarelli et al. 2024). Alkaline situations lead to decreased tissue sensitivity to parathyroid hormone (PTH), thereby inhibiting the release of calcium in bone and lowering the absorption of calcium by the kidney and intestine (Abramowicz et al. 2026). Subsequently, cows get into parturition with impaired calcium homeostatic processes, which predispose them to clinical and subclinical hypocalcemia (Chetan Kumar et al. 2025).

The use of prepartum diets including DCAD composition assist mild metabolic acidosis to enhance tissue sensitivity to PTH (Frizzarini 2024). The augmented sensitivity of the PTH receptors promotes osteoclastic bone resorption augmenting the delivery of the calcium into the blood (Vieira-Neto et al. 2024). Also, metabolic acidosis increases the renal synthesis of vitamin D by increasing the production of 1, 25-dihydroxyvitamin D3, which improves the absorption of calcium by intestines (Vieira-Neto et al. 2024). These synchronized endocrine reactions help cows to sustain calcium homeostasis upon the abrupt calcium requirement that comes with the production of colostrum and the commencement of lactation (Hasif et al. 2025).

DCAD manipulation has other effects on calcium metabolism in comparison to bone mobilization (Yogeshpriya et al. 2024). The enhanced calcium status promotes smooth muscle contractility that is critical in maintaining normal rumen motility, uterine contractions and the functioning of teat sphincter (Chetan Kumar et al. 2025). Proper amount of calcium in the initial lactation period decreases incidences of secondary conditions like retained placenta, dystocia, displaced abomasum, and mastitis (Ma et al. 2024). Calcium homeostasis has extensive systemic consequences including efficiency of the digestive system, reproductive recovery, and immune defense mechanisms (Zheng et al. 2025).

Several controlled trials have proved that negative DCAD value prepartum diets play a big role in reducing the chances of hypocalcemia in multiparous cows (Sami et al. 2024). A decrease in DCAD of about 200 to 100 mEq/kg dry matter has always been found to reduce clinical milk fever and subclinical hypocalcemia (Kour et al. 2024). These dietary changes will not only increase the levels of calcium circulating at calving but will also increase general metabolic viability in the early lactation period (Nikkhah et al. 2023). Generally, the most effective DCAD manipulations generally aim to achieve urine pH of 6.0 to 6.8 of the Holstein cows as a useful indication of effective metabolic acidification (Melendez and Chelikani 2022).

The negative DCAD diets enhance postpartum feed consumption and lactate output indirectly by maintaining neuromuscular activity and reducing the probability of the disease (Ametaj 2025a). The improved calcium homeostasis increases the ruminal motility and promotes the gut consummation of the feed and its absorption during the first quarter of lactation (Zhang et al. 2022). Moreover, calcium homeostasis helps to decrease systemic inflammation and immune competence to help increase transition success and overall health (Nikkhah et al. 2023).

DCAD manipulation should also be cautiously undertaken to prevent acidification (Hotel 2025). Very low DCAD values can lower palatability, slow down feed consumption, and escalate strain (Kour et al. 2024). As a result, effective DCAD use would be possible with appropriate ration development, control over the mineral content of the diet, and periodic assessment of physiological signs in cows, including urine pH levels and blood calcium levels (Zachwieja et al. 2022).

In conclusion, the manipulation of calcium metabolism via DCAD optimization is one of the most effective methods of nutrition aimed at preventing the development of hypocalcemia and promoting the health of transition cows (Kang et al. 2025). The negative DCAD diets improve metabolism stability at early lactation by increasing the PTH responsiveness, stimulating the vitamin D, and enhancing calcium mobilization (Frizzarini 2024).

Fats supplementation

Dietary fat supplementation has been a popular intervention that has been conducted to enhance energy balance and minimize excess lipid mobilization throughout the transition period (Wang et al. 2023). Enhanced dietary fat enables cows to satisfy augmented energy requirements without paying much attention to elevated ruminal fermentation load, which reduces the chance of ruminal acidosis (Elmhadi et al. 2022). The dietary fat intakes are mostly absorbed through intestinal lymphatic system instead of through the portal circulation directly to the liver (Tso et al. 2025).

Nutritional fatty acid supplementation in late pregnancy has also been revealed to lower circulating amounts of fatty acids that are not bound by esterification (NEFA) by lowering the requirement to mobilize adipose tissue (Xiao et al. 2026). It has been shown that cows that receive more energy diets prior to calving which includes the addition of fats at about 2 percent of dry matter have lower peripartum NEFA levels and a lower rate of triglycerides pile-up in hepatic tissue after calving (Montazeri et al. 2024). These dietary supplements lower the chances of ketosis and fatty liver in transition cow (Wang et al. 2023).

Polyunsaturated fatty acids (PUFA) and omega-3 fatty acids have been demonstrated to change the inflammatory signaling pathways, lipid metabolism, and the activity of immune cells (Poggioli et al. 2023). The research on immunometabolism shows that fatty acids are signaling molecules that stimulate the expression of inflammatory genes, oxidative stress response genes, or genes of metabolic adaptation (Zhang et al. 2024). The omega-3 fatty acids have the potential to lower the secretion of pro-inflammatory eicosanoids which are produced by omega-6 fatty acids to maintain metabolic stability in the early lactation phase (Alagawany et al. 2022). Such an anti-inflammatory action helps to improve liver functioning, decrease oxidative stress, and general metabolic integrity in transition cows (Fabjanowska et al. 2023).

The dietary fats also have effect on insulin sensitivity and glucose (Ofori et al. 2024). The augmented supply of energy-rich fatty diets could enhance insulin sensitivity, enabling a better partitioning of nutrients into lactation without leading to the actual mobilization of excess adipose tissue (Mousaie et al. 2025).

Amino Acid and Lipids

Amino acid nutrition is considerable to transition cow metabolic adjustment, especially to assist hepatic lipid metabolism and synthesis of milk proteins (Kang et al. 2025). One of these nutrients include Choline, which has been termed as a quasi-vitamin, and carries out various crucial metabolic roles (Drackley 2025). Choline, a structural molecule of phosphatidylcholine, the major phospholipid found in cellular membranes, is the precursor of betaine, which is engaged in a methyl group transfer reaction (Kenny et al. 2025). Among the most important choline functions in transition cow nutritional practices are its involvement into the synthesis and secretion of very-low-density lipoprotein (VLDL) (Lunsin et al. 2024).

The exportation of triglycerides from hepatocyte must be carried out by VLDL (Chen et al. 2024). In the initial lactation period, intense movement of adipose tissue enhances the production of hepatic triglycerides (Hu et al. 2025). Lacking sufficient phosphatidylcholine, the formation of VLDL will be constrained, which results in the formation of hepatic triglycerides and fatty liver (Li et al. 2025c). It has been indicated that rumen-protected choline supplementation increased hepatic lipid exportation, decreased hepatic fat, as well as improved overall metabolic activity during the transition period (Lunsin et al. 2024). Enhanced hepatic lipid metabolism favors gluconeogenesis and endocrine balance hence enhancing lactation performance and metabolic wellbeing (Hu et al. 2025).

The amino acids methionine and lysine are universally known to be essential amino acids in synthesis of milk and milk proteins in dairy cows (Huang et al. 2023). In addition to protein synthesis functions, these amino acids have a role to play in hepatic lipid metabolism and mitochondrial energy pathways (Kakazu et al. 2025). Methionine is another important methyl donor used in the production of phosphatidylcholine and in the production of carnitine used in the shuttling of long-chain fatty acids into the mitochondria to undergo beta-oxidation (Panov et al. 2024). Increased beta-oxidation will lead to hepatic energy metabolism and decrease triglyceride storage (Talley and Mohiuddin 2023).

Lysine supplements methionine in that it helps in the production of protein and metabolism (Luo et al. 2025). These amino acids facilitate antioxidant defense systems and protect oxidative stress which comes with excessive mobilization of lipids (Egbujor et al. 2024).

Nutraceutical and Mineral Supplementation

The importance of mineral supplementation in maintaining the stability of the animal metabolite during transition phase as well as for prevention of disorders in dairy cows cannot be undervalued (Ashar et al. 2026). A few additive mineral compounds and nutraceuticals are discussed to enhance calcium balance, energy metabolism and general health in the transition period (Jain et al. 2022).

Zeolite A and Calcium

Zeolite A is also in common use as a mineral additive in the prevention of hypocalcemia (Su et al. 2025). It acts by binding calcium that decreases intestinal calcium being absorbed in prepartum period (Su et al. 2025). This regulated calcemic deficit develops a mildly adverse calcium equilibrium prenatally to calving, which initiates calcium release out of bones (Masoumi Pour et al. 2022). Consequently, this causes cows to be better equipped to respond to the abrupt rise in calcium need in the period of colostrum production and during early lactation (Athonvarangkul and Wysolmerski 2023). Research has demonstrated prepartum Zeolite A supplementation helps to prevent incidences of subclinical hypocalcemia and milk fever especially in multiparous cows (Su et al. 2025).

The Monensin and Energy Metabolism

Monensin is generally used as a controlled-release capsule (CRC) to enhance energy metabolism in the transition period and lactation (Lauronen 2023). The influence of monensin in ruminal fermentation is that it increases propionate synthesis and decreases the synthesis of acetate and methane (Rodríguez et al. 2023). Increased supply of propionate helps cows to produce glucose in the liver which improves energy balance in cows (Rathert-Williams et al. 2023). It has been described by research that a cow supplemented with monensin has reduced circulating levels of beta-hydroxybutyrate (BHBA) and a decrease in the subclinical ketosis risk (Lauronen 2023). Monensin supplementation has also been linked to an increased level of postpartum blood glucose and enhanced feed efficiency, which adds to improved adaptation to metabolic conditions in the initial stage of lactation (Gonzalez-Chappe et al. 2025).

Trace Minerals

Trace minerals such as selenium, zinc, and copper, are also involved in antioxidant defense and immune activities (El-Sayed et al. 2024). Enough supplementation of selenium promotes the activity of glutathione and peroxidase that suppresses the effect of oxidative stress in early lactation (El-Sayed et al. 2024). Zinc plays a role in repairing tissues, immune cells and udder health, whereas copper helps in the enzyme system that is used in the metabolism of energy and immune response (El-Sayed et al. 2024). An overview of supplements and their effects have been described in Table 1.

Future Prospectives

Although there has been a major development in the study of the transition cow metabolism and the prevention of diseases, there are still a few research gaps (Kang et al. 2025). Evolving technologies and science will improve the ability of predicting diseases, precision in nutrition and support of the immune system in transition dairy cows (Džermeikaitė et al. 2025).Precision nutrition seeks to personalize feeding plans and cow needs using sophisticated monitoring devices (Losacco et al. 2025). Metabolic stress or severe negative energy balance in a cow can be detected using automated feeding systems, wearable sensors and real-time approaches of metabolic monitoring (Lee et al. 2026).The other fast-growing area with high potential of early detection of diseases is metabolomics (Zhu et al. 2023). It is a method that involves small metabolic products such as blood, milk or urine to determine the early metabolic changes before clinical symptoms are evident (Li et al. 2024). Nevertheless, more studies are needed to confirm the biomarkers in the field and to come up with cost effective methods of measuring the biomarkers to conduct regular herd surveillance (Li et al. 2025b). Functional immunonutrition also receives more attention as scientists acknowledge the close relationship that exists between metabolism and immune activity (Raczyńska et al. 2025). Dietary interventions aimed at boosting immune functions during the period of transition may prevent the occurrence of diseases and increase productivity (Andreou and Papaneophytou 2025). The preliminary research results are positive, but additional research is required to identify the best levels of supplementation and benefit results over long-term in herds (Castillo et al. 2025). The future research in terms of transition cow is likely to be aimed at precision feeding, detecting illnesses early in the metabolomics framework, and immunonutrition approaches (Emam et al. 2025).

Table 1: Summary of supplements and their mechanisms along with applications and effects

Sr. No.	Supplement / Nutrient	Primary Action / Mechanism	Metabolic & Biochemical Parameters	Endocrine & Molecular Indicators	Rumen & Digestive Parameters	Health & Welfare Outcomes	Production & Reproductive Outcomes	Ref
1.	Propylene Glycol	Enhances hepatic gluconeogenesis and energy balance	↑Blood Glucose ↓NEFA, ↓BHBA, ↓liver triglycerides, ↑glycogen storage	↑Insulin secretion, ↑IGF-1 activity, ↓ cortisol	↑Propionate supply, improves rumen energy metabolism	Reduces ketosis and fatty liver	Improves milk yield, faster postpartum recovery, improved fertility	(Tan et al. 2024)
2.	DCAD Diets	Induces compensated metabolic acidosis improving calcium mobilization	↑ Serum Ca, ↓blood bicarbonate, ↓urine pH, ↑bone Ca mobilization	↑ Parathyroid hormone receptor sensitivity, ↑ Vitamin D activation	Improves mineral absorption efficiency	Prevents milk fever and neuromuscular disorders	Improves feed intake, reduces postpartum disorders	(Kour et al. 2024)
3.	Rumen-Protected Choline	Enhances VLDL synthesis and hepatic fat export	↓ Hepatic lipid accumulation, ↑ liver enzyme efficiency, ↓ AST/ALT stress markers	Improves methyl donor pathways, supports phospholipid synthesis	Improves nutrient transport across intestinal epithelium	Prevents fatty liver and improves immune competence	↑ Milk production, improved reproductive cyclicity	(Huang et al. 2023)
4.	Methionine & Lysine	Improves protein synthesis and fatty acid oxidation	↑ Plasma essential amino acids, ↑ carnitine synthesis, ↑mitochondrial β-oxidation	Enhances gene expression for milk protein synthesis and antioxidant enzymes	↑ Microbial protein synthesis, improves nitrogen efficiency	Improves immune and liver function	↑ Milk protein %, improved embryo survival	(Khan et al. 2023)
5.	Dietary Protected Fats	Provides high-density energy and fatty acid supply	↓ NEFA mobilization, ↑ plasma energy metabolites, ↑ cholesterol transport	Modulates prostaglandin synthesis and steroid hormone production	Maintains rumen fermentation stability	Reduces ketosis and metabolic stress	↑ Milk fat %, improves reproductive hormone balance	(Zeng et al. 2023)
6.	Zeolite A	Binds dietary calcium and stimulates prepartum Ca mobilization	↑ Serum Ca, ↑ bone mineral mobilization efficiency	Improves PTH responsiveness and Ca regulatory hormone sensitivity	May improve mineral retention and digestion	Prevents subclinical and clinical hypocalcemia	Improves uterine contraction and calving success	(Su et al. 2025)
7.	Monensin	Alters rumen microbial ecology favoring propionate production	↓ BHBA, ↑ blood glucose, ↑ hepatic energy supply	Improves insulin sensitivity and metabolic efficiency	↑ Propionate, ↓ acetate, ↓ methane emission, ↑ rumen fermentation efficiency	Reduces ketosis and improves metabolic adaptation	Improves feed efficiency and milk production	(Osorio-Terán et al. 2025)
8.	Niacin (Vitamin B3)	Reduces excessive lipolysis and supports liver metabolism	↓ Plasma NEFA, ↓ ketone bodies, ↑ hepatic energy utilization	Modulates lipid metabolic enzyme expression	Improves rumen microbial activity	Supports liver health and reduces metabolic stress	Improves lactation persistence and body condition stability	(Singh et al. 2024)
9.	Vitamin E & Selenium	Enhances antioxidant defense and immune modulation	↓ Oxidative stress biomarkers, ↑ glutathione peroxidase activity	Enhances cytokine regulation and immune signaling pathways	Supports rumen epithelial integrity	Reduces mastitis, retained placenta, and uterine infections	Improves reproductive efficiency and calf vitality	(Khan et al. 2024)
10.	Omega-3 Fatty Acids (EPA, DHA)	Anti-inflammatory and immunomodulatory effects	↓ Pro-inflammatory cytokines, ↑ lipid mediator balance	Regulates prostaglandin synthesis and follicular gene expression	May improve rumen lipid metabolism	Reduces inflammatory and metabolic disorders	Improves follicular growth and embryo survival	(Xu et al. 2025)
11.	Betaine	Supports methyl metabolism and osmotic cell protection	↑ Hepatic methyl donor activity, ↓ liver fat deposition	Supports DNA methylation and metabolic gene expression	Enhances intestinal epithelial stability	Improves metabolic stress tolerance	Supports milk yield and energy metabolism	(Buonaiuto et al. 2025)
12.	Magnesium Supplementation	Enhances calcium metabolism and neuromuscular activity	↑ Ca absorption efficiency, ↑ muscle contraction ability	Supports PTH signaling and hormonal regulation	Improves rumen motility and digestion	Reduces hypocalcemia risk and improves feed intake	Enhances postpartum recovery and milk yield	(Fatima et al. 2024)
13.	Yeast Probiotics	Stabilizes rumen microbiota and fermentation	↑ Fiber digestibility, ↑ microbial protein synthesis, ↑ VFA production	Improves immune signaling through gut microbiome interaction	Stabilizes rumen pH and fermentation profile	Reduces acidosis and digestive disorders	Improves feed efficiency and milk yield	(Wang et al. 2024)
14.	Plant Extracts/ Phytochemicals	Antioxidant and anti-inflammatory activity	↓ Reactive oxygen species, ↑ antioxidant enzymes	Modulates inflammatory gene expression	Improves gut microbial diversity	Improves immune resilience and metabolic stability	Supports reproductive and lactation performance	(Xiao et al. 2022)

Conclusions

The transition period is one of the most important phases of dairy cows. There are significant changes to cows in their nutrition, metabolism, hormones, and immune function at this time, so they can produce colostrum and initiate lactation. The increased energy demand is associated with markedly reduced DMI which results in negative energy balance (NEB), excessive mobilization of fat and elevation of blood NEFA and BHBA concentrations, factors that induce a state of ketosis and fatty liver. Meanwhile, calcium demand increases that elevates the risk of developing clinical or subclinical hypocalcemia, which affects muscle, immune and reproductive function adversely. Metabolic changes also have a suppressing effect on the immune system and on oxidative stress with a higher risk of diseases like mastitis and metritis, as well as lower reproductive capacity. Good nutritional management needs to be in place to minimize the occurrence of transition-related disorders. Adaptability to a stage of control energy dry cow diet, slow feed changes and appropriate grouping of the cows. Supplementation of non-fiber carbohydrates promotes rumen adaptation and glucose supply and will decrease NEFA and BHBA. DCAD Negative diets help to enhance calcium mobilization and minimize hypocalcemia. When targeting metabolic health, dietary fats, rumen-protected choline, methionine, lysine, zeolite A, monensin, antioxidants and trace minerals are all supplemented to ensure optimum health, production and reproduction.

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