NANGARHAR UNIVERSITY
INTERNATIONAL JOURNAL OF BIOSCIENCES
Review Article
e-ISSN: 2957-9988
NUIJB Vol 4, Issue 3 | 2025

Received: 21 Jul 2025 Accepted after revision: 2 Sep 2025 Published Online: 30 Sep 2025

Economic Burden and Preventive Strategies for Ketosis and Milk Fever in Dairy Cows: A Systematic Review

Tawfeeq Mohammad Monir[1*]

[1]Department of Clinic, Faculty of Veterinary Science, Kabul University, 1006, Jamal Mina, Kabul, Afghanistan

[*]Corresponding author email: monir.tawfeeq@gmail.com

ABSTRACT

Ketosis and milk fever (hypocalcemia) are common metabolic disorders affecting dairy cows, particularly around calving. These disorders significantly impact productivity in dairy farming. They impose substantial economic burdens through direct losses such as decreased milk production and indirect costs including animal treatment, increased culling rates, and labor demands. Several causative factors have been proposed for the occurrence of these disorders in cattle. Despite their global economic importance, limited research exists on the economic and preventive implications of ketosis and milk fever in developing countries such as Afghanistan, where dairy farming plays a critical role in rural livelihoods. The aim of this study is to highlight the economic and preventive significance of ketosis and milk fever, offering insights to farmers, veterinarians, and policymakers to enhance disease management and minimize losses. This article systematically analyzed peer-reviewed studies published between 1982 and 2025, using several electronic search engines. The study found that ketosis and milk fever were prevalent in dairy farms, which result in significant economic losses. Preventive measures including proper nutritional management, use of monensin, balancing of dietary cation-anion, and timely calcium supplementation are proven effective in minimizing the incidence and severity of mentioned disorders. It can be concluded that ketosis and milk fever lead to major global economic losses in dairy farming, but targeted nutritional and management strategies can substantially reduce their burden.

Keywords: Ketosis; Economic losses; Milk fever; Management; Preventive strategies

INTRODUCTION

Metabolic diseases are a group of disorders that primarily affect dairy cows. These diseases are also referred to as production diseases, and some, like milk fever and ketosis, are also categorized as managerial diseases. Metabolic diseases typically occur around parturition or the transition period (*McArt et al*., 2018). Dairy cows, due to their high milk production, are more susceptible to metabolic diseases compared to other domestic animals. The incidence of these diseases is higher during the calving period and continues until the peak of lactation is reached (Tadesse & Belete, 2015). The susceptibility of animals to milk fever and ketosis depends on genetic and management factors. Most metabolic diseases in farm animals, including dairy cattle, result from an imbalance between energy intake and expenditure. Due to these challenges, many animals fail to meet their daily energy needs, which is often exacerbated by the relatively deficient feed offered to them (Sharma *et al*., 2013).

Over the past two decades, the average annual milk production per cow due to advancements in genetics, breeding, nutrition, and management techniques has significantly increased. However, as milk production per cow has increased, metabolic diseases have become more common. This is because large amounts of nutrients are drained from cows through milk, and replenishing these nutrients through feed is challenging, especially during the first three weeks after parturition, when feed dry matter intake is limited (Gabor *et al.*, 2016). As a result, the proper nutrition and management of high-producing cows have become increasingly complex and critical. During the transition period, various changes, including hormonal shifts, the transition from a non-lactating to a lactating state, a decrease in feed intake, and a change in diet from roughage-based feed to rapidly fermentable carbohydrates, occur. These changes are crucial factors contributing to the occurrence of metabolic diseases (Ametaj, nd). Severe changes in metabolic activity and immune response disorders are closely associated with the development of metabolic dysfunction in cows during the transition period (Contreras *et al*., 2010; Sordillo *et al*., 2009).

Metabolic diseases cause significant economic losses to dairy farms due to a severe decrease in milk production, reduced fertility rates, high treatment costs, and the culling of affected animals from the herd (Senthilkumar *et al*., 2013). These diseases are economically significant worldwide. The reduction in milk production leads to financial losses for farmers (JohnChristy & Thirunavukkarasu, 2006; Ngategize & Kaneen, 1985). Moreover, metabolic diseases can result in other complications, such as changes in meat quality, weight loss, and increased costs related to medicine, fertility, and treatment (Singh & Shiv, 2008). Afghanistan is an agricultural country with abundant permanent pasture, which is well-suited for animal husbandry. Millions of animals, including 5.3 million cattle, play a key role in the economy of farmers and the country through their production (CSO, 2017). There is no published data about importance of economic losses and preventive strategies of ketosis and milk fever in Afghanistan.

The objective of this review article is to briefly discuss ketosis and milk fever, helping farmers and clinicians understand their economic importance and take timely preventive measures.

METHODS

To prepare this manuscript, a systematic search was conducted across multiple electronic search engines, including PubMed, Scopus and Web of Science using predefined keywords such as ketosis, milk fever, preventive strategies and economic losses of mentioned disorders. Up to February 2025, the available literature regarding the above predefined keywords were about 272, which was extracted from the mentioned search engines. After screening of the abstract, only those papers included in this article that matched with the scope of the keywords, published after 1981 in English language and discussed about the: hypocalcemia, management and preventive strategies of metabolic diseases, nutritional and metabolic disorders; and economic impact of mentioned diseases on dairy farms. After removal of 43 duplicate records, 229 articles remained for title and abstract screening. Based on predefined inclusion and exclusion criteria, 96 articles were excluded due to irrelevance, lack of full text, or being conference abstracts. A total of 133 full-text articles were assessed for eligibility, of which 76 were excluded due to insufficient data on economic or preventive aspects. At the end, 57 articles met all inclusion criteria and were included in this review. The details of the study selection process can be seen in Figure 1.

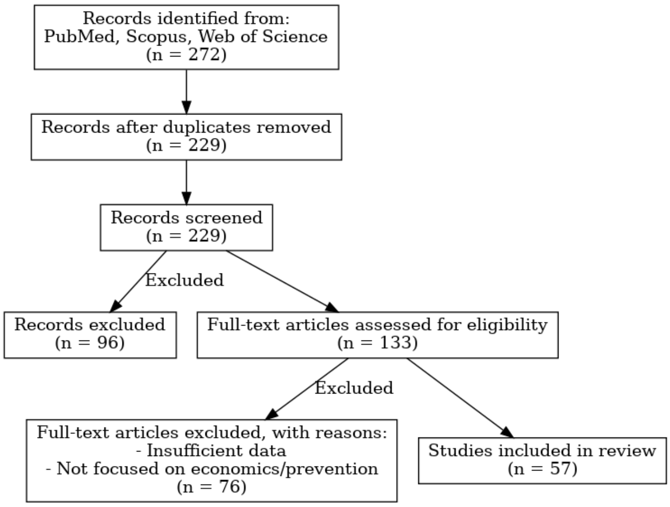

Fig 1. PRISMA flow chart of the study selection process.

RESULTS AND DISCUSSIONS

Ketosis and milk fever (hypocalcemia) are among the most prevalent metabolic disorders in dairy cattle, particularly affecting high-producing cows during the transition period around calving. These conditions arise due to significant physiological and nutritional imbalances during early lactation, leading to disruptions in energy and mineral metabolism.

KETOSIS

Ketosis is considered one of the most common metabolic diseases in dairy cows. This disorder primarily occurs in cows at the end of pregnancy and during early lactation. During these stages, cows experience a negative energy balance and cannot meet the energy demands required for intense milk production at the onset of lactation (Gross *et al*., 2011). Due to this negative energy balance, carbohydrate metabolism changes, resulting in the production of ketone bodies (acetoacetate, β-hydroxybutyrate, and acetone) in milk and urine (Tadesse, 2019). Several risk factors increase the susceptibility of cattle to ketosis, particularly subclinical ketosis. These include high milk production, high body condition score (BCS) during the transition period, and the occurrence of multiple postpartum diseases (McArt *et al*., 2012). Another proposed risk factor is breed susceptibility (Tatone *et al.*, 2017). Ketosis manifests in clinical and subclinical forms (Melendez *et al.*, 2006). Clinical ketosis can be identified through clinical examination and symptoms such as gradual loss of appetite, reduced milk production, rapid weight loss, depression, decreased ruminal activity, pica, and an acetone-like odor in the milk and breath of affected animals. In some cases, nervous signs such as excitement, hyperesthesia, and depraved chewing can also be observed (Fleming, 2015; Scott *et al.*, 2011). Subclinical ketosis is more challenging to detect through clinical signs. Affected animals exhibit an abnormal increase in circulating ketone bodies in the blood, urine, and milk. Most dairy cows are affected by subclinical ketosis, which increases the risk of clinical ketosis, retained placenta, displaced abomasum, and metritis (McArt *et al.*, 2012).

Economic importance: Clinical and subclinical ketosis causes significant economic losses in dairy farms. These losses stem from reduced milk production, increased veterinary costs, decreased fertility, and earlier culling, as outlined below:

1. *Decrease in milk production:* Ketosis, which typically occurs during early lactation, negatively impacts milk production. This condition arises from a negative energy balance, leading the cow to mobilize body fat reserves to meet energy demands. Excessive fat mobilization causes an accumulation of ketone bodies in the bloodstream, disrupting metabolic processes and impairing milk production. Ketosis reduces milk yield by decreasing appetite and feed intake, resulting in insufficient energy for milk synthesis (Duffield *et al.*, 2009). Affected cows may display symptoms such as reduced milk output, lethargy, and weight loss. Ketosis also impacts milk quality, increasing milk fat concentration while decreasing protein content, which affects its marketability. Additionally, the disorder raises the risk of other health issues, such as fatty liver disease, which further reduces productivity and increases veterinary costs (Duffield *et al.*, 2009). Studies have reported reductions in milk yield for cows with subclinical ketosis, ranging from 5.5% (Duffield *et al.*, 2009) to 6.9% (Chapinal *et al.*, 2012) and 7% (Ospina *et al.*, 2010). It also can cause failure of animal to return to normal production after recovery (Constable *et al.*, 2017). It can be concluded that a decrease in milk quantity and quality can cause severe economic losses to farmers and the country.
2. *Decrease in fertility rate:* Affected cows show abnormalities in fertility rates because ketosis interferes with the hormonal balance necessary for ovulation, often leading to delayed ovulation or anestrus (Butler, 2003). It is clear that high concentrations of β-hydroxybutyrate (BHB) and non-esterified fatty acids (NEFAs) alter the secretion of gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH), impairing the normal ovarian cycle (Walsh *et al.*, 2007). Cows affected by ketosis show reduced conception rates due to impaired oocyte quality and a compromised uterine environment. High ketone levels can cause oxidative stress, which negatively impacts oocyte quality and early embryonic development (Leroy *et al.*, 2008). Some studies have shown that cows with subclinical ketosis had a 15–20% lower conception rate compared to healthy cows (Ospina *et al.*, 2010).
3. *Increase displaced abomasum:* In ketosis, negative energy balance occurs, leading to elevated ketone levels, particularly β-hydroxybutyrate (BHBA). BHBA has been shown to reduce abomasal motility (Cameron *et al.*, 1998). Hypomotility allows gas to accumulate in the abomasum, increasing the risk of abomasal displacement (Sharma *et al.*, 2013). Several other mechanisms have also been proposed to clarify the role of ketosis as a risk factor for abomasal displacement.
4. *Increased occurrence of metritis:* An increased occurrence of metritis has also been reported in affected animals (Duffield & Bagge, 2002). This metabolic disorder, characterized by elevated levels of ketone bodies, can contribute to the development of metritis. Metritis typically occurs after calving and is an inflammatory disease influenced by various factors, including metabolic disorders. Ketosis disrupts normal metabolic processes in cows, leading to a weakened immune system, impaired neutrophil function, and

compromised uterine health post-calving (Grummer, 1995).

More than 90% of subclinical ketosis cases occur within the first two months of lactation. The prevalence of subclinical ketosis has been reported at approximately 40% in dairy cows. Studies demonstrate that each cow suffering from subclinical ketosis can incur a financial loss of $78 USD. In a herd of 100 cows, where 40% are affected by the disease, annual losses can amount to $3,120 USD. These costs arise from treatment charges, veterinary fees, culling of affected cattle, and the occurrence of postpartum diseases (Geishauser *et al.*, 2001). Such economic losses are significant, particularly in large farms, and highlight the importance of addressing ketosis as a critical disorder in dairy herds.

Prevention: Since ketosis is a disease with multifactorial causes, several hypotheses for its prevention have been proposed. These are briefly discussed below:

1. *Nutritional management*: One of the important risk factors for ketosis is negative energy balance. Therefore, it is essential to ensure that cows receive a balanced diet with adequate energy, especially during the calving and early lactation periods. This helps prevent excessive fat mobilization and subsequent ketosis (Duffield, 2000). The quantity and composition of the diet should be adjusted gradually. The ration for lactating animals must be nutritionally balanced and include necessary minerals. Cobalt supplementation should be added if required, as it plays a role in energy metabolism (Fleming, 2015).
2. *Use of Monensin for prevention of ketosis:* Monensin has been shown to have a positive effect on rumen microflora. It is hypothesized that monensin alters the balance of sodium and potassium within bacterial cells. When this balance shifts, bacteria require more energy to restore equilibrium, causing a shift in the ruminal bacterial population. This phenomenon primarily, though not exclusively, affects Gram-positive bacteria, favoring Gram-negative bacteria and leading to an overall beneficial change in ruminal microflora (Schären *et al.,* 2017). Monensin can be administered at a dose of up to 25 mg per cow per day in the ration for 4–6 weeks postpartum (Sharma *et al.*, 2013).
3. *Pregnancy fattening control:* Excessive fattening of cows during pregnancy should be avoided. The body condition score (BCS) of animals should be maintained between 3.5 and 4 on a 5-point scale. Regular monitoring of the diet during pregnancy is essential to prevent over conditioning (Sharma *et al.*, 2013).

In general, the preventive measures should address the underlying causes and pathogenesis of ketosis. Key points for prevention include maintaining an ideal body condition, avoiding excessive feeding during late pregnancy, preventing sudden changes in feed, and gradually increasing the lactation ration in proportion to rising milk yield (Payne, 1977).

MILK FEVER

Milk fever, also known as post-parturient hypocalcemia or parturient paresis, results from a severe and acute decrease in blood calcium levels. It is one of the most significant metabolic diseases affecting adult dairy cows, typically occurring within 48 hours after parturition (Khan *et al.* 2015; Kaneko, 1989). Milk fever is a non-febrile disease with an annual incidence rate of clinical milk fever within herds ranging from less than 1% to as high as 60%. Approximately 75% of all milk fever cases occur within 24 hours of calving, with additional cases arising during delivery or after 24 hours postpartum. Cases that occur without parturition are referred to as non-parturient hypocalcemia**,** while those without clinical signs are termed subclinical hypocalcemia (Oetzel & Goff, 2009). The primary risk factors for milk fever are categorized into internal and external/environmental factors (Peterson & Beede, 2002). Parturition or number of parities, stages of lactation, age, milk yield (Fleischer *et al.*, 2001; Taylor *et al.*, 2001; Rehage & Kaske, 2004), breed, body condition, length of dry period, and diet composition are among the mentioned factors that contribute to the occurrence and severity of the milk fever (Houe et al., 2001; McDowel, 2002).

A deficiency of calcium (Ca) in the diet does not immediately result in noticeable changes in health or production, as calcium levels are initially compensated by mobilizing calcium from skeletal reserves through the action of the parathyroid hormone. However, during the dry period, parathyroid activity may be temporarily suppressed, impairing calcium mobilization and predisposing cows to hypocalcemia. Subclinical hypocalcemia, characterized by low blood calcium levels without overt clinical symptoms, often results in greater economic losses than clinical cases. Hypocalcemia is defined as a total blood calcium concentration below 2 mmol/L, with or without clinical signs of paresis (Constable *et al.*, 2017), which is approximately equivalent to 1 mmol/L of ionized Ca (Oetzel, 1996). The condition is typically accompanied by hypophosphatemia and, in most cases, hypermagnesemia (Phillippo *et al.*, 1994).

Cows developing milk fever generally exhibit clinical signs that can be categorized into three stages:

*Stage One***:** This stage often goes unnoticed as the clinical signs are subtle. Affected animals may appear excitable, restless, nervous, or anorexic. Recumbency is not observed in this stage.

*Stage Two***:** The cow becomes recumbent and assumes a sternal position. Moderate to severe depression is evident, and the cow may turn its head toward its flank. Partial paralysis is often observed.

*Stage Three***:** The cow progresses to lateral recumbency, becomes completely paralyzed, bloated, and severely depressed. Without treatment, animals in this stage usually die within a few hours (Oetzel, 2013).

Economic importance: From an economic perspective, milk fever can cause significant direct and indirect losses, which are discussed briefly below:

1. *Treatment Costs:* Treatment costs include veterinary fees, medical expenses, transportation costs, and feed supplementation for recovery.
2. *Milk Reduction:* A major economic loss in affected dairy cattle is the reduction in milk production. According to Kossaibati and Esslemont (1997), milk reduction in affected Holstein cows was estimated to be around 200–500 liters per animal.
3. *Mortality and Culling:* Mortality and culling of affected animals represent another significant economic loss for farmers. Although the mortality rate of animals with milk fever is relatively low, affected animals may not reach their full production potential and are often culled from the herd (Thirunavukkarasu *et al.*, 2010).
4. *Predisposition to Other Parturient Problems:* Clinical milk fever predisposes affected animals to several other parturient problems, such as retained placenta, displaced abomasum, uterine prolapse, fertility disorders, and mastitis (Oetzel, 2011; Bzune *et al.*, 2020).
5. *Reduced Feed Intake and Rumen Function:* Milk fever can lead to reduced feed intake, decreased rumen and intestinal motility, and increased susceptibility to infectious diseases (Goff 2008; Seifi *et al.*, 2011). Different data according to economic losses of milk fever have been reported in different countries including Israel (Bar & Ezra, 2005), and India (Thirunavukkarasu *et al.*, 2010).

Prevention: While most cows suffering from clinical milk fever can be successfully treated with the intravenous administration of calcium salts, these animals become more susceptible to other infectious and metabolic diseases. Therefore, preventing milk fever is of utmost importance. Several strategies have been proposed to prevent milk fever in cows (Hansen *et al.*, 2002).

1. *Dietary Management:* Effective dietary management during the transition period is crucial for preventing milk fever in susceptible cows. Most studies recommend restricting dietary calcium intake at least 10 days before parturition. This approach stimulates the parathyroid gland to release parathyroid hormone, which enhances calcium resorption from bones and increases renal production of 1,25-dihydroxyvitamin D. Consequently, after calving, calcium absorption is optimized, reducing the risk of hypocalcemia (Sharma *et al.*, 2013). Supplementing the diet with magnesium during the prepartum period also plays a vital role in preventing milk fever. Adequate magnesium levels are essential for proper calcium absorption and metabolism (DeGaris & Lean, 2008).

2. *Balancing Dietary Cation-Anion Ratios (DCAD):* Balancing the dietary cation-anion difference (DCAD) in the ration is an effective strategy for preventing milk fever and improving overall production (Patel *et al.*, 2011). Acidifying the diet by reducing cations (e.g., sodium and potassium) while increasing anions (e.g., chloride and sulfur) promotes calcium mobilization and absorption, helping to prevent hypocalcemia (Goff, 2008).
3. *Administration of Calcium*: Oral calcium supplementation around calving is effective in preventing milk fever. Calcium should be administered starting 24 hours before parturition and continued up to 24 hours postpartum. A dose of 40–50 grams of calcium preparations, such as calcium chloride or calcium carbonate, can be given in liquid or bolus form (Thilsing-Hansen *et al.*, 2002).
4. *Vitamin D Administration*: Injecting vitamin D metabolites or their analogs immediately before parturition enhances calcium mobilization and helps prevent milk fever. However, the required dose of vitamin D for this purpose is close to the toxic threshold. Administering such high doses is controversial, as it may lead to adverse effects or clinical signs of toxicity (Littledike & Horst, 1982).

CONCLUSION

In conclusion, metabolic diseases such as ketosis and milk fever are major health concerns in dairy cows, especially during the transition period. These disorders result from nutritional and physiological imbalances, significantly affecting animal health, milk production and fertility. High-producing dairy cows are more vulnerable due to their increased nutritional demands. Ketosis arises from negative energy balance, while milk fever is caused by acute calcium deficiency. Both conditions lead to substantial economic losses through decreased productivity, increased treatment costs, and higher culling rates. Effective prevention through proper nutritional management, early diagnosis, and specific strategies like diet balancing and controlled supplementation of calcium and energy can greatly reduce their incidence. Strengthening extension services, farmer training, and government subsidies for preventive supplements can improve management and reduce the burden of metabolic diseases. Integrating such strategies will promote sustainable dairy production and enhance both animal health and farmer livelihoods. Future research should evaluate regional economic impacts and the effectiveness of preventive interventions for ketosis and milk fever.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

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