Review: Milk Fever and Its Economical Impacts in Commercial Dairy Cattle Production

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Abstract: Production diseases are those diseases induced by management practices, where high producing dairy cows fail in metabolic imbalances. Milk fever (parturient paresis) is an important production disease of dairy cows around periparturient period. Because of the high volume of milk produced during this time and a subsequent increased demand for calcium, these cows often develop milk fever (hypocalcaemia), abnormally low levels of calcium in the blood. Calcium is required for release of acetylcholine at the neuromuscular junction, affected animals will begin to experience muscle weakness. The clinical symptoms of milk fever include inappetence, tetany, low body temperature, paresis, lateral recumbency, and eventually coma and death if left untreated. Milk fever is sporadic but on individual farms the incidence may be high among susceptible cows. High producing dairy cows are the most susceptible to milk fever during the periparturient period. Several factors have been consistently associated with an increase in the incidence of milk fever. These include parturition and initiation of lactation, advanced age, breed, and diet. Cows with serum calcium lower than 7.5 mg/dL are as considered as hypocalcaemic. Parturient paresis is treated intravenously with calcium boro gluconate. Affected cows have an excellent prognosis if treated early. Economic losses due to milk fever include losses from deaths, premature culling, treatment costs and decreased milk production in the subsequent lactation. Therefore milk fever management is economically most important, as it results in not only reduction in milk production, but also loss of animals. Multiple strategies have been utilized to prevent hypocalcaemia. Furthermore, as the dairy profitability is determined by the biological cycles of milk production and reproduction, emphasis should be given to the nutritional management of dairy cows in both dry and periparturient periods.

Keywords: Calcium, Dairy Cows, Milk Fever & Periparturient Period.
1. Introduction

Production diseases of dairy cows are those diseases induced by the management practices; metabolic diseases are typical examples (Oded, 2003). They are manifestations of the cow’s inability to cope with the metabolic demands of high production and occur when the level of production is inconsistent with nutrient intake (Mulligan and Doherty, 2008). Milk fever is an important production disease occurring most commonly in adult dairy cows within two to three days after parturition (Radostits et al., 2000). It is a metabolic disorder that occurs immediately after or close to calving as a result of a low level calcium (Ca) in the blood that is referred to us hypocalcaemia (Khan et al., 2015). In a small proportion of cows, hypocalcaemia becomes severe and results in paresis, recumbency and occasionally death (Bhanugopan and Lievaart, 2014).

Milk fever is one of the most common mineral related metabolic condition affecting dairy cows at parturition (Khan et al., 2015). Parturient paresis is cow affection and occurs immediately after childbirth which is clinically characterized by hypocalcemia, motor paralysis, sensory nerve devices, general muscle weakness, circulatory collapse and consciousness depression (Radostits et al., 2000). Most commonly milk fever affects high producing and well performing dairy cows about to reach their maximum production potential. The selection for body traits, especially those related to udder conformation placing cows at risk of milk fever. So selection for high production results in cows that are more prone to milk fever (Hansen, 2000).

Milk fever is caused by a temporary blood calcium deficiency (hypocalcaemia) which usually occurs around the time of calving (Brandly and Cornelius, 2001). During the dry period, calcium demand is relatively low. Hence, intestinal absorption and bone resorption of calcium is relatively inactive during this time. The onset of lactation results in sudden loss of calcium through milk. When the calcium homeostatic mechanism is unable to meet the demand of calcium for milk production, hypocalcaemia occurs (Tsioulpas et al., 2007). About 50% of dairy cows in their second lactation and above have blood calcium concentrations that fall below the threshold for subclinical hypocalcaemia after calving (Reinhardt et al., 2011).

Milk fever can be clinical or subclinical based on whether an animal may or may not show clinical signs. The symptoms include ataxia, poor appetite, reduced rumen motility, Low body temperature, slow respiration, quick and weak heart beats, paresis due to reduced muscles function that may develop in to complete paralysis and coma (Goff, 2008). It can be diagnosed based on the history of the animal at calving, clinical signs, age of dam and response to intravenous calcium borogluconate solution (Radostits et al., 2007). Treatment of milk fever should be done as early as possible for good recovery and to avoid complications. Most commonly calcium borogluconate is used for treating milk fever (Oetzel, 2011).

Milk fever is a common noninfectious disease of dairy cows throughout the world. It is common outcome of modern dairy industry that is pushing for maximization of profit (Thirunavukkarasu et al., 2010a). The risk factors for hypocalcaemia could be grouped into intrinsic risk factors, which are associated within the animal itself and extrinsic risk factors, which are outside of the animal’s body which are commonly known as environmental factors (Radostits et al., 2000). Generally milk fever is sporadic but on individual farms the incidence may rarely reach 25 to 30% of susceptible cows. The incidence of milk fever increases with age of the cow and milk yield (Sharma, 2015). In Ethiopia, it was found that poor reproductive and productive performance of dairy cows. The prevalence rate of milk fever is 17.5% in Hawassa (Nigussu and Terefe, 2015) and 30.2% in Gondar (Anteneh et al., 2012).

The key to prevention of milk fever is management of a close up dry cow or management during late pregnancy (Sharma, 2015). Multiple strategies must be designed for the management of hypocalcemia and to enhance calcium mobilization in dairy cows particularly in periparturient period (Amaral-Phillips, 2014). Milk fever is a serious problem in many countries, because of the enormous economic consequences of the disease. The most important economic loss of milk fever is due to reduction in milk production, loss of animals due to culling and mortality and the cost of treatment of the animals (Thirunavukkarasu et al., 2010b).
Therefore, the objectives of this seminar paper are:

- To give an overview on milk fever in dairy cattle.
- To show the economic impacts of milk fever in the dairy industry.

2. General Features of Milk Fever

The name milk fever is misleading since the cow does not have a fever (Sharma et al., 2005). There is always a marked and rapid lowering of the blood calcium so that the name parturient hypocalcemia is quite appropriate (Thilsing-Hansen et al., 2002b). This disease has been known by a number of terms including parturient paresis, milk fever and parturient apoplexy. When a milk fever results from imbalance in blood calcium, phosphorus and magnesium levels, it is known as milk fever complex (Sharma et al., 2005). It generally affects older and high producing cows in their productive stage that is mostly after their third to seventh calving (Goff, 2008).

The disease is life threatening itself and it is predisposing for several other disorders (Kara et al., 2009). Milk fever should be considered as a gateway diseases that greatly reduce the chance for full productivity in the ensuing lactation. Hypocalcemia reduces all muscle contraction including the teat sphincter muscle responsible for closure of the teat orifice after milking, thus increasing the risk of mastitis (Kimura et al., 2006). A mild degree of hypocalcaemia develops in the majority of cows during the peripartum period and has been linked to calving problems, retained placenta, metritis, ruminal stasis and depression of the immune system (Khan et al., 2015).

2.1 Cause and Pathophysiology

2.1.1 Cause

Milk fever is caused by a severe deficiency of metabolizable calcium ion in the circulation (Brandly and Cornelius, 2001). Onset of lactation is related to the development of milk fever (Fig. 1); because calcium is one of the most abundant minerals in cow’s milk and the concentration of calcium in the colostrum is almost double that in the milk later in lactation of the cow (Tsioulpas et al., 2007). Calcium in milk often constitutes the major part of the absorbed calcium. A cow producing 10 liters of colostrum loses about 23 gram of Ca in a single milking (Kamiya et al., 2010). Therefore, initiation of lactation challenges a cows’ ability for calcium homeostasis. Colostrum and milk synthesis increases around parturition and dry mater intake transiently decreases; the result is a transient period of hypocalcemia (Reinhardt et al., 2011).

![Figure 1: Plasma concentrations of total calcium before and after calving in mature Jersey cows with or without clinical milk fever](image)

**Source:** Kimura et al., 2006
Calcium is eliminated from the cow to endogenous fecal calcium, clearance in glomerular filtration, placental calcium transport to the fetus, bone deposition and calcium secretion in the mammary gland (El-Samad et al., 2002). When approximately 50% of the circulating blood calcium is lost milk fever is likely to occur (DeGaris and Lean, 2008). Hypocalcemia occurs as the dairy animal’s complex mechanisms for maintaining calcium homeostasis fail during a sudden and severe calcium outflow. The delay in the operation of calcium homeostatic mechanisms is vital in causing milk fever (Oetzel, 2011).

Generally calcium homeostasis can be affected by three major factors. The first is excessive loss of calcium in the colostrums beyond the capacity of absorption from the intestines and mobilization from the bones to replace it. The second factor is impairment of absorption of calcium from the intestine at parturition and the last factor is insufficient mobilization of calcium from storage in skeleton, which could arise because of parathyroid insufficiency since the gland is relatively quiescent in dry period (Mulligan et al., 2006). So the parathyroid hormone (PTH) insufficiency is caused by inadequate functioning of parathyroid gland (Radostits et al., 2007).

2.1.2 Pathophysiology
During the dry period, the demand of calcium is relatively low. Hence, intestinal absorption and bone resorption of calcium is relatively inactive during this time. Parturition is accompanied by sudden increase in calcium sequestration for the production of milk. The calcium requirements rise to 2 to 5 times that of dry period (Lean et al., 2006). This daily calcium out flow through milk will not be matched with decreased plasma calcium. This places major strain on calcium homeostatic mechanism. Decreased plasma calcium cause hyperexcitability of nervous system and weakened muscle contractions, which result in both tetany and paresis (Aiello, et al., 2008).

The fall in blood calcium level stimulates the calcium homeostatic mechanism to improve intestinal absorption and bone resorption. Therefore, the decrease in plasma calcium causes a compensatory increase in parathyroid hormone and calcitriol, but it takes time for both to exert their full effect (Harris, 2002). Bone calcium mobilization by parathyroid hormone takes at least a week and improved efficiency of calcium absorption by influence of calcitriol takes a day or two. So, nearly all animals at parturition develop hypocalcemia, but high yielders tend to develop milk fever. The pathogenesis of the disease is more associated with the action of PTH that is responsible for regulation of calcium homeostatic mechanism (Bezerra et al., 2014).

Hypocalcemia affects muscular contraction mainly in three ways. Firstly, calcium has a membrane stabilizing effect on the peripheral nerves. So hyperesthesia and mild tetany is seen in early stages of milk fever. Secondly, calcium is required for the release of acetylcholine at the neuromuscular junction. The inability to release acetylcholine causes paralysis by blocking the transmission of nerve impulse to the muscle fibers. Thirdly, calcium is directly required by muscle cells for contraction (Iggo, 1994). There is decreased contractility of cardiac muscle and lowered stroke volume cause reduction in arterial blood. Then this reduced peripheral perfusion resulted in hypothermia and depression of consciousness (Erkihun and Lingerih, 2015).

Hypocalcemia also reduces gastrointestinal (GIT) function. Serum calcium content below 5 mg/ dL reduces abomasal motility and rumen function and thus reduces energy balances, which is manifested as elevated blood nonesterified fatty acid (NEFA) (Grummer, 1996). Periparturient cows also experience immune suppression. Intracellular calcium signaling is a key early feature in immune cell activation, so the increased demand for calcium in these cows affect intracellular calcium stores of immune cells and leads to the immune suppression (Kimura et al., 2006).

2.2 Clinical Signs
Many cases of milk fever do not externalize the clinical signs in animals. Hypocalcaemia can be clinical or subclinical based on whether an animal may or may not show clinical signs. Clinical milk fever is the most severe hypocalcaemia results in a cow that is unable to rise (from lying to standing position).
and is the most easily recognized form of hypocalcaemia with blood calcium concentration less than 5 mg/dL (Goff, 2008). Subclinical hypocalcaemia results in less severe disturbances in blood Ca and does not have any outward sign. During subclinical hypocalcaemia, blood calcium concentration ranges between 5.5 and 8.0 mg/dL (Wubishet et al., 2016).

The symptoms include, initially the animal is ataxic, nervous and hyperactive. There is Poor appetite, reduced rumen motility, bloating, Low body temperature, slow respiration, impalpable pulse, weak but rapid heart beats (80-100 per minutes) with very hard to hear due to reduced ability of muscles to contract, dilated pupils and dry muzzle are a common signs (Goff, 2008). Other symptoms include turned head back to the flank, splayed out hind legs, paresis (difficulty to rise from lying down). Finally, coma and sudden death may occur (Oetzel, 2011).

Based on the degree of hypocalcaemia and time of occurrence, the clinical signs of milk fever divided into three stages. Stage I milk fever is early signs without recumbency. It may go unnoticed because its signs are subtle and transient. Affected cattle may appear excitable, nervous, or weak. Cows in stage II milk fever are in sternal recumbency (Fig. 2). They exhibit moderate to severe depression, partial paralysis and typically lie with their head turned into their flank (Oetzel, 2011). Body temperature is subnormal, muzzle dry and the heart rate will be rapid (Tadesse and Belete, 2015). Stage III hypocalcemic cows are completely paralyzed, typically bloated, in lateral recumbency (Fig. 2) and progressively lose consciousness that leading to coma. There is a marked fall in temperature and increased heart rate. Cows will not survive more if not treated (Radostits et al., 2007).

**Figure 2:** Commercial dairy cows that are in the various clinical stages of milk fever (hypocalcemia)

Source: Mohammad, 2015

### 2.3 Diagnosis of Milk Fever

Diagnosis of milk fever is based on history taking, clinical examination and laboratory diagnosis. During history taking all the detailed information of the cow including age, breed, stage of lactation, milk yield and calving day should be collected. Milk fever commonly occurs in mature dairy cows usually 5-9
years old, within 72 hours after parturition. The incidence increases in high producing dairy cows. Jersey breeds are commonly affected cows (Radostits et al., 2007).

The laboratory determination of blood calcium level and good response to intravenous calcium solutions are the most accurate method to diagnose a case of milk fever. The normal serum Ca concentration is 8 - 10 mg/dL (Thirunavukkarasu et al., 2010b). Cows with serum calcium lower than 7.5 mg/dL are as considered as hypocalcaemic. Animals with serum calcium level of 5.5 to 7.5 mg/dL show sign of stage I hypocalcaemia. Stage II hypocalcaemia seen with calcium levels of 3.5 to 6.5 mg/dL and stage III seen when calcium concentration falls below 3.0 mg/dL. Blood samples are often taken later if there has been no improvement (Hunt and Blackwelder, 2002).

2.3.1 Differential Diagnosis

The differential diagnosis of milk fever can be subdivided as metabolic, toxemia and traumatic disorders. Metabolic diseases showing symptoms resembling milk fever include hypoglycemia, hypomagnesaemia and hypophosphotamia. Toxic conditions that create doubt with milk fever include acute toxic mastitis and acute diffuse peritonitis. Traumatic conditions may cause symptoms resembling milk fever includes maternal obstetrical paralysis and musculoskeletal injury including downer cow’s syndrome due to pressure damage to muscles and nerves (Adam, 2013). Most cases can be differentiated from milk fever, as hypocalcaemia has a rapid response and good recovery to administration of IV calcium borogluconate (Bewley and Schutz, 2008).

2.4 Treatment

Treatment of milk fever should be done as early as possible, especially if recumbency is present, as recumbency can cause severe musculoskeletal damage (Oetzel, 2011). Commonly milk fever is treated with oral calcium solutions and intravenous (IV) calcium borogluconate (Goff, 2008). Supplementation of calcium borogluconate by oral route is the best approach to hypocalcemic cows that are still standing, such as cows in stage I hypocalcemia or which have undetected subclinical hypocalcemia (Oetzel, 2011). Cows absorb an effective amount of calcium into its bloodstream within about 30 minutes of supplementation. Drenching of calcium borogluconate near calving also serves as the prevention of milk fever (Goff, 2004).

The fastest way to restore normal plasma calcium concentration is to administer an IV injection of calcium salts. For cows in stage II and III of milk fever should be treated immediately with a slow IV administration of 500 ml of 23% calcium borogluconate (Melendez et al., 2002). Extremely high dose of calcium may cause fatal cardiac complications (Doze et al., 2008). Subcutaneous calcium administration can also be used to support blood calcium concentrations around calving (Goff, 2008). Subcutaneous calcium injections are irritating causes tissue necrosis; administration should be limited to no more than 75 ml of a 23% calcium borogluconate (Mohebbi, and Azadnia, 2012). The prognosis depends on the stage of the condition; cows in severe stage may present several complications and poor prognosis (Huntjens and Aalseth, 2005).

3. Epidemiology

Milk fever is one of the common production disease of dairy cows throughout the world and a necessary outcome of modern dairy industry that is pushing for maximization of profit (Thirunavukkarasu et al., 2010a). Generally milk fever is sporadic but on individual farms the incidence may reach high among susceptible cows. The incidence of milk fever is higher in dairy cows than beef cows and increases with age of the cow and milk yield (Sharma, 2015). Parturient paresis is a disease of high producing dairy cattle. It is estimated that 3% to 8% of cows are affected by this disease with some herds having prevalence as high as 25% to 30%. Parturient paresis in dairy cows may occur before calving, but most cases occur within the first 48 hours following calving (Goff, 2004).
The periparturient or transition period of 4 weeks before and 4 weeks after calving is characterized by a greatly increased incidence of disease. The periparturient period of dairy cows refers to the time frame near parturition (Smith, 2005). There is high variability in milk fever incidence among herds (McLaren et al., 2006), which implies that there are possibilities to affect the milk fever incidence by differences in management. The incidence of clinical milk fever tends to be lower in first parity cows with the risk increasing with subsequent lactations (Whitaker et al., 2004). The hypocalcaemia at calving is age related in which most cases occur in animals older than five years of age (Tadesse and Belete, 2015).

Although milk fever was known to occur sporadically in dairy cows, recently it is dramatically increased in small holder dairy farms. The occurrence of milk fever predisposes the cow to productive problems, especially among highly productive dairy cows (Wubishet et al., 2016). The prevalence of milk fever was significantly associated with milk yield, parity and breed. Cows with milk yield of less than 25, 25 to 30 and greater than 30 liters per day had 21.83%, 22.4% and 50.92% milk fever respectively. The occurrence of milk fever was 17%, 17% and 73.3% in cows with less than three, three to four and greater than four parities respectively. The prevalence of milk fever is higher in greater than 50% Friesian blood than 50% Friesian blood cows in Ethiopian (Anteneh et al., 2012).

3.1 Risk Factors

The factors that contribute to occurrence of milk fever and which influence the incidence and severity of milk fever includes; parturition or number of parity (Roche and Berry, 2006), stage of lactation; first-lactation dairy cattle rarely develop milk fever because they produce less colostrum and they can rapidly mobilize calcium from bone owing to the high osteoclastic activity in their growing skeleton (McDowel, 2002), age, milk yield breed, body condition, length of dry period and diet composition (Fleischer et al., 2001). Generally, the risk factors for milk fever could be grouped into intrinsic risk factors, which are associated within the animal itself and extrinsic risk factors, which are outside of the animal’s body which are commonly known as environmental factors (Radostitis et al., 2007).

3.1.1 Intrinsic Risk Factors

A. Number of Parity and Milk Yield

There was a strong association between milk fever and parity. Increased prevalence rate of milk fever is associated with increased number of calving and hence parity is an important risk factor for milk fever, 9% increased risk for each successive lactation (Taylor et al., 2001). The occurrence of milk fever is significantly associated with milk yield. Because from a total of 116 cows affected with milk fever observed in Gonder town 55 (50.92%) were producing 30 liters of milk per day (table 3). From local breeds only 6 (15%) had milk fever and from which 110 (31.9%) cross breed cows had the disease. This could be attributed to high milk yield of the cross breeds than the locals (Anteneh et al., 2012).

B. Age of the Cow

The risk of a cow developing milk fever will increase with age. From the third lactation onwards, dairy cows produce more milk, resulting in a higher calcium demand. In addition to increased milk production, ageing also results in a diminished ability to mobilize calcium from bone stores and a decline in the active transport of calcium in the intestine, as well as impaired production of vitamin D3. The skeletal bones of heifers are still in a growth phase and therefore have a large number of osteoclasts present, which can respond to PTH more readily than the bones of mature cows (Rezac, 2010). Thus hypocalcaemia is age related and most marked in cows from third to seventh parturition (Jawor et al., 2012).

C. Breed of the Cow

Certain breeds of dairy cows have been shown to be more susceptible to milk fever than others. For instance cross breed cows are more susceptible to milk fever than local breeds (Table 2). This indicates that, there is a genetic predisposition of cows to milk fever and this is well recognized in
certain breeds of high producing Jersey and other breeds (Tadesse and Belete, 2015). This is associated with higher milk production per unit of body weight, reduction of intestinal vitamin D₃ receptors (Peterson and Beede, 2002). Jersey breeds has lower numbers of intestinal receptors for 1, 25-(OH)₂ D₃ (1, 25 dihydroxy vitamin D₃) than same aged Holsteins. Lower receptors would result in a loss of target tissue responsiveness and sensitivity to 1, 25-(OH)₂ D₃ resulting in an increased tendency to develop milk fever (hypocalcaemia) (Weiss et al., 2015).

D. Body Condition Score (BCS)

Excessive BCS prior to calving has been recognized as a risk factor for the development of metabolic problems. High BCS enhance the risk of milk fever. Dairy cows that are over conditioned at calving are up to four times more likely to develop milk fever (Ostergaard et al., 2003). This is due to dairy cows with higher BCS at calving have a higher calcium output in milk, making them more prone to milk fever and over conditioning results in decreased feed intake during gestation period, as they take small amount of calcium containing feed. This is caused by reduced appetite in the critical period around calving (Harris et al., 1999).

Cows with excessive body condition at calving, or excessive weight loss after calving, demonstrate overall decreased reproductive performance and increase in the likelihood development of milk fever (Avendano-Reyes et al., 2009). An optimum body condition score for reducing the risk of developing milk fever should be maintained between 3.25 and 3.75 (Thilsing-Hansen et al., 2002b).

3.1.2 Extrinsic Risk Factors

A. Dietary Factors

The diets providing dry cows a high daily intake of calcium are associated with an increased incidence of parturient paresis. At this level the maintenance requirement of calcium can be met predominantly by passive absorption since active absorption of dietary calcium and bone resorption are then suppressed. Cows in this condition are not able to quickly replace plasma calcium lost in milk and become severely hypocalcaemic (Boda and Cole, 2003). Higher calcium intake impairs the uptake of calcium. Prepartum diets high in cations like sodium and potassium are associated with an increased incidence of milk fever (Jarjou et al., 2010).

Diets of high in anion, especially chlorides and sulfides are associated with decreased incidence of milk fever. The addition of anions to the diet of dairy cows prior to parturition effectively reduced the incidence of milk fever by inducing a metabolic acidosis, which facilitates bone resorption of calcium (Rezac, 2010). Excessive dietary phosphorus intake during late gestation can also induce milk fever and the severity of hypocalcaemia by raising blood phosphorus concentrations to the point that phosphorus directly inhibits renal synthesis of 1,25-(OH)₂ D₃ and thus reduces the intestinal calcium absorption mechanisms (Oetzel, 2011).

B. Complete Milking

Complete milking is an absolute removal of milk from the cow at time of milking. Complete milking in the first in the first 48 hours (two to three days) after calving appears to be a precipitating factor for the occurrence of milk fever. When there is complete milking, the cow will immediately continues to secrete milk. This causes an equivalent loss of calcium from the body, as the cow exports large quantity of calcium in to the milk. Therefore, complete milking particularly in those susceptible cows can predispose the animal to milk fever (Henshaw et al., 2010).
4. Prevention and Control Strategies

All cases of milk fever can be prevented through proper management. Management of milk fever is very important because it should be considered as a gateway diseases that greatly reduce the chance for full productivity and reproduction of dairy cows (Kimura et al., 2006). Specific management program is relevant to control the incidence of milk fever among high risk cows. The key to prevention of milk fever is management of a close up dry cow or management during late pregnancy. The common way of preventing milk fever is to limit calcium intake during the dry period to adapt to calcium deficiency and able to respond to milk calcium demand in early lactation (Sharma, 2015).

Strategically prevention of milk fever is economically important to the dairy farmer because of minimize production loss, death loss and veterinary costs associated with milk fever. In order to understand how to prevent this condition, one must understand why it becomes a problem (Tadesse and Belete, 2015). Multiple strategies have been utilized to prevent hypocalcemia and mobilize calcium in dairy cows through nutritional management including feeding anionic salts, low calcium ion diets and vitamin D supplementation (Amaral-Phillips, 2014). Several milk fever control principles are applied in commercial dairy farms today (Radostits et al., 2007).

4.1 Nutritional Management

4.1.1 Feeding Acidifying Rations (Dietary Cation-Anion Difference (DCAD))

The regulation of DCAD of rations is the effective strategies in preventing milk fever by benefiting from anion salts in dairy cows feeding in calving period (Townsend, 2003). It is a common prevention strategy by supplementing anionic salts to reduce diet cation-anion difference (Overton et al., 2004). This is most efficiently achieved by the ingestion of rations having a surplus of acidifying anions (Jorgenson et al., 2001). The goal of this type of supplementation is to reduce absorbable cations such as sodium and potassium, while increasing available anions like chlorine and sulfur monoxide in the diet (Goff, 2008).

The strong cation-anion difference is necessary in the diet to transition cows to prevent them contracting milk fever (McNeill et al., 2002). Metabolic alkalosis impairs the physiologic activity of PTH and induces conformational changes in the PTH receptor, which prevents tight binding of PTH to its receptor. Anionic salts reduce the incidence of milk fever by increasing the mobilization of Ca from bones. They are helpful when there is a high incidence of milk fever or when it is difficult to control Ca consumption during the dry period. Anionic salts are effective in rations with high Ca levels (150 gram per day). Addition of anionic salts reduced the incidence of clinical milk fever from 18.5% to 7.7% and the incidence of parturient hypocalcemia from 50.0% to 28.2% (Sharma, 2015).

It is now widely accepted that the homeostatic mechanisms that result in milk fever prevention work more efficiently when dietary cation-anion difference is negative (Goff, 2004). Negative dietary cation-anion differences reduce milk fever by increasing the calcium level in serum by improving resorption and absorption of calcium (Sakha et al., 2014). Adding any anions to the rations before calving is not only useful for the prevention of milk fever, but also for the prevention of subclinical hypocalcaemia, which cause further problems like retained placenta and displaced abomasums (Saffar and Nouri, 2008).

4.1.2 Low Calcium and Phosphorus Intake in Late Pregnancy

One of the classical strategies often proposed for milk fever prevention is the restriction of calcium rich feed intake precalving. This has the effect of making sure that PTH and the active form of vitamin D₃ are in higher concentrations in circulation on the day of parturition when calcium export in colostrums increases suddenly (Wilson, 2001). It is possible to prevent milk fever, as well as subclinical hypocalcemia, by supplementing the dry cow ration with sodium aluminium silicate (zeolite A), which has the capacity to bind calcium and causes it to be passed out in the feces. (Thilsing-Hansen et al., 2002a; Pallesen et al., 2007)
Other factors in the preventive feeding are phosphorus. Phosphorus increases milk fever risk because phosphorus has a negative impact on calcium homeostasis (DeGaris and Lean, 2008). A cow with a phosphorus intake of more than 80 gram per day has an increased risk to develop milk fever, because the phosphorus will block the renal production of vitamin D₃ (1, 25 dihydroxy-cholecalciferol), which plays an important role in calcium homeostatic mechanism by stimulating intestinal calcium absorption. For dairy cows it is better that, diet should contain as low as four gram of phosphorus per kilogram of the diet to prevent the negative effect of phosphorus on calcium homeostatic mechanism (Goff, 2008).

4.1.3 Peripartum Dietary Magnesium Supplementation

Ensuring adequate magnesium supplementation is vital for the prevention of milk fever. Because magnesium plays a very important role in calcium metabolism, as it is a key intermediate in the resorption of calcium from bone by parathyroid hormone. High levels of magnesium could induce a lower renal calcium excretion (DeGaris and Lean, 2008). Increasing magnesium supplementation has the greatest influence amongst dietary strategies for the prevention of milk fever (Lean et al., 2006). Milk fever is usually accompanied by an increased concentration of plasma magnesium level to restore the normal blood calcium level (Klimiene et al., 2005).

4.1.4 Controlling Dietary Carbohydrate Intake

The influence of grain feeding in the dry period is not a major risk factor for the occurrence of milk fever. But feeding large amounts of concentrate such as grain in the dry period increases the incidences of milk fever, due to the fact that overfed dairy cows, more easily lose their appetite around calving and thereby absorb less intestinal calcium than required. Therefore limiting prepartum carbohydrate intake is essential to reduce the incidence of milk fever in dairy herds (Houe et al., 2001).

4.1.5 Prepartum Administration of Vitamin D, Vitamin D Metabolites and Analogues

A practice by some farms is supplementing high amounts of vitamin D to prepartum dry cows either in the feed or parenterally. Supplementation requires that up to 10 million IU (international unit) of vitamin D must be injected or fed daily for 10-14 days before calving. These vitamin D doses pharmacologically increased intestinal calcium absorption and prevents milk fever (Goff, 2008). The timing of the treatments is very important. Injection given 2 to 8 days before parturition has been considered optimal (Radostits et al., 2000). Therefore, injection of high doses (10 million IU) of vitamin D to the susceptible dairy cows before calving period is important for prevention of milk fever as it stimulates the intestinal calcium absorption (Amanlou and Abuzar, 2008).

4.1.6 Oral Calcium Drenching Around Calving

Oral drenching with calcium preparations can prevent a significant proportion of milk fever cases when given to parturient cows. Administration of calcium solutions during the period from 24 hours before calving to 24 hours after calving, essential reduces the incidence. There are many formulations available for oral calcium drenching. The effect have been done with preparations containing easily absorbed calcium salts such as, calcium carbonate and calcium chloride preparations, providing 40-50 gram of calcium per dose as a bolus or a liquid (Thilsing-Hansen et al., 2002b).

The positive side effects of oral calcium supplementation following efficient milk fever prevention are reductions in hypocalcaemia associated diseases and improvement of the reproductive and productivity performance of the dairy cows. Oral calcium drenching can also prevent a significant proportion of relapses when given as a supplement to intravenous calcium therapy of milk fever cases (Houe et al., 2001).
4.2 Management Practices

4.2.1. Body Condition Score Management

Achieving the correct BCS at calving and dry period is critical for the prevention of milk fever (Kim and Suh, 2003). Over conditioned cows at calving are up to four times more likely to develop milk fever. The main reasons could be, firstly dairy cows with higher BCS at calving have a higher calcium output in milk, making them more prone to milk fever. Secondly, over-conditioned dairy cattle have a reduced feed intake relative to thinner cows, in the last week of pre-calving. This reduce intake of calcium and magnesium to the levels of hypocalcaemia. It is important to prevent the dry cows from being too fat. Cows with marked body condition loss in the dry period are also at greater risk of milk fever (Charbonneau et al., 2006). Therefore, it is recommended that the energy intake of cows in mid and late lactation is controlled to ensure an optimum BCS (proposed to be 3.25 to 3.75) (Ostergaard et al., 2003).

4.2.2. Shortening of the Dry Period

The length of the dry period is not a critical predisposing factor for milk fever. Cows with long non-lactating periods are predisposed to becoming excessively fat, since cows do not regulate intake according to their physiological requirements. Besides obesity, a long dry period may result in a more quiescent calcium homeostasis. There is less post parturient drop in blood calcium of cows with a mean dry period of 4 days only as compared to a period of 8 weeks. However, shortening the dry period may cause a significant reduction in milk production in the subsequent lactation (Thilsing-Hansen et al., 2002b).

4.2.3. Reduced Milking in Early Lactation

The principle of reducing milking in early lactation is to decrease the amount of milk drained from the cow, which in turn reduces the concentration of essential minerals loss from the body through milk (Henshaw et al., 2010). Although it is easy to apply an effect of reduced milking in early lactation, it is not an efficient method. Furthermore it is unacceptable method for many dairy farmers to reduce milking in early lactation as it is not economical and results in decreased milk yield (Thilsing-Hansen et al., 2002b).

5. Economical Impacts of Milk Fever

Economically, milk fever is an important disease that can reduce dairy cow’s productive life by 3.4 years. Mostly in untreated cases of milk fever, 60-70% cows will die (McDowel, 2002). Economic losses due to clinical cases of milk fever are substantial and include losses from deaths (around 8% of affected cows), premature culling (around 12% of affected cows), treatment costs as well as costs of additives required for affected cows to regain their production and the decreased milk production in the subsequent lactation (Khan et al., 2015). In addition, each episodes of clinical milk fever increases the risk for other parturient diseases such as retained placenta, ketosis, displaced abomasums and environmental mastitis (Oetzel, 2011).

All production diseases including milk fever at a time are the results of managemental practices, but necessary outcomes of modern dairy industry which are essentially pushed for maximum reproductive and production potential (Oded, 2003). Therefore, management practice and genetic improvements cause an increased susceptibility to a number of metabolic and infectious diseases that can result in huge economical consequences in the dairy industry (Oltenacu and Broom, 2010). Milk fever can cause much economical crisis to the dairy farmer unless essential management practice is implemented. In addition to its direct effect, it leads to several indirect costs. Both milk fever and subclinical hypocalcaemia exacerbate the level of immune suppression experienced by periparturient dairy cattle (Kimura et al., 2006).

Milk fever in dairy production reduces the efficiency with which inputs are converted into out puts and hence result in decreased overall productivity. There are costs directly associated with the disease including the cost of veterinary treatments and the herdsman’s time spent dealing with the affected animals. The indirect cost of the milk fever is due to increased risk to associated health problems (Tadesse and Belete, 2015). The reproductive capability of the animal, a major concern in its economic value in
dairy farming, is frequently related to periparturient events, as undesirable health related events during this period might result in tremendous economic losses to farmers (RCI, 2000).

5.1. Direct Impacts of Milk Fever

Milk fever is a serious problem in many countries, because of the enormous economic consequences of the disease. The most important direct economic losses due to milk fever is losses due to reduction in milk production of affected cows, loss of animals through death and culling and the cost of treatment of the animals. Thus, milk fever management is economically most important, as it results in not only reduction in milk production, but also loss of animals. The timing of occurrence of milk fever is such that it occurs at the most productive period of a lactating dairy cows, which results in an important economic loss to the dairy farmers (Thirunavukkarasu et al., 2010b).

5.1.1. Economic Loss due to Reduced Milk Yield and Treatment Expenditure

A. Expenditure on Treatment of Affected Cows

This included the cost of medicines, veterinarian’s fee, wages on additional labour for taking them to veterinary centers and for looking after them and cost of feed supplements to bring the affected animals back to their original milk yield. The costs are calculated due to milk fever in India (Table 1); and found that, farmers lost in average 13.55 American dollars (converted of Rupees (Rs) 618) for each cow for just the treatment. The expenditure was maximum on medicine, Rs 304 (49.2%), followed by veterinarians’ fee, Rs 206 (33.3%) and Rs 108 (17.5%) for feed supplements given to the affected cows (Thirunavukkarasu et al., 2010b). Milk fever is second only to mastitis in terms of number of veterinary treatments in Sweden (SDA, 2010).

B. Economic Loss due to Reduced Milk Yield

The dairy industry has changed dramatically with a trend in direction of larger herds and higher production per cow, which seems to be associated with a decrease in fertility and increases, susceptibility to production diseases (Lucy, 2001; Stevenson, 2001). Generally, the dairy profitability is directly related to the level of milk production (Erkihun and Lingerih, 2015). Beyond milk yield reduction this condition is a common cause of poor labour (dystocia), stillborn calves and apparent sudden death of calves (Kara et al., 2009). In India, the average milk loss per milk fever affected cow was 36.42 litres during the period of illness; the loss was estimated to be of Rs 346 per affected cow (Thirunavukkarasu et al., 2010b).

The economic loss due to milk fever in Holstein cows is 200 litres per animal, costing 40 pound, for a mild case and 500 litres per animal, costing 100 pound, for a severe case of milk fever (Bar and Ezra, 2005). The average loss due to reduction in milk yield per affected animal is higher for a high producing dairy cow than low yielding cows. Milk fever in Finnish Ayrshire alone caused a milk loss of 1.1 to 2.9 kilogram per day during the first 4 to 6 weeks following parturition (Rajala-Schultz et al., 1999).

5.1.2. Economic Losses due to Culling and Mortality

A. Economic Losses due to Culling

Some of the animals affected by milk fever do not regain their earlier milk yield. Therefore, the decline in productivity of these milk fever affected animals usually calls for the need to cull them, as their rearing become uneconomical. Dairy owners cull older, high producing cows from a herd, because of a history of repeated case of milk fever (Murray et al., 2008). Additionally, the loss of muscle tone in the teat sphincter and the uterus may increase the risk of mastitis, retained fetal membranes, endometritis and uterine prolapse. Cows with milk fever may be at increased risk of infertility compared with their healthy herdmates (Ahmadzadeh et al., 2010). Cows not having milk fever were 2.25 times more likely to conceive than those that had milk fever. Therefore, dairy farmers cull out these cows for their poor performance (Chebel et al., 2004).
B. Economic Losses due to Mortality

Death of animals is one of the direct losses due to milk fever. Usually a loss due to deaths is about one in 20 affected cows. Reduction in the productive lifespan of each affected cows is about three years. In general, the mortality of milk fever affected animals is rare. It may be due to the fact that animals can be successfully treated with calcium injections for milk fever (Thirunavukkarasu et al., 2010b). Milk fever also increases the risk of other production diseases, primarily because it has a detrimental effect on smooth muscle function, which in turn may increases mortality. Around 8 percent of milk fever affected animals died due to severe hypocalcemic complication and delaying treatment, while about 12 percent of dairy cows affected by milk fever are culled (Hutjens, 2003).

Table 1: The estimated economic losses due to various effects of milk fever in India

<table>
<thead>
<tr>
<th>Number of affected cows</th>
<th>516</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss due to treatment (Rs.)</td>
<td>617.67 (57.80)</td>
</tr>
<tr>
<td>Loss due to milk loss (Rs.)</td>
<td>345.99 (32.37)</td>
</tr>
<tr>
<td>Loss due to mortality and culling (Rs.)</td>
<td>105.04 (9.83)</td>
</tr>
<tr>
<td>Total (Rs.)</td>
<td>1068 (100)</td>
</tr>
</tbody>
</table>

Source: Thirunavukkarasu et al., 2010

5.2. Indirect Impacts of Milk Fever

Milk fever is an important metabolic disease that predisposes dairy cows to several health problems which indirectly increases the expenses of dairy farmers through death of cows, culling, treatment and management regimes. The indirect cost of the milk fever is due to increased risk to associated health problems, increased risk of calving problems and the possible risk of fatality (Tadesse and Belete, 2015). Generally, it may lead to reduced feed intake, poor rumen and intestine motility, increased risk for displaced abomasum, reduced fertility, increased susceptibility to infectious diseases and increased risk for early lactation removal from the herd. These conditions are challenging to the dairy industry and may cause poor productivity of dairy herds, hence severe economic consequences (Seifi et al., 2011).

5.2.1. Milk Fever, Dystocia and Uterine Prolapse

Milk fever and subclinical hypocalcaemia reduce the ability of the transition cow to effect smooth and skeletal muscle contraction (Goff, 2004). Loss of uterine muscle tone due to hypocalcemia in cows suffering from milk fever is a major cause of uterine prolapse. Cows with milk fever are developing dystocia six times more than that of normal cows. This is because of a reduced ability of smooth and skeletal muscle contraction causes for cow’s long period in labour, which predisposes to dystocia (Tadesse and Belete, 2015). Therefore milk fever is very important in causing dystocia and uterine prolapsed, that increases additional expenses and losses to the dairy farmer (Whiteford and Sheldon, 2005).

5.2.2. Milk Fever and Fertility

Clinical hypocalcaemia significantly reduces the process of uterine involution and a significantly reduced likelihood of having a corpus luteum (indicative of ovulation since parturition) than normal cows (Mulligan et al., 2006). These results in reduced fertility in dairy cows due to its effect on uterine muscle
function, slower uterine involution and reduced blood flow to the ovaries. There are also indirect effects of milk fever on the fertility of the dairy cow, which is mediated through dystocia, endometritis and retained placenta. As fertility of the cow is the main point in dairy industry, milk fever is an important risk for economical loss to the dairy farmer (Rob and Bryn, 2010).

5.2.3. Milk Fever and Mastitis

Mastitis is the most economically important disease of dairy cattle; accounting for 38% of the total direct costs of the common production diseases. It is an important disease throughout the world and accounts for huge losses in the dairy industry (Sharma et al., 2005). Cows that have suffered from milk fever are eight times more likely to develop mastitis than normal cows. This phenomenon is mainly due to a reduction in smooth muscle function at the teat sphincter and hence an easy routine for infection after milking and an exacerbated suppression of immunity in milk fever cows when compared with normal cows (Goff, 2004).

5.2.4. Milk Fever and GIT Function

There is a reduction in the motility of rumen and abomasum in clinically hypocalcaemic cows. This reduction in ruminal and abomasal motility will likely cause a reduction in feed intake (Whiteford and Sheldon, 2005). This reduced feed intake and decreased rumen motility leads to reduced energy balances that leads to excess fatty acid mobilization which is manifested in the body as increased NEFA. Calcium concentration around calving will result in reduced motility and strength of abomasal contractions and hence abomasal atony and distension of abomasums that may ended in the death of the dairy cows (Goff, 2003).

5.2.5. Milk Fever and Retained Placenta

There is an increased risk for the occurrence of retained placenta following milk fever, with milk fever cows being up to three times more likely to experience retained placenta than normal cows (Houe et al., 2001). Subclinical hypocalcaemic dairy cows usually experiences retained fetal membrane. Retained fatal membrane further may leads the cow to other complications such as endometritis. This reduces the overall fertility and productivity of the cow that put an eligible economic consequence to the dairy farmer (Melendez et al., 2002).

6. The Status of Milk Fever in Ethiopia

Ethiopia has the largest livestock population being the first in Africa and the 10th in the world and holds a large potential for the dairy development due to the country’s large number of livestock population (Tegegne et al., 2000). However, the livestock sector in general and the dairy industry in particular do not provide the expected contribution to the national income due to several factors (IFPRI, 2006). The growth of milk production in Ethiopia has been slow and the annual milk production is estimated to be 1,089,488,251 liters (BoFED, 2007), which does not meet even the domestic demand. Among the major clinically manifested diseases of dairy cows in Ethiopia, milk fever is the one that affect intensive dairy production (Regasa, et al., 2009).

Major health challenges of dairy cattle consists of ketosis, milk fever, metritis, lumpy skin diseases (LSD), bloating, mastitis and uterine prolapsed. The prevalence rate of hypocalcaemia is 17.5% in Hawassa town. Difference may occur due to management and the type of breeds of cow reared (Nigussu and Terefe, 2015; Shiferaw, 2003). The prevalence of milk fever is high on privately owned dairy cows in Gondar town and nearby peasant farmers association. Among 384 cows of two breeds (cows with 50 percent Friesian blood and those with greater than 50 percent Friesian blood); the prevalence of milk fever is 30.2%. There is also a significant relationship between milk fever and parity and breed (Anteneh et al., 2012).
Table 2: Percentage of milk fever in different breeds of cows in Gondar

<table>
<thead>
<tr>
<th>Breeds of cow</th>
<th>No. of cows</th>
<th>No. of positive cows</th>
<th>Percentage of milk fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% Friesians</td>
<td>40</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Greater than 50% Friesian</td>
<td>344</td>
<td>110</td>
<td>31.9</td>
</tr>
<tr>
<td>Total</td>
<td>384</td>
<td>116</td>
<td>30.2</td>
</tr>
</tbody>
</table>

Source: Anteneh et al., 2012

As indicated in the table (Table 2) cows with greater than 50 percent Friesian blood has a higher prevalence of milk fever than those with 50 percent Friesian blood. There is also high prevalence of milk fever in cows with increased milk yield (Table 3). So milk yield appeared to be an important risk factor of milk fever (hypocalcemia) because from a total of 116 cows affected with milk fever in Gonder town and nearby farmer associations 55 (50.92%) are producing 30 liters or more of milk per day (Anteneh et al., 2012).

Table 3: Percentage of milk fever in cows with different milk yield groups in Gondar

<table>
<thead>
<tr>
<th>Milk yield per day (L)</th>
<th>No. of cows</th>
<th>No. of positive cows</th>
<th>Percentage of milk fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 25</td>
<td>142</td>
<td>31</td>
<td>21.83</td>
</tr>
<tr>
<td>25-30</td>
<td>134</td>
<td>30</td>
<td>22.4</td>
</tr>
<tr>
<td>Greater than 30</td>
<td>108</td>
<td>55</td>
<td>50.92</td>
</tr>
<tr>
<td>Total</td>
<td>384</td>
<td>116</td>
<td>30.2</td>
</tr>
</tbody>
</table>

Source: Anteneh et al., 2012

Bovine mastitis, milk fever, LSD and calf disease are among the major dairy diseases affecting dairy cattle production in dairy farms of Mekelle. Dairy farmers are unaware of subclinical mastitis, milk fever and other metabolic diseases. Therefore, milk fever and other metabolic disorders are still diseases that would threaten the growing of dairy industry. Milk fever is the third ranked disease of dairy cows in Mekelle with prevalence rate of 7.69% (Emuru et al., 2015).

In Mekelle, most dairy farms mineral supplement is only focused on common salt feeding. Other important minerals like calcium are not known as feed supplement by the dairy owners. The matters worse is that, colostrum contains twice as much calcium as milk (2g/L versus 1g/L) and there is a tremendous loss of calcium in the birth fluids. Then failure to fulfill the requirements predisposes the cow to milk fever which is expensive to treat in Ethiopia (Emuru et al., 2015).
7. Conclusions and Recommendations

Milk fever is a common metabolic disturbance of dairy cows resulting from hypocalcaemia that occurs in adult high producing dairy cows around calving. It is uncommon before the third parturition and the incidence is highest from the third to sixth parturition. Milk yield, parity and breed of the cows are some of the factors which contribute to the occurrence of milk fever. Economically, it reduces milk yield and fertility that leads to culling of high producing dairy cows from a herd. Therefore, prevention of milk fever is the key to reduce the economic impacts of the diseases. Management practices like nutritional strategies, body condition management and shortening the dry period are critical for the prevention of the disease.

In Ethiopia milk fever is one of the challenges in intensive dairy production. This disease is also an impairing factor in urban, periurban and rural semi-intensive dairy farmers, particularly to those who rears high producing improved dairy breeds. Low understanding of proper dairy management, ration formulation and the occurrence of production diseases accompanied by low access to proper hypocalcemic treatment contribute to the incidence and economic effect of the disease. Although the incidence is not as much of that in exotic or hybrids, milk fever also occur in better producing local breeds which are found almost throughout the country.

Based on the above conclusion the following recommendations are forwarded:

- Policy makers of dairy industry development should give attention to milk fever and other production diseases to encourage the country’s maximum dairy producing potential.
- Education of dairy farmers is very important to aware them about milk fever and proper ration formulations for their dairy cows.
- Commercial dairy farmers should have an integrated herd health program, to control metabolic diseases through optimal feeding and management regimens.
- The government should insure available treatment options, particularly for semi-intensive dairy farmers in urban, periurban and rural areas where there is a low access to treatment.
- Further study should be conducted on the prevalence of milk fever and its economic impact in the dairy industry of Ethiopia.

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9. Conflict of Interest: Authors State No Conflict of Interest

10. List of Abbreviations

1. 25-(OH)2 D3 Dihydroxy vitamin D3
2. BCS Body condition score
3. Ca Calcium
4. DCAD Dietary Cation-Anion Difference
5. g/L gram per Liter
6. GIT Gastrointestinal tract
7. IU International unit
11. References


