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### **Review Article**

# Milk Fever (Parturient Paresis) and Its Economic Impact in Dairy Cattle Production

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### Abstract

Milk fever (parturient paresis) is a metabolic disturbance or production disease of dairy cows that occur just before or soon after calving due to low calcium (Ca<sup>++</sup>) level (hypocalcaemia) in the blood. It is associated with the drain of calcium within the fetus and milk during pregnancy and calving, respectively. It can be clinical or sub-clinical based on clinical signs. High producing dairy cows are the most susceptible to milk fever during the peri-parturient period. Milk yield, parity, age, breed, Body Condition Score (BCS), and diet composition of the cows are the most common factors that contribute for the occurrence, incidence and severity of milk fever. Economically, it reduces milk yield and fertility that leads to culling of high producing dairy cows from a herd. Diagnosis of milk fever is based on history taking, clinical examination and laboratory diagnosis. It is commonly treated with oral calcium solutions and intravenous (IV) calcium borogluconate. Prevention of milk fever is economically important to the dairy producers to minimize production losses, death losses and veterinary costs associated with the disease. Multiple strategies have been utilized to prevent hypocalcaemia including feeding anionic salts, low calcium ion diets, vitamin D supplementation, dietary magnesium supplementation, and managing the body condition score of cows during the peri-partum period. Hence, prevention of milk fever is the key to reduce the economic impacts of the diseases in dairy industry.

### **INTRODUCTION**

Milk fever is one of the most common mineral-related metabolic diseases of dairy cows that occur just before or soon after calving as a result of low calcium level (Ca<sup>++)</sup> in the blood [1]. It is one of the metabolic diseases occurring most commonly in adult cows within 48 hours after parturition, but it may occur several weeks before or after parturition. On the day of parturition, dairy cows commonly produce 10 liters or more of colostrum containing 23g or more of calcium, approximately 6 fold as much calcium as the extracellular calcium pool contains [2].

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 [3]. 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 [4].

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#### **Keywords**

- Milk fever
- Parturient paresis
- Hypocalcaemia
- Dairy cows
- Peri-parturient period
- Economic impact

Milk fever can be clinical or sub-clinical based on whether an animal may or may not show clinical signs [5]. The clinical signs 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 [6]. 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 [7]. 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 [8,9].

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 [10]. 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 [2].

The key to prevention of milk fever is management of a close up dry cow or management during late pregnancy [11]. Multiple strategies must be designed for the management of hypocalcemia

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and to enhance calcium mobilization in dairy cows particularly in peri-parturient period [12]. 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 [10]. There are many research works on the incidence of milk fever, preventive strategies and risk factors of milk fever. However, there is no compile information on milk fever and its economics importance. Therefore, the objectives of this seminar paper on milk fever and its economic impacts in the dairy industry.

### **GENERAL FEATURES OF MILK FEVER**

Milk fever is a non-febrile disease of adult dairy cows caused by an acute calcium deficiency [8]. Low level of blood calcium can lead inability of a cow to rise feet up the ground as calcium is vital for muscles and nerves function, that results into a metabolic disorder termed as milk fever. 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 [11]. It generally affects high producing exotic breeds in their productive stage and older dairy cows which have reduced ability to mobilize calcium from their bone [13].

Milk fever is considered as a gateway diseases that greatly reduce the chance for full productivity in the ensuing lactation. A mild degree of milk fever develops in the majority of cows during the peri partum period and has been linked to calving problems, retained placenta, uterine prolapse, metritis, mastitis, ruminal stasis, depression of the immune system and generally reduced reproductive performance and resulting in reduction of productive life by 3-4 years [9]. In a small proportion of animals, hypocalcaemia becomes severe and results in paresis, recumbency and, occasionally, death [1].

### **ETIOLOGY**

Milk fever is caused by a severe deficiency of metabolisable calcium ion (Ca<sup>++</sup>) in the circulation [8]. During onset of lactation milk fever might be develop since calcium is one of the most abundant minerals in cow's milk and the concentration of calcium in the colostrum is almost double than in milk later lactation of the cow [3]. Calcium in milk often constitutes the major part of the absorbed calcium. A cow producing 10 liters of colostrum loses about 23g of Ca in a single milking [14]. 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 hypocalcaemia [4].

Hypocalcaemia occurs as the dairy animal's complex mechanisms for maintaining calcium homeostasis fail during a sudden and severe calcium outflow [8]. Calcium homeostasis can be affected by three major factors. (1) Excessive loss of calcium in the colostrum beyond the capacity of absorption from the intestines and mobilization from the bones to replace it. (2) Impairment of absorption of calcium from the intestine at parturition and (3) Insufficient mobilization of calcium from storage in skeleton, which could arise because of parathyroid insufficiency since the gland is relatively quiescent in dry period [15] (Figure 1).

### **CLINICAL SIGNS**

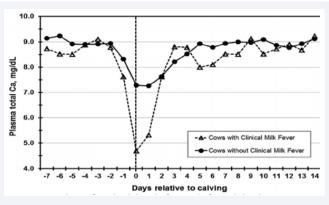
Hypocalcaemia can be clinical or subclinical based on whether an animal may or may not show clinical signs [5]. Clinical milk fever is the most severe hypocalcaemia results in cow's inability to stand after calving [9] and is the most easily recognized form of hypocalcaemia with blood calcium concentration less than 5 mg/dL [6]. 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 [17].

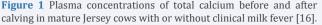
The symptoms include, initially the animal is ataxic, nervous and hyperactive. There is poor appetite, reduced rumen motility, low body temperature, slow respiration, impalpable pulse, weak but rapid heartbeats (80-100 per minutes) with very hard to hear due to reduced ability of muscles to contract, dilated pupils and dry muzzle are a common signs [6]. 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 [8].

Based on the degree of hypocalcaemia and time of occurrence, the clinical signs of milk fever divided into three stages. Stage I is characterized by mild excitement and tetany without recumbency. This phase often goes unobserved because its signs are subtle and of short duration (often less than 1 hour) [17]. Affected cattle may appear excitable, nervous, anorexia, weakness, weight shifting and shuffling of hind leg. Cows in stage II milk fever are in sternal recumbency. They exhibit moderate to severe depression, cold extremities, mild bloat, and partial paralysis and typically lie with their head turned into their flank [8]. Body temperature is subnormal, muzzle dry and the heart rate will be rapid [18]. Stage III hypocalcemic cows are completely paralyzed, typically bloated, in lateral recumbency and progressively loss consciousness that leading to coma. There is a marked fall in temperature and increased heart rate. Cows will not survive more if not treated [7,8].

### DIAGNOSIS

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 [9]. 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 [19]. 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 [20] (Figure 2).

### **TREATMENT**

Treatment of milk fever should be done as early as possible. Commonly milk fever is treated with oral calcium solutions and intravenous (IV) calcium borogluconate [6]. 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 [8]. Bhanugopan and Lievaart [9] also reported the most commonly treatment of milk fever is a calcium/magnesium drip delivered subcutaneously.

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 [22]. Extremely high dose of calcium may cause fatal cardiac complications [23]. Subcutaneous calcium administration can also be used to support blood calcium concentrations around calving [6].

### **EPIDEMIOLOGY**

Milk fever is one of the common production diseases of dairy cows throughout the world. It 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 [17]. The prevalence of milk fever was significantly associated with milk yield, parity and breed [24].

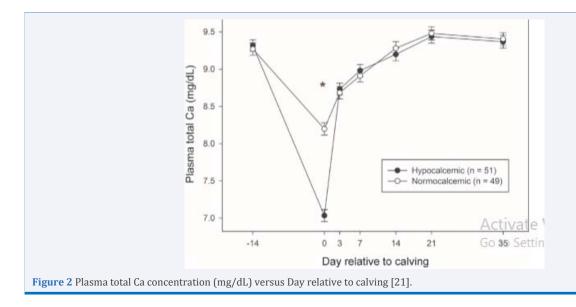
### **RISK FACTORS**

Factors that contribute to occurrence of milk fever and which influence the incidence and severity includes age, stage of lactation and parity, body condition and diet composition, breed and length of dry period [25]. In general, the risk factors for milk fever could be grouped into intrinsic risk factors, which are associated within the animal itself and extrinsic risk factors.

### Intrinsic risk factors for hypocalcaemia

Number of parity and milk yield: Increased prevalence rate of milk fever is associated with increased number of calving (parity) and milk yield [2,24]. Bernard et al. (2017) [26] showed that the incidence of milk fever in jersey cows and Holstein with more than four parities was significantly higher than those in their second, third and fourth parities. Neves et al. (2017) [27] also reported animals in their third or greater parities were 70% more likely to be affected by sub clinical hypo calcaemia than second-lactation animals. Second-lactation animals, as compared with older parities, are able to better maintain Ca<sup>++</sup> turnover rates in the immediate postpartum period. Venjakob et al. [28] showed none of the cows in first lactation was suffering from clinical milk fever. Prevalence of clinical milk fever was 1.4%, 5.7%, and 16.1% for  $2^{nd}$ ,  $3^{rd}$ , and  $\geq$  4th parity cows, respectively. Different researchers suggested that this is because of the reduced ability to mobilize calcium from bones, a decline in intestinal transport of calcium and the reduced ability to produce calcitriol in older cow [28].

According to Bernard et al. [26] report Jersey and Holstein cows producing more than 6114 L and 9149 L per 305-day lactation had significantly higher incidence of milk fever than those producing less than 6114 and 9149 liters per 305-day lactation, respectively. Aberaw [2] showed the prevalence of milk fever is higher in cows producing more than 25 liters of milk per day. Obviously, milk yield in dairy cows, from third lactation onwards, start to increase, which lead to high calcium demand for milk production. This may due to higher loss of calcium through milk.



**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. Moreover, increased age is known to impair Ca metabolism; for instance, bone and intestine vitamin D receptors decline with aging [27]. Thus hypocalcaemia is age related and most marked in cows from third to seventh parturition [29]. Reinhardt et al. [4] also reports subclinical hypocalcaemia in postpartum cows increased with age and was present in 25% of first lactation cows and 41-54% of second or greater lactation cows.

**Breed of the cow:** Certain breeds of dairy cows have shown more susceptibility to milk fever than other breeds. Specifically the incidence increases in high producing dairy cows such as Jerseys and Guernseys, are the most susceptible than Holstein and Brown Swiss breed. This might be due to higher milk production per unit of body weight in the most susceptible breeds. In general cross breed or temperate breeds are more susceptible to milk fever than tropical zebu breeds [9]. This could be attributed to their high milk yield and low ability to maintain their calcium homeostasis of cross breed and temperate breed. In addition, the other important reason of higher susceptibility to milk fever is lower number of intestinal receptors for 1,25-Dihydroxy vitamin D3 (1,25(OH) D3), which responsible intestinal calcium absorption and bone calcium resorption [30].

**Body condition score (BCS):** Excessive BCS prior to calving has been recognized as a risk factor for the development of metabolic problems. The occurrence of milk fever also increases in cows with higher BCS, possibly due to decreased calcium intake [31]. Contreras et al. [32] reported cows with BCS at dry-off  $\leq$  3.00 had a lower incidence of milk fever than those  $\geq$  3.25. Roche and Berry [33] also found that cows with a BCS above 2.5 at calving had an increased risk of milk fever.

On the other hand, Chapinal et al. [34] found no relationship between dry BCS  $\geq$  3.75 and milk fever outcome. The development of milk fever in over-conditioned cows may be due to the decrease in DMI, at the same time decreasing calcium intake consequently results hypocalcaemia at calving.

### **Extrinsic risk factors**

**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 suppressed. Cows in this condition are not able to quickly replace plasma calcium lost in milk and become severely hypocalcaemic [35]. 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 [9].

## PREVENTION AND CONTROL STRATEGIES OF MILK FEVER

The occurrence of milk fever or subclinical hypocalcaemia is related to increased incidence rates of several other transition cow disorders. As a result, 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. Multiple strategies have been utilized to prevent hypocalcaemia and mobilize calcium in dairy cows through nutritional management including feeding anionic salts, low calcium ion diets and vitamin D supplementation [12].

### Feeding of low-calcium diets

Feeding with low calcium diets during dry period is one of milk fever prevention strategy (Jesse et al., 2018)33. This was achieved through feeding the cows with less than 50g per day. Therefore, to do so, high calcium forages such as alfalfa, have to be eliminated from animal's diet. Forages such as corn silage and grass hay have to be routinely used in dry from to reduce calcium composition within it [25]. Bhanugopan and Lievaart [9] reported feeding hay, straw and grain during the dry period was a general nutrition strategy used by all the farmers. Feeding grain reduces the risk of MF because it helps the rumen adapt to the high-energy feeds given post-calving and grain is also low in calcium.

### **Dietary cation-anion balancing (DCAB)**

Dietary cation-anion balancing is a nutritional tool for reducing milk fever in early lactation as well as improving health and production of the cow [37]. It is a common prevention strategy by supplementing anionic salts to reduce diet cationanion difference and was implemented in the dairy industry [38]. 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 [6].

It is very difficult to control hypocalcaemia if total ration of K is >1.8%. Since high potassium diets usually induce milk fever, pre-calving potassium levels should be kept as low as possible. As dry fodder contains more potassium, feeding of dairy animals with higher amount of dry fodder should be discouraged to prevent milk fever. Inclusion of silage and succulent / green fodder as a major portion of the dry cow's diet is essential, as it has lower potassium content [10].

### Oral calcium drenching during calving

Oral calcium supplementation is one of the prevention of milk fever around calving [9]. According to Amanlou et al. [39] results, cows given 2 infusions of subcutaneous Ca within the first 18 hrs postpartum were less likely to develop metritis and clinical and subclinical endometritis and hypocalcaemia than non-treated control cows.

### 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 [36]. Milk fever is usually accompanied by an increased concentration of plasma magnesium level to stimulate calcium homeostatic mechanisms, which is essential for restoring the normal blood calcium level [40].

### Peripartum dietary Zeolite A supplementation

Zeolitesarecrystalsformedfromamicroporousaluminosilicate skeleton of alkali and alkaline earth cations [41]. Including

Zeolite in the rations of dry dairy cows to activate the calcium homeostatic mechanisms before calving avoid postpartum hypocalcaemia [42]. Zeolite supplementation significantly increase the plasma Ca level before and after calving and thus it alleviate the negative Ca<sup>++</sup> balance during per parturient period [43]. Feeding a daily dose of about 0.5-1.0 kg zeolite A creates functional calcium deficiency and substantially reduces the risk for milk fever [8].

### Vitamin D supplementation

A practice by some farms is supplementing high amounts of vitamin D to prepartum dry cows either in the feed. Supplementation requires that up to 10 million IU of vitamin D must be injected or fed daily for 10-14 days before calving. These vitamin D doses pharmacologically increased intestinal  $Ca^{++}$  absorption [9].

### **Body condition score management**

Achieving the correct BCS at calving and dry period is critical for the prevention of milk fever [44]. 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 [45].

### **ECONOMIC IMPACTS OF MILK FEVER**

Milk fever is one of the production diseases which affect the production and productivities of cows. It has both direct and indirect impact as follows:

### **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 [10].

**Expenditure on Treatment of Affected Cows:** This included the cost of medicines, veterinarian's fee, wages on additional labor 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 [10].

**Economic Loss due to Reduced Milk Yield:** The average milk loss per affected cow was 36.42 liters during the period of illness. In monetary terms, the loss was estimated to be of Rs 346 per affected cow [10]. Another study conducted by Renan et al. showed that cows with metabolic diseases produced less milk than healthy cows. Lower milk yield was also observed by Zhang et al., [46].

Economic Losses due to Mortality and Culling of Milk Fever-affected Animals: 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 [10].

Some of the animals affected by milk fever do not regain their earlier milk yield. Therefore, the decline i+-n productivity of these milk fever affected animals usually calls for the need to cull them, as their rearing become uneconomical. The total loss due to mortality and culling of cows and calves was observed to be of Rs 54,200 and Rs 6,600 due to milk fever during the study period [10].

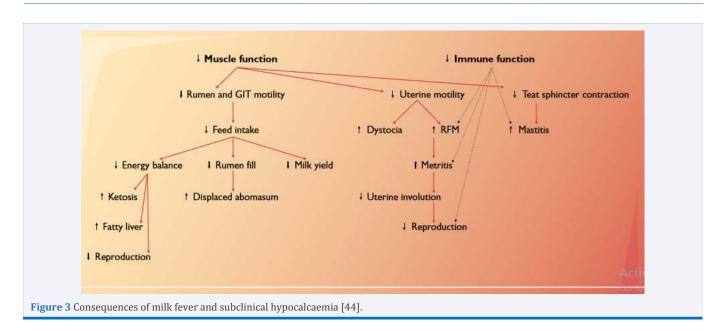
### **Indirect Impacts of Milk Fever**

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 regimens. 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 [18].

Milk Fever, Dystocia, Uterine Prolapse and Retained placenta: Milk fever and subclinical hypocalcaemia reduce the ability of the transition cow to effect smooth and skeletal muscle contraction [47]. Loss of uterine muscle tone due to hypocalcaemia 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 labor, which predisposes to dystocia [18]. Martinez et al. [48] reported that cows with subclinical hypocalcaemia were at greater risk of developing dystocia and uterine Prolapse. The same author reported that cows with subclinical hypocalcaemia were at greater risk of developing retained placenta defined as a placenta that was not expelled within 12 hrs after parturition. Melendez et al. [22] reported a significantly lower plasma Ca<sup>++</sup> concentration in cows with retained fetal membranes in comparison to cows with normal placental expulsion. Gild et al. [49] also reported subclinical hypocalcaemic cows suffered from retained placenta.

**Milk Fever and Mastitis:** 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 [48]. Aleri et al. [50] showed that reduction in the calcium concentration contributes to an increased incidence of mastitis.

**Milk Fever and Fertility:** Milk fever is a metabolic disease which can cause negative effects on the reproductive performance of dairy cows, which can increase the number of services per conception and reduce conception rate [51]. Postpartum cows that develop hypocalcaemia had leukocytes with a compromised ability to respond to stimuli which in turn leads to ovarian dysfunction (e.g., low plasma estradiol, prolonged luteal phase, and cysts and the subsequent reduced animal fertility [52].



The size and diameter of uterine horns and endometrial thickness have greater in cows with hypocalcaemia than healthy cows which can cause a greater delay in uterine involution and a significantly reduced likelihood of having a corpus luteum (indicative of ovulation). 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 [17]. 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 [53].

**Milk Fever and GIT Function:** Cows with hypocalcaemia exhibit reduced muscle contraction, which results in reduced motility of the digestive organs including the abomasum and rumen [51]. This reduction in ruminal and abomasal motility will likely cause a reduction in feed intake [54]. 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 abomasalatony and distension of abomasums that may ended in the death of the dairy cows [47] (Figure 3).

### **CONCLUSION**

Milk fever is a common metabolic disturbance of dairy cows resulting from hypocalcaemia that occurs in adult high producing dairy cows during calving. Factors that contribute to the occurrence and which influence the incidence and severity of milk fever are: age of the cow, stage of lactation and parity, body condition score, diet composition, and breeds. Milk fever has both direct and indirect economic impacts in dairy industry. The most important direct economic losses due to milk fever are 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. On the other hand, increased incidence of infertility, dystocia, retained placenta, metritis, mastitis and displacement of abomasum are the indirect impacts. Therefore, prevention of milk fever is the key to reduce the economic impacts of the diseases. Management practices like nutritional strategies and body condition management are critical for the prevention of the disease. Based on the above conclusion, the following recommendations are forwarded: training of dairy farmers is very important to aware those about milk fever and proper ration formulations for their dairy cows. The owners of dairy farms should be reduce the energy source of feed especially concentrate to avoid over conditioning of the cow around calving. Awareness should be created for farmers to observe their dairy cattle from 48-72 hrs before and after parturition for evidence of milk fever. Further study should be conducted on the epidemiology and economic impacts of milk fever in dairy industry.

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