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Review article

Comprehensive review on prevalence of caseous lymphadenitis (CLA) in dairy goats: A systematic review and meta-analysis

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Abstract

Caseous lymphadenitis (CLA) presents a significant challenge to the dairy goat industry worldwide, negatively affecting animal health, productivity, and economic sustainability. It is a disease caused by *Corynebacterium pseudotuberculosis,* and its symptoms include the development of abscesses in lymph nodes and other organs. Generally, animals affected by CLA experience reduced milk output, reproductive problems, and higher morbidity and death rates. Furthermore, CLA could harm the well-being of animals by causing pain, discomfort, and disruption of normal behaviours. This review aims to determine the prevalence of CLA cases affecting dairy goats, map the geographical distribution of the disease in dairy goat herds throughout different locations, determine hotspots of CLA incidence and comprehend regional differences. Additionally, the study included relevant information on CLA prevalence in Asia. This comprehensive review is expected to help develop educational strategies for CLA prevention and control among dairy goat farmers. Moreover, an assessment of the economic impact of CLA in dairy goat operations on a global scale was performed. The losses associated with CLA are reduced milk production, lower meat yield, and increased veterinary costs. Besides, the variability of clinical presentation and the limits of conventional diagnostic methods make diagnosing CLA in dairy goats difficult. However, new developments in diagnostics, such as serological testing and polymerase chain reaction (PCR) assays, present chances for early detection and targeted control strategies. Examples of management strategies for CLA in dairy goat herds include vaccination, strict biosecurity protocols, and targeted treatment of infected animals. To surmise, the dairy goat industry can strive to mitigate the effects of CLA and maintain the well-being of dairy goat populations by tackling these challenges and executing comprehensive management strategies.

Keywords: Caseous lymphadenitis, Dairy Goat, Milk

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INTRODUCTION

Dairy goats, regularly referred to as the "cow of the poor," have long been recognised for their ability to supply milk and dairy products in many environments. These adaptable animals are often irreplaceable by other livestock and have been necessary to agricultural practices all over the globe. In particular, their widespread usefulness is especially evident in regions where resources are restricted and in various climactic conditions (Nayik et al., 2022). Today, the number of goats is approaching one billion worldwide and is still rising (Miller and Lu, 2019). This rapid increment can be attributed to the goats that are raised mainly for milk production. Additionally, when appropriately managed, goats can help the environment by preventing fires, controlling weeds, preserving biodiversity, and minimising some of the effects of climate change (Rosa et al., 2012). This is largely due to their eating habits and dietary preferences (Miller and Lu, 2019). In addition to milk, dairy goats also provide other benefits, including skin, meat, and manure, which are used as fertiliser. (Miller and Lu, 2019).

Nowadays, goat milk is increasingly valued for its high nutritional content and easy digestion. Previous studies have shown that those with dairy sensitivity or lactose intolerance frequently tolerate goat milk better than cow milk (Haenlein, 2004). Goat milk is also an important source of nourishment in many cultures since it is high in vitamins, calcium, and other essential nutrients (Navamniraj et al., 2023). Moreover, research shows that goat milk proteins are less allergenic than cow milk proteins, making it a suitable alternative for people who are sensitive to cow's milk (Lopez et al., 2003). As demand for functional proteins in the food sector rises in several areas, improving the methods for producing and separating milk proteins with certain functions becomes more critical (El-Agamy, 2007).

The concept of quality has evolved significantly in recent years (Ribeiro and Ribeiro, 2010). Goat milk, which contains significant amounts of calcium and phosphate essential for humans, is receiving much attention. About 1.2 g of calcium and 1 g of phosphate per litre can be found in goat milk, and these amounts are comparable to those found in cow milk (Jenness, 1980). In contrast, human milk has much lower concentrations, with only about one-fourth as much calcium and one-sixth as much phosphate. Besides, goat milk provides human infants with a significant surplus of calcium and phosphorus relative to their energy needs, and they can readily absorb both minerals from the milk (Turck, 2013). Its high buffering capacity also appears to be helpful in treating stomach ulcers (Lutchman, 2024). In general, goat milk is tolerated by 40–100% of individuals who are allergic to cow milk proteins (Park, 1994).

Caseous lymphadenitis (CLA) is a zoonosis, chronic, and subclinical disease that is highly prevalent in flocks and animals, such as sheep and goats. In general, CLA is caused by *Corynebacterium pseudotuberculosis* (*C. pseudotuberculosis*). Nonetheless, the pathogen can also infect cattle, horses, and, on rare occasions, humans. Hence, for this reason, CLA is classified as an occupational zoonosis (Dorella et al., 2006). To date, *C. pseudotuberculosis* has been discovered and isolated from laboratory animals, llamas, camels, deer, porcupines, and pigs (Williamson, 2001). CLA is a widespread disease that has impacted many livestock in Europe, Asia, Africa, North and South America, Australia, and New Zealand. When there is a CLA outbreak, the incident often results in significant economic losses, especially for farmers, due to the stigma attached to abscesses, the condemnation of skins and carcasses, and reductions in reproductive efficiency, as well as in the production of wool, meat, and milk (Arsenault et al., 2003).

The clinical signs of this disease include abscessing in both superficial and visceral lymph nodes. Commonly, the superficial type causes swelling and abscessing of the peripheral lymph nodes, while the visceral form can cause systemic problems that weaken the surrounding tissue. *C. pseudotuberculosis* can spread rapidly throughout the herd if the surrounding environment has been compromised (De Sá Guimarães et al., 2011). A herd or flock may have an endemic disease that is challenging to treat due to poor response to medications, environmental persistence, and difficulty in identifying subclinical infections. This disease has a major negative economic impact on the small ruminant sector, as it can lead to reduced meat production, damaged wool and leather, poor reproductive success, internal environment death, and culling of affected animals (Williamson, 2001).

The objective of this comprehensive review was to summarise the current state of research on CLA in dairy Goats, identify knowledge gaps, assess the existing body of studies, and offer suggestions for future research. A thorough review of the literature was conducted using electronic databases, such as PubMed, Google Scholar, Scopus, and Web of Science, using search terms like 'CLA,' 'Milk,' and 'Dairy Goat'. The criteria used to select relevant studies and sources were peer-reviewed articles published between 1970 and 2024 in English. However, since only peer-reviewed publications were included in this study, it may introduce a possible bias. Furthermore, as only research published in English was examined, language biases can occur. Lastly, ethical approval was not necessary, as this study did not involve human subjects or sensitive data.

OVERVIEW OF CLA

CLA is a contagious bacterial disease caused by the bacterium *C. pseudotuberculosis*. In 1888, Nocard, a French microbiologist, first identified *C. pseudotuberculosis* as a microorganism that resembles *C. pseudotuberculosis* in a case of ulcerative lymphangitis in cattle (Pépin and Paton, 1999). The disease is characterised by abscess formation in the lymph nodes, lungs, and other visceral organs (Fontaine and Baird, 2008). *C. pseudotuberculosis* is a Gram-positive rod-shaped, intracellular, facultative aerobic bacterium with worldwide distribution (Almeida et al., 2016).

Globally, CLA occurs in herds of sheep and goats, with the most probable cause for its spread being the importation of infected animals (Baird and Fontaine, 2007). The disease can be transmitted when the animals are in direct or indirect contact with pus-containing *C. pseudotuberculosis* (Nairn and Robertson, 1974). Infected animals can contaminate the land, water, feed, pastures, and facilities with their faeces, nasal secretions, and pus from spontaneously draining abscesses. Even animals that do not show any clinical signs can spread the bacteria through their respiratory system (De Sá Guimarães et al., 2011). In 2008, after assessing the coefficients of transmission of *C. pseudotuberculosis* via respiratory tract infection and pus from spontaneously draining abscesses, O'Reilly et al. found that lung abscesses have a more significant role in keeping the infection active in the herd (endemic phase) (O'Reilly et al., 2008).

Generally, CLA is a bacterial disease characterised by the development of abscesses in the skin, internal organs, and both exterior and internal lymph nodes (Williamson, 2001). When a disease shows only a few distinct clinical symptoms, a post-mortem study is often required to make the diagnosis; this makes it challenging to gather information regarding the incidence of diseases (Brown et al., 1985). It has been reported that the location of abscess formation varies between sheep and goats, with the visceral form occurring more frequently in sheep and the superficial form in goats (de la Fuente et al., 2017). External abscesses in the head and neck lymph nodes are more common in goats. Meanwhile, the subiliac and pre-scapular lymph nodes are more frequently affected by CLA infections in sheep (De Sá Guimarães et al., 2011). *C. pseudotuberculosis* can survive for a long period in the soil. However, when placed in an environment such as soil and goat facilities with different temperatures and experimental contamination, the bacterium can only survive up to eight months (Williamson, 2001). In addition, it can persist for three weeks in bedding straw, two months in hay, four months in shearing stalls, and more than eight months in the ground. The bacterium has also been found in areas with pus contamination even after a five-month period (Thongkwow et al., 2019).

CLA ON SMALL RUMINANTS

C. pseudotuberculosis can be found in a variety of mammalian species. However, small ruminants raised on farms are most susceptible to this bacterial infection since they tend to develop chronic CLA (Windsor, 2011). Most studies that investigated prevalence rates, farming techniques, and slaughterhouses related to CLA are generally focused on Australian wool sheep. Surveys conducted in 1995 revealed that cheesy glands were incredibly common and could be found affecting approximately 91% of farms in Victoria, 88% of farms in Western Australia, and 97% of farms in New South Wales (Walker, 1996). After a CLA vaccination was introduced in 1983, the average occurrence of the diseases in adult sheep populations was significantly reduced. For instance, in Western Australia, the incidence of CLA dropped from 58% in 1973 to 53% in 1984. Animals with CLA often have swollen lymph nodes that measure between 5 cm and 15 cm in diameter. In Australia, the prefemoral, pre-scapular, mediastinal, and bronchial nodes are the ones that are primarily impacted (Windsor, 2011). In North America, external abscesses are most commonly found in the parotid and submandibular areas of the head (Menzies and Muckle, 1989). This virus can spread in confinement houses through contaminated feeders. Furthermore, the contagious bacterium can live in sheep dips for at least 2 hours and up to several weeks in faeces and fomites (dips contaminated by open skin or bronchial abscesses are a potential source of infection). CLA in sheep is a widespread and economically significant disease in most sheep-farming nations, caused by *Corynebacterium pseudotuberculosis* biovar ovis (Ruiz et al., 2020). It has a negative impact on wool production, meat, and milk, as well as the condemnation of carcasses, skins and the animal's reproductive abilities (Williamson, 2001).

DAIRY GOATS FARMING

Today, the most common breeds of goats used in milk farming include Saanen, Jamnapari, and Toggenburg (Devendra and Haenlein, 2016). The Saanen breed is internationally acknowledged as the most advanced breed and is known for its highest milk production rate (Hedrich, 2008). This type of goat has upright ears and is entirely white or light cream in colour. As the human population grows, the demand for food, particularly animal-derived products, has increased (Leroy et al., 2022). As a result, there are now more goat farms to cater for the demand for goat goods like milk and meat (Derks et al., 2013). The increase in the market demand for goat milk over the past 20 years has led to the establishment of commercial dairy goat farms in several Southeast Asian countries (Liang and Paengkoum, 2019). The secondary dairy species are essential for fulfilling the dietary and nutritional demands of the general population in developing and underdeveloped nations. Milk from smaller animals, such as goats, buffaloes, sheep, and camels, are essential daily dietary sources of protein, phosphate, and calcium, especially as cow milk is scarce and meat intake is minimal. Additionally, the milk of certain species, such as goat milk, has been suggested as a diet alternative for those with cow milk allergy due to their significant innate hypoallergenic qualities (Qausar et al., 2023)

For the past 20 years, the high market demand for goat milk has led to the growth of the commercial dairy goat industry in numerous Southeast Asian nations (Liang and Paengkoum, 2019). However, according to Devendra and Liang (2012), most goats in Asia, particularly dairy goats, are owned by small-scale farmers who often lack land and resources. Despite their significance in providing nourishment, food security, and socioeconomic status, goats raised in Asia's challenging conditions are frequently overlooked in national development strategies. Nevertheless, with the rising demand that is fuelled by the belief in goat milk's medicinal potential, some East and Southeast Asian countries, including China, Japan, Malaysia, Indonesia, Thailand, and Vietnam, now have a greater demand for goat milk compared to cow milk (Liang and Paengkoum, 2019). As a consequence, these countries are seeing an increase in the number of sizable and moderately sized dairy goat farms to meet the growing demand. Unfortunately, many of these farms experience challenges in terms of their sustainability and success rates (Liang and Paengkoum, 2019). In 2017, an estimated 217.7 million dairy goats existed worldwide, accounting for 21% of the global goat population. The majority of these goats were located in Asia (52%) and Africa (39%), while the rest were distributed across Europe, the Americas, and Oceania. India is the world's biggest producer of goat milk, with over six million tonnes produced as of recently. Today, the worldwide goat milk output has reached 18.66 million tonnes, with other major producers, including Bangladesh, Sudan, Pakistan, France, Greece, Turkey, and Spain (Sepe and Argüello, 2019). Nonetheless, a significant number of these farms experience challenges in terms of their sustainability and success rates (Liang and Paengkoum, 2019). Production methods, feeding systems, breeding programs (seasonal or year-round), research and development initiatives, and the breed are the main factors that affect the quantity and quality of milk produced by goats

The inclusion of goat milk in human diets increased its value, yet this situation ironically led to a steady decrease in its global economic significance and impact. Goat milk has superior digestibility, a wider alkalinity range, and a stronger buffering capacity compared to cow's milk. Additionally, it is known for its reliable therapeutic benefits when included in the human diet (Sepe and Argüello, 2019). Goat milk is easier to digest than cow milk because it contains smaller fat globules, unique protein polymorphisms, higher levels of as^2 casein and lower levels of as^1 casein. It also shows better digestion when acidified, compared to cow milk. Moreover, goat milk contains short- and medium-chain fatty acids that give it a unique capacity to supply energy, which is particularly essential for developing youngsters (Gallier et al., 2020). Currently, less than 1.6% of the world's dairy production is made from goat milk (Liang and Paengkoum, 2019).

OUTBREAK CASES OF CLA

The overall population of Australian sheep has decreased recently, but as of mid-2011, there were an estimated 74.7 million sheep across 43,760 estates. Based on the records, CLA likely arrived with the first sheep brought to Australia over 200 years ago. Between 1991 and 1992, the projected losses caused by CLA were estimated at AU$ 30–40 million annually. This high cost was due to the expenses required for carcass condemnations to prevent unsightly lesions in retail sheep-meat products, especially for live sheep or products intended for export (Windsor, 2014). Although CLA has become less important for Australian sheep farmers, with only a few documented clinical cases, studies conducted in 1995 revealed that the disease remains prevalent and has affected about 97% of farms in New South Wales, 91% in Victoria, and 88% in Western Australia. Despite this, the estimated prevalence of CLA in adult sheep populations has been steadily decreasing, with estimates at 26% (Pépin and Paton, 1999; Windsor, 2011).

Several environmental variables influence the occurrence of diseases in small ruminants, such as inadequate hygiene and herd size, the layout of the habitat, and skin injuries. Currently, one of the biggest challenges that farmers and producers face is to manage the long-term CLA-infected regions (Burmayan and Brundage, 2021). Another CLA outbreak occurred in August 2019 at the sheep unit of California State Polytechnic University, Pomona. A veterinarian at Los Angeles

County noticed an abscess on a goat's closed mandibular lymph nodes while using the university's animals at the petting farm and reported the findings to the university. For two weeks, the suspected goat was kept isolated for diagnostic purposes (Burmayan and Brundage, 2021).

In Australia, CLA prevalence has increased to as high as 61% (Middleton et al., 1991). Similarly, in the USA, the prevalence has been estimated to reach 43% (Windsor, 2014). Using two combination diagnostic tests (AGPT and Elisa), a survey of CLA on small ruminant farms in Malaysia revealed an average disease prevalence of about 30% (Pacheco et al., 2007). Swab samples were collected from the abscessed areas and cultured on blood agar for 48 hours at 37°C. PCR results from the cultured samples identified the growth as *C. pseudotuberculosis*, which is consistent with previous findings (Çetinkaya et al., 2002). Suspected cases of lymph node abscesses were contained in an isolation pen with a 25-foot buffer on either side to prevent the infection from spreading. CLA was first recorded in South Africa by Jowett in 1909. A prevalence of 2.4% of CLA was observed in Merino sheep under one year old and 7.4% in older sheep from the Karoo. CLA outbreaks appeared to be more frequent in the drier parts of South Africa, such as the Karoo, Eastern Cape, and Free State provinces (Zavoshti et al., 2011). Furthermore, in the case of superficial abscesses, which are known to assist in the spread of the disease, often go untreated as most farmers and animal owners do not seek veterinary assistance due to their ignorance (Osman, 2012). In other countries, CLA prevalence has been reported to range from about 8% to as high as 90% (Çetinkaya et al., 2002).

The disease has also been reported in Malaysia, specifically in two Perak districts: Kinta and Hilir Perak. Small ruminant farms in these areas were the focus of bacterial infection studies in sheep and goats. A total of 8 farms with an overall population of 579 animals were examined. Animal serum samples were analysed using the Agar Gel Precipitation Test (AGPT) and the Enzyme-Linked Immunosorbent Assay (ELISA). The AGPT test yielded positive results in 8.5% of the animals. 36 samples (17%) were found to be positive when both the AGPT and the ELISA techniques were used; 9 samples (4%) were found to be positive only when the AGPT method was used; 14 samples (6%) were found to be positive only when the ELISA method was used; and 157 samples (73%) were found to be negative when both methods were used (Komala et al., 2008; Abdullah, 2017). There are very few reports of CLA in humans, and when it happens, it is usually caused by the consumption of raw meat or milk from infected animals or through direct exposure to infected animals (Peel et al., 1997). The primary methods used to diagnose CLA include the isolation of the pathogenic bacterium from the abscess, observation of distinctive clinical signs, and serological testing such as the immunodiffusion test, hemolysis inhibition test, complement fixation test, and ELISA (Çetinkaya et al., 2002; Abdullah, 2017). The rapid spread of the organism, once introduced, makes disease control and prevention challenging. However, a range of immunisations has recently been developed to eliminate CLA (Roslindawani et al., 2016) and has shown promising results. This case study describes the treatment of recurring CLA cases on a Malaysian goat farm. Figure 1 illustrates the progression of CLA within a flock, beginning with the introduction of a latently infected animal. The figure demonstrates how the disease spreads over time, leading to successive outbreaks within the population. Key stages in the progression include the silent introduction of the infection, the development of clinical cases, and the eventual establishment of widespread transmission, which can significantly impact flock health and productivity

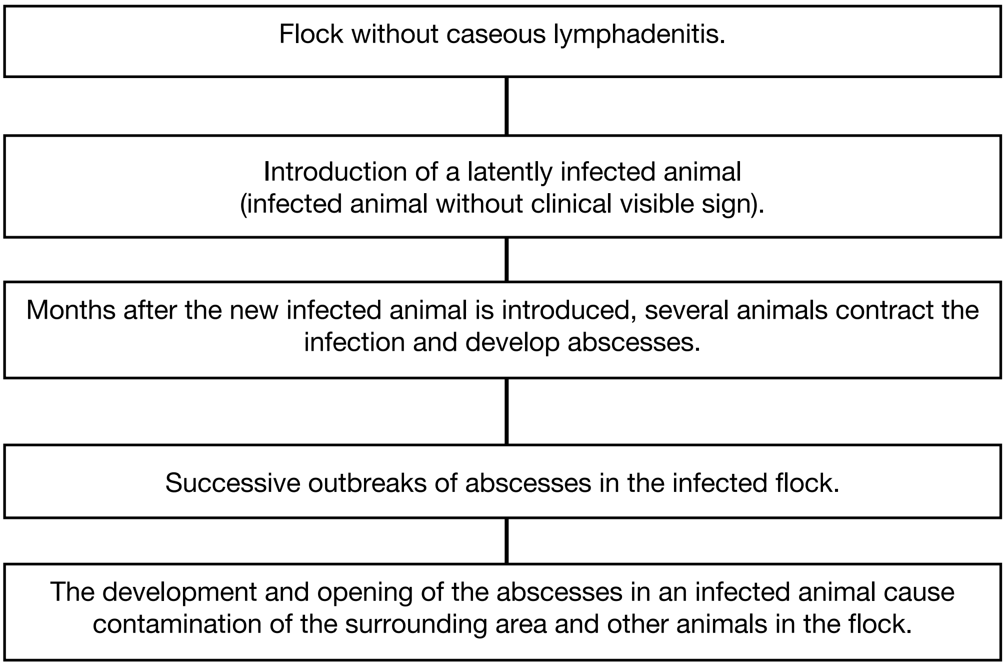

Figure 1 The flow of the progression of caseous lymphadenitis in a flock, from the introduction of a latently infected animal to successive outbreaks.

EFFECT OF CLA ON DAIRY GOAT

Globally, CLA is regarded as one of the most economically devastating chronic zoonotic diseases that has ever affected small ruminants, specifically both sheep and goats (Abdullah, 2017). For example, several clinical cases of CLA were identified in a milking goat herd in April 2008 via lesion bacteriological culture (Sharpe et al., 2010). Among the clinical indicators that were recorded include low milk production, poor physical state, persistent cough, and purulent discharge coming from swollen superficial lymph nodes. A farmer in the south of Ireland purchased the 290 mature goats that were part of an established milking herd from a farm in the midlands that was shutting its dairy business due to the CLA outbreak (Sharpe et al., 2010). Nowadays, almost every major goat- and sheep-rearing country in the globe has a high prevalence of CLA. In nations with large sheep populations, such as Australia, the infection leads to significant financial losses due to the downgrading and condemnation of infected carcasses during the meat inspection process (Komala et al., 2008). "Thin ewe syndrome" is a condition that is linked to visceral lesions of CLA, and it has been determined to be one of the main causes of the losses. Although this kind of CLA is not usually fatal, it results in a substantial loss of profit due to low milk production and reduced wool production manufacturing (Komala et al., 2008).

According to Al-Gaabary (2009), CLA is an endemic disease in areas with a lot of sheep and goats. Although most infected animals only showed visual abscessation and no other overt clinical pathology, the disease has significant economic implications for the goat and sheep industries (Abutarbush, 2010). This repercussion stems from reduced weight gain, decreased reproductive effectiveness, and lower production of milk and wool, as well as the condemnation of carcasses, the depreciation of skins and hides, and the need to cull diseased animals (Chakraborty et al., 2014). The pathogen spreads to healthy animals that come into contact with the infected animals when the diseased animal's lymph nodes burst and drain. The contagious exudates are purulent. Bacterial exudates or pus can enter the body through skin abrasions, breaks or mucous membranes. Moreover, the risk of infection increases when the animal is sheared, castrated, docked, head-butted, or licks another animal's draining abscess (Fikre and Abraha, 2014). When the draining lymph nodes contaminate the hay, straw, shavings, and/or soil, it results in environmental pollution. The microorganisms are especially resilient during the first 24 hours in environments like dips and can survive for months in damp, dark places such as shearing sheds (Spier et al., 2012). The external sign of CLA in an infected goat at Pasir Akar Farm in Terengganu is shown in Figure 2. One of the disease's distinctive clinical signs, the picture emphasises the obvious expansion of superficial lymph nodes. The significance of early identification and monitoring to control the infection's spread throughout the herd is shown by this visual evidence. Visceral CLA in the rib of an infected sheep was shown in Figure 3. The development of abscesses within deeper tissues is demonstrated by this internal manifestation of the disease.

Figure 2 Shows the enlargement of superficial lymph nodes of infected goat at Pasir Akar Farm, Terengganu (external).

Figure 3 Shows a visceral caseous lymphadenitis in sheep rib (internal).

ECONOMICAL EFFECT

Between 1986 and 1988, approximately 18.7% to 20.3% of condemned carcasses at the Cato Ridge Abattoir in KwaZulu-Natal Province had CLA lesions (Paton, 2010). The carcass condemnations alone resulted in an annual loss of about R400 000 (RM103 405), with additional significant losses from unmeasured trims to the carcasses. These condemnations accounted for 0.24% to 0.3% of all the sheep and goats slaughtered at that abattoir during that period. In South African abattoirs in the 1990s and 1991, the most common cause of carcass condemnation in sheep was CLA (Paton, 2010). Economic losses associated with CLA include poor wool development, wasting, reduced milk production and quality, early culling, carcass condemnation, reproductive issues, and occasionally death (Paton et al., 1994). An estimated 17 million dollars are lost annually in Australia alone due to the disease, which has an indirect substantial economic impact on small ruminant farms in the US, Canada, and Australia (Çetinkaya et al., 2002). Furthermore, since CLA is not a condition that has to be reported in many nations, its true prevalence is often overlooked, which allows the disease to develop undiagnosed (Windsor, 2011). The map in Figure 4 shows the nations between 1996 and 2004, reported to the World Animal Health Organisation (OIE) on their sanitary conditions with reference to CLA. The map gives a worldwide overview of CLA reporting over this time, showing the disease's geographic prevalence and highlighting how crucial international reporting and monitoring systems are to controlling animal health.

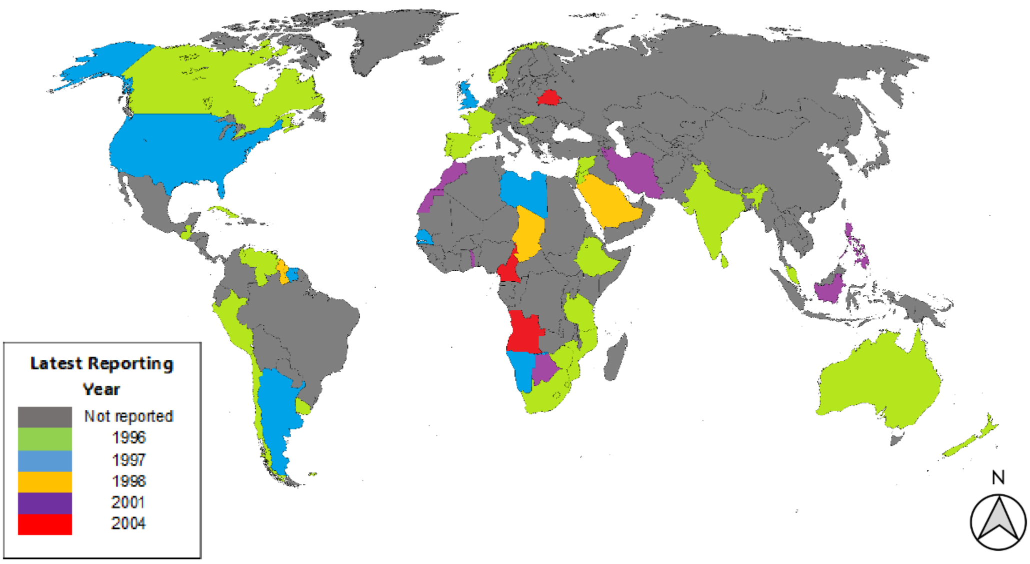

Figure 4 Map of countries that reported their sanitary situation as caseous lymphadenitis to the World Animal Health Organization (OIE) from 1996 – 2004.

RISK FACTORS OF TRANSMISSION OF CLA

The size of the herd, scratching against walls, pipes, or pillars, and herd disinfection all had a major impact on the prevalence of CLA (Pioquinto et al., 2023). Other environmental risks that might cause infections and raise the likelihood that the animals become infected include pointy nails, barbed wire, and splintered wood (Williamson, 2001; Çetinkaya et al., 2002). Larger herds had higher CLA frequency than smaller herds, according to a prior study (Kaba et al., 2011). In larger herds, increased competition for space leads to more animal interaction, and this can significantly raise the risk of infected animals spreading the disease to others with open wounds. Additionally, scratching against walls, pipes, or pillars has been demonstrated to be substantially linked to the development of CLA. Goats tend to lick, rub, and scrape their heads and shoulders against fences, walls, or other hard surfaces, which can cause sores in these areas and increases the likelihood of superficial abscesses in the parotid, mandibular, and pre-scapular lymph nodes (Yitagesu et al., 2020). Pathogens may also be present on the walls and pillars that animals rub against. Since there is a strong correlation between CLA prevalence and goat herd disinfection, regular disinfection is essential for lowering the prevalence of CLA in goat herds (Pioquinto et al., 2023). According to the data collected in this study and previous research, disinfection is crucial for managing CLA. It has been emphasised that if farms neglect standard hygiene practices, they raise the risk of CLA prevalence and spread (Guimarães et al., 2011). Furthermore, the main risk factors linked to CLA spread include poor ventilation in barns, lack of abscess treatment procedures, and animal age, with younger animals being the most affected (El Khalfaoui et al., 2024). When it came to the age distribution of sheep in flocks, the younger sheep, those that were between 6 and 24 months old, had a higher prevalence of superficial CLA. The immaturity of young sheep's immune systems makes them more susceptible to contamination (Williamson, 2001). Likewise, decreased body weight in CLA-infected goats was related to the visceral form of the disease (Fikre and Abraha, 2014). This could be attributed to reduced appetite and compromised nutrient digestion and absorption (Odhah et al., 2019).

DIAGNOSE AND TREATMENT OF CLA

The superficial form of CLA is characterised by infection of external lymph nodes, including the parotid, submandibular, pre-scapular, pre-femoral, femoral, and popliteal lymph nodes. Figure 5 shows the location of lymph node enlargement. The figure provides a visual reference for recognising and diagnosing the disease in afflicted animals by illustrating the common sites where lymph node enlargement develops.

The visceral form, on the other hand, is distinguished by abscessing of internal organs, such as the uterus, spleen, liver, kidneys, lungs, and internal lymph nodes, including the mediastinal and bronchial lymph nodes (Guimaraes et al., 2011). Internal abscesses are normally associated with weight loss and weakness, commonly referred to as thin-ewe syndrome in sheep (Washburn, 2023). Goats are more likely to have external abscesses in the lymph nodes of the head and neck, whereas sheep tend to have damaged subiliac popliteal and pre-scapular lymph nodes (Brown et al., 1987). Goat abscesses contain a thin, pasty exudate, while in sheep, the contents have a laminar structure when sliced, like the layers of an onion, due to the formation of layers of fibrous tissue and thick caseous material (Ali et al., 2016).

Methods known as enzyme-linked immunosorbent assays (ELISA), which employ bacterial cells, toxins, and produced by *C. pseudotuberculosis* such as *pld,* have been shown to be effective in managing and eradicating CLA (Laak, 2014). When diagnosing CLA in small ruminants, indirect ELISA based on secreted proteins demonstrated a diagnostic sensitivity and specificity of 93.5% and 100%, respectively (Binns et al., 2007). In addition, molecular methods have also been used to diagnose CLA. Table 1 summarizes the advantages and disadvantages of using the ELISA for detecting CLA

The polymerase chain reaction (PCR) has been used as a faster and more precise diagnostic method compared to conventional techniques for detecting *C. pseudotuberculosis* (Çetinkaya et al., 2002). In PCR, DNA segments are repeatedly amplified through cycles of denaturation, amplification, and replication. Specific DNA primers are used to detect the presence of the target bacterium (Waters and Shapter, 2014). The diagnostic sensitivity of multiplex PCR, which is based on amplifying the genes 16S rDNA, rpoB, and *pld*, was 94.6% for both clinical material and isolates of *C. pseudotuberculosis* (Pacheco et al., 2007). This method facilitates the diagnosis process by distinguishing *C. pseudotuberculosis* from other infections commonly identified in abscesses. Table 1 also summarizes the advantages and disadvantages of conducting the PCR for detecting CLA.

Infected animals are treated by draining abscesses, cleaning, and applying chemical cauterisation with 10% iodine or by incising the afflicted superficial lymph nodes (Washburn, 2023). However, since internal abscesses may be present, this procedure might not be as effective as expected. All disposable materials, including plastics and paper used to cover the area, should be burned and buried after the abscess is drained to prevent environmental contamination. On top of that, surgical tools should be cleaned both before and after the procedure. Antibiotic treatment is another therapeutic approach that has not proven to be very effective despite the fact that *C. pseudotuberculosis* is adaptable to nearly all antibiotics studied in vitro (Brown et al., 1987). The reason is that these living bacteria within abscesses are protected by a confined capsule, and as such, it can be difficult to manage solely using antibiotics (Piontkowski and Shivvers, 1998).

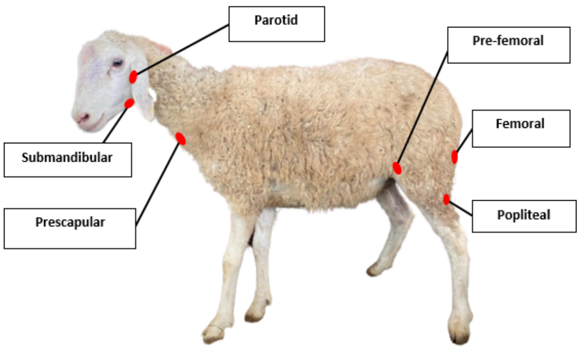

Figure 5 Shows the site of enlargement of the lymph nodes.

Table 1 Advantages and disadvantages of ELISA (Sakamoto et al., 2018)

Advantages	Disadvantages
1. Simple procedure 2. Easy to perform with a simple procedure 3. High specificity and sensitivity 4. ELISA is based on antigen-antibody reaction 5. High efficiency 6. Generally safe and eco-friendly 7. Large volumes of organic solvents and radioactive materials are not necessary	1. Labor-intensive and expensive to prepare antibody 2. Expensive culture media and sophisticated methodologies are needed 3. High possibility of false positive/negative 4. Insufficient blocking of immobilised antigen results in false results 5. Antibody instability 6. Since an antibody is a protein, it must be transported and stored refrigerated

Table 2 shows the advantages and disadvantages of using PCR (Liu et al., 2019)

Advantages	Disadvantages
1. High sensitivity compared to staining and culture 2. Possibility of antimicrobial resistance tests 3. Performed in 4-8 hours 4. Demonstrated to be more economical than staining and culture when used occasionally 5. Improved capacity to identify uncommon organisms like viruses	1. Potentially lower specificity compared to culture and staining 2. The use of certain primers requires a limited set of causative agents 3. Becomes less cost-effective when performed with a multi-organism PCR approach 4. Supply costs, machinery fees, training expenses

Bacteria vaccinations

A vaccine made from formalin-killed *C. pseudotuberculosis* cells can protect sheep from the fatal effects of a subacute infection but not from the development of lesions in chronic cases (Cameron, 2016). In a recent study, an experiment in field research using a formalin-killed whole-cell vaccine showed a significant decrease in the prevalence of CLA in sheep, with signs of a similar result in the goat population (Menzies, 1991). For instance, lambs immunised with the *C. pseudotuberculosis* bacterin displayed a notable rise in antibody titers at the time when external, spontaneous abscesses developed (Brogden et al., 1985). Although the killed *C. pseudotuberculosis* does not completely prevent the disease, it does reduce the number of granulomas in both sheep and goats (Brogden et al., 1985).

DNA Vaccination

Since the development of DNA vaccination technology, researchers have examined the effectiveness of DNA vaccines against *C. pseudotuberculosis* while trying to understand how these antigens are targeted to antigen-presenting cells to improve both the effectiveness and the duration of the immune response (Brum et al., 2017; Rezende et al., 2020). Although few experiments have been conducted, interesting results have emerged. For example, when genetically detoxified PLD (ΔPLD) was combined with CTLA-4, it produced a much greater antibody response in sheep than DNA coding for ΔPLD alone. It also offered some degree of protection against *C. pseudotuberculosis,* which is comparable to that which is given by a formalin-inactivated subunit vaccine (Chaplin et al., 1999).

Live vaccinations

Live attenuated vaccines have been proposed since experimentally infected lambs with *C. pseudotuberculosis* have demonstrated resistance to a future challenge, even in cases when the infection is severe (Piontkowski and Shivvers, 1998). An inactivated *pld* gene-containing live recombinant vaccine, administered to sheep challenged with wild-type *C. pseudotuberculosis*, demonstrated strong humoural and cellular immune responses, as well as protection (PEPIN et al., 1993). In sheep, Toxminus, a phospholipase D (*pld*)-deleted strain of *C. pseudotuberculosis*, produced reduced toxicity, increased protection, and a decrease in the quantity and severity of typical CLA granulomas in comparison to the unvaccinated control group (Hodgson et al., 1992). A promising 100% protection against *C. pseudotuberculosis* was reported when Toxminus was modified by inserting the genetically inactivated *pld* as a live vaccine vector for oral immunisation in sheep (Hodgson et al., 1992). As live attenuated vaccinations may be employed at a low cost, their potential use as vaccine vectors is promising (Simmons et al., 1997).

CONTROL OF CLA

As part of an effective program to control CLA, all animals in the flock, including newly acquired ones and those recently entering the herd, should undergo clinical inspection and periodic serology. Any animals that exhibit clinical symptoms or test positive for the disease should be culled. This is because when an animal is infected with *C. pseudotuberculosis,* it can barely ever recover (Saeedand Alharbi, 2014). The major cause of infection for a flock is the introduction of infected or abscessed animals into the herd. If nothing is done, this can result in a high frequency of abscesses after two or three years. The situation emphasises how crucial it is to use biosecurity protocols in all flocks, especially when introducing new animals. Therefore, the employment of strategies like smooth wire fences, troughs, and non-sharp edge buildings, cleaning surgical, ear-tagging, and shearing tools, using single-use disposable needles consistently, managing insects effectively, and disinfecting newborns' navels and other wounds with 10% iodine is necessary to lower the environmental risk of wounding (Pépin and Paton, 1999). Additionally, 10% formaldehyde should be used occasionally to disinfect herd facilities, even if the method is not recommended to be administered on swollen lymph nodes due to its irritating and caustic impact on tissues (skin, mucosa, and lungs) (De Sá Guimarães et al., 2011). The control strategies differ according to the infection prevalence. Nevertheless, all animals should be tested by ELISA before they can be imported, and they must be initially quarantined when reaching the farms. Only herds that have been certified free of CLA for three years should be allowed to enter any country. Moreover, lambs and kids should be raised separately from their mothers, installations and equipment should be thoroughly cleaned, and clinically infected animals should be isolated and subjected to ELISA testing. Other than that, vaccination and strict sanitary measures should be put in place in nations where the prevalence is high (Pépin and Paton, 1999; Ali et al., 2016). In endemic herds, the disease can be eradicated by culling all animals that show any symptoms or those that test positive for antibodies. However, this approach is difficult because of the agent's rapid dissemination across the herd and the challenge of identifying animals with subclinical infections (Çetinkaya et al., 2002).

EFFECT OF CLA ON MILK

Impact on Milk Yield

The CLA disease is characterised by the development of abscesses in the internal organs and lymph nodes. Any animals that are infected will have several health problems with their milk production lowered. For dairy goats, CLA directly reduces their ability to produce milk (Nabih et al., 2018). This reduction occurs because of the abscess development and the systemic sickness linked to CLA (Fontaine and Baird, 2008). Goats suffering from CLA generate less milk than their healthy counterparts as their energy and resources are being used to fight and heal from the infection. Persistent CLA infections can lead to long-term decreases in milk production and may even cause the complete loss of the animal's ability to produce milk (Abutarbush, 2010).

Milk Quality and Composition

The somatic cell count (SCC), which measures inflammation and possible contamination in milk, frequently rises in the presence of CLA abscesses (Li et al., 2014). A higher SCC is linked with low-quality milk due to the changes in the composition, where the milk contains lower levels of fat and protein. This makes the milk not fit for processing or consumption due to possible bacterial contamination (Puggioni et al., 2020). Using the PCR, virulence genes, including [*pld*] and [*rpoB*], were screened to identify *C. pseudotuberculosis*. Among the tested animals, 30.5% had clinical mastitis, while the remaining 69.5% appeared healthy and produced normal milk. Out of the 180 clinically healthy half-milk samples, 96 (53.33%) had Subclinical mastitis, as determined by SCC (SCC ≥1,000,000 cells/ml). *Staphylococcus aureus* (37.5%) and *C. pseudotuberculosis* (7.14%) were the most common bacteria, followed by coagulase-negative staphylococci (41.96%) (Nabih et al., 2018).

CONCLUSIONS

CLA poses a substantial threat to the dairy goat industry as it can negatively affect animal health, production, and the economy. Dairy goats, especially in intensive farming environments, are more vulnerable to CLA because their close proximity increases the risk of disease transmission. In addition to compromising animal well-being, abscesses in lymph nodes and other organs can cause a decrease in milk supply, reproductive problems, and higher mortality. As such, strict biosecurity standards, early identification, and intensive control measures are required to effectively manage CLA in dairy goat populations. Programs for vaccination have demonstrated promise in lowering the frequency and severity of CLA; nevertheless, issues including vaccine effectiveness and administration logistics need to be addressed. Furthermore, advanced diagnostic methods like PCR allow for early detection of CLA, and thus, quick prevention strategies can be implemented to stop this disease from spreading. Finally, improved surveillance and monitoring of CLA incidence in dairy goat herds can help guide targeted control measures and lessen the negative effects of outbreaks on herd health and productivity.

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AUTHOR CONTRIBUTIONS

Nik Danial Asyraf Nik Mustaffa: Conceptualization, methodology, data analysis, writing original draft preparation.
Chai Min Hian: Data curation, review and editing of the manuscript.
Yazan Al-Rashdan: Project administration and funding acquisition.
Khalid Mahmood Al-Jaff: Project administration and funding acquisition.
Mohd Faizal Ghazali: Visualization and validation.
Noor Syaheera Ibrahim: Project administration, final review, and supervision.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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