Associated Risk Factors with *Neospora caninum* and *Neosporosis:* A Review

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Abstract:

Neospora caninum is an obligate intracellular protozoan parasite causing neosporosis, a disease presenting great importance in a variety of domestic and wild animals worldwide, particularly dogs and cattle are the most affected hosts. It is among the common causes of bovine abortion and one of the primary threats to intensively raised dairy and beef cattle, causing huge reproductive and economic losses. Serological tests, including seroreactivity tested by ELISA and IFAT were the most common methods used for the diagnosis of infection. The parasite has a complex life cycle that entails three major stages: sporozoites, tachyzoites and bradyzoites. Vertical transmission is the form of transmission in cattle; the parasite is passed from dam to fetus trans placentally. Dogs are the final hosts of the parasite that excretes oocysts with the faeces and contaminates environment particularly feed and water. Closeness to infected dogs is significantly related to higher prevalence of infection thus a close association between cattle and sick dogs has been highly incriminated. Exact worldwide figures are not available. Pharmacological treatments against *N. caninum* have been explored, and compounds such as piritrexim, monensin, pyrimethamine and trimethoprime have demonstrated inhibitory activity against the parasite ultimate development in cell culture. There is, however, no truly effective cure. Consequently, the control of vertical transmission is still the most realistic and the most effective approach to control, thus requiring enhanced biosecurity measures in order to manage dogs on farms as well as more sustainable therapeutic or vaccine-based interventions.

*Keyword***:** *Neospora caninum*, Risk factors, Dignosis, Treatments

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Introduction:

Neospora caninum is an obligate intracellular protozoan parasite that has emerged as one of the most important causes of reproductive disorders in animals, particularly in cattle and dogs. Since its first identification in the late 1980s, *N. caninum* has been recognized as a major etiological agent of abortion in cattle worldwide, leading to considerable economic losses in the livestock industry(Zhang *et al.,* 2022). The disease caused by this parasite, known as neosporosis, affects a wide range of domestic and wild animals, with variable clinical outcomes ranging from asymptomatic infections to severe neurological disorders and reproductive failure(Tomasina *et al.,* 2023). In cattle, vertical transmission from dam to fetus is the most common route of infection and a key factor in the persistence of *N. caninum* within herds. Horizontal transmission, primarily through ingestion of oocysts shed by canids, also plays a critical role in disease epidemiology. The clinical and subclinical impacts of neosporosis extend beyond individual animal health to herd productivity, making it a global concern for veterinarians and livestock producers(Tao *et al.,* 2025).

Over the last three decades, substantial progress has been made in understanding the biology, immunopathogenesis, diagnostic methods, and control strategies related to *N. caninum*. However, despite these advances, there is still no effective vaccine or therapeutic regimen available, and the parasite continues to pose challenges in animal health management(Song *et al.,* 2021).

This review provides an updated overview of *Neospora caninum* and animal neosporosis, focusing on its epidemiology, pathogenesis, diagnosis, and current approaches to control. By summarizing recent findings, this work aims to highlight knowledge gaps and future research directions necessary to mitigate the impact of this parasite on animal health and the livestock industry.

Life Cycle

Neospora caninum constitutes a coccidioidal pathogen with an extensive host range. It closely resembles *Toxoplasma gondii* in structure and life cycle, but there are two key differences **(i),** neospora primarily infects cattle, Dogs and their canine relatives serve as the primary hosts of N. caninum. **(ii),** Toxoplasmosis primarily affects people, goats and sheep with cats serving as the sole definitive host of *T. gondii*. The life cycle of the parasite has three primary infective stages: tachyzoites, Bradyzoite, and oocysts (Morganti et al., 2024).. The tachyzoite and tissues cyst phases manifest intracellularly within intermediary hosts. Tachyzoites are approximately 6 µm long and 2 µm wide, while tissue cysts are round or oval, reaching approximately 107 µm in length(Ikonnikova *et al.,* 2023).

These cysts are often located in the central nervous system, with cyst walls up to 4 µm thick, and contain bradyzoites measuring 7–8 × 2 µm. Tissue cysts can also be found in other tissues outside the nervous system, particularly in muscle. The environmentally resistant stage of the parasite is the oocyst, which is excreted in the feces of dogs or wolves in a non-sporulating form and then sporulates outside the host within a period that may exceed 24 hours. Although the precise duration of *N. caninum* oocysts' survival in the environment has not yet been determined, its taxonomic closeness to *T. gondii* suggests that its survival capacity may be similar to that of *T. gondii* oocysts(Ikonnikova et al., 2023).
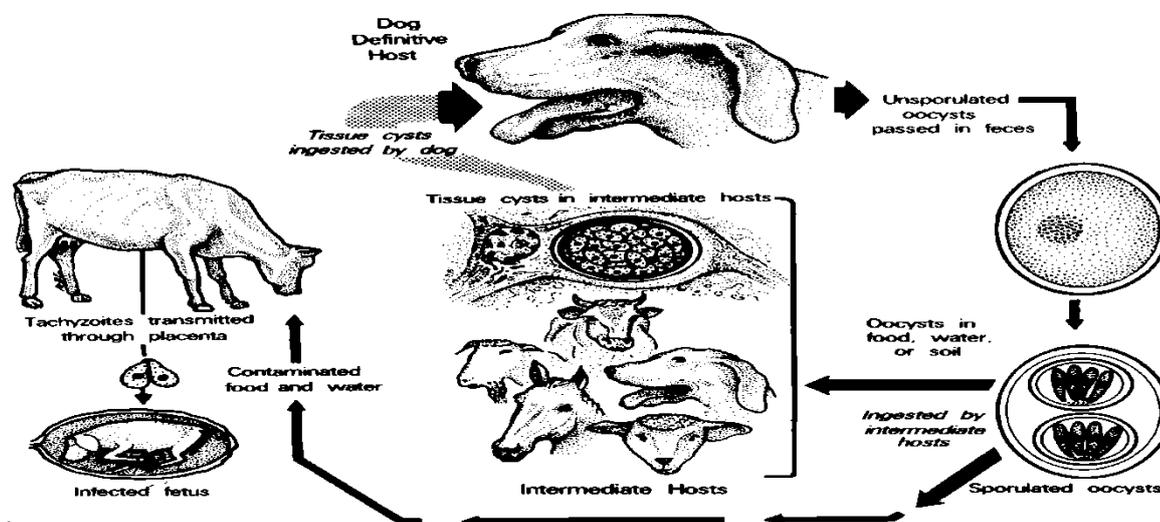
Figure 1. Life cycle of *Neospora caninum*(Dubey et al., 2007).

Clinical manifestations

In both dairy and meat cattle, *Neospora caninum* causes abortion. Abortion can occur in cows of any age between three months of pregnancy and term. Fetuses can die in the womb, resorb, mummify, undergo autolysis and die stillborn, be born alive with clinical symptoms, or be born clinically normal but persistently infected. (Rosbottom *et al.,* 2011). Cows with *N. caninum* antibodies (seropositive) had an increased probability of abortion compared to seronegative cows, a trend noted in both dairy and beef cattle(Morales et al., 2023). However, up to 96% of calves from seropositive mothers who are born with congenital infections do not exhibit any clinical problems. The frequency of congenital infection may be unaffected by the dam's age, the number of lactations, and the history of abortions; nevertheless, research indicates that vertical transmission works better in younger, consistently infected cattle than in older ones (Rimayanti *et al.,* 2025).Clinical manifestations have been recorded in animals younger than 2 months. Calves infected with *N.caninum* might show neurological manifestations, be underweight, be unable to stand, or be born asymptomatic (Uesaka *et al.*, 2018). Hind limbs, forelimbs, or both may exhibit flexion or hyperextension. Musculoskeletal abnormalities such as flexion or hyperextension of the forelimbs, hind limbs, or both are frequently described. Neurological assessment often reveals signs including ataxia, diminished patellar reflexes, and impaired conscious proprioception. Ocular involvement, such as exophthalmia and asymmetry of the eyes, can also occur. In certain cases, congenital malformations, including hydrocephalus and spinal cord compression, have been associated with the infection(Selim *et al.*, 2023).Reproductive losses represent the most significant impact of neosporosis. Abortions may occur sporadically or in outbreak form. Reports indicate that up to one-third of fetuses in dairy herds from endemic regions may be lost within a short period. Outbreaks are generally classified as epidemics when more than

10% of susceptible cows. Although less common, repeated abortions due to *N. caninum* have been documented in a minority of infected cows (<5%)(Basso et al., 2022).

Prevalence

Infections of *N. caninum* have been reported from many areas worldwide, such as the Americas, Europe, Korea, Japan, Thailand, Australia, and New Zealand.. Bovine abortion and neonatal mortality associated with neosporosis have been reported from the following countries: Italy, Argentina, Australia, Belgium, Canada, Brazil, France, Germany, Costa Rica, Hungary ,Denmark, Japan ,Ireland, , Korea, Mexico, the Netherlands, New Zealand, Portugal, Poland, Spain, South Africa, United Kingdom, United States of America, and Zimbabwe(Nayeri, Sarvi, *et al.,* 2022). The United States of America, New Zealand, the Netherlands, and Germany have all conducted quantitative studies that have shown that between 12 and 42 percent of the fetuses that are aborted from dairy cow are infected with *N. caninum* (Table 1). The serological frequency in cattle differs by country and region, influenced by the type of serological test employed and the cut-off level utilized to ascertain exposure. In certain dairy farms, as much as 87 percent of cows are seropositive(Anvari *et al.,* 2020).

Table (1). Diagnostic of *N. caninum*-related abortion in cattle based chosen research(Dubey, 2003)

Country	Number of fetuses examined	Percentage infected
Argentina	240	12.1
Australia	729	21.0
Brazil	46	39.1
Germany	135	12.6
Mexico	211	77
Switzerland	242	21.0
The netherlands	2,053	17
Usa	698	24.4
Usa	266	42.5

Differences in strains and their pathogenicity

Although clinical illness is uncommon, infections in a wide variety of hosts are quite common. There is a possibility that the strain of *N. caninum* is connected with clinical illness(Caspe *et al.,* 2024). Despite the fact that numerous strains of *N. caninum* have their own molecular signature, which can be detected by multilocus microsatellite analysis, the genetic makeup of *N. caninum* isolates from different hosts is comparable(Abdelbaky *et al.*, 2024).

In the context of epidemiological research, the molecular properties of a strain can prove to be applicable. According to Basso *et al.*,(Basso *et al.*, 2022), A consistent source of infection was identified in Germany in bovine neosporosis outbreaks brought on by external point sources. Based on the geographical location for aborted bovine fetuses, *N. caninum* isolates in Spain were grouped together, as shown in another experiment conducted by Pedraza-Díaz et al. in 2009(Rojo-Montejo *et al., 2009)*. A limited amount of information is available regarding the strain variation in terms of their

pathogenicity. In the limited research that were conducted, it was observed that certain strains of *N. caninum* exhibited greater virulence in mice compared to different strains. Furthermore, these strains exhibited variances during the process of in vitro cultivation. The question of whether or not the virulence of *N. caninum* in mice could be a reflection of the effect of the infection in other hosts is not yet known.

Several isolates from different labs have been used to cause abortion or fetal infections in cattle. However, it would not be possible to do a large comparison in pregnant calves because it would cost too much(Barr e*t al.,* 1991). A study found that injecting cows with a Spanish bovine strain did not hurt the fetus, even though the cows were only 70 days pregnant at the time of the injection (Rojo-Montejo *et al.,* 2013). On the other hand, one baby died when a beef strain was introduced to beef calves at 110 days of pregnancy for an experiment(Almería & López-Gatius, 2013). Research focused on assessing the pathogenicity of *N. caninum* in cattle presents interpretative challenges. Due to experimentally infected dogs typically shedding only a limited number of oocysts, this stage is frequently unavailable. Researchers often use tachyzoites to infect cattle for experiments(Selim *et al.*, 2023). However, oocysts are more likely to infect these animals after birth, and the disease outcome may be different based on the stage of the parasite that infects the animal. It might be harder to do research using tachyzoites that come from cell cultures because *N. caninum* isolates that have been kept in a lab for a long time might have changed in how infectious they are and how they behave biologically. The way an experiment causes a miscarriage may be different depending on the type, passage number, or inoculation method used. For example, none of the 19 cows that were intraconjunctively inoculated with 10^8 NC1 tachyzoites had an infected calf (De Yaniz *et al.,* 2007).

Pathogenesis of abortion

Bovine neosporosis primarily affects the placenta and fetus, begun by maternal parasitemia, which can happen because of either a first illness in the mother (exogenous) or the return of an infection that was present during pregnancy (endogenous) (Nyzhnyk et al., 2022). Once the parasites are present, *N. caninum* can settle in the caruncular septum of the mother before moving to the uterine villus of the fetus. In order for abortion to happen, the baby or its placenta must be hurt so that it can't live., with several factors potentially interacting to varying degrees to affect this outcome (da Costa *et al.,* 2022). Parasites can cause damage to the primary placenta, which can put the fetus's life at risk or cause the release of prostaglandins in the mother, leading to luteolysis and abortion.

Fetal harm may arise from direct tissue injury resulting from the proliferation of *N. caninum* within the fetus or from inadequate oxygen and nourishment due to placental impairment. Additionally, it has been suggested that maternal immunological rejection of the fetus may occur, associated with the release of maternal pro-inflammatory cytokines in the placenta or hormonal imbalance. While all proposed processes are interrelated, one or more may possess more importance in particular cases, and all may be affected by the stage of gestation(Abdelbaky *et al.*, 2024).

Significant damage in essential embryonic organs may immediately lead to fetal demise (Gibney *et al*., 2008). The outcome of infection is largely influenced by the host immune response, in which the synthesis of regulatory cytokines (e.g., IL-10) and pro-inflammation cytokines (e.g., interferon-gamma) occurs, along with direct tissue damage caused by tachyzoite replication, play a decisive role in determining fetal survival or mortality(Fayisa, 2024). Interestingly, elevated prolactin concentrations in cows infected with *Neospora caninum* have been associated with a protective role during pregnancy(Wei *et al.*, 2025). Moreover, progesterone is believed to enhance gestational maintenance by modulating Th1/Th2-mediated immune responses in cattle. A recent observation highlighted a possible interaction between *N. caninum* and *Coxiella burnetii*, where non-aborting cows seropositive for both Pathogens demonstrated elevated plasma levels of progesterone in comparison to other studied animals(Mohammed *et al.,* 2023). Nonetheless, the administration of artificial progesterone to pregnant cows did not mitigate neosporosis-related abortions but instead increased the likelihood that cows with high *N. caninum* antibodies titres would have an abortion(Khan *et al.*, 2020). The stage of pregnancy at the time of infection may have some bearing on the likelihood of transmission and fetal disease. Given that the placenta seems to be more permeable in the last trimester, the transmission rate increases with gestational age, which may be related to placental vascularization(Abdelbaky *et al.,* 2024).

Immune Response

Parasites have to get into host cells in order to avoid the host's immunological response. Among these protective systems is the CD8+ T cell response (Jordan and Hunter ,2010) , CD8$^+$ T lymphocytes are recognized as central players in the host response against intracellular protozoa of the phylum Apicomplexa (Jordan & Hunter, 2010). These cells exert their protective role either through the secretion of cytokines that enhance the immune milieu or by functioning directly as cytotoxic T lymphocytes capable of destroying infected host cells. The production and efficacy of CD8$^+$ T-cell responses are significantly influenced by cytokines like IL-2 and IL-12, which enhance proliferating T-cell , persistence, and maturation into effector cells (Shallberg *et al.*, 2022). Additional experimental research shown that CD8 T cells offer significant protection against neosporosis, assisting the humoral immune system in preventing the spread of parasites and containing infection (Correia *et al*., 2022). Clinically, intestinal manifestations of infection usually emerge within 5–8 days following ingestion of tissue cysts; however, tracing the exact distribution of these cysts within host organs and tissues remains a considerable diagnostic challenge (Morelli *et al*., 2021).

Risk factors

Understanding the risk factors that contribute to *N. caninum* infection and abortion in cattle is essential for designing effective control strategies against bovine neosporosis. Several studies have reported that the presence of farm dogs is one of the main contributors to infection, since dogs act as definitive hosts and can transmit the parasite through oocyst contamination of feed or the farm environment (Zaghawa *et al.,* 2023). Certain practices, such as dogs consuming placental tissues or aborted fetuses, have been demonstrated to augment the probability of infection in cattle. Therefore, managing the interaction between farm dogs and livestock is a key preventive measure.

Variations in farm management practices, such as feeding, pasture management, Cattle density with their housing might impact the likelihood of infection. A survey of 5,594 dairy and beef cows in Argentina revealed that infection-positive animals were 84% more inclined to undergo abortion than their seronegative counterparts. The findings suggested an increased likelihood of infection in dairy cattle compared to beef herds, potentially attributable to unspecified differences in herd management practices between the two types (Novoa *et al.,* 2023)

In chronically, congenitally infected cattle, supplementary factors may elevate the likelihood of neosporosis-induced abortion. According to new research from two Holstein-Friesian dairy groups, heifers and cows that are pregnant had a higher chance of having an abortion if there were more days with an average humidity level below 65% in the second trimester (Basset *et al.,* 2024).

Some studies have suggested that environmental conditions and reproductive factors may play a role in increasing the likelihood of *N. caninum*-associated abortion(Bartels *et al.,* 1999; Nayeri, Moosazadeh, *et al.*, 2022). High rainfall rates during the second trimester of pregnancy in multiparous cows have been associated with an increased risk of abortion. This risk has also been shown to be higher in cows with higher antibody titers against the parasite, as well as in cows that were bred with Friesian sperm instead of Limousin or Belgian Blue sperm (Bartels et al., 1999).

N. caninum is a major cause of abortion, but coinfection can exacerbate the severity of the disease. For example, Coinfection with bovine herpesvirus type 1 (BoHV-1) was observed in 28% of 948 cattle and identified as a possible risk factor for Neospora in Italy (Rinaldi *et al.,* 2007). A survey in Vietnam revealed a notable relationship among bovine viral diarrhea (BVD) seropositivity and Neospora infections(Fávero *et al.,* 2017).

An additional investigation demonstrated that *N. caninum* seropositivity has a negatively affected reproductive traits such as first-insemination conception rate and calving intervals, with a significant interaction between BVD infection and neosporosis. The effect of neosporosis on first-insemination conception rate was more pronounced in BVD-negative cows than in BVD-positive cows, while no similar association was observed with Mycobacterium avium subtype paratuberculosis or bovine leukemia virus (BLV) infection(Vanleeuwen *et al.*, 2010).

A study from Canada looked at how temperature (drought), soil pH, and agroecological zone affect the ability to test positive for *M. avium* paratuberculosis, *N. caninum*, BLV, and BVD. There was no major change in the number of those who were positive for *N. caninum*(Vanleeuwen *et al.*, 2010).

Diagnosis

An investigation of the blood from a cow that has undergone an abortion is merely indicative of exposure to *N. caninum*. In order to make a conclusive diagnosis of neosporosis, A histological study of the fetus was necessary. For diagnostic purposes, the most appropriate specimens include the brain, heart, liver, and placenta, as well as bodily fluids or blood serum. Additionally, the diagnostic rate is increased when various tissues are evaluated(Ansari-Lari, 2021). Notwithstanding the fact that

neosporosis lesions can be seen in a number of organs, the embryonic brain is the organ that is most frequently damaged. Thorough histologic examination of hematoxylin and eosin (HE) stained slices of semi-liquid brain tissue was advised in cases of neosporosis, a type of localized encephalitis marked with both necrotic and absence of inflammation (Hecker *et al.*, 2023).

The diagnostic efficiency of polymerase chain reaction (PCR) for *N. caninum* largely depends on the laboratory facilities, the degree of fetal tissue autolysis, and the quality of the sampling process(Mioni et al., 2022). Although immunohistochemistry (IHC) remains the most direct approach to demonstrate the presence of *N. caninum* within characteristic lesions of aborted fetuses, its sensitivity is limited, making it less reliable as a stand-alone diagnostic tool. In contrast, PCR has proven to be more sensitive, as *N. caninum* DNA can be successfully amplified even from formalin-fixed, paraffin-embedded (FFPE) brain tissues of bovine fetuses. In addition to molecular methods, several serological assays are employed to detect antibodies against *N. caninum*(Nayeri, Moosazadeh, *et al.,* 2022). These include Enzyme-Linked Immunosorbent Assays (ELISAs), the Indirect Fluorescent Antibodies Testing (IFAT), and the Neospora Agglutination Test (NAT). Immunoblotting also provides valuable confirmation of *N. caninum*-specific antibodies. Furthermore, the development of avidity-based ELISA assays has shown promise in distinguishing between recent (acute) and chronic (persistent) infections in cattle, which is particularly useful for differentiating between endemic infections and epidemic abortion outbreaks(da Costa *et al.,* 2021).

The detection of *Neospora caninum* antibodies in fetal serum can serve as evidence of infection; however, a negative serological result does not necessarily exclude the disease. This limitation is due to the fact that fetal antibody production depends on several factors (Nayeri, Moosazadeh, *et al.,* 2022). Notably, even a low indirect fluorescent antibody test (IFAT) titer of 1:25 is considered diagnostic for *N. caninum* infection in fetuses(dos Santos Hofmeister et al., 2025). The use of immunoblotting with *N. caninum*-specific antigens further enhances diagnostic accuracy. Although multiple body fluids from the fetus can be utilized for serological testing, peritoneal fluid is regarded as the most reliable sample. In addition, presuckling serum collected from calves provides a valuable tool for confirming congenital infection(Corbellini et al., 2006).

The age and production class of the animal can influence the appropriate diagnostic cut-off level for serological tests. Despite the intimate relationship between *N. caninum* with *T. gondii*, and Sarcocystis species, as well as additional apicomplexans, cross-reactivity remains insufficiently described. Antibodies levels are typically elevated in cows that have aborted owing to neosporosis compared to those with normal gestation, but relying on the serum titer alone is not sufficient to determine the direct cause of the abortion(González-Warleta *et al.*, 2018). *T. gondii* and *Sarcocystis cruzi* must be included in a possible diagnosis of protozoan-induced miscarriages in cattle. These parasites can be distinguished from *N. caninum* by immunohistochemical techniques or by detection of parasite DNA using PCR. *S. cruzi* is capable of forming schizonts in vascular endothelial cells, but its presence in the brains of aborted fetuses is extremely rare (<0.1%). *N. caninum* is typically located in extravascular tissues, and its infection is not associated with the presence of immature schizonts,

which distinguishes it from *S. cruzi* infection. *T. gondii* infections in bovine fetuses are very rare(Sánchez-Sánchez *et al.,* 2021). The discovery of a statistical significance connection among seropositivity and abortion within the cohort of at-risk dams underscores the involvement of N. caninum in cow abortion (Rimayanti *et al*., 2025).

Treatment and Control

Several toxoplasmosis treatments targeting *N. caninum* have been examined. Piritrexim, monensin, lasalocid, pyrimethamine, and trimethoprim inhibit the intracellular proliferation of N. caninum in infected cell cultures(Samkange, 2023). Sulfadiazine diminished clinical neosporosis in experimentally infected mice (Lindsay and Dubey, 1990). Putting sulfadiazine into a person after they have developed clinical signs does not work. Many medicines have been shown to work against Neospora tachyzoite in vitro, but chemotherapy has not been thought to work against encysted bradyzoite in vivo (Müller *et al.,* 2022). Due to the length of milk withholding, the treatment of dairy cows is impractical. Pregnant cows can be treated with medication to prevent vertical transmission of infection and abortion(Imhof et al., 2024). Heifers are not fully protected against Neospora-caused abortion in the first trimester, even when treated with 40–120 mg/animal/day of monensin (Sánchez-Sánchez et al., 2018).

In vivo tests were conducted using standard mouse models, focusing on medication toxicity and pharmacokinetics, to evaluate effectiveness against a variety of conditions, including acute infections as well as placentally transmitted diseases. Toltrazuril, ponazuril, thiazoles, and the bumped-BKI-1294 kinase inhibitor are among the medications that have demonstrated efficacy in treating neosporosis (Correia et al., 2022; Shams et al., 2022). Chemotherapeutic approaches have demonstrated effectiveness in lowering parasite numbers, vertical transmission, and abortion rates when used to control *N. caninum* infections in cattle. Cuteri *et al*. (2005) conducted a field trial with 936 Friesian cattle spread across 18 herds in Italy, administering trimethoprim together with toltrazuril and sulphadiazine. (Cuteri *et al.*, 2005). The seroprevalence rate dropped from 68.7 percent to zero percent, and the abortion rate dropped sharply from 188 to nine percent in just one year. The pharmacokinetics of toltrazuril sulfone (Ponazuril) were studied in six calves by Dirikolu *et al.* (2009) to enable ongoing parasite suppression, noting significant absorption and an extended elimination half-life (Dirikolu et al., 2009). In a study conducted by Haerdi *et al.* (2006), neonatal calves of seropositive mothers were found to have lower levels of parasite infection and were completely eradicated after being treated with toltrazuril. This suggests that toltrazuril may help affected herds produce offspring free of parasites (Haerdi et al., 2006). The study conducted by Kritzner *et al*. (2002) examined the effects of Ponazuril on 19 experimentally infected calves. A 6-day treatment effectively eradicated the bulk of parasites found in the brains along with other organs of the rats who were treated)Kritzner *et al.,* 2002(. Conversely, Calves that were not treated had substantial parasite loads and concomitant health problems. Toltrazuril and ponazuril are effective chemotherapeutic drugs that can be used to manage cow neosporosis, according to these studies.

In general, managing neosporosis was challenging and ineffective, either entirely or in part. A minimum of 8 weeks of treatment might be required of patients. Canines showing signs of neurological disease have a poor prognosis and a very extensive treatment time (Fisher *et al.*, 2024). When muscular contractures occur, the best course of action is to intervene quickly. There have been reports of it being more effective in cases of cutaneous neosporosis (Jiménez-Pelayo *et al.,* 2019). The primary pharmacological agent employed for the treatment of canine neosporosis is clindamycin. It is the sole lincosamide possessing further antiprotozoal effects (Wang *et al.,* 2022). Thus, this medication works well against tachyzoites of *N. caninum*. Clindamycin and sulfonamides work together to prevent neoplasia. Additionally, pyrimethamine and sulfonamides work together to increase the effectiveness of antiprotozoal drugs. (McFarland *et al*., 2016). Clindamycin is thought to exert minimal to no influence on bradyzoites but does impact the proliferation of *N. caninum tachyzoites*. Consequently, tissue cysts may persist for around two months post-therapy, and the exposure of bradyzoites to an immune response as a potential treatment for chronic neosporosis warrants study and further investigation(Lyon, 2010). All members of the parent group must be tested for *N. caninum* antibodies levels upon the diagnosis of neosporosis in any member, while those who show seropositive should get treatment. Puppies who are seropositive must not be administered immunosuppressive drugs(Enshaeieh *et al.,* 2021). Due to the absence of prophylactic treatment, the parasite can be transmitted from an infected female dog to her progeny numerous times.

Vaccination

At present, Neosporosis is a leading cause of abortion in cows, and there is currently no fully protective vaccine or effective treatment to prevent it. Bovilis Neoguard (Intervet International B.V., Boxmeer, The Netherlands), the sole commercially registered vaccine, was made up of inactivated N. caninum tachyzoites (3×10^6 ml^{-1}) that were mixed with 5% stabilizer, 10% Havlogen adjuvant, and 5% phosphate-buffered saline. (Mazuz *et al.,* 2021). Despite its initial release, Due to its low level of protection, this vaccine was later taken off the market (approximately 20%) and its unintended effect of enhancing transplacental transmission, which led to embryonic mortality (Mansilla *et al.*, 2015). More recently, promising experimental findings indicated that pregnant cattle demonstrated strong immunogenic responses, particularly through IFN-γ activation, when exposed to a soluble tachyzoite lysate fraction combined with a soy-based aqueous adjuvant (sNcAg/AVEC) (Mansilla *et al.*, 2012).

Live tachyzoite-based vaccinations have been demonstrated to significantly decrease abortion rates and increase antibody production against *N. caninum*. These vaccines are produced from naturally attenuated or low-virulence strains such Nc-Nowra, Nc-Spain1H, and the Argentine strain Nc-6 (Imhof *et al.,* 2024). Despite these benefits, live vaccines present inherent drawbacks, including the potential reversion to pathogenicity following inoculation and the challenges associated with maintaining viable parasites on a large scale (Hou *et al.,* 2023). For these reasons, inactivated and subunit vaccines have attracted considerable interest; however, their protective efficacy has been limited. For example, recombinant NcGRA7 (50–200 μg) encapsulated in oligo-mannose microsomes (M3-NcGRA7), as well as bacterial recombinant proteins such as rNcSAG1, rNcHSP20, and rNcGRA7, were not effective in preventing infection in pregnant cattle (Reichel et al., 2015). Therefore, the development

of innovative vaccine strategies remains essential. Promising approaches include the use of genetically engineered live attenuated strains, such as tachyzoites deficient in **Ca²⁺-dependent protein kinase 2**, which may offer more durable and reliable protection against neosporosis (Khan *et al.,* 2020).

Control

Appropriate control and preventative measures are the most effective ways to eliminate *N. caninum* due to the economic significance of neosporosis and the absence of effective therapies and vaccines. The proper therapy of neosporosis requires serological testing to gather seroprevalence data. (Guido et al., 2016). Mitigating the likelihood of vertical or horizontal transmission can aid in the prevention and management of neosporosis. One of the main reasons Neospora infections might last in herds is because of vertical transmission (Marugan-Hernandez, 2017). Consequently, measures to prevent vertical transmission represent the most effective strategy for managing neosporosis in cattle populations, given the existing body of knowledge.

Only herds with a minimal prevalence of disease can execute the most drastic approach, specifically the culling of all infected animals and their affected progeny. In herds where the infection rate is moderate to high, it is more practical and cost-effective to exclude infected calves from replacement (Haddad et al., 2005). More research is shown that heifers infected at birth are much more likely to have abortions and vertical transmission to the virus to their progeny, particularly through their first pregnancy. This procedure was recommended because of this increased risk. As part of general herd management, seropositivity to Neospora can be used as a criterion for dairy cow selection, and only seronegative heifers can be used as replacement stock (Rimayanti *et al.,* 2025). It is possible to preserve valuable seropositive animals as breeding stock by transferring embryos from seropositive cattle to seronegative receivers (Pabón *et al.,* 2007).

Given that dogs significantly contribute to the disease's dissemination and transmission, implementing dog quarantine to interrupt the parasite's The life cycle aids management by preventing horizontal transfer among main and intermediary hosts (Stott *et al.,* 2025). Moreover, There can't be any aborted fetuses or placentas from cows or kids on the host. To avoid getting an oocyst illness, cows should only eat and drink sealed food and water. It is very important to keep dog poop from getting into the food. Moldy cow feed may contain mycotoxins, so don't give it to them (Hamzavi *et al.*, 2023). Stressors and dietary deficiencies are additional factors that may contribute to a compromised immune response and are challenging to regulate(Monney et al., 2011). To stop the spread of disease, plans must be made to get rid of all animals, including mice, rats, and rabbits (Gharekhani & Yakhchali, 2022). The same methods should be used for poultry, since pigeons and chickens could be intermediate hosts for the parasite. To make a control program work, it's important to figure out how much tests and control measures cost compared to how much money they save by lowering the number of infections and abortions caused by *N. caninum* (Liu *et al*., 2020).

Conclusion

Neosporosis is a parasitic disease of cattle found worldwide. It is due to the protozoa *N. caninum*. The disease is very severe in pregnant cows as it often leads to abortions and heavy losses with reproduction. The dog is the only animal known to harbour the parasite and to excrete infective oocysts in their faeces, contaminating the agricultural environment and foodstuffs. Oocysts are ingested most through the consumption of these by cattle and other domesticated animals, who serve as intermediate hosts. Neosporosis is a significant economic challenge because of decreased productivity leading to the increased number of abortions and costs tons of money to treat. Because there are currently no effective vaccines or treatments, the most effective way to slow down the spread and impact of *N. caninum* is through strong prevention and control. These measures include restricting dog access to cattle feed, enhancing farm biosecurity and initiating targeted monitoring programs.

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Author contribution

Rana Mohammed Ibrahim is the sole author of this review article. She conceptualized the topic, collected and analyzed the relevant literature, and wrote and revised the entire manuscript.

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