Q Fever Seroprevalence in Dairy Goats: Implications for Public Health, Risk Factors, and Reproductive Outcomes

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Abstract

Dairy goats have a high threat of Q fever, which is produced by the bacterium *Coxiella burnetii* and affects animal welfare and human health. There are different rates of Q fever in dairy goats from an epidemiological perspective, and different variables such as age, sex, and many other factors as pillars of several infections. This chapter explores clinical presentations of Q fever, especially about reproductive disorders such as abortions and stillbirths, which increase the incidence of the disease in goat herds. It also explains the symptoms of acute and chronic Q fever; while acute Q fever features symptomatic features like fluelike symptoms, fever, tiredness, severe headache, muscle and joint pains, and coughing. It also aims the redouble efforts for biosecurity and proper management regimes to minimize a variety of challenges associated with *C. burnetii* transmission. The World Health Organization (WHO) standard protocols may entail doxycycline (100 mg twice/day) and hydroxychloroquine (200 mg thrice/ day) for at least 18 months depending on clinical response and serological test results. In addition, for patients with infections in the vascular system and/ or joints, Rifampin or surgery can be added to specific therapeutic regimens. The chapter looks at several serological diagnostic methods such as IFAT, ELISA, and PCR in an evaluation of the infection rates in goats. These studies call for more Q fever studies and better knowledge of Q fever for the maintenance of goat health and reduction of zoonotic risk.

Keywords: Q Fever, Seroprevalence; *C. burnetti;* Dairy Goats; Q Fever etiology; Public health

Cite this Article as: Ibrahim NS, Mustaffa NDABN, Ahmad K, and Nauman M, 2025. Q fever seroprevalence in dairy goats: Implications for public health, risk factors, and reproductive outcomes. In: Abbas RZ, Akhtar T and Arshad J (eds), One Health in a Changing World: Climate, Disease, Policy, and Innovation. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 341-348. https://doi.org/10.47278/book.HH/2025.196

A Publication of Unique Scientific Publishers

Chapter No: 25-048

Received: 09-Jan-2025
Revised: 25-Apr-2025
Accepted: 12-May-2025

Introduction

Definition and Overview of Q Fever

An unexplained disease was reported in 1937 by Edward Holbrook Derrick who named it Q fever or Query fever after stating discovery of a disease affecting Australian butcher workers. *Coxiella burnetii* is a Gram-negative bacterium which is an obligate intracellular pathogen belonging to the family Coxiellaceae, and order Legionellales. Q fever, caused by bacteria *C burnetii,* infects a wide range of people. Information concerning the possibilities of *C. burnetii* infection is impressive: as this bacterium can infect all types of animals, aquatic and land-dwelling. According to (Miller et al., 2021), this bacterium looks a little hardy; it is resistant to decay, can stay for some time in the environment, and can spread via air.

Domestic animals are the primary reservoir of this type of infection and people are infected by breathing inside contaminated aerosols containing bacteria (Barberio, 2016). Human-to-human transmission is exceptionally rare, and cattle, sheep, goats, and other home-reared animals contribute to 80% of cases. As Q-fever is subclinical, infected animals have a stillbirth, miscarriage in the later stages of pregnancy, and other complications. Two methods are possible for the bacteria to spread within the environment: through abortions and the birth of infected newborn animals. Hence, *C. burnetii* is also shed in fecal, urine, vaginal mucus, and feces (Plummer et al., 2018).

Mastitis is not a major concern in pregnant ruminants; however, its infections raise the risk of abortions, which occur in the first partum following infection (Plummer et al., 2018). While low pregnancy order reflects frequent secondary fertility, reproductive pathologies are not usually superimposed on recurrent pregnancy. In the parturition exposed to the earlier study by Berri et al (2007), the infection was prevalent during the first parturition, but the bacterium was absent from the placenta or any of the liquid body observed during the second parturition. Therefore, current scientific data about the absence of the pathogen in subsequent parities is scarce, and nothing is known about the clinical manifestations of endemically infected goats. *C. Burnetii* still causes pneumonia in goats as well as stillbirth and poor offspring in goats. This is the case especially when diagnosing Q fever infection in goats some of the clinical symptoms are very vital. Ahmad et al. (2024) reported that 90% of the female goat a carrier of the disease hence more prevalent in them than in the male ones.

This chapter aims to identify Q fever outbreaks in livestock in public health, evaluate the risk factors for Q fever infection in dairy goat and present the effect of Q fever in dairy goat productivity.

Importance of Q Fever in livestock and public health

Q fever remains another unnoticed zoonosis in Pakistan (Ullah et al., 2022). The cause, *Coxiella burnetii*, is very resistant to heat, dryness, and most decontaminators and so is a continuing source of infection for man and animals. Since the disease is often subclinical in animals, it is not manifested until poor pregnancy rates are observed in the herd. The infection caused chronic vascular disease and serious endocarditis in humans later. The molecular epidemiology and evolution of this virus, especially in ruminants, is not well known. In this context, it will be easier to investigate links to outbreaks through analysis based on genomic information. Human morphological studies remain insufficient to explain the temperate pathogen's pathophysiology and, therefore, molecular studies are warranted. The eggs and larvae of Q fever zoonosis should be prevented through increased awareness programs and by ensuring that dairy milk is treated through pasteurization.

Clinical Signs in Humans

Tissot-Dupont et al. (2008) classified Q fever infections as acute as primary infections or chronic localized Q fever. Most patients infected acutely are incubated for 2-3 weeks, and the clinical picture of acute diseases is identical to a febrile catarrhal disease, whereas 50% of the early stages of infections are subclinical. Infections with high inflammations tend to produce photophobia and severe headaches that may be retroorbital in nature (Marrie, 2010). The other signs include wipe, fever, cold, and muscle aches. Fever sometimes lasts 1–2 weeks and may persist for an additional 1–2 weeks (Torreggiani et al., 2016). In some cases, acute Q fever might become atypical pneumonia. Also, symptoms include flulike signs, and in Q fever pneumonia it can be a relatively mild pneumonia to severe pneumonia. Furthermore, inspiratory crackles and a non-productive cough are present frequently (Miller et al., 2021).

The most common sign of chronic Q fever infections is the Valve involvement with endocarditis being the frequent clinical sign. Most valves that are normally affected by endocarditis include 60-70% of all chronic Q fever. Q fever endocarditis presents symptoms that include weakness, dullness, chills, fatigue, anorexia, low-grade fever, and progressive night sweats. Besides heart failure or valve disease, these patients may also end up having splenomegaly and hepatomegaly (Mazokopakis et al., 2010). Research has shown that with focalized infections, many patients experience valve replacements and most patients with Q fever endocarditis use cardiac valve malfunction (Fenollar et al., 2001; Tissot-Dupont et al., 2008).

Etiology and Epidemiology of Q Fever

C. burnetii is a rod-shaped pleomorphic bacterium that has a width of 0.2 to 0.4 µm and a Length of 0.4 to 1 µm with gram-negative membrane (Ebani, 2023). Regarding the classification, it falls under the order Legionellales, gamma subgroup Proteobacteria (Raoult et al., 2005). Eldin et al. (2017) revealed that the US Centers for Disease Control (CDC) ranked *C. burnetii* as a possible Class B bioterrorism pathogen because of its high infectivity and ability to survive in environmental conditions. Zamboni et al. (2002) reported that the bacteria have devised strategies for coping with the hostile intracellular environment of vacuoles through a doubling time of 20-45 hours. Q fever occurs due to *C. burnetii* whose molecular characteristics are described in Figure 1.

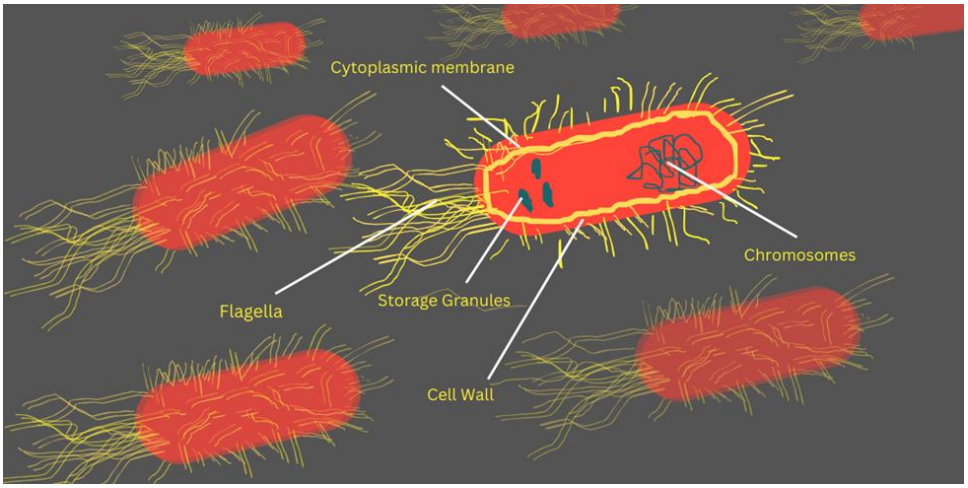

Fig. 1: *C. burnetii* bacteria causes Q fever in dairy goats.

C. burnetii replicates within the parasitophorous vacuole of eukaryotic host cells and has a doubling time of 20 to 45 hours according to Mertens and Samuel (2007). Three cellular forms, namely the large cell variant (LCV), the small cell variant (SCV), and the small dense cell (SDC) characterize the bacterium internal cycle illustrated in Figure 2 (Angelakis and Raoult, 2010).

The LCV of *C. burnetii*, is located within the parasitophorous vacuole of the host and is metabolically active. OV and LCV are larger and more pleomorphic compared with other variations and contain discrete scattered chromatin with well-outlined cytoplasmic and outer membranes that stain for LPS. If it is, this variant can multiply within host cells for several reasons; first, this choice has a higher metabolic rate second, it is weaker to external incentives. A few are slow-growing organisms that take between 20 to 45 hours to double depending on their classification (Howe & Mallavia, 2000; Barberio, 2016).

The SCV is a diminutive structure, which can exist for extended periods extracellularly and demonstrate stability in response to various stresses. That is why SCVs are more stable in unfavorable conditions owing to the small dimensions and dense nucleoid filaments (Shepherd et al., 2023). Even though they are described as latent and non-cryptogenic they attribute the ability to transform to LCVs within an optimal

intracellular environment. The SCV is an infectious agent in natural particles, which can only invade its hosts through inhalation since it is resistant to both physical and chemical barriers (Howe & Mallavia, 2000; Shepherd et al., 2023).

However, SCV and SDC have several features that are more distinguishable in their improved physical stability of the SDC. Throughout the *C. burnetii* life cycle, SDCs have been observed to form during the LCV lysis or asymmetric division procedures. One more advantage that would make these cells more resistant than infective agents is their pressure resistance. Since they protect the bacteria from harsh adverse environmental conditions, the SDCs are vital for the bacterial life cycle (Barberio, 2016; Shepherd et al., 2023).

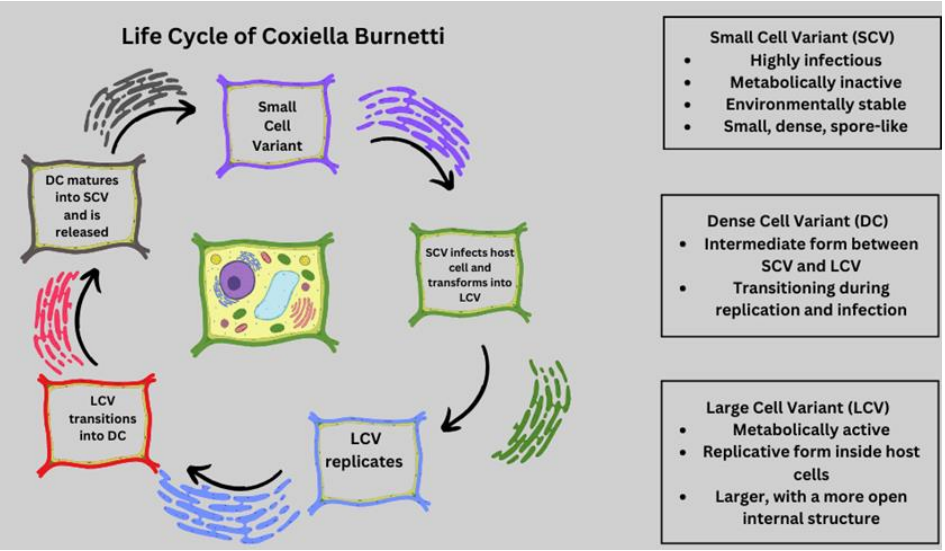

Fig. 2: Life cycle of *C. burnetii* which includes three cell types: large cell variant (LCV), small cell variant (SCV), and small dense cell (SDL).

From the results of experimental and epidemiologic investigations, it was established that the major sylvatic hosts of *C. burnetii* are the small ruminants, including goats, sheep, and cattle. Mcquiston et al. (2002) avow that dogs and cats get diseased with *C. burnetii* and spread the infection to humans. Q fever in cattle, for example, may result in stillbirth, abortions, and problems associated with delivery. Offspring born to laboratory-infected sheep are either stillborn or weak/sickly because of their pyrexia, anorexia, and tachypnea as disclosed by Barberio (2016). While Q fever can involve many forms or symptoms, Q fever most commonly presents the acute form such as hepatitis or pneumonia, and the chronic form such as endocarditis. Such conditions as non-symptomatic, non-oxidative infections are quite possible. Q fever diagnosis is made serologically, and the immunofluorescence assay is the most used method. q fever serology should be conducted in any altremosic patient and those presenting with negative blood cultures (Guirao-Arrabal et al., 2024).

The most prominent way of aerosol transmission in *C. burnetii* infection in man is through inhalation of contaminated fomites. *C. burnetii* aerosols can contaminate wool directly from the parturient fluids of sick animals; placenta; or newborn animals (Moraga-Fernández et al., 2023). The creature that is highly susceptible to death in an environment may stay alive for weeks in sites where animals were previously identified. This is the reason that *C. burnetii* has transmitted characteristics that may be aided by the wind to its dissemination (Clark & Soares, 2018).

So, Q fever may affect individuals who have not been exposed to animals for quite some time. Most likely it is ingested, presumably through drinking raw milk (Andreana et al., 2017). Despite their rarity, human Q fever cases linked with contact with an infected parturient mother have been rarely observed (in an obstetrician during an abortion).

Serological Method for Diagnosing Q Fever

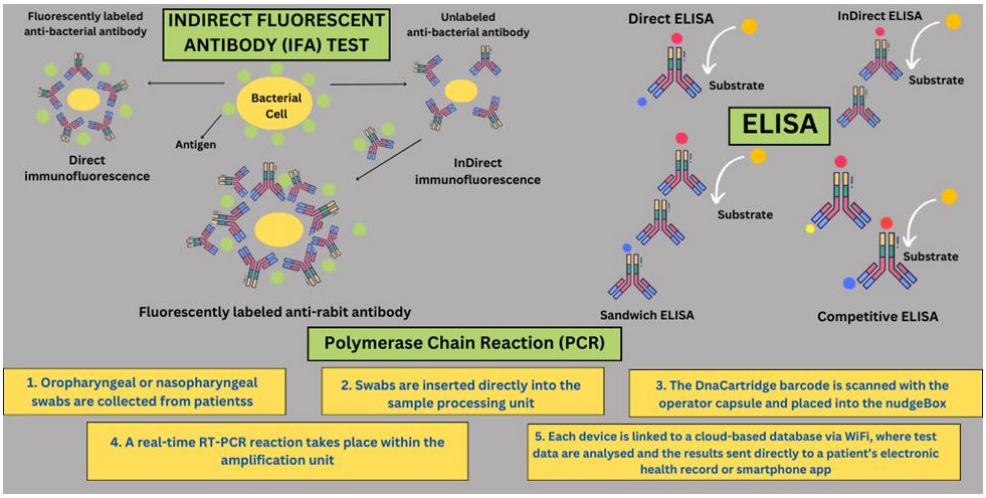

Fig. 3: Different techniques to diagnose Q fever include Indirect Fluorescent Antibody Test (IFAT), Enzyme-Linked Immunosorbent Assay (ELISA), and Polymerase Chain Reaction (PCR)

Different methods have been developed to diagnose Q fever in dairy goats including the Indirect Fluorescent Antibody Test (IFAT), Enzyme-Linked Immunosorbent Assay (ELISA), and Polymerase Chain Reaction (PCR) (figure 3).

The IFAT plays the role of the gold diagnostic method of acute Q fever. This technique involves the use of *C. burnetii* antigens to test for antibodies in two samples of sera; one collected during the acute phase of illness and another at a later phase usually when the patient is recovering, then an increase in antibodies titer is an indication of the infection. This test is significant as a positive result signifies the presence of IgG than IgM antibodies which may persist longer than the duration of infection and cause a false positive result. However, in a previous study, it was noted that IFA is a useful technique to determine the seroprevalence of Q fever in goats. Possibly, the criteria developed for the IFA test in goats may not be relevant when used in cattle. It is unfit for assessing the cattle population for disease since its possibility might be low and this implies a high risk of missed cases known as false negatives (Wood et al., 2019).

The ELISA (enzyme-linked immunosorbent assay) is a procedure that uses a plate format for the detection and quantification of peptides, proteins, antibodies, and hormones. They include (Stellfeld et al., 2020; Ahmad et al., 2024) used in the quick diagnosis and screening of other related conditions including Q fever. Several serological studies utilized ELISA from three distinct manufacturers: This includes IDEXX Q, IDvet ID Screen®, and PrioCHECK™. The IDEXX Q Fever Ab Test applies a *C. burnetii* Nine Mile phase I strain derived from ticks. By contrast, the IDvet ID Screen® Q fever Indirect Multi-species is derived from a French isolate originating from a bovine species. Meanwhile, the PrioCHECK™ Ruminant Q Fever Ab Plate Kit uses ovine antigen of phases I & II developed from the French isolate (Eibach et al., 2012; Klemmer et al., 2018; Ahmad et al., 2024).

Diagnostic tests often employ PCR methodologies like real-time PCR and conventional PCR to detect *C. burnetii* DNA. Since *C. burnetii* can now be detected specifically in biological and clinical specimens by PCR. PCR methods are applied to screen blood, serum, cerebrospinal fluid, bone marrow, aneurysms, and tissue biopsies for *C. burnetii* (Anderson et al., 2013). High specificity and sensitivity have been achieved when PCR using primers in repetitive, transposon-like elements (trans-PCR) for the detection of *C. burnetii* in several clinical samples (Boulos et al., 2004; Klaasen et al., 2014).

In Germany applying the PCR approach, the Q fever cases among agricultural workers in goat and lamb herds have been investigated. PCR of blood samples revealed slightly higher values in goats regarding the incidence of the infection. This difference might have been associated with the fact when the goat herd first got affected or could have been due to the difference in susceptibility of the goat to the illness. No differences in the PCR outcomes arising from different shedding mechanisms were statistically distinguishable (Eibach et al., 2012).

Seroprevalence Studies in Dairy Goats

Monitoring prevalence rates of infection within goat populations and identification and estimation of risk factors involved with transmission require data from seroprevalence surveys. Recent research has established that seroprevalence levels in dairy goats depend on the sex, age, and method of managing the goats.

Saanen dairy goats in Malaysia were investigated, and an overall prevalence of 7/100 positive for the antibodies was observed. As for the current investigation, 10 and 60 percent of the goats had weak positive and medium-positive titers for *C. burnetii*, respectively. Surprisingly, no samples were found to have high or extremely high positive titer, of which it can be deduced that the community was moderately infected. Based on the 91.7% of the negative results attained in the 6-month-old goats, the study clearly showed that the mature goats particularly the 5 and 6-month-old goats have remarkably higher seroprevalence levels compared to the young ones. This pattern also recalculates the way age affects a person's susceptibility to Q fever (Ahmad et al., 2024).

The objective of a study implemented in Brazil is to identify the ORF and FR of *C. burnetii* infection in a selected group of dairy goats with a history of reproductive issues, surveying 312 goats' serum samples and 23 cotyledon specimens. IgG antibodies against *C. burnetii* were evaluated by the ELISA; bacterial DNA was identified by the PCR: 55.1% of sera could be considered positive; placental extracts were positive for DNA from *C. burnetii* in 8.7 % of cases according to the data. Seroconversion was also evident for both infected animals. Altogether, these investigations are pioneering to observe an increase in the number of abortions in Brazil and goat infections with *C. burnetii*, stress the importance of adhering to it at the animal monitor, and establish that its nature is abortive in goat population in the region.

Another large seroprevalence survey identified 66·7%Agriculture of dairy goat farms in the Netherlands as being positive for *C. burnetii*. Several factors that are assessable and predictive of increased seroprevalence rates in the population were established by the study. These risk factors are having bulk milk-producing neighbors and a high density of goats neighboring other farms. The findings provided here clearly indicate that both improved environment and overall management contribute to the epidemiology of Q fever in dairy goats (Lange, 2020).

Risk Factors for Q Fever Infection in Dairy Goats

This pathogen, *C. burnetii*, threatens both humans and dairy goats because it causes Q fever. For effective control of Q fever, it is important to understand the risk factors which are always related to the disease. Four types of factors may be distinguished: There therefore exists environmental, farm level, animal level, and human-animal interactions indexes.

Q fever infection risk in dairy goats depends to an extent on factors within the farm environment. Other segments include hygiene procedures and controls, feed handling conditions, and housing environment. According to research, animal farming where no strict barriers to infection and contamination from birth locations and cleanliness are put in practice, are more prone to develop *C. burnetii* infection (Hou et al., 2022). Prenatal absence of a defined birthing place, for instance, raised the chances of seropositivity by 3.17 occasioning to studies. Further, Q fever rates were directly correlated with the probability of farms testing positive with the odds ratio at 2.53 for each order of magnitude of farms per acre. This means feed and waste management plays a vital role because contaminated feed or bedding serves as a refuge from germs.

Data about animal-level factors show that the immune system, age, and parity have great influence over an animal's health, making it easy for the animal to be infected with Q fever. One study showed that a higher prevalence was found in elderly goats compared to young goats. In line with this observation, the present study. Age was significantly related to the infection rates; infection rates in the goats aged greater

than five years were higher than those of the goats aged less than one year. This increase may be due to pregnancy-associated reactivation of latent infections in women or the lifetime exposure of the bacteria. Parity also has an impact on immunological reactions and differently positioned goats, for instance, with the first birth, can have different immunological reactions than nulliparous animals (Ahmad et al., 2024). The immunological status of some animals determines their susceptibility because stressed or immunosuppressed animals have higher susceptibility.

Close contact with animals poses a substantial risk for the transmission of Q fever. Potential disease sources include the animals themselves because those handling goats or involved in goat farming are constantly in contact with live animals that may well be diseased. The seroprevalence of the responders who identified themselves as dairy goat producers from the total number of responders was 73.5%, mentioned in the Netherlands. Some of the practices that expose people to *C. burnetii* include milking cows, cleaning stables, and handling manure. It is therefore important to avoid any contact with these animals with other livestock while performing these procedures. The use of masks and gloves is mandatory to minimize the risk of zoonotic transmission (Schimmer et al., 2012).

Prevention Strategies for Q Fever

Previously it was frequently used tetracycline, but doxycycline has taken its place due to the favorable drug kinetics profile and fewer gastrointestinal side effects. The first choice of an antibiotic for acute Q fever in adults and children eight and over is doxycycline, given in two 100 mg doses, to be taken daily for two weeks. Cox and empiricists pointed out that clarithromycin and roxithromycin, modern macrolides can provide similar clinical efficacy when administrated for Q fever pneumonia as that of doxycycline. In case of allergy or contraindication, the recommended drugs to be used instead of rifampin and cotrimoxazole are (Dupont & Raoult, 2007). However, short-course doxycycline therapy is now regarded as safe in children, except those below eight years old who should receive cotrimoxazole (800/160 twice daily), among children with rickettsia (Wormser et al., 2019).

The treatment of chronic Q fever requires at least 18 months of antimineralization therapy, with hydroxychloroquine (200 mg three times a day) and doxycycline (100 mg two times a day) (Kersh, 2013). It is recommended to perform a retinal examination at least every 6 months while hydroxychloroquine should only be taken after a glucose-6-phosphate dehydrogenase deficiency test. A decrease in anti-phase I IgG and IgA antibody titers to 1:200 or less is indicative of a clinical cure because the suggested minimum treatment time of 18 months remains inconclusive (Abramova et al., 2020). Hydroxychloroquine concentrations between 0.8 and 1.2 mg/l and doxycycline > 5 mg/l have been associated with improved response in clinical trials (Parker et al., 2006). Alternate therapy is doxycycline with ofloxacin (200 mg three times a day) for patients unwilling to take a combination of doxycycline and hydroxychloroquine for at least three years (Raoult et al., 2002).

Controlling Q fever during pregnancy is very challenging since some first-line antibiotics are ineffective or contraindicated during pregnancy, doxycycline, hydroxychloroquine, and fluoroquinolones and the only effective antibiotic is cotrimoxazole. Cotrimoxazole medical treatment does not influence chronic infection development or placental invasion; nevertheless, it presumably reduces the risk of abortion (Ford et al., 2014). In a recently published study, it was found that the patients, who received cotrimoxazole, for a more prolonged period than at least 5 weeks had a greatly reduced risk of complications to their fetuses than the patients who did not take the medicine (Carcopino et al., 2007). All pregnant women should be treated with cotrimoxazole for a longer duration than the indicated five weeks, and the mother should have serology tested after delivery. For chronic disease patterns, doxycycline and hydroxychloroquine will have to be administered to her for twelve months; breastfeeding is contraindicated during this period.

Impacts of Q Fever on Dairy Goat Health and Productivity

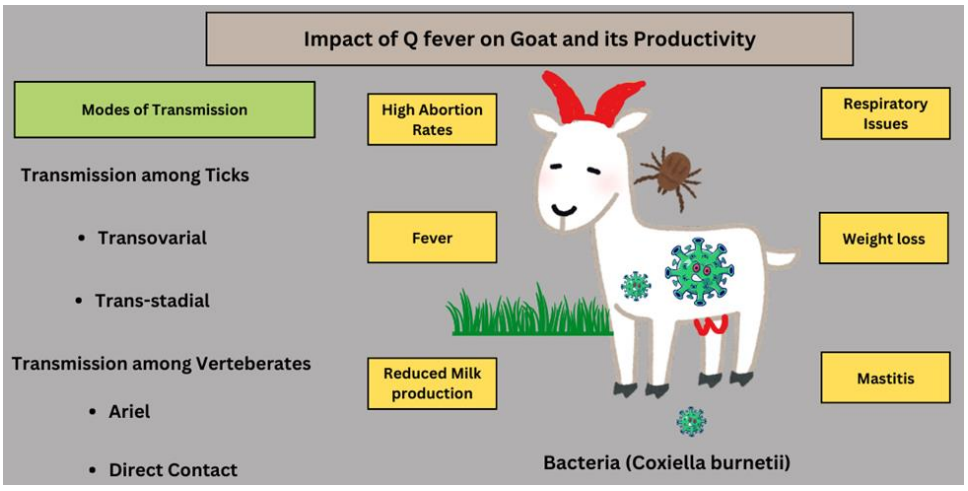

Fig. 4: The dynamics of Q fever transmission provide insight into the disease's causes and impacts on both humans and animals.

That is why *C. burnetii* bacteria causes Q fever, which poses a great threat to dairy goat health and their ability to reproduce, produce milk, and contribute to dairy farming profitability (Figure 4).

The one main compilation of Q fever in dairy goats is that it is associated with fertility problems. A condition that affects infected goats includes reduced conception rates, abortions, infertility, and the production of weaker offspring, goats. It was noted above that Q fever is the cause of up to 90% of abortions in affected populations (Raboisson et al., 2024; Zendoia Ion et al., 2024). Most of them can be found in the

reproductive tracts and may cause chronic infections that may relapse during pregnancy; the infections may lead to endometritis and placental retention. This can affect the short-term breeding cycle as demonstrated by conception rates below target, persistently high repeat breeding, and potentially long-term fertility (Bauer et al., 2021).

Q fever harms both the amount and quality of produced milk. Those animals experiencing the condition may cause a low amount of milk production, and other diseases such as metritis or mastitis may worsen the situation (Raboisson et al., 2024). The available literature shows that infection with *C. burnetii* alters the composition of milk, which may affect the quality and marketability of the milk (Shujat et al., 2024). One of the greatest challenges of globalization in terms of economic problems is when there is a decrease in milk production since that influences farm income and yields.

Apart from the acute physical impacts of Q fever, the sickness comes with severe economic repercussions. Forcing farmers to cut milk production and animal breeding are uneven in their businesses and this puts them financially backward. Like other zoonotic diseases, controlling Q fever is costly in terms of caring for affected animals, putative biosecurity measures, and potential animal casualties. The cost of reproductive disorders associated with Q fever, in terms of production, is shown in a new econometric model for dairy farmers to reflect the huge losses (Raboisson et al., 2024). Since immunization improves reproductive performance and lowers the incidence of miscarriages and other related issues, it can sustainably reduce losses in herds with moderate to high Q fever incidences (Sam et al., 2023; Raboisson et al., 2024).

Conclusion

Focusing on the factors relating to the prevalence or incidence of infection, this chapter presents an extensive review of the extensive impact of Q fever on dairy goat herds. Since the previous study found that older goats get infected more frequently, the finding suggests that the two factors, gender, and age, are predictors of the probability of getting infected with the *C. burnetii* bacteria. Since Q fever is transmitted through animals its effects are not limited to the animals themselves and may threaten the health of the community. Management practices must thus be crucial to arrest or slow down the disease's progress in goat herds and minimize the risks posed to people. Therefore, there is a need to enhance proper washing, adopt proper bio-security measures, and make the producers understand the dangers of the disease. As a result, further research is required to study specific correlations between M. E. *C. burnetii* with host animals and its molecular epidemiology. Outpatient treatment for acute and chronic Q fever is based on proper diagnosis, adherence to the course of therapy, and systematic reassessment of the patient's response to the therapy to minimize the risk of relapse. Thus, it can be concluded that raising diagnostic capabilities as well as knowledge of the interested parties can contribute to the minimization of the adverse effects of Q fever on cattle health and encourage safer approaches in the dairy production industry.

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