A systematic overview of bovine brucellosis and its implications for public health

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Abstract

Comprehensive study reveals the complex nature of bovine brucellosis, with special emphasis on its potential for transmission to humans. By adopting a systemic methodology thorough literature search was done, including publications published during 1897 to 2022, form academic databases, research repositories, and scholarly credible literature sources. The criteria for being included in this study ensured an in-depth investigation of the previous and current facets of the disease. The methodological extraction and processing of data enabled for the categorising of pertinent findings into particular groups, which enhanced the comprehension of characteristics, transmission trends, clinical aspects, diagnostic tools, treatment options, prevention strategies, vaccination, and public health concerns. This study highlights the importance of this zoonotic threat indicating the compelling need of effective solutions of this problem by keeping in view the zoonotic variables and epidemiological views. Understanding disease origins and transmission patterns help design effective control strategies that are tailored to each mode of transmission. A detailed evaluation of symptoms shows that humans and animals need appropriate diagnosis. Comprehensive treatment and preventative measures are supported by the review. The study of vaccination as a preventive measure underlines its importance in eliminating bovine brucellosis. Public health issues require knowledge, surveillance, and economic concerns. In conclusion, this comprehensive study not only explores uncharted research grounds but also serves as a beacon for researchers and policy makers. Through an in-depth analysis of the interaction between bovine brucellosis and public health, findings in this study provide crucial information that is useful to a wide range of stakeholders. This systemic review provides a clear and comprehensive perspective of the public health implication of bovine brucellosis by emphasising the need of specific interventions and preventive measures.

1. Introduction

Bovine brucellosis is a disease whose etiological agent is a bacteria. This is the most common disease in cattle and is distributed in almost every part of the world. It is the most prevalent zoonotic disease as declared by food and agriculture organisation and the world health organisation (Corbel 1997; Schelling et al. 2003; Khurana et al. 2021). It was a perception that brucellosis have been spotted in the late roman epoch. It was nominated as brucellosis because of its correspondence with an organism called as brucellae from the cheese that was carbonised (Khan and Zahoor 2018). In the catalog of zoonotic diseases associated with bacteria brucellosis is on the top of these diseases and almost 500,000 new cases are delineated yearly in the areas thought to be endemic to the disease (Olsen and Palmer 2014; Byndloss et al. 2016; Johansen et al. 2018). In Mediterranean regions, brucellosis is the most prevailing disease and in the past this disease had a common relation with military camps. Complete illumination of this disease was done by Sir. Hughes, Zammit, and David Brucein Malta (Cutler et al. 2005; Christopher 2010).

2. Materials and methods

The methodology utilised in this comprehensive article entailed a methodical and thorough investigation into the different aspects of bovine brucellosis, with a particular emphasis on comprehending its zoonotic implications and addressing crucial elements such as etiology, transmission, clinical
manipulations, diagnosis, treatment, and prevention.

2.1 Literature search

An extensive literature search was conducted across several academic databases, research repositories, and authoritative sources to find paperwork related to bovine brucellosis. Only scholarly publications that have undergone a rigorous evaluation process by experts in the field, research papers, critical evaluations of existing literature, reports on specific cases, and pertinent books published from 1897 to 2022 were taken into account for potential inclusion. The selected criteria for this inclusion was based on the thorough evaluation of the past and present aspects of the bovine brucellosis.

2.2 Selection criteria

The collated literature was themed to an insightful scrutinising process to ensure its credibility, and relevance with the basic concerns of the review paper. The scholarly assessment included studies that proposed meaningful insights into the bovine brucellosis as a zoonotic threat. These studies evaluated various facets like the potential causes, transmission cycles, clinical manifestations in both humans and cattle, diagnostic approaches, treatment, control and prevention strategies, vaccination, and public health implications.

2.3 Extraction and integration of the data

Relevant data, arguments and findings were systematically compiled from the authorised scholarly literature. The extracted data was classified according to various aspects of the brucellosis, such as its features, transmission dynamics, clinical signs, diagnostic protocols, treatment options, control programs, immunisation methods, and public health implications.

2.4 Table and figure integration

A table about the details of vaccination related to brucellosis incorporated referring an informative summary for researchers by enhancing the accessibility to information that is important for the brucellosis prevention and control. Moreover, two scientific figures emphasising the transmission pathways and pathogenesis of bovine brucellosis were also incorporated to improve the visual aspects of understanding.

2.5 Qualitative analysis of the literature

Qualitative analytical methods were used to explore signifying characteristics, and valuable considerations throughout the analysed literature. The analysis of the data was performed in relation to zoonosis, epidemiology, and public health measures. The adopted methods enabled a comprehensive analysis of the keynote aspects of bovine brucellosis and its importance as a zoonotic concern. This comprehensive review article is a sincere effort to offer a detailed and organised analysis of complex connection between bovine brucellosis and its expected concerns for mankind by insightful scholarly selection and analysis of relevant literature.

3. Zoonoses and its importance

Zoonosis is a Greek word, “zoon” means animal and the “noses” means illness. In accordance with World Health Organization (WHO) any disease or infection which can be transferred from animals to humans or from humans to animals is considered as zoonosis (WHO 2020). About 61% human pathogens are zoonotic in nature (Taylor et al. 2001). According to the etiology zoonotic diseases can be of viral origin like Acute Immuno-Deficiency Syndrome (AIDS), rabies, avian influenza, ebola; bacterial origin like anthrax, brucellosis, Lyme disease, salmonellosis, plague, tuberculosis; fungal origin like ringworm; chlamydia origin like psittacosis; parasitic origin like malaria, toxoplasmosis, trichinosis, echinococcosis, giardiasis, protozoal, and acellular non-viral diseases like mad cow disease or transmissible spongiform encephalopathies (Chomel 2014). In many cases, domestic animals play an important role in the transfer of diseases to humans. Vertebrate animals are the etiology of about 60% of human infections (Taylor et al. 2001; Klous et al. 2016). All the domestic animals including sheep, goat, dog, cat, cattle, pigs, and horses are the major reservoirs for the transmission of zoonotic pathogens to humans (Samad 2011).

4. Etiology

Brucella abortus is the causative agent of abortion in cattle and causes undulant fever (brucellosis) in humans which was brought to light by Bang (Bang et al. 1897). Bacteria from the genus brucella is the etiological agent of the most important bacterial zoonotic illness of domestic livestock and wildlife, as well as humans. Bacteria are present within the cells and they are non-motile, non-spore forming, gram-negative, and coccobacilli in shape. Different species of bacteria affect different animals as like B. melitensis causes disease in small ruminants, B. canis causes illness in dogs, B. suis is the causative agent in pigs, and B. abortus is the bacteria that mostly affects large animals (Godfroid 2002; Diaz 2013; Jamil et al. 2021).

5. Characteristics of brucella

Brucella are partially acid fast coccobacilli that are non-capsulated, non-spore-forming, gram-negative, and intracellular facultative species. Brucella are highly resistant bacteria and can bare freezing and thawing, but the disinfectants that are active against the gram-negative species can kill these bacteria as well. The brucella present in milk can be eliminated and killed by pasteurisation. This bacterium is 0.6-1.5 µ in length and 0.5-0.7 µ in diameter. Brucella are positive in urease, oxidase, and catalase tests (Fretin et al. 2005; Kiros et al. 2016). Brucella has an association with α-2 subdivision of the proteobacteria along with other species like rhizobium, agrobacterium, rhodobacter, bartonella, orchobactrum, and the rickettsia (Yanagi and Yamasato 1993; Kiros et al. 2016).

6. Transmission of disease

Transmission of brucellosis from one cattle to another can occur by direct or indirect contact with the cattle that was previously diseased or with the secretions of diseased cattle. The disease can be transferred by ingestion or through the broken skin and mucous membranes, or rarely even through the intact skin (Poester et al. 2013; Tadesse 2016). Pregnant animals carry a lot
of bacteria in their uterus and the placenta, uterine discharges as well as an aborted foetus act as a source of the disease. For newborn calves, the milk from the infected dam is the major source of the disease. This disease can also be transferred to healthy cattle during artificial insemination if the bull used for artificial insemination semen was infected and it can spread disease to many herds because of the use of Brucella infected semen or the spread can also occur by the inhalation of the bacteria. In cattle infection can also be acquired by ingestion of contaminated feed and drinking of water contaminated by the causative agent that is excessively found in the uterine discharges and birth materials (Acha and Szyfres 2003). Both vertical and horizontal routes are cause the spread of disease in humans (Meltzer et al. 2010). Laboratory and professional workers are always at risk of getting an infection especially in the regions where the disease is prevalent and it has been reported that almost 12% of laboratory staff get the infection during fieldwork (Kose et al. 2014; Tadesse 2016). Brucellosis is the most common bacterial zoonotic disease that spreads in humans via the respiratory, oral, and conjunctival routes whether by contact with infected animals or by the consumption of unpasteurised milk from the infected animal or by the utilisation of the dairy products produced from the infected milk (Crawford et al. 1990; Pappas et al. 2006). The spread of disease to humans totally depends on the severity of the disease in the animals, mostly veterinary doctors and farmers get the disease because of their profession in which they come in contact of animals frequently (Musallam et al. 2016; Proch et al. 2018). Direct contact of the human mucosa or abrasions with the aborted foetus from infected animals and their secretions may lead to the disease (Quinn et al. 2002; Fugier et al. 2007). Water contaminated with excreta, raw vegetables, and undercooked flesh from the infected animal can transmit the disease even when the bacterial load is minimal (Radostits et al. 2000).

8. Clinical findings of brucellosis in cattle

Brucellosis is an all-inclusive disease that usually causes abortion in the last trimester, stillbirth, retention of foetal membranes, and the birth of weak calves that usually die within a short time after birth. It can also lead to a decrease in the milk yield, cause a delay in calving, and mostly cause infertility in males (Celebi et al. 2007; Curro et al. 2012; Garofolo et al. 2016; Arif et al. 2017). In males, the clinical picture of brucellosis is characterised by orchitis, vesiculitis, epididymitis, and fever. Testicular abscesses and orchitis in severe cases may lead to lifetime infertility in bulls (Curro et al. 2012). In males, hygroma can also occur in chronic infections (Corbel 1997). The time period of brucellosis varies from weeks to months, and the incidence of abortion in infective herds varies from 30-80% (Kiros et al. 2016). Those calves who are born after completion of pregnancy normally die very soon mostly due to interstitial pneumonia or fibrinous pleuritis and these conditions also appear in aborted foetuses as well (Neta et al. 2010). In cattle, suffering from brucellosis, the problem of cervical bursitis is also not uncommon (de Macedo et al. 2019).

9. Clinical picture of brucellosis in humans

Clinical signs of brucellosis present in humans include depression, weight loss, nervousness, sexual impotence, fatigue, chills, insomnia, night sweats, uneasiness, joint pain, constipation, loss of appetite, and fever (Koshi et al. 1971; Mousa et al. 1987; Acha and Szyfres 2003; Kochar et al. 2007; Mantur et al. 2007). Intermittent fever is common in patients with brucellosis of acute and chronic type while undulant fever is common in patients with subacute brucellosis (Khan and Zahoor 2018). Unexpected termination of pregnancy during the first and second trimester takes place in pregnant women (Kurdoglu et al. 2015; Vilchez et al. 2015; Yang et al. 2018).
Infection in newborn babies can be transferred from breastfeeding if the mother is infected (Al-Eissa 1990; Palanduz et al. 2000; Tikare et al. 2008). Neuro-brucellosis is common in humans along with the reproductive type in which patients show clinical manifestations like meningitis, myelitis, peripheral neuropathies, stroke, radiculitis, encephalitis, and neuropsychiatric features.

10. Diagnosis

For the diagnosis of brucellosis, laboratory testing is necessary because it is difficult to properly diagnose the disease merely based on the clinical signs which are non-specific and sometimes atypical in nature. The methodology used for diagnostic testing depends upon the goals of testing for example diagnosis for confirmation of disease, National screening program, diagnosis for certification and international trade, and for surveillance of the disease in a country where it has been eradicated (Godfroid et al. 2010). The diagnosis of the brucellosis is mainly divided into two categories. The first one includes the tests for the detection of the disease causing agent, for example different staining methods, culture methods, and Polymerase Chain Reaction (PCR). The second category includes the tests used for the detection of immune response i.e. Rose Bengal test (RBT), Complement Fixation test (CFT), Enzyme Linked Immunosorbent Assay (ELISA), Serum Agglutination test (SAT), Bulk milk tests, and milk ring tests. Tests involving detection of the agent are also called direct tests while tests involving detection of immune response are called indirect tests. Indirect tests may be in vitro like test on blood and milk or in vivo like allergic tests (Le Flèche et al. 2006). Direct diagnosis includes staining, culture, and bio typing and molecular methods of identification using PCR based techniques (Godfroid et al. 2010). Staining is non-specific in nature but more often used in aborted material analysis. Identification of Brucella species from the culture depends upon the morphological structure and staining results. Metabolic profile is also checked for identification (Corbel and Banai 2005). Agglutination tests with antibodies are used for the bio typing of Brucella species. In molecular methods the best authenticity of the test is by identifying the specific sequences of genes (Baddour and Alkhalfia 2008). PCR techniques for brucellosis have less diagnostic sensitivity and more specificity (near to 100%) (Bricker 2002; Marianelli et al. 2008). Surety of diagnosis is only by the DNA detection of Brucella species through PCR or by isolating the Brucella species (Whatmore 2009). If PCR and culture techniques are combined, best results can be obtained (Leyla et al. 2003). The indirect diagnosis of brucellosis includes three main categories. First category is serological testing like SAT, CFT, Brucella Agglutination Test (BAT), Indirect Enzyme Linked Immunosorbent Assay (iELISA), Competitive Enzyme Linked Immunosorbent Assay (cELISA) and Fluorescence Polarisation Assay (FPA). The second category is of milk tests which includes Milk Ring Test (MRT), FPA and iELISA. The third category is of cellular tests e.g. skin tests (Cloeckaert et al. 1995; Foster et al. 2007). The serological tests detect the Brucella species except B. ovis and B. canis (Foster et al. 2007). The detection of agglutinins mainly of IgM type is the principle of SAT (Slow agglutination test). It is no longer recommended in bovines but in case of human brucellosis it is mostly used (Alton et al. 1988). Rapid agglutination tests include Rose Bengal (RB) and buffered plate agglutination tests. The simplicity and sensitivity of these tests is more than SAT (Greiner et al. 2009). Office International des Epizooties (OIE) recommends ELISA and CFT (Complement fixation test) as prescribed trade tests. The detection of anti-brucella antibodies can be performed by CFT. The test is less sensitive and more specific due to which it is being replaced by ELISA (McGiven et al. 2003). ELISA tests which detect IgG antibodies of its subclasses are of two types - indirect ELISA (iELISA) and competitive ELISA (cELISA) (Saegerman et al. 2004). The main quality of iELISA is its high sensitivity but it shows certain non-specific reactions. So cELISA was developed having higher specificity (Nielsen et al. 1995; Weynants et al. 1996). The tests that are recommended to be used in control and eradication of the disease but not in the diagnosis for trading purpose by OIE are milk tests. In the milk ring test Brucella whole cell antigens having specific colour are mixed with milk. If animal is infected the presence of anti-Brucella antibodies will form a complex with antigens and appear as a purple ring on the surface of milk .This test is very cheap and is used in case of cow milk only. Fluorescence polarisation assay (FPA) and ELISA tests can also be performed on milk. But in case of serum they are more sensitive than milk (Nielsen and Gall 2001; Nielsen 2002). These two are mostly used for cattle and small ruminants as recommended by the OIE. The other test used for diagnosis of brucellosis is skin test. This is allergic type of test in which inoculation of the protein extract of Brucella spp is done and specific immune response is detected by measuring the thickness of skin at the injection site pre and post inoculation. This test is much specific but sensitivity is less and this test cannot differentiate weather the animal is infected or vaccinated (Weynants et al. 1996).

11. Treatment

Brucella is an intracellular bacterium and is well adapted to the environment and survives within the macrophages, so usually, antibiotic treatment in domestic animals is less successful (Farid et al. 1961; Seleem et al. 2008). The mingling of different antibiotics is more effective than a single treatment or drug as it minimises the chances of reoccurrence of the disease (Ranjbar et al. 2020). A combination of doxycycline and streptomycin is thought to be the best regime for the therapy of brucellosis (Seleem et al. 2009). A combination of doxycycline with rifampicin for six weeks with streptomycin for 2-3 weeks is also effective for the treatment of brucellosis. Another clinical intervention is the use of doxycycline for 6 weeks with gentamicin (5mg/kg) for 1 week parentally which is also thought to be the best practice (Ariza et al. 2007).

12. Control and prevention

The purpose of the inspection and control programs is to minimise the infected animals, so that the risk of zoonosis is also reduced and public health issue resolved. The control programs shall include the measures such as identification of the disease in infected herds, stopping the spread of disease to non-infected animals, eliminating the reservoir of the disease in
order to control the spread to susceptible animals, and ensuring the non-reoccurrence of the disease (Gwida et al. 2010). The movement of animals in disease-free areas can be the source of disease transfer. Only certified brucellosis-free areas should be allowed to export animals. Animal products can also be transported nationally or internationally with respect to the principles of the international zoo sanitary code of OIE.

13. Vaccination

*B. abortus* S19 vaccine in cattle and *Brucella melitensis* Rev.1 or Strain H38 vaccine in small ruminants have been used for about six decades to prevent the economic losses as a result of abortion and sterility (Blasco 1997; Moriyon et al. 2004; Avila et al. 2013). During past years another strain of *B. abortus* has been used to immunise the cattle of all age groups by using strain RB51 (Schurig et al. 1991). Another benefit of vaccination with RB51 strain is that it is not detected during serological surveillance tests while other strains give seropositive results making it difficult to differentiate between an infected and vaccinated animal (Stevens et al. 1994). Although the efficiency of RB51 strain vaccine in cattle is still under question, it doesn’t provide protection in small ruminants at all (Crawford et al. 1990). In case of humans and wildlife still no vaccination is available (Godfroid et al. 2005; Perkins et al. 2010).

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<td><strong>Vaccines</strong></td>
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14. Public health Implications

Brucellosis being an established zoonosis have important public health implications and is quite common in developing countries (Diaz 2013). Although human brucellosis is not contagious (Fosgate et al. 2002) the brucellosis agent may be transferred to human beings via occupational contact e.g. farmers, veterinarians, and personal working in meat packing plants or slaughter houses (Robson et al. 1993). Consuming unpasteurised milk and milk products of dairy animals may be a major route of this disease transmission (Almuneef et al. 2004), under cooked meat of brucellosis infected animal, eating meat of aborted foetus, detaching umbilical cord of newborn with your teeth, or while taking the skin off of stillborn calves, kids or lambs are also key routes of disease transmission (Awad 1998). Entry of bacteria via respiratory route can also occur through aerosol or dust contaminated with the causative agent (Godfroid et al. 2005). Brucellosis vaccines used for animals are live attenuated and have a residual virulence in human beings if these vaccines are not handled carefully (CDC 1998; Banai et al. 2002). As brucellosis is a public health concern so different control and disease eradicating methods are implemented to control the disease in animal host and to avoid transfer to human beings (Crawford et al. 1990). For this purpose vaccination in animals is the primary measure. In cattle immunisation is with *B. abortus* RB51 and B19 strains while in sheep and goat *B. melitensis* Rev.1 strain is used (CDC 1998; Banai et al. 2002). Besides vaccination other methods to control the disease like testing and slaughter of positive animals or depopulation of the whole herd are also used to eradicate animal brucellosis (Crawford et al. 1990; Corbel 1997). The incidence of human brucellosis is associated with the prevalence of disease in cattle in the vicinity; vaccination of young female cattle is a good disease control practice, along with increased public awareness about the routes of transmission of the disease (Weidmann 1991; Tulu 2022).

15. Discussion

The exploration of bovine brucellosis in this comprehensive review centered on the unveiling of complicated magnitudes of this zoonotic threat, having emphasis on core aspects such as etiology, clinical manifestations, transmission, diagnosis, treatment, and prevention. The dynamic methodology adopted in the scientific literature search provided a systematic analysis with extraordinary clinical understanding of the disease’s implications as a zoonotic threat.

15.1 Zoonotic threat and public health significance

Bovine brucellosis underscores its relevance in the broader context of public health as a potent zoonotic disease. This study demonstrates that brucellosis as a significant threat to both animals and humans. The link between zoonotic factors and epidemiological perspectives signifies the importance of comprehensive strategies for disease control and prevention as the need of time (Weidmann 1991; Tulu 2022).

15.2 Etiological insights and transmission dynamics

The analysis about the etiology of bovine brucellosis revealed the significant aspects about the characteristics of brucella through review of the literature and demonstrates the diverse modes of transmission, emphasising the complex connection between cattle and humans (Fretin et al. 2005; Meltzer et al. 2010; Musallam et al. 2016). Clear understanding of the epidemiological factors contributing to the prevalence of the disease is crucial for proposing effective control measures and strategies (Jamil et al. 2021; Tulu 2022).

15.3 Clinical manifestations and diagnosis

The clinical signs of bovine brucellosis in cattle and the subsequent manifestation of the disease in humans are crucial points of discussion in this review article. Analysing the clinical picture in both humans and animals is essential for effective and in time diagnosis of the disease (Garofolo et al. 2016; Arif et al. 2017; Yang et al. 2018). Authentic analysis emphasises the importance of accurate diagnostic methods for the differential diagnosis of bovine brucellosis (Godfroid et al. 2010).

15.4 Treatment strategies and control measures

The review article crucially examines various treatment options...
and control measures used to manage bovine brucellosis (Ariza et al. 2007; Seleem et al. 2009). The hurdles related to therapeutic options in both cattle and humans are recognised, emphasising the need for comprehensive control and prevention approaches are highlighted to mitigate the risk of disease prevalence (Gwida et al. 2010).

15.5 Vaccination as an effective prophylactic measure

A particular portion is devoted to exploration of vaccination strategies as a prophylactic intervention against bovine brucellosis. The incorporated table presents an in-depth summary of available vaccines. The discussion highlights the vital role of vaccination in mitigation and eradication of the disease both in humans and animals (Moriyon et al. 2004; Perkins et al. 2010).

15.6 Public health implications

The article explores the impacts of bovine brucellosis on public health, particularly the need of public awareness, disease surveillance, and effective methods of communication (Fosgate et al. 2002). The review also underscores the prospective economic impacts of brucellosis on farming practices along with the significance of public initiatives in minimising these effects.

15.7 Future perspectives

The comprehensive analysis of the scholarly literature presented in this review sets the stage for future research initiatives by highlighting gaps in knowledge and potential areas for further investigation, providing a roadmap for researchers and public health policymakers to address the emerging concerns associated with bovine brucellosis.

16. Conclusions

To conclude, this extensive study has illuminated bovine brucellosis' complex nature, human transmission, and various elements. The careful literature search and data synthesis have provided a complete picture of the disease, from its history to its contemporary challenges. The talk emphasises the importance of rigorous and all-encompassing procedures for bovine brucellosis, which can spread from animals to humans. This study suggests a proactive approach to controlling and preventing the issue due to a complex understanding of causes, spread patterns, and symptoms. Due to the disease's clinical complexity and multiple transmission pathways, precise diagnostic methods are needed. These strategies emphasise the importance of diagnostics. This review suggests comprehensive control measures, such as vaccination which helps prevent and eliminate bovine brucellosis with a hope to control its prevalence to humans. Bovine brucellosis' public health effects emphasise the need for enhanced awareness, surveillance, and economic considerations. Prospective perspectives identify avenues for continued research and policymaking, helping us understand and control this zoonotic threat. This comprehensive study on bovine brucellosis offers academics, practitioners, and policymakers' valuable information.

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