Review/Derleme

Iğdır Üniversitesi Tarım Bilimleri Dergisi

Agro-Science Journal of Iğdır University

List of contents accessible via DergiPark

e-ISSN: 3023-7017 **Volume:** 2 **Issue:** 1 **Year:** 2024

Babesiosis As a Potential Hazard in Animal Production and Its Global Emerging Zoonotic Threat for One Health

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Keywords:
Babesia
Hemolysis
Zoonotic
One Health

ABSTRACT

Babesiosis is a lethal illness spread by ticks that affects both humans and animals globally. The livestock industry is severely impacted and is experiencing severe financial losses. The common species that cause babesiosis in cattle are Babesia B. bovis and B. bigemina. Rhipicephalus (Boophilus) species are the primary vectors for B. bovis and B. bigemina. The two main mechanisms that Babesia species use to cause acute illness are circulatory disruption and hemolysis. Animals with the infection experience an increase in body temperature, anorexia, trouble breathing, weakness, anemia, and jaundice. The complicated link between the causal agent, host, and vector has made the development of a vaccine for bovine babesiosis difficult because the condition is transmitted by ticks. Another recent problem that needs to be addressed is human babesiosis. In numerous regions of the world, zoonotic babesiosis represents a significant health danger. Due to its development, it is imperative that effective control measures be put in place to stop it from spreading over this area. This study demonstrates the sharp rise in the disease's prevalence around the globe and the urgent necessity for developing efficient plans and early detection techniques. This review also examines zoonotic Babesia species and provides a thorough overview of those species that have been linked to both animal and human infections. There have been 11 investigations that have found zoonotic Babesia species in animals, while 16 have found them in people. To ensure one health approach, this ailment must be effectively controlled.

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Received: 30/05/2024 **Accepted:** 23/06/2024 **Published:** 30/06/2024

How to cite:
Ijaz, S., Ghazali, M.H., Faraz, A., Ishaq, H.M., Hussain, S.M., Saleem, F., Tariq, S., Irshad, N., Tahira, S., Jamil, S., Khan, R., Sharif, A., Akram, A., Liaqat, C., Fayyaz, K., (2024). **Babesiosis As a Potential Hazard in Animal Production and Its Global Emerging Zoonotic Threat for One Health**. *Agro-Science Journal of Iğdır University*, 2(1), 110-118.

INTRODUCTION

Babesiosis is a widespread disease that poses significant public health implications and affects a variety of mammalian species (Bock, Jackson, De Vos, & Jorgensen, 2004; Waked & Krause, 2022), and it has also had a significant negative economic impact on the cattle sector due to the occurrence of the two most significant babesiosis species in cattle, B. bovis and B. bigemina (Zintl et al., 2014). Babesia, a genus of intra-erythrocytic parasites, are the culprits behind this ailment (Bajer et al., 2022; Hunfeld, Hildebrandt, & Gray, 2008). According to (Jacob et al., 2020; Sahinduran, 2012), they are apicomplexan protozoan parasites from the family Babesiadae and suborder Piroplasmida. Piroplasmosis, Texas cattle fever, Red-water, and Nantucket Tick fever are additional names for the illness that are used internationally (Ozubek et al., 2020; Sahinduran, 2012). After trypanosomiasis, it is the second most prevalent blood-borne parasite disease (Hamsho, Tesfamarym, Megersa, & Megersa, 2015). The movement of animals and the habitat of ticks in various locations both affect disease transmission. B. divergens is another typical species that is frequently seen in cattle. According to (Bock et al., 2004), the three most significant and well-studied species that have an impact on the cattle sector are B. bovis, B. bigemina, and B. divergens.

According to a different study, B. mymensingh, a new species of Babesia that can induce clinical illness in cattle, has been found. The species B. major, B. ovata, B. occultans, and B. jakimovi can also infect cattle. These Babesia species-specific strains all require ticks as their vectors and ideal environmental circumstances in order to spread. According to (Fakhar et al., 2012), B. ovis and B. motasi are known to be pathogenic pathogens in sheep and goats, respectively. These species infect nearly every type of mammal, and as a result of zoonotic infections, they eventually spread to humans (Waked & Krause, 2022). In many regions of the world, zoonotic babesiosis is largely brought on by three species: B. divergens, B. microti, and B. venatorum (Homer, Aguilar-Delfin, Telford III, Krause, & Persing, 2000). While B. microti primarily spreads through rodents in North America and Asia (Control & Prevention, 2012), Babesia divergens originated from cattle and has been documented in cases of human babesiosis in Europe (Gray, Zintl, Hildebrandt, Hunfeld, & Weiss, 2010). Babesia venatorum is widespread throughout the world and frequently originates in Europe (Control & Prevention, 2012). The principal carriers of babesiosis are ticks from the genus Ixodes, and the geographic distribution of these ticks affects the prevalence of the pathogens implicated (Young et al., 2019).

Babesiosis Zoonotic Incidence and Clinical manifestations

Babesiosis can affect both wild and domesticated animals, and its severity varies depending on a number of variables. The immunological health of the animal, the infectious dose, the virulence of the strain, and the degree of tick infestation all affect how severe a *B. divergens* infection in cattle will be (Purnell, Brocklesby, Kitchenham, & Young, 1976). The ticks that carry zoonotic Babesia species during their intricate life cycles, spreading these diseases either mother to offspring via infectious egg or by vector, are known to infect a variety of mammals and a few avian species as hosts. The reservoirs for B. divergens, B. venatorum are cattle, roe deer, and other ruminants, while the reservoirs for B. are white-footed mice, cottontail rabbits, and other small mammals (Silaghi et al., 2012).

Bovine babesiosis poses the greatest financial risk to the livestock sector, endangering 500 million cattle globally (Onoja et al., 2013). The illness has the worst consequences on the cattle industry because it kills allinfected animals having low immunity since it affects adult animals at the point of production rather than young animals (Onoja et al., 2013). Due to its high mortality rate, particularly among dairy cattle imported from Babesia-free regions e.g Ireland, this disease also makes it difficult to raise the production of local animals (Zintl et al., 2014). As it is blood parasite and host-specific illness, is common in tropical nations of the world and is characterized by anemia, hemoglobinuria, progressive weakness, jaundice, mortality, particularly in large ruminants. Anal sphincter spasms caused by B. divergens infection may allow feces from pipe stems to flow through. In endemic locations, the frequency of clinical cases is quite low due to repeated exposure to infections, and the immune-deficient animals that have recently been brought or who have not had early exposure to pasture are typically the ones who are harmed (Zintl et al., 2014). A recent meta-analysis and comprehensive review on the occurrence of bovine babesiosis worldwide was conducted by Jacob et al. (2020), which comprised a total of 163 pertinent papers from 63 different countries with a total of 81099 samples. The results of a continent-by-continent research showed that South America (64% of cases) had the maximum occurrence of bovine babesiosis. However, the prevalence was 61% in Australia, 52% in North America, 27% in Africa, 22% in Europe, and the lowest was 19% in Asia as shown in figure 1. The research of the years 2016 to 2019 revealed a growth in the prevalence of bovine babesiosis (25%) that should act as a red flag for the future health of the cow herd (Jacob et al., 2020). Based on the Babesia species, (Jacob et al., 2020) also performed subgroup analysis for estimating the occurrence of individual species and discovered that B. bigemina had the highest prevalence, which was 22%, followed by B. bovis with 20%, B. occultans with 16%, B. major with 15%, and B. divergens with the lowest prevalence, which was 12%.

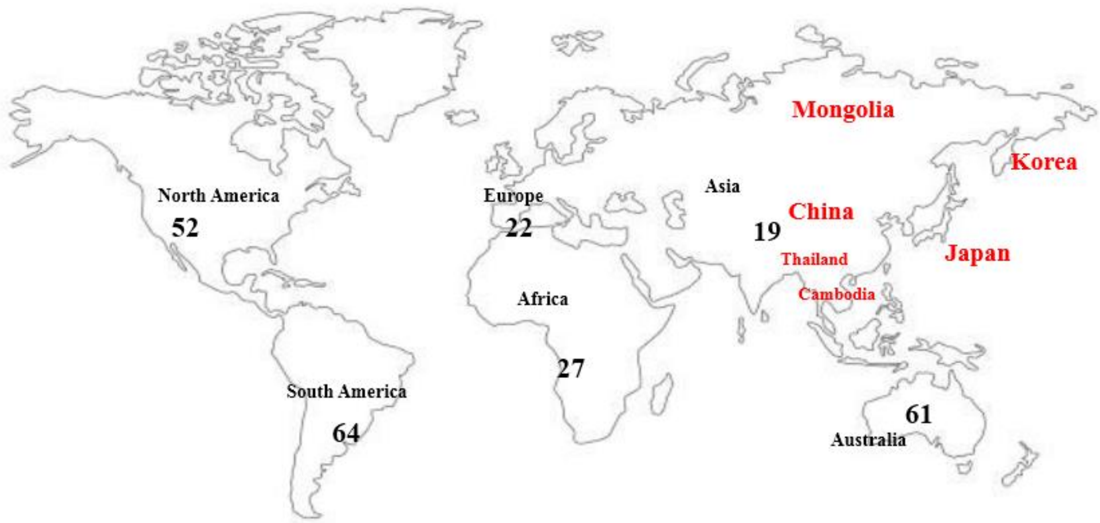

Figure 1. Screening geographical prevalence of babesiosis in animal and human populations. Countries marked with red showing zoonotic babesiosis occurrence (Rar et al., 2016) whereas in black displaying bovine babesiosis incidence (Jacob et al., 2020).

It is transmitted to humans through infected tick bites (Piesman & Spielman, 1980), but it can also be transferred between mothers during pregnancy (Asante et al., 2013) and through blood transfusions (Nzenze et al., 2013). It shows symptoms include headache, exhaustion, appetite loss, temperature. The elderly is more vulnerable to developing severe symptoms like enlargement of liver, loss of kidney function, hemolytic anemia, enlargement of spleen, and splenic complications, which can be fatal (Sanchez, Vannier, Wormser, & Hu, 2016). Acute babesiosis's splenic consequence is interestingly unrelated to the host immune system or the rise in parasitemia, unlike other serious complications. Blood smear examination is frequently employed as an identifying implementation (Dumic et al., 2020; Krause et al., 2003).

Babesiosis is consequently spreading zoonotically in Asia, which is made worse by a dearth of molecular identifying tools, clinical applicable testing skills, inadequate medical knowledge, and low throughput capacity to identify the pathogens at fault (Zhou et al., 2014). Human babesiosis is under-represented in Asia due to its low incidence, and its existence in this continent has not been adequately explored. However, it is understood that specific Babesia species are to blame for babesiosis spreading throughout Asia. For instance, Babesia microti and *Babesia sp*. KO1 appear to be the main disease-spreading agents in Japan (Tsuji et al., 2001), Korea (Kim et al., 2007), Taiwan (Shih, Liu, Chung, Ong, & Wang, 1997), and Mainland China, respectively. B. venatorum and Babesia sp. XXB/Hang Zhou have also been identified as potential disease-causing agents (Zhou et al., 2013). Additionally, it was noted that rodents and the ticks that live on them are important sources of Babesia spp. throughout Asia, including B. microti and B. microti-like as shown in figure 1(Rar et al., 2016). There is a dearth of data on the real occurrence and frequency of zoonotic babesiosis throughout world especially in Asia, as well as its species distribution and reservoir diversity.

Epidemiology of babesiosis

Victor Babes, who detected illness outbreaks with the typical characteristics of hemoglobinuria in cattle in Romania in 1888, is credited with being the first person historically to detect Babesia and Theileria in bovine blood. Following Victors' finding, Smith and Kilborne in 1893 discovered that Rhipicephalus annulatus was the vector for transferring B. bigemina (Smith & Kilborne, 1893). (Agoulon et al., 2012) confirmed and published the first case of human babesiosis in 1956, demonstrating the zoonotic significance of bovine babesiosis and the role of B. divergens as the causative agent.

Bovine babesiosis is more common in subtropical and tropical regions and can be found where tick vectors are abundant (Esmaeilnejad et al., 2015). Tick populations significantly increase during hot weather or the summer months as a result of temperature rise (Mohamed & Ebied, 2014)epidemiology of B. divergens in Europe has changed significantly during the past several years, with considerable declines in illness incidence in Norway (Hasle et al., 2010), Ireland (Zintl et al., 2014)and Hungary (Hornok, Edelhofer, Szotáczky, & Hajtós, 2006). Significant populations of *B. bovis* and *B. bigemina* can be found in Asia, Africa, Central and South America, Southern Europe, and Austria. The occurrence of Babesia species across the globe is shown in Table 1.

Table 1. Geographical distribution of Babesia species.

Babesia spp.	Affected spp.	Major tick vector	Global distribution	References
Babesia major	Cattle	*Haemaphysalis punctate*	Asia, Africa, Europe, and Northwest Africa	(L'Hostis & Seegers, 2002; Zintl et al., 2014)
Babesia divergens	Cattle	*Ixodes persulcatus and Ixodes ricinus*	Great Britain, Northwest Europe, Spain, Ireland	(Edelhofer, Müller, Schuh, Obritzhauser, & Kanout, 2004)
Babesia bovis	Buffalo and Cattle	*Boophilus annulatus, Boophilus microplus, and Boophilus geigyi*	Asia, Australia, Southern Europe, Central and South America, Africa but it is less prevalent in Africa	(Silva et al., 2009)
Babesia bigemina	Buffalo and Cattle	*Boophilus geigyi, Boophilus microplus, Boophilus decoloratus, and Boophilus annulatus*	Africa, Asia, Central and South America, Australia, and Southern Europe	Altay et al. 2008

For human babesiosis, more than 100 individuals from different areas in China have tested positive for B. microti. In 2011, in Zhejiang province, Babesia microti was identified for the first time in the Chinese population. This was verified using PCR (Yao et al., 2012). Babesia crassalike has also been linked to human babesiosis in China, where it was initially discovered in 2015. Since then, evidence from a sample size of 1125 participants with tick bite histories suggests that it is a novel Babesia species that caused 58 instances of babesiosis in Heilongjiang between 2015 and 2016 (Jia et al., 2018). The human population in China is also infected by Babesia venatorum, which is a common parasite. 48 positive cases of this species were identified from a sample of 2912 people who had a history of tick bites in a research conducted in the province of Heilongjiang, according to that study's findings (Jiang et al., 2015). According to PCR amplification and sequencing results, B. divergens, a different species that has only been described in two instances from the Shandong area, seems to be less frequently linked to Chinese human babesiosis infection (Qi et al., 2011). Babesia sp. XXB/Hangzhou, a different unique species of Babesia that can cause human babesiosis, was also identified in China in 2015, albeit only in one instance in a 42-year-old man in Hangzhou, Zhejiang province (S.-Q. Man et al., 2016). The assessment of zoonotic babesiosis in Korea discovered that small mammals and wild mammals that had been rescued from the area had tested positive for B. microti, which was verified using PCR in two studies with a prevalence of 2.1% and 5.7%, respectively (Table 2). Four investigations in Japan have identified zoonotic Babesia species from animals, with the findings confirmed by PCR. A total of three studies found that B. microti was present in wild rats, with prevalence rates of 13.4%, 45.2%, and 14.6%, respectively. *B. divergens*, another significant zoonotic Babesia species, was discovered in Japan's wild sika deer, with a prevalence of 6.6%. In Japan, there was just one case of PCR-confirmed human babesiosis where patient received around 2 liters of blood via transfusion after being taken to the hospital for a gastrointestinal issue and bleeding. The gastrointestinal ulcer was healed after one month, however the patient also had anemia and black urine. Following the discovery of Babesia-like intraerythrocytic parasites on a blood smear stained with Giemsa, *B. microti* was subsequently identified using IFA and PCR (Wei et al., 2001). With a prevalence of 5.3%, *Babesia microti* has been found in wild rats and has been recorded in Cambodia, Laos, and Thailand. 7% of 100 asymptomatic farmers in the Mongolian province of Selenge who underwent screening for the B. microti pathogen were found to have antibodies to the pathogen, and 3% of them had detected B. microti DNA in their blood.

Table 2. Some recent Zoonotic cases of Babesia.

Year of Study	Country	Method of Identification	Host	Species	Prevalence %	Reference
2008–2009	Korea	PCR/Seq	Rescued wild Animals	*B. microti*	5.7	(Hong et al., 2017)
2008–2009	Cambodia, Laos, Thailand	Nested PCR	Wild rodents	*B. microti*	5.3	(Karnchanabanthoeng, Morand, Jittapalapong, & Carcy, 2018)
2009–2011	China	PCR/Seq	Small mammals	*B. microti*	2.4	(Gao et al., 2017)
2012–2018	Japan	PCR	Wild Sika deer	*B. divergens*	6.6	(Zamoto-Niikura et al., 2020)

Prevention Measures

The spread of tick vectors and their rising prevalence in favorable circumstances make it difficult for the dairy and cattle industries and one health approach to control babesiosis. It can be prevented and controlled using three major strategies: immunization, restrict the vector, and chemoprophylaxis. (Y. Man et al., 2022) To attain and preserve enzootic stability, appropriate integration of these three techniques is crucial. In order to treat iron insufficiency, oral supplementation is also a viable option (Y. Man et al., 2022). Globally, it is also common practice to use acaricidal medications on a regular basis to eradicate tick habitats from farms. A way forward to manage the virus is to maintain biosecurity measures with good hygiene and to regularly immunize susceptible herds (Asrar et al., 2022). However, in order to safeguard the existing herd,vaccination has been reccomendedstringent quarantine is used for freshly purchased animals that are imported from locations where ticks are prevalentalso recommend the use of live attenuated vaccinations in all uninfected animals. (Jackson, Waldron, Weier, Nicoll, & Cooke, 2001).

Future Strategies

To minimize the financial losses resulting from that disease, there are a lot of gaps in the research and use of tick-control measures that need to be filled. Babesiosis prevention does not currently have a sub-unit vaccination, thus this is a possible topic that has to be covered in future research. Another area of interest would be the application o techniques to the identification of structural protein variations in *Babesia spp.*, genetically modified parasitic organisms grown in a lab environment can produce potential vaccine candidates. Another plan for the management of this illness is the creation of subunit vaccines made up of multiple antigens from sexual and asexual life stages of Babesia spp. Additional investigation is needed to understand the various *reservoirs* that could be involved in the growth of the tick population. In order to reduce the use of animals and humans for researching the impacts of pathogenic Babesia species, artificial feeding mechanisms for ticks should be created (Hatta, 2020; Vimonish et al., 2020). The development of effective vaccines against tick populations may also be facilitated by the use of nanoparticle technologies (de la Fuente, Estrada-Peña, & Contreras, 2020).

CONCLUSION

China and Korea have conducted a thorough search and discovered that the maximum number of zoonotic species of babesiosis in animals and human case reports, with *B. microti* and *B. divergens* appearing to be the most prevalent zoonotic species circulating in Asia. Rodents and other wild mammals were the most frequent zoonotic hosts found.in Asia where these zoonotic species are occurring, guiding management actions of stopping the spread of illness., The primary developing health concern is the spread of the disease, which is transmitted by a vector to several hosts before spreading among people. To effectively manage and prevent this disease, this public health perspective must be considered, especially for people under the one health concept.

AUTHOR'S CONTRIBUTION

Sara Ijaz and Muhammad Hussain Ghazali planned research and wrote paper, Asim Faraz revised the manuscript, Farena Khan, Sehrish Tariq, Nida Irshad and Sitwat Tahira helped in writeup and research, Shama Jamil, Raheel Khan and Ayesha Sharif helped in write-up.

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