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Hemoparasites Co-infections in Bovines in the Tropics

AUTHORS DETAIL

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INTRODUCTION

Tropical regions of the world are located between Tropic of Capricorn and Tropic of Cancer, among the territories of more than one hundred countries from America, Europe, Asia, Africa and Oceania (Fig. 1). Tropical regions represent only a 7% of terrestrial surface, but biological diversity found in these regions is the richest of all climates, containing more than 50% of world's species (Beck 2019). However, the optimal conditions for bovines also serve as the best conditions for a number of parasites and other microorganisms that have been adapting and evolving since hundreds of years ago (Rosenberg and Zilber-Rosenberg 2011; Cavicchioli et al. 2019).

Livestock production around the world is one of the most important source of food for world population, given the fact that bovines may be used for meat, milk or double purpose production in the developing countries located in tropical regions. Approximately 453 million bovines are just in the Sub-Saharan Africa and South Asia (Oosting et al. 2014). Meanwhile, according to FAO (http://www.fao.org/faostat/en/?#data/), tropical regions have provided more than 31 thousand million tonnes of world cattle meat and milk production in the last five years (Beck 2019).

At the same time, the economic effects of infectious diseases affecting livestock producers quality due to the losses by detriment in weight gain, daily milk production, reproductive capability, diagnosis and treatment expenses, and mortality. Unfortunately, very limited studies conducted yet to determine the real economic impact of hemoparasitic diseases in the world, however, some works obtain results on the little scale or with a short sample size that can underrepresent the real effects of these diseases. Bovine anaplasmosis, for example, has been estimated to produce an economic loss of more than $100 million dollars per year in the US only (Kocan et al. 2010). A recent study showed that expenditure due to theileriosis represents 13.83% of the farm costs of a dairy farm in Pakistan (Rashid et al. 2018). Economic losses due to babesiosis has also been estimated in thousands of million dollars per year (Ozubek et al. 2020). However, economic significance has to be evaluated considering the effects of both diseases and vectors in order to develop control strategies that allows the reduction of both factors to improve animal health and thereby to achieve One health (Rodríguez et al. 2009; Kocan et al. 2010).

Bovine Hemoparasites in the Tropics

The co-infections in bovines is not rare and the evolution has made parasites and host to adapt according to each other and to maintain certain steadiness, producing the enzootic stability of diseases (Esteve-Gasent et al. 2020). The problem comes when this stability breaks and negative effects show on the host species in the form of clinical signs of disease, reduction or lack of production, poor genetic improvement or economic losses due to treatment expenses, damages to production and death of the animals (Rodríguez et al. 2009). There are following hemoparasitic infections causing economic impact on bovines found in the tropical regions of the world.

a. *Anaplasma* spp

Anaplasma (*A.*) *marginale* is a gram-negative bacterium, belonging to the order Rickettsiales, which cause enzootic bovine anaplasmosis in Europe, Asia, Africa and Latin America (Kocan et al. 2010). *Anaplasmataceae* family contains other species of *Anaplasma* that infects cattle, such as *A. centrale* (*A. marginale* subsp. *centrale*) or *A. phagocytophilum* which has a wider range of hosts and is a zoonotic microorganism (Kocan et al. 2010).

In bovines, *A. marginale* is the most pathogenic species of the genus which parasitizes erythrocytes of cattle causing fever, jaundice, loss of appetite, weight loss, abortions, low milk production and death (Kocan et al. 2010). Transmission of *A. marginale* occurs through the ticks belonging to the genus *Rhipicephalus (Boophilus) microplus* and *Dermacentor* (*D.*) *andersoni*, *D. variabilis*, *D. albipictus*, *D. hunter* and *D. occidentalis* (Kocan et al. 2003, 2010; Ueti et al. 2007; Guzmán-Cornejo et al. 2016). Hematophagous insects (*Tabanus* spp., *Anopheles*, *Psorophora*, *Haematobia irritans* and *Stomoxys calcitrans*) can also transmit the microorganism mechanically (Ristic and Kreier 1984; Blouin and Kocan 1998; Bautista-Garfias et al. 2021).

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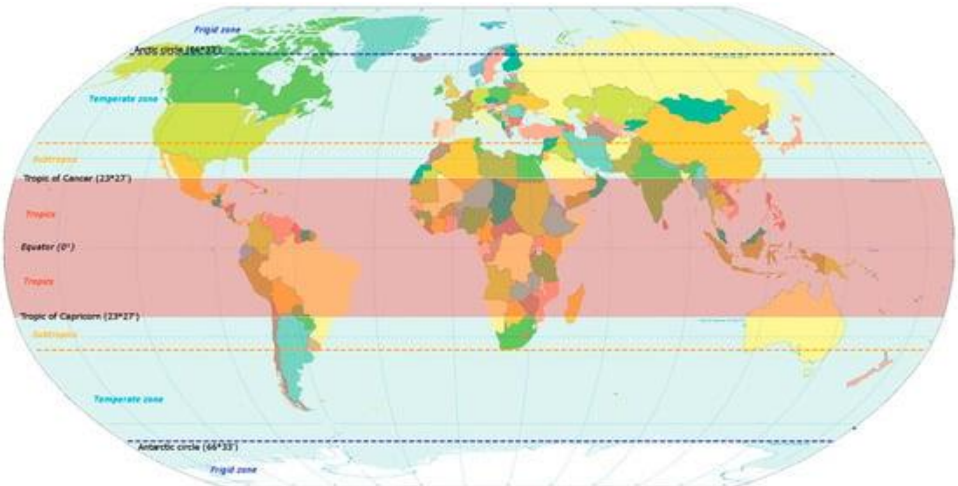

Fig. 1: Tropical regions of the world. Delimited by the Tropic of Cancer and Tropic of Capricorn, the region is characterized by the presence of a great diversity of species. (Mavridou et al. 2018).

Once recovered from acute initial infection, bovines become chronically infected presenting cycles of rickettsemia every 6 to 8 weeks. In these persistent cases, microscopic identification of pathogen will be difficult and serologic (indirect or competent ELISA) or molecular (PCR, qPCR, LAMP, RLBH) diagnosis will be more precise, sensitive and specific (Carelli et al. 2007; Wen et al. 2016; Paoletta et al. 2018; Salinas-Estrella et al. 2022a).

b. *Babesia* spp

Bovine babesiosis is an infectious disease caused by protozoan parasites *Babesia* (*B.*) *bovis* and *B. bigemina* which are considered as most pathogenic species for bovines (Henker et al. 2020), and are widely distributed around the world. Ticks are the biological vector of these pathogens including *Rhipicephalus* (*R.*) *microplus* and *R. annulatus* (Mosqueda et al. 2012; Esteve-Gasent et al. 2020). The infection produces fever, anemia, haemoglobinuria, apathy, anorexia, drop in productivity, and in some cases nervous movements and death (Bock et al. 2004). Severity of disease depends on bovine immune status, age, strain of the parasite and number of infecting microorganisms (El-Dakhly et al. 2020). Recovered animals become chronic asymptomatic carriers and a source of infection for non-infected animals (Chávez-Larrea et al. 2021). Conventional treatment of bovine babesiosis is based on imidocarb or diminazen azeturate. More recently many other drugs have been used to treat bovine babesiosis including triclosan, nerolidol, artesunate, epoxomicin, gossypol and atovaquone (Mosqueda et al. 2012). Control of this disease relies on tick control, surveillance diagnosis, and adequate nutrition to maintain an optimal immune status. Vaccines are yet to be developed against *Babesia* spp. (Esteve-Gasent et al. 2020). Several approaches in vaccine development include immunization with attenuated strains, cell culture and genome-based vaccinology (Mosqueda et al. 2012, 2017).

c. *Borrelia* spp

Borrelia spp. are gram-negative spirochaetes which are 5–20 µm long and up to 0.5 µm wide, and causes disease in humans and animals. Among these, *Borrelia* (*B.*) *theileri*, a causative agent of bovine borreliosis is well-known to infect cattle and other mammals (horse, sheep, goats and deer). This disease has already been diagnosed in the cattle of South Africa, Nigeria, Australia, Brazil, Mexico and Argentina (Yparraguirre et al. 2007; Cordeiro et al. 2018; Morel et al. 2019; Qiu et al. 2021). The infection begins by attachment and prolonged feeding of infected vectors i.e., *Rhipicephalus* ticks (*R. microplus*, *R. evertsi*, *R. annulatus*, and *R. decoloratus)* (Smith et al. 1978; Matton and Melckebeke 1990; Yparraguirre et al. 2007; Cordeiro et al. 2018; Qiu et al. 2021). Bovine borreliosis is a low pathogenicity disease; however, signs such as fever, hemoglobinuria, lethargy and anemia can be present in the infected animal (Callow 1967). This disease usually occurs associated with babesiosis and/or anaplasmosis worsen the hematological parameters of the animal, especially in splenectomized cattle (Smith et al. 1985). While, in Africa, borreliosis is associated with babesiosis, theileriosis, anaplasmosis and eperitrozoonosis (Koch et al. 1990).

B. burgdorefi sensulato- complex is the causal agent of Lyme disease in humans and can also infect cattle. The main vectors of *B. burgdorferi* in tropic regions (South America, Africa and Australia) belongs to the *Ixodes* (*I.*) *ricinus* species complex (*I. ricinus*, *I. scapularis*, *I. pacificus* and *I. persulcatus*). The clinical signs associated with the acute disease include fever, stiffness-swollen joints, lethargy, anemia, decreased milk production, erythematous rash, chronic weight loss, lameness and spontaneous abortions (Post et al. 1988; Parker and White 1992; Wells et al. 1993). *B. burgdorferi* persist in the nature within an enzootic cycle involving ticks and mammals and the geographical area can

Table 1: Main diagnosis test to *B. burgdorferi*

	Diagnosis test	Reference
Identification of the agent	Giemsa-stained blood smears	Matton and Melckebeke 1990
	Polymerase chain reaction (PCR)	Lebech 2002
	Dark-field immunofluorescence microscopy	Wittenbrink et al. 1994
	Bacterial culture	Zhioua et al. 1999
Serological	Indirect fluorescent antibody	Parker and White 1992; Burgess et al. 1993
	Antibody capture enzyme-linked immunosorbent assay (ELISA)	Burgess et al. 1993
	Serotyping using monoclonal antibodies against OspA and OspC bacterial surface proteins	Wagner et al. 2012

Table 2: Occurrence of Bovine theileriosis in tropics

Specie	Disease	Vector	Geographical Distribution	Symptoms	References
T. Parva	East Coast fever, corridor disease and Zimbabwean Theileriosis	*Rhipicephalus species, Appendiculatus (R. zambesiensis,* and *R. Duttoni)*	Eastern, central and southern Africa	High fever, swelling of the lymph nodes, dyspnea, and high mortality. (Death occurring approximately three weeks after infection).	Bishop et al. 2004; Kiara et al. 2018; Selim et al. 2022
T. Annulata	Tropical theileriosis	Hyalomma species, (*H. anatolicum, H. rufipes, H. impeltatum and H. dromedarii)*	Middle Eastern of Africa, and south Asia (india)	Swelling of the lymph nodes, pyrexia, anemia, dyspnea, emaciation, and diarrea. In chronic diseases some neurological and reproductive signs may develop.	Bishop et al. 2004; Kiara et al. 2018; Liu et al. 2022; Selim et al. 2022
T. Mutans	Benign bovine theileriosis,	*Amblyomma species, (A. variegatum)*	Caribbean islands, Western, Eastern, Central and Southern Africa and	Mild disease	Flanagan and Le Roux 1957; Kiara et al. 2018; Selim et al. 2022
T. Velifera	Benign bovine theileriosis, Benign bovine theileriosis	*Amblyomma* species, *(A. variegatum*	Western, Eastern, Central and Southern Africa	Mild disease	Kiara et al. 2018
T. Taurotragi		*Rhipicephalus* species	Eastern, Southern and Central Africa	Mild disease	Kiara et al. 2018
T. Orientalis, (Ikeda)		*Haemaphysalis species (H. longicornis)*	Australia	Anemia, pallor, lethargy, pyrexia, elevated heart rate, recumbency, weakness, and death in extreme cases.	Perera et al. 2014; Oakes et al. 2019; Marendy et al. 2020

be affected by climatic factors and host density. The life cycle of *B. burgdorefi* is complex and takes 2 to 6 years depending on the tick species. It begins when an infected tick feeds on its host releasing saliva or coxal secretions on the biting site. The bacteria need 48 h of tick attachment before enters the host and its transmission begins depending on the *Borrelia* specie (Gern 2009).

The recommended diagnosis test in cattle is a smear of peripheral blood, stained by Giemsa, nevertheless, a high number of spirochetes are required for proper diagnosis (Matton and Melckebeke 1990). Several other diagnostic test for *B. burgdorferi* has been enlisted in Table 1.

For treatment of cattle borreliosis, the recommended antibiotics include oxytetracycline and procaine penicillin. Oxytetracycline is commonly used for human borreliosis and is effective for treatment of bovine borreliosis, although with limited success, in treating a Bovine Lyme Borreliosis (Matton and Melckebeke 1990). Even though in 5 days of treatment a significant improvement is observed, it is important to finish the treatment for the clearance of spirochaetes from the blood circulation (Post et al. 1988).

d. *Theileria* spp

Theileriosis is a tick borne hemoparasitosis caused by the family Theileridae (order Piroplasmida, genus Theileria), which parasitize wild and domestic animals where the appropriate tick vectors are found (Bishop et al. 2004; Kiara et al. 2018).

Theileriosis is an economically important disease and range from mild (inapparent reactions) to fatal, therefore some species that infect cattle are relatively benign (asymptomatic) whereas others as *Theleiria* (*T.*) *parva* and *T. anulata* are responsible for a severe illness (Uilenberg 1981; Irvin and Morrison 1987; Mans et al. 2015; Lawrence and Mans 2017). African buffalo represent an important wildlife reservoir for cattle infection (Young et al. 1978). The pathological significance along with tick vector and geographical distribution of various species infecting cattle has been illustrated in Table 2.

Theileria life cycle involve intracellular stages in the vectors and the host. The protozoan infects and develop in the leukocytes (schizont) or erythrocytes (piroplasm) depending on the species (Ali et al. 2017): *T. parva* infect T and B lymphocytes, while *T. annulata* infect monocytes, dendritic cells and B-lymphocytes (Baldwin et al. 1988; Spooner et al. 1989; Stephens and Howard 2002).

Infected tick feeding secretes sporozoites (infective form) from salivary glands into bovine blood, infecting leukocytes and multiply inside them by merogony. The schizont associates with the mitotic spindle during cell division, therefore, the parasites are able to divide synchronously with the bovine cells. It ensure infection remains in daughter cells, facilitating multiplication and differentiation to merozoites, which are released and invade erythrocytes forming piroplasms (Hulliger et al. 1964; Dobbelaere et al. 2003; Von et al. 2010; Torina et al. 2020). In susceptible bovine, infection usually results in death within 3 to 4 weeks approximately.

The immune response of the host acts against extracellular stages (sporozoites or merozoites), the antigen of the macroschizonts and piroplasmic stages on the surface of the invaded cells (Seifert 1996).

Treatment for the prevention and control of infection in the initial stage includes the anti-protozoal Buparvaquone, which is considered as an effective drug against theileriosis. However, even after preventive treatments of theilleriois, the disease still represents a serious threat to livestock. Currently, low-pathogenicity parasites derived from infected cells in vitro are used as vaccines in many countries (Liu et al. 2022).

e. *Trypanosoma* spp

Trypanosomosis is caused by a hemoprotozoan parasite *Trypanosoma*, which affects domestic, wild animals, and humans across the world. In Africa, Asia and South America, *Trypanosoma* (*T.*) *vivax, T. congolense, T. evansi, T. equiperdum, T. cruzi,* and *T. theileri* represent a potential risk for a cattle population of more than 500 million (Jones et al. 2001; Osório et al. 2008; Van den Bossche et al. 2010; Gelaye et al. 2020). In bovine trypanosomosis, *T. vivax* is the most pathogenic and important agent infecting cattle (Jones et al. 2001). However, the specie that causes American Trypanosomosis in humans is *T. cruzi,* and it has been found in many wild (rodents, bats and marsupials) and domestic animals such as dogs and pigs (Ramsey et al. 2012).

The transmission of *Trypanosoma* spp. from vector occurs either through stercorarian (infective stage developed in the digestive tube) or salivarian route (infective stage developed in salivary glands) (Haag et al. 1998). In this regard, parasites are usually transmitted by tsetse flies (in Africa) and mechanically by other blood-sucking arthropods, such as *Haematobia irritans*, *Stomoxys calcitrans*, and *Tabanus* spp. (Osório et al. 2008). Additionally, although less common, the *Trypanosoma* spp. is also transmitted by ticks, including: *Rhipicephalus microplus*, *Ixodes ricinus*, *Hyalomma anatolicum*, and *Amblyomma cajennense* (Latif et al. 2004; Krige et al. 2019; Zeb et al. 2019; Luu et al. 2020).

In Latin America, the infection is present in 10 out 13 countries of South America (Jones et al. 2001; Dagnachew et al. 2015). Molecular characterization of *Trypanosoma* parasites corroborates the West African origin of South American isolates, which were possibly introduced by cattle imported from Africa at the end of the 19th century; however, a genetic distance separated these parasites from the East African isolate (Hill et al. 2005). Additionally, morphometric studies suggest a difference in the surface antigens diversity and its inability to infect and grow in tsetse flies between the American *Trypanosoma* spp. and the African parasite through DNA labeling, and biochemical analysis of isoenzymes (Haag et al. 1998; Jones, 2001).

The severity and symptomatology of the infection depend on the host and the *Trypanosome* spp. Thus, the presence of a parasite in the blood results in anemia, causing progressive weight loss, anorexia, detrimental effects on fertility, reproduction, and economic losses in milk and meat production in infected bovines (Holmes et al. 2000). Hematological alterations observed in natural and experimental infections include the simultaneous development of leukopenia, lymphopenia, and neutropenia as well as variations in the concentration of total serum proteins. Currently, we know that bovine trypanosomiasis prevalence is related to host factors such as age, sex, breed, purpose, and abiotic factors such as management system, population density, extension of exploitation, presence and control of vectors, geographic regions, agroecological zones, climatic season and application of trypanocidal treatments (Holmes et al. 2000). In this regard, Anti-*Trypanosoma* drugs will continue to play a significant role in the bovine trypanosomosis integrated control. However, the inappropriate use of these chemical compounds results in the development of resistance, which represents a continuous threat to their sustainable use (Miruk et al. 2008). Finally, the advance in elucidating the mechanism involved in the pathogenic differences, drug resistance, and genetic composition could be an approach to diagnosis and control (Dagnachew et al. 2015; Gelaye et al. 2020).

Epidemiology of Most Common Hemoparasites Co-infections in Bovines

Recently, vector-borne diseases have shown a new geographic distribution worldwide. Many of these diseases are caused by hemoparasites. The critical point of this distribution relies on several conditions, including vector's adaptation to new climatic conditions and the migration and transportation of vectors and cattle, respectively. Therefore, the diseases and sick animals have begun to appear in geographical regions never reported before (Shope 1991; Gray et al. 2009; Chávez-Larrea et al. 2021). According to a study, *Babesia* spp. was reported in cattle in Quito, Ecuador at an altitude of 2469 meters above the sea level (m.a.s.l.), which is the highest altitude reported for babesiosis and the vector *R. microplus* (Chávez-Larrea et al. 2021).

The hemoparasites that affect red blood cells of bovines mainly belong to the genus *Anaplasma* spp., *Babesia* spp., and *Theileria* spp.; however, some other microorganisms have been described too, including species of genus

Ehrlichia, *Trypanosoma*, *Setaria*, and *Mycoplasma* (Kamyingkird et al. 2020, Ngasaman et al. 2021). Among the most representative species of each genus are: (bacteria) *Anaplasma marginale*; *Ehrlichia ruminantium, E. minasensis*; (protozoan) *Babesia bovis, B. bigemina, B. divergens, B. major, B. jakimovi, B. ovata, B. ocultans*; *Theileria orientalis* complex (*T. mutans, T. buffeli, and T. sergenti*), *T. annulata, T. parva, T. orientalis, T. taurotragi, T. velifera*; *Trypanosoma evansi*; (mycoplasmas) *Candidatus Mycoplasma haemobos* and *M. wenyonii* (Niethammer et al. 2018; El-Dakhly et al. 2020; Agina et al. 2021).

Age of the animal may be an associated risk factor regarding the clinical or subclinical presentation of disease, as adult cattle present serious clinical illness of bovine anaplasmosis as compared to calves (Kocan et al. 2003).

In many cases, only one type of hemoparasite is found in sick animals; however, in other cases, the animals are diagnosed with more than one hemoparasite, which exacerbates the clinical signs and, the health deteriorates rapidly (Tembo et al. 2018). Some of the most important co-infections reported worldwide in the years 2017-2022 are shown in Fig. 2. Table 3 shows a broader view of the prevalence of hemoparasites in cattle in recent years.

Many recent prevalence studies are based on PCR testing to detect the pathogenic DNA in the sample (Rodríguez et al. 2009; Mans et al. 2015). Unfortunately, several reports are based on opportunity, incidental finding or searching for specific pathogens and are not representative of the real prevalence of a country. There is a lack of comprehensive epidemiological studies worldwide to know the status of hemoparasite co-infections that are causing serious health problems and thus affecting cattle production (Cordeiro et al. 2018; Cavicchioli et al. 2019; El-Dakhly et al. 2020; Chávez-Larrea et al. 2021).

Diagnosis, Treatment and Control of Hemoparasite Coinfections in Bovines

The diagnosis of hemoparasitic infection is usually made on the basis of clinical signs but it give false negative results due to several factors such as lack of information on the clinical history, unspecificity of the clinical signs and non-declared management practices or treatment. So, laboratory tests are always needed to support the presumptive diagnosis. The most common, easy and inexpensive is observation of stained blood-smears with an optical microscopy using Giemsa staining (Al-Hosary et al. 2015), however, it may be more useful during the acute phase of disease when there is a high amount of circulating hemoparasites. In addition, microscopy allows to obtain more information about the general state of blood cells such as its shape, size and ratio of RBCs and WBCs which can help to confirm or discard a diagnosis. However, it requires an experienced microscopist to clearly identify the pathogens and species present in the slides (Mosqueda et al. 2012).

Serological tests (Complement fixation test, ELISA and its variants, IFA and immunochromatographic strips) are fast and effective for detection of antibodies in a herd, but it will be detected after the start of an immune response (Torioni de Echaide et al. 1998; Mosqueda et al. 2012; Vieira et al. 2017; Tayebwa et al. 2018; El-Sayed et al. 2019; Torina et al. 2020; Salinas-Estrella et al. 2022a). Hence, false negative results are the risk at the beginning of infection, whereas false positive results may present when there are cross-reactions of antibodies with its site of recognition (Rodríguez et al. 2009; Esteve-Gasent et al. 2020).

Molecular tests based on PCR or its variants are very useful in low parasitemia cases and facilitates sequencing and identification of pathogen species. Duplex or multiplex PCR or qPCR, and RLBH are examples of molecular tests that allows diagnosis of coinfections simultaneously which is ideal in those places where coinfections are a great problem (Ananyutthawongese et al. 1999; Decaro et al. 2008; Bilgiç et al. 2013; Paoletta et al. 2018).

Pathogens represent a major threat to cattle and one of the main constraints for the improvement of the livestock industry. Therefore, having a better control of diseases transmitted by cattle ticks and other vectors would greatly contribute to improve meat and milk production (Johansson et al. 2020). Development of resistance to acaricides and antibiotics leads to requirement of more sustainable and reliable measures for control of vector-borne diseases. For instance, wildlife management, alternative husbandry practices or a combination of strategic tick control and vaccination and preventive serological testing must be a part of production practices to complement the management (Jia et al. 2020; Johansson et al. 2020; Salinas-Estrella et al. 2022b).

Conclusion

Hemoparasites such a protozoan parasites (*Babesia*, *Teilleria and Trypanosoma* species) and intracellular-obligate bacteria (*Anaplasma* and *Borrelia* species) are some of the pathogens transmitted by arthropods, which have limited the production of livestock in tropical regions, since their climatic characteristics provide ecological niches, which are auspicious to the development of vectors (ticks and Tsetse fly).The economic losses caused by these diseases are mainly due to cattle death, drop of production, cost of treatment, preventive measures and vector control. Lack of commercial vaccination represents a serious problem in places with a high incidence. Antibiotic resistance in humans is a problem occurring worldwide and is still on the path of control. In this sense, indiscriminate use of antibiotics in animals contributes to the problem, but treatment of bovine infectious diseases relies on a few pharmacological compounds. In addition, there is a lack of comprehensive epidemiological studies worldwide to know the exact status of hemoparasite co-infections that are causing serious health problems and thus affecting cattle production. Use of diagnostic tests are a great

Table 3. Representative cases of prevalence of hemoparasites distributed worldwide.

Disease	Species	Prevalence	Method	Country	References
Anaplasmosis	*A. marginale*	n= 216 87.9%	Nested PCR	Pakistan	(Bisen et al. 2021)
		n=520 10.30 %	PCR	Thailand	(Junsiri et al. 2020)
		n= 104 21.15%	Semi-nested PCR	Bolivia	(Ogata et al. 2021)
		n= 223 95.5%	Quantitative PCR	Cuba	(Díaz-Sánchez et al. 2020)
		n= 650 20%	cELISA	Egypt	(Selim et al. 2021a)
		n= 200 77%	iELISA	Brazil	(Ramos et al. 2020)
		n=62 42%	Quantitative PCR	Russia	(Fedorina et al. 2019)
Babesiosis	*Babesia* spp.	n=264 18.93%	PCR	Ecuador	(Chávez-Larrea et al. 2021)
	B. bigemina	n= 150 19.33%	PCR	Egypt	(El-Dakhly et al. 2020)
	B. bovis	n=725 27.9%	PCR	Mongolia	(Otgonsuren et al. 2020)
	B. bigemina	23.6%			
	B. divergens	n=95 37.89%	Indirect Immunofluorescence	Germany	(Springer et al. 2020)
	B. bovis	n=40 7.5%	Multiplex PCR	Iran	(Rajabi et al 2017)
	B. bigemina	92.5%			
	B. bovis	n=487 69.8%	ELISA	Indonesia	(Guswanto et al. 2017)
	B. bigemina	27.5%			
	Babesia spp.	n=60 15%	PCR	Bolivia	(Ogata et al. 2021)
Theileriosis	*T. annulata*	n=96 54.16%	PCR	India	(Selim et al. 2021b)
	T. orientalis,	n=260 36.5%	PCR	China	(Wang et al. 2018)
	Theileria spp.	n=61 72.13%	PCR	Malaysia	(Agina et al. 2021)
	T. parva	n=479 22.7%	ELISA	Cameroon	(Silatsa et al. 2020)
	T. mutans	41.1%			
	T. velífera	n=392 13%	PCR/Reverse Line Blot (RLB)	Ethiopia	(Hailemariam et al. 2017)
	T. mutans	66.1%			
	T. orientalis	51.8%			
Trypanosomiasis	*Trypanosoma evansi*	n=61 4.92%	PCR	Malaysia	(Agina et al. 2021)
	Trypanosoma (Duttonella) vivax	n=15 80%	PCR	Brazil	(Vieira et al. 2017)
	T. vivax	n=45 35./%	PCR	Venezuela	(Eleizalde et al. 2021)
Ehrlichiosis	*Ehrlichia ruminantium*	n=182 6.6%	Semi-nested PCR	Cameroon	(Esemu et al. 2018)
	Ehrlichia ruminantium	n=392	PCR/Reverse Line Blot (RLB)	Ethiopia	(Hailemariam et al. 2017)
	E. minasensis	0.5% 0.26%			
Hemoplasmosis	Hemoplasmas *C. Mycoplasma haemobos* and *Mycoplasma wenyonii*	n=208 32.2%	PCR	Uganda	(Byamukama et al. 2020)
	C. M. haemobos	n=400 9.5%	PCR	Japan	(Tatsukawa et al. 2021)
	M. wenyonii	40.3%			

	C. M. haemobos	n=410 56.59%	PCR	Germany	(Niethammer et al. 2018)
	M. wenyonii	8.54%			
	C. M. haemobos	n=27 96%	PCR	Mexico	(Quiroz-Castañeda et al. 2019)
	M. wenyonii	96.29%			

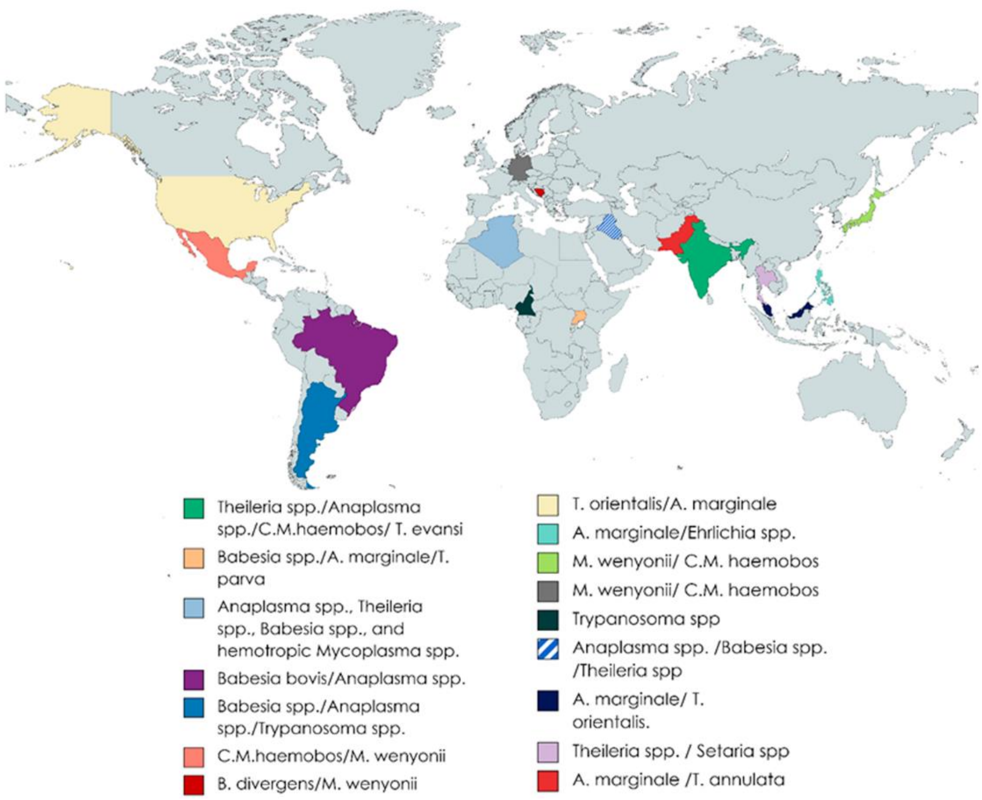

Fig. 2: Worldwide distribution of representative co-infections of hemoparasites that infect cattle in 2017-2022. Created with Mapchart.net (Vieira et al. 2017; Niethammer et al. 2018; Paoletta et al. 2018; Tayebwa et al. 2018; Quiroz-Castañeda et al. 2019; Paguem et al. 2019; Quiroz- Henker et al. 2020; Agina et al. 2021; Ngasaman et al. 2021)

tool for surveillance and prevention of outbreaks, contributing to avoid or at least control negative effects of diseases. Therefore, it is of great importance, to characterize infectious diseases of bovines in the tropics and to promote control strategies in order to mitigate the impact of those diseases on bovine production around the world.

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