Review Article
The Implications of Malaria in Livestock: Reservoirs, Challenges, and Future Directions

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Abstract
Malaria, a mosquito-borne infectious disease caused by the parasite Plasmodium, has been predominantly associated with humans. However, recent studies have uncovered a potential reservoir for Plasmodium spp., within livestock populations. Malaria, caused by the parasitic protozoan Plasmodium spp., is a deadly disease that affects millions of people worldwide. Although human is the primary host for the malaria parasite, it has been discovered that certain animals can also serve as reservoirs. One such potential reservoir is livestock populations, as they have been found to carry Plasmodium spp. parasites. This article will discuss the implications of livestock being potential reservoirs for malaria and the importance of understanding this relationship for effective disease control. Livestock populations have long been overlooked as potential reservoirs for malaria transmission, but recent advancements in diagnostic techniques and surveillance studies have sparked interest in exploring this field. By prioritizing thorough assessments of zoonotic transmission risks, we can gain valuable insights into the role of livestock in malaria transmission and develop effective strategies to reduce the burden of this devastating disease.

Keywords: Future direction, Livestock, Malaria, Plasmodium, Reservoirs

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Introduction

Vector-borne diseases (VBDs) affect humans and other animals due to infectious agents, including viruses, bacteria, and parasites, which are spread by arthropod species that come into close contact with people and other animals. Many of these transmitters are bloodsucking insects that spread infection to new hosts by ingesting them during a blood meal from an infected host (Sabzavari et al., 2017; Hosseini-Chegeni et al., 2020; Jameie et al., 2020). The distribution of VBDs is influenced by a complex set of environmental, ecological, demographic, and social variables (Plowright et al., 2017; WHO, 2020). Malaria is distributed worldwide across tropical and subtropical areas (Figure 1). Malaria is a fatal illness that affects people worldwide and has a long-term effect on both the economy and quality of life (Tanner et al., 2015; Cervellati et al., 2017). Malaria threatens nearly half the global population; around 2.3 billion reside in Asia (Figure 2) (Tanner et al., 2015; Najjari et al., 2022). Other animals, such as birds, turtles, reptiles, and some mammals, are also susceptible to malaria, which lowers their wellbeing and chance of survival (Martínez-de la Puente et al., 2020). Anopheles mosquitoes, female vectors of the Plasmodium parasite, bite victims and transmit the infection (Tanner et al., 2015; Shi et al., 2023). According to the most recent global malaria report, the number of malaria cases in 2022 was 249 million, which is higher than in 2021 (Figure 3). In 2022, 608000 fatalities from malaria were predicted (WHO, 2022). Malaria, caused by the Plasmodium parasite, remains a significant global health issue, affecting millions each year (Najjari et al., 2022; Garrido-Cardenas et al., 2023).

There are reports of many new malaria cases worldwide during 2021 (Figure 4). Evidence links malaria’s prevalence to host density (Awosolu et al., 2021). Still, an inverse association with the density of non-host species was found due to their diluting impact on disease transmission (Mayengue et al., 2020). Human malaria is caused by five different Plasmodium species, with Plasmodium falciparum and Plasmodium vivax posing the most serious threats. The most lethal malaria parasite is P. falciparum. In the majority of countries, P. vivax is the dominant malaria parasite. Plasmodium malariae, Plasmodium ovale and Plasmodium knowlesi are other malaria species that can also infect people (Sinden & Gilles, 2017; Nagoba & Pichare, 2020; WHO, 2022). Hundreds of different species of parasites infect birds, reptiles, and other animals, in addition to the ones that infect humans. These species have all exquisitely developed to meet the unique obstacles inherent in their individual hosts’ survival (Siao et al., 2020).

Anthropogenic activities like urbanization and animal husbandry can affect the prevalence of malaria (van de Straat et al., 2022). The impact of livestock on the spread of malaria is a factor that has been overlooked. If cattle are a malaria reservoir, their presence may raise the frequency of the disease in taxonomically similar local fauna; however, this will be determined by the host-specificity of the malaria strains (Hasyim et al., 2018). Conversely, animals may reduce the spread of malaria by giving vectors non-host blood meals (Mayengue et al., 2020). On a different level, livestock farms may contribute to an increase in malaria prevalence by altering the surrounding environment, such as providing water sources that promote the growth of vectors or allowing disease to spread through gatherings of wild animals drawn to the farms. The incidence of malaria may also be affected by urbanization, depending on how well host species have adapted to the urban environments (Mayagaya et al., 2015; Fornace et al., 2021) and the degree to which these regions offer appropriate dwellings for the growth of vectors (Mburu et al., 2021).

The likelihood of livestock serving as reservoirs for malaria caused by Plasmodium spp. has several implications that can impact human and animal health and the efficacy of malaria control efforts (Mburu et al., 2021). If certain Plasmodium species can effectively complete their life cycle in livestock and be transmitted to mosquitoes, there is a potential risk of zoonotic transmission to humans (Sato, 2021). Zoonotic transmission could complicate malaria control efforts, especially in areas where humans and livestock live nearby (van de Straat et al., 2022). Livestock serving as reservoirs for Plasmodium spp. may contribute to increased malaria transmission intensity, mainly if the parasites are efficiently transmitted from animals to mosquitoes and, after that, to humans (Franco et al., 2014; Hasyim et al., 2018; Mburu et al., 2021).

Animals can serve as a reservoir for communicable pathogens and as a source of blood meal for arthropod vectors of human illness, which is why animals are essential in the epidemiology of many of the most significant human diseases (Isaquote et al., 2021; Mottaghian et al., 2023). The adoption of human disease management measures aimed at animal populations has resulted from the realization of this link (Franco et al., 2014; Sabzavari et al., 2017; Hosseini-Chegeni et al., 2020; Jameie et al., 2020; Hassan et al., 2022). The multitude of potential livestock-related impacts on malaria contribute to the seemingly inconsistent results of most research that has been done. Livestock can deter mosquitoes that seek blood from attacking humans by redirecting their vectors (Hasyim et al., 2018; Mayengue et al., 2020; Mburu et
al., 2021), thereby lowering the malaria parasite’s rate of transmission (Hasyim et al., 2018) and stopping its multiplication in human beings. However, animals can also serve as extra supplies of blood or as places for larvae to breed (Donnelly et al., 2015; Mayagaya et al., 2015; Hasyim et al., 2018), which may improve the density and or survival of vectors (Donnelly et al., 2015; Ohm, 2018). Therefore, the likelihood that the vector will survive the parasite’s extrinsic incubation period is increased, and the parasite will become infectious and bite other individuals (Donnelly et al., 2015). Thus, the proportional importance of each factor determines the net effect of cattle on the risk of malaria. A seemingly straightforward remedy in regions where having livestock close to humans boosts the spread of malaria might be to alter livestock management practices to relocate the animals between villages and vector breeding sites away from people’s homes (Franco et al., 2014). Consequently, a different approach has been suggested: Treat cattle with pesticides or acaricides to target the zoophilic mosquito’s non-human host (Njoroge et al., 2017). This tactic has been successfully applied for a long time to reduce the direct economic losses caused by ectoparasites owing to decreased production, as well as the illnesses they spread to animals and frequently people (Franco et al., 2014).

The presence of livestock reservoirs may influence the epidemiology of malaria in a given area. It could affect the dynamics of Plasmodium transmission, prevalence, and the effectiveness of control measures (Mburu et al., 2021). The presence of livestock may influence the feeding behavior

Figure 1. Status of indigenous malaria cases in 2021.
of mosquito vectors. If mosquitoes preferentially feed on animals, this could affect the overall dynamics of *Plasmodium* transmission, potentially diverting mosquitoes from humans to livestock (Hasyim et al., 2018). *Plasmodium* infections in livestock may have health implications for the animals themselves. While some animals may tolerate the infection without presenting clinical signs, others may experience adverse effects, such as anemia and reduced productivity (Kaewthamasom et al., 2018; Al-Badrani & Alabadi, 2021; Al-Badrani et al., 2023). Malaria in livestock can impact the livelihoods of communities that rely on these animals for agriculture, transportation, and food security. Decreased productivity due to malaria can affect income and food availability (Kassie et al., 2020).

![Figure 2](image1.png)  
**Figure 2.** Number of malaria cases in Southeast Asia from 2012 to 2021

![Figure 3](image2.png)  
**Figure 3.** Distribution of malaria cases worldwide in 2021
The identification of livestock as potential reservoirs may necessitate the adaptation of malaria control strategies. Integrated approaches that target both human and animal hosts and mosquito vectors may be required for adequate control (Onen et al., 2023). Interdisciplinary collaboration among human health, veterinary medicine, entomology, and environmental science would help with research and control efforts. Plasmodium infections in livestock can be challenging to identify and diagnose. Developing and implementing specific diagnostic tools for veterinary use is necessary to accurately assess the prevalence and role of animals in malaria transmission (Slater et al., 2022). Raising awareness and educating communities about the potential role of livestock in malaria transmission is crucial. This measure includes promoting good animal husbandry practices and preventive measures to reduce the risk of zoonotic transmission (Yasmeen et al., 2021).

Understanding the implications of livestock as potential reservoirs for malaria is essential for designing effective and context-specific control strategies. It requires a holistic approach that considers the interactions between humans, animals, mosquitoes, and the environment to achieve sustainable malaria control and elimination goals (Naserrudin et al., 2023). While previous research has primarily focused on human hosts as the main reservoir for transmitting malaria, recent studies have suggested that livestock populations could play a significant role in the disease’s spread and maintenance. This article aims to review the challenges associated with considering livestock as a potential reservoir for malaria and explore future directions for research in this field.

**Challenges in identifying livestock as a reservoir for malaria**

Determining whether livestock populations can act as reservoirs for malaria is a complex task. Several challenges require careful attention to obtain accurate and reliable information regarding the role of livestock in malaria transmission (Iwashita et al., 2014; Hasyim et al., 2018). These challenges include adequate surveillance systems, identifying and characterizing potential mosquito vectors, and creating appropriate diagnostic tools to detect the parasite in livestock. Addressing these challenges allows researchers to understand livestock’s role in malaria transmission better and develop effective disease prevention and control strategies. (Meireles et al., 2023). Identifying livestock as a reservoir for malaria presents several challenges due to the complex interactions between humans, animals, and Plasmodium parasites. While certain Plasmodium species can infect livestock, their role as reservoirs for human malaria transmission is not well-defined (Chaves et al., 2022). Here are some challenges in identifying livestock as a reservoir for malaria.
Host-specific adaptation by malaria parasites

*Plasmodium* species often have host-specific characteristics, and little is now known about the molecular mechanisms preventing host change (Proto et al., 2019). *Plasmodium* species usually show high host specificity, meaning they are adapted to infect specific host species. The ability of a parasite to complete its life cycle in a particular host is a crucial factor (Sato, 2021). The malaria-causing protozoan parasites communicate a disease to various vertebrate hosts, including mammals, birds, and reptiles. The evolutionary forces that resulted from this association have significantly impacted the parasite and host genomes. The mechanism of frequent ectopic recombination among gene family members is a critical component of the malaria parasites’ ability to produce genetic variation within their antigen-encoding gene families constantly. Hence, malaria remains a persistent disease globally (Siao et al., 2020). Many *Plasmodium* species infect various vertebrate hosts, making it possible to compare the adaptations unique to each host. Comparing many parts of cell biology, such as transcriptional machinery components, has shown surprising shifts in fundamental ways (Su et al., 2020; Sato, 2021) to chromatin modifiers (Kishore et al., 2013) and lipid metabolism (Venugopal et al., 2020; Siao et al., 2020), offering a comprehensive understanding of the evolutionary forces forming these parasites, including elements crucial to the human illness such as immunological evasion, pathogenesis, and dynamics of transmission.

Incompatibilities between the vector and the host, the vector and the parasite, or the host and the parasite may cause *Plasmodium* host specificity. Host-parasite interactions have been firmly linked to *Laverania* species-specificity, especially during *Plasmodium* blood stages. Although several genes responsible for erythrocyte invasion have been gained and lost among *Laverania* species, overall *Laverania* core genome conservation is rather excellent (Otto et al., 2018), and two crucial erythrocyte invasion genes were transferred into an ancestor of *P. falciparum* in one instance by horizontal gene transfer (Sundararaman et al., 2016). By manipulating the antigens expressed on the surface of red blood cells, parasites in their vertebrate host evade antibody-mediated clearance, prolonging the infection duration. Extensive variety throughout the multi-gene families encoding these surface antigens is necessary for this process, known as antigenic variation (Deitsch & Dzikowski, 2017). Furthermore, distinct parasite strains need to encode distinct repertoires of variant antigens to allow reinfection of a previously infected host. As a result, persistence within a host population is made possible by producing new variations, even when the mainstream, prospective hosts have gained clinical immunity, as with human *P. falciparum* infections. The primary process behind the diversity of variant genes is recombination between gene copies (Siao et al., 2020). The recombination of non-syntenic genes can also happen during asexual replication when the malaria parasites are haploid, in addition to sexual recombination (Claessens et al., 2018).

Incomplete life cycle of *plasmodium* in livestock

*Plasmodium* infects red blood cells in animals such as birds, reptiles, as well as humans. *P. knowlesi* is the *Plasmodium* species that causes malaria, an infectious disease (Sato, 2021). The parasite *Plasmodium* has a complicated life cycle, and mosquitoes are used as a medium for disease transmission. One of the most intricate and fascinating life cycles of any creature is that of the malaria parasite, which presents great research opportunities for cell biology, molecular biology, and immunology (van der Watt et al., 2022). This life cycle is complex, including the parasite switching between asexual reproduction in a vertebrate host and sexual reproduction in an invertebrate host (mosquito). Malarial parasites also use birds and reptiles as hosts and mammals as vertebrate hosts (Venugopal et al., 2020).

For the past 120 million years, the evolution of *plasmodium* species has followed the evolution of vertebrates. Thus, the *plasmodium* has encountered different hosts and then adapted to those hosts, demonstrating the main driving force behind the *plasmodium’s* development (Rougeron et al., 2022). The gorillas are kept apart from the other animals. *Plasmodium mexicanum* and *P. floridense* are found in reptiles, whereas *Plasmodium relictum* and *Plasmodium juxtanucleare* are found in birds (Sharp et al., 2020). *Plasmodium bubalis* was identified by polymerase chain reaction (PCR) in three cases from 11 buffaloes that exhibited anemia and thrombocytopenia in malaria-infected buffaloes (Albadrani et al., 2023). Chickens, turkeys, and other birds can develop clinical and infrequently lethal diseases due to *Plasmodium* spp. infections. Mixed infections were seen in quails, pigeons, chickens, ducks, turkeys, and guinea fowl, with a higher incidence in the former. The most frequent co-infections were caused by *Plasmodium* and *Haemoproteus* species, and their spread may explain the presence of vectors linked to them in the regions where they have been reported (Tembe et al., 2023). There have been reports of domestic livestock, including buffalo, horses, dogs, and goats, as well as crossbred goats from Etawa, becoming infected with *P. falciparum* and *P. vivax* (Sumanto et al., 2021). Some *Plasmodium* species that infect livestock...
may not reach the infectious stage (gametocytes) in the same way they do in humans, limiting their potential to contribute to human malaria transmission. Livestock may be dead-end hosts for certain Plasmodium species, preventing effective transmission to mosquitoes (Al-Badrani & Alabadi, 2021; Sato, 2021).

Host immunity and malarial parasite persistence in livestock

Tropical and subtropical countries suffer greatly from parasitic infections, which increase mortality, morbidity, and socioeconomic inequality (Hosseini et al., 2022; Shi et al., 2023). The interaction between the host immune system and the parasite’s survival strategy frequently determines how the infection turns out and how severe the illness gets. Recovery can be aided by a robust and efficient host immune response, which can stop parasite reproduction and lessen the severity of the disease. On the other hand, if the parasite can avoid or inhibit the immune response, the infection may continue and result in a serious or chronic illness. Occasionally, excessive or dysregulated immune reactions brought on by parasite infections can cause the host immune response to contribute to the pathophysiology of the disease, resulting in tissue damage, inflammation, and immunological-mediated diseases (Shivahare et al., 2023). The immune response to Plasmodium spp. varies between human hosts and mosquito vectors. The main factor contributing to the virulence of the Plasmodium parasite is its ability to evade the host’s immune system (Chandley et al., 2022). Host immunity in both humans and livestock can affect the persistence and transmission of Plasmodium parasites. Immune responses in animals may limit the development and transmission of Plasmodium parasites, reducing their potential as reservoirs (Sato, 2021).

Several differentiation stages in the Plasmodium life cycle are distinguished by the expression of proteins unique to that stage (Chandley et al., 2022). Although the host immune system can reduce the parasite burden, malarial parasites possess several efficient immune evasion techniques. The complement system is considered a key component of innate immunity and serves as the body’s first line of defense against parasites. The malaria parasite can evade the host complement system at some stages of infection (Kiyuka et al., 2020). Moreover, P. falciparum inhibits the membrane attack complex in severe malaria cases, which results in complement evasion (Schmidt et al., 2015). An essential defense against Plasmodium is humoral immunity. The host’s protection against malaria is mainly derived from antibody-mediated reactions. ADCC (Ab-dependent cellular cytotoxicity), ADCI (Ab-dependent cellular inhibition), growth inhibition, and host cell invasion inhibition are among the main functional actions of antibodies (Gomes et al., 2016; Shukla et al., 2021). Natural killer cells are recognized to mediate innate immune activities alongside phagocytic cells. They do this by secreting interferon-γ, which facilitates the clearance of parasites, and by killing infected cells directly (Stegmann et al., 2015).

Diagnostic challenges of plasmodium infections in livestock

Diagnosing Plasmodium infections in livestock can be challenging, and the tools used for human malaria diagnosis may not be directly applicable. The availability of specific diagnostic tools adapted for veterinary use is limited, and there may be a lack of standardized methods (Slater et al., 2022). Asymptomatic malaria represents a significant obstacle to the control and eradication of the disease. Asymptomatic people are a possible reservoir for malaria parasites and frequently do not seek treatment for their infection, which perpetuates the spread of the disease (Degefa et al., 2016; Djoufouma et al., 2022; Yimam et al., 2021). To address this issue and quicken eradication, the WHO advises turning malaria surveillance into a fundamental intervention (WHO, 2015).

Epidemiological screening and surveillance have long faced the difficulty of determining a suitable and precise diagnostic for the identification of malaria parasites, which is necessary to offer information on malaria control methods and lower its morbidity and mortality.

Several methods are currently available for diagnosing malaria, ranging from the traditional approach that uses microscopy to the innovative technique that uses the quick molecular method. Here, asymptomatic malaria-positive individuals are treated, and eventually, the transmission of the disease is stopped by employing active case detection (ACD) techniques such as mass or targeted population screening in the wake of an index case found at a health institution (Wickremasinghe et al., 2014; WHO, 2015). Plasmodium parasite infection has been extensively determined using immunodiagnostic techniques, such as ELISA, flow cytometry, and immunochromatography-based RDT (Fitri et al., 2022). Rapid diagnostic tests (RDTs) and microscopy are used to make an early diagnosis because ACD is typically conducted in the community (WHO, 2015; Aidoo et al., 2018). However, the limited capacity of routinely used malaria diagnostic methods to identify low-density asymptomatic infections limits the efficiency of ACD (Aidoo et al., 2018; Hemingway et al., 2016; Lo et al., 2015).
The gold standard technique for identifying parasite species and estimating parasitemia is microscopic analysis of thick and thin blood films. Nonetheless, the primary issues in many nations are a shortage of skilled microscopists and incorrect diagnoses brought on by low parasitemia (WHO, 2016). Because of their speed, affordability, and ease of use with little training requirements, conventional RDTs, or conventional RDTs, have also been crucial in the fight against malaria. They are unable to identify low-density Plasmodium infections because of their low sensitivity, which has a detection limit of around 100–200 parasites/µL (Das et al., 2017; Hemingway et al., 2016; Laban et al., 2015; WHO, 2016).

Identifying Plasmodium spp. within livestock populations is challenging due to the similarity of malaria parasites in humans and animals (Sato, 2021). Current diagnostic techniques predominantly focus on detecting human malaria parasites, limiting our ability to differentiate between the species or strains found in animals. Developing improved diagnostic tools specifically targeting Plasmodium spp. in livestock is crucial. Detecting Plasmodium spp. in livestock requires specific diagnostic tools tailored for veterinary use. While some tools commonly employed in human malaria diagnosis can be adapted for animal use, there are also veterinary-specific approaches (Slater et al., 2022). The choice of diagnostic tool depends on factors such as the purpose of the diagnosis, the available resources, and the specific requirements of the veterinary setting. Combining multiple diagnostic methods may enhance the accuracy and reliability of Plasmodium detection in livestock.

Complexities of disease transmission dynamics in livestock

Malaria is primarily prevalent in tropical areas, where the temperature and topography offer ideal circumstances for the Anopheles species that spread the disease (Mafwele & Lee, 2022). It is critical to recognize that a wide range of complicated factors, such as climate, land use, and human behavior, impact the spread of malaria and that understanding these circumstances is necessary (Nissan et al., 2021; Mafwele & Lee, 2022). Plasmodium parasite transmission dynamics involve interactions between humans, animals, mosquitoes, and the surrounding environment. Understanding the complexity of these interactions and determining the specific contributions of different hosts to transmission is challenging (Meibalan & Marti, 2017). Several studies have used polymorphic, unlinked genetic markers found in the parasite genome to characterize the genetic diversity in wild populations of malaria parasites (Oyedoji et al., 2020). The host preference of Anopheles mosquitoes, the primary malaria vectors, can influence the potential for transmission between humans and animals. If mosquitoes primarily feed on humans, the likelihood of Plasmodium transmission from livestock to humans may be reduced. To explore the connection between the documented zoophagy and possible Plasmodium parasite infection of vectors, further research is necessary. A more thorough grasp of residual transmission will result from this approach. Understanding the vulnerability of vertebrate hosts to vector-borne illnesses requires understanding mosquito behavior and trophic preferences. Human malaria transmission occurs when mosquitoes prey more on people than other animals (Gueye et al., 2023).

The target of controlling and, in some cases, eliminating malaria has led to a greater emphasis on the importance of thorough, excellent, and ongoing monitoring to guide program development and malaria intervention measures (Recht et al., 2017; Yi et al., 2023). Identifying livestock as potential reservoirs for malaria requires comprehensive research, including molecular studies, epidemiological surveys, and an understanding of host-parasite interactions. While challenges exist, addressing these complexities is crucial for a more accurate assessment of the role of livestock in malaria transmission dynamics. Understanding the transmission dynamics of malaria within livestock populations is vital for designing effective control measures and implementing strategies to reduce the burden of the disease (Franco et al., 2014). Interactions between different host species, vectors, and environmental factors influence the spread and persistence of Plasmodium spp. Evaluating the contribution of livestock, particularly domesticated animals and wild reservoirs, to the overall transmission cycle has remained a challenge. Comprehensive field studies combining entomological and epidemiological data are essential to elucidate these dynamics further.

Zoonotic potential of specific Plasmodium species

Malaria is instigated by five species of the genus Plasmodium, which are apicomplexan protozoan parasites and are thought to be specialized for humans (Sato, 2021), while up to 30 communicate the disease to non-human primates (Faust & Dobson, 2015). Public health and wellbeing are greatly threatened by the perceived and actual risks associated with the emergence of novel infectious illnesses in humans (Hosseini-Chegeni et al., 2020; Jameie et al., 2020). Exposure of humans to live vertebrate animals, their byproducts, or polluted habitats can transmit zoonotic illnesses (Sabzavari et al., 2017;
Rahman et al., 2020). One concern with malaria is the possibility of zoonotic transmission, or from one parasite species to another, of types of Plasmodium that were previously thought to infect only non-human hosts. As a result, the capacity to communicate a disease to various hosts creates an imperfect connection that is seldom reliant on a single element but rather on several distinct and variable biological drives (Amambua-Ngwa et al., 2019). Although most Plasmodium species are thought to be incapable of using zoonotic transmission to spread malaria parasites that do not infect humans, disregarding the possibility of this happening might result in the creation of a potentially fatal human blood-borne illness (Clark & Taylor-Robinson, 2021).

Ecological studies on malaria parasites have shown that, despite the belief that they were specialists, they infect a wide variety of host taxa, providing enough opportunity to diversify infectious zoonotic illness (Hoberg & Brooks, 2015). Malaria parasites (P. falciparum, P. vivax, P. malariae, and P. ovale) are the four species that typically infect people. Two more recent discoveries, P. knowlesi and Plasmodium cynomolgi, may also be included in this list (Ramasamy, 2014; Cox-Singh, 2018; Clark & Taylor-Robinson, 2021). Over the past 20 years, the zoonotic malaria parasite P. knowlesi has drawn more and more attention from medical professionals. While P. knowlesi has been identified as a zoonotic species that can infect monkeys and humans, there is limited evidence of other Plasmodium species in livestock contributing significantly to human malaria transmission (Lee et al., 2022). The severity of the illness is further highlighted by the appearance of other zoonotic malaria, such as Plasmodium simium and P. cynomolgi (Chua et al., 2019; Hang et al., 2021). The transmission of the disease exacerbates the special relationships between the parasites, vectors, and their human host species (WHO, 2015; Clark & Taylor-Robinson, 2021).

Given the surge in zoonotic infections, we can no longer overlook potentially innovative treatments, especially those with an ecological focus (Belay et al., 2017; Hotez, 2018; Vanhove et al., 2021). This condition raises serious public health concerns about malaria-host systems that have not yet been resolved (Hotez, 2018; Gutiérrez-López et al., 2020). As was previously mentioned, several studies have demonstrated that various parasitic species react to ecological and environmental stresses in different ways, which expedites changes in these systems (Dayananda et al., 2018; Hotez, 2018; Aleuy & Kutz, 2020). This information suggests that blood-borne parasites adapt to this environmental change by looking for new hosts and developing innovative means of spreading malaria. Consequently, several cases show that plasmodia may be able to move among hosts, which is highly likely (Santiago-Alarcon et al., 2012; Pulgarín-R et al., 2018; Nazemosadat et al., 2022). The ability of parasites and vectors to adapt, as well as human habitation and behavior, all impact the possibility of zoonosis. The emergence of zoonotic malaria may be caused by several factors, including changes in human dwelling patterns and ecology, the incidence of susceptible Anopheles mosquitoes and human hosts in the same area, the rate of human-primate-mosquito interactions, vector adaptation, and the potential for genetic recombination between the Plasmodium species that infect humans and closely related non-human primate species, which could mean increased virulence (Ramasamy, 2014). It should be understood, therefore, that non-specific protein expressions in a complex molecular interaction help Plasmodium species adapt to their Anopheles mosquito vectors (Smith & Jacobs-Lorena, 2010).

Considering livestock as a reservoir for malaria also raises concerns regarding zoonotic transmission to humans. However, limited evidence suggests the possibility of Plasmodium spp. transmission from animals to humans, the actual risk and public health significance, remain largely unknown. Investigating potential zoonotic transmission pathways and assessing the associated risks are fundamental for understanding the overall impact of livestock populations on malaria transmission (Rahman et al., 2020).

The presence of animals, such as cattle that specific malaria vectors use as blood meal hosts may impact malaria parasite transmission dynamics. Cattle may provide enough blood meals for vectors, reducing the number of times they bite people (Mayagaya et al., 2015). Conversely, the existence of cattle might increase the amount of blood meals available, extending the life of infected mosquitoes and raising the possibility of malaria transmission (Mburu et al., 2021). The ultimate host of a mosquito is determined by a complex array of circumstances, including the accessibility and number of hosts, even though malaria vector species differ in their host preferences (Takken & Verhulst, 2013). After using long-lasting insecticidal nets, malaria vectors may find it difficult to interact with people for a blood meal. As a result, the vectors can decide to feed on the subsequent non-human hosts that become accessible (Takken & Verhulst, 2013), such as cattle (Kreppel et al., 2020).

The presence of cattle in rural areas may significantly impact malaria transmission. Zooprophylaxis, defined as “the use of wild or domestic animals, which are not the
reservoir hosts of a given disease, to distract the bloodseeking mosquito vectors from the human hosts of that disease,” is one method by which cattle may influence the spread of malaria (Asale et al., 2017). Mosquitoes feeding on these animals would be less likely to pick up malaria parasites. Numerous investigations have backed up the zooprophylaxis theory (Donnelly et al., 2015; Massebo et al., 2015). Some research demonstrates that the impact is contingent upon livestock confined away from habitations (Asale et al., 2017).

Alternatively, cattle may influence the spread of malaria by a process known as zoo potentiation, in which their presence may provide new supplies of blood for the vectors to ingest, extending their lives and increasing their densities (Donnelly et al., 2015). For example, in some nations, the presence of cattle was linked to a higher risk of malaria and a greater number of malaria vectors (Hasyim et al., 2018; Mburu et al., 2021; Chan et al., 2022). The primary species of malaria vector, the number of potential extra hosts, and the distance between human hosts and cattle are likely to affect whether the occurrence of cattle reduces or increases the probability of malaria transmission. When cattle are kept away from humans at night, and the primary vectors are not inclined to feed on humans, zooprophylaxis can be beneficial (Donnelly et al., 2015). Additionally, a model has proposed that the incidence of cattle close to human habitations would supply the vectors with enough blood meals, a fact that would improve the vectors’ ability to reproduce, increasing the vector population and danger of malaria transmission (Mayagaya et al., 2015; Mburu et al., 2021). Furthermore, the manifestation of cattle may result in an upsurge in the population of malaria vectors, particularly during the monsoon season, since the hoof prints of the animals may be regarded as extra-appropriate larval homes (Mburu et al., 2021).

In this context, zooprophylaxis refers to removing vectors from livestock animals so the infection cannot spread. In certain circumstances, vector populations can be managed without mosquitoes acquiring pesticide resistance by combining insecticide spray with zooprophylaxis (Asale et al., 2017). A zooprophylactic effect can be achieved by increasing blood feeding on cattle, which lowers the risk of human illnesses (Asale et al., 2017; Hasyim et al., 2018). Therefore, the usefulness of zooprophylaxis and the causes of the success found in zooprophylactic environments have remained controversial (Franco et al., 2014; Hasyim et al., 2018). The debate over the relative importance of zooprophylaxis and zoopotential in reducing malaria frequency may be somewhat explained by the range of livestock species and activities that have been examined, as well as the varying appeal that these factors have for various zoophilic vectors (Franco et al., 2014; Mayagaya et al., 2015).

Assessment of zoonotic transmission risks

Studying the genetic diversity of malaria parasites found in livestock and humans, investigating potential inter-species transmission routes, and assessing the infectivity of these parasites to humans are necessary to evaluate the zoonotic transmission risks (Clark & Taylor-Robinson, 2021). Plasmodium species, the parasites responsible for malaria, typically exhibit host specificity, meaning they are adapted to infect specific host species. While P. falciparum is the main cause of malaria in humans, there is limited evidence of zoonotic potential in certain Plasmodium species that infect animals (Sato, 2021).

While there is evidence of Plasmodium infections in livestock, the zoonotic transmission of these parasites to humans is not well-established. Plasmodium species that primarily infect animals may not efficiently complete their life cycle in humans, and the prevalence of such zoonotic transmissions is generally considered low (Sato, 2021). P. knowlesi, originally thought to infect only monkeys, has been identified as a cause of human malaria in Southeast Asia. The transmission of P. knowlesi to humans occurs through the bites of infected mosquitoes, often from the Anopheles leucosphyrus group, feeding on monkeys and humans (Imai et al., 2014; Lee et al., 2022). While P. knowlesi is not directly associated with livestock, its ability to infect humans and monkeys highlights the potential for zoonotic transmission from animals to humans (Lee et al., 2022). Further research is needed to understand the factors influencing the transmission dynamics of Plasmodium parasites between animals and humans. Surveillance, molecular studies, and a multidisciplinary approach are critical for assessing and managing the zoonotic potential of Plasmodium spp. in livestock.

Diagnostic tools and techniques

Developing accurate and reliable diagnostic tools tailored specifically for detecting Plasmodium spp. in livestock populations is essential. Novel techniques, such as next-generation sequencing and genotyping methods, can aid in differentiating between animal-specific and human-specific malaria parasites, enabling a deeper understanding of the transmission dynamics (Slater et al., 2022). Detecting Plasmodium spp. in livestock populations, particularly in the context of veterinary medicine, is essential for understanding and managing the impact
of these parasites on animal health (Franco et al., 2014). While malaria in humans is primarily caused by P. falciparum, in livestock, various Plasmodium species may cause diseases such as bovine, ovine, or caprine malaria. Here are some diagnostic tools commonly used for detecting Plasmodium spp. in livestock.

Blood smear microscopy

Blood smear microscopy is a traditional and widely used method for diagnosing Plasmodium infections in animals. The condition is diagnosed by a pathologist who manually examines the patient’s thick and thin blood smears under a microscope. Owing to inadequate healthcare infrastructure, these skilled pathologists could not be accessible in many regions of the world. A thick smear can identify malaria more precisely and quickly than a thin smear. Conversely, a thin smear can indicate the kind of malaria and its severity (Das et al., 2015; Jan et al., 2018). Furthermore, manual inspection is a laborious and time-consuming method of detecting malaria and demands the full concentration of the pathologist (Fatima & Farid, 2020).

Rapid diagnostic tests (RDTs)

Parasite-based diagnosis is now more widely available in malaria-endemic regions of the world through RDTs. Immunochromatographic assays detect parasite antigens in whole blood samples (Iwuafor et al., 2018). Compared to microscopy or clinical diagnosis, RDTs hold several benefits. An accurate diagnosis is crucial to manage cases, monitor, and eventually eliminate malaria. RDTs, similar to those used in human malaria diagnosis, are available for veterinary use. These tests typically detect specific antigens produced by Plasmodium parasites in blood samples. RDTs are relatively quick and easy to use, making them suitable for field settings (Gómez-Luque et al., 2020).

Polymerase chain reaction (PCR)

Molecular techniques, like PCR, can be utilized for sensitive and specific detection of Plasmodium DNA in blood samples. PCR allows for identifying specific Plasmodium species and can be helpful in research. PCR is more sensitive than microscopy and conventional RDTs and can identify infections with parasite densities as low as 0.2 parasite/µL. However, due to the high cost of the reagents, equipment, and skilled staff required, large-scale field use of PCR is not feasible (Mathison & Pritt, 2017; Naeem et al., 2018; Mbanefo & Kumar., 2020).

Loop-mediated isothermal amplification (LAMP)

It has been shown that the LAMP approach is a strong and dependable way to identify and detect microbial and viral pathogens (Garg et al., 2022). The isothermal nucleic acid amplification method, known as LAMP, is becoming increasingly well-liked due to its ease of use and quick outcomes. LAMP assays for Plasmodium spp. can be adapted for field use and are less complex than traditional PCR (Sattabongkot et al., 2014; Wong et al., 2018). LAMP reactions can be visually inspected for color changes, making them suitable for resource-limited settings. LAMP has demonstrated its superiority over PCR by specifically amplifying target DNA even when non-target sequences are present (Khan et al., 2018; Foo et al., 2020).

Serological tests

ELISAs, a type of serological test, can identify antibodies the host produces in reaction to Plasmodium infection. These tests are valued for detecting exposure to the parasite but may not distinguish between current and past infections (Plucinski et al., 2021). Over the years, the advancements mentioned above have greatly benefited the creation of new assays. Developing stable hybridisms as sources of monoclonal antibodies and enhancing immunoassay platforms were two significant developments (Slater et al., 2022). These analyses have demonstrated that malaria is the primary cause of fever in antigen-positive individuals across various locations with varying malaria transmission intensities (Plucinski et al., 2020); however, further research is needed to determine how reliable these results are in other contexts.

Immunofluorescence assays (IFA)

Antibodies against asexual blood-stage malaria parasites are typically detected during the serological malaria diagnosis. IFA involves using fluorescently labeled antibodies to detect Plasmodium parasites in blood smears. For the past few decades, IFA has proven to be a trustworthy serologic test for malaria (McMorrow et al., 2011; Slater et al., 2022). IFA is sensitive and specific but subjective and time-consuming (Talapko et al., 2019). It provides a sensitive and specific means of identification but requires specialized equipment (Slater et al., 2022).

Antigen detection assays

Antigen detection assays, similar to those used in human malaria diagnosis, can be adapted for veterinary use. These tests detect specific Plasmodium antigens in blood samples (Figueiredo et al., 2018; Plucinski et al., 2021).
High-throughput sequencing

Next-generation sequencing technologies can provide in-depth information about the genetic diversity of *Plasmodium* spp. in livestock populations. This approach is more suited for research purposes and may not be practical for routine diagnostic use (Brashear & Cui, 2022). Genetic and genomic information may be utilized to find new vaccine targets, create a successful vaccination plan, pinpoint protective antigens in a vaccine, including complete organisms, and assess the vaccine’s effectiveness (Su et al., 2023). Dielectrophoretic and magnetophoretic procedures are among the potential novel strategies for malaria parasite-infected red blood cells, even though many other techniques have lately been developed and examined (Kasetsiriokul et al., 2016). Combining multiple diagnostic methods may enhance the accuracy and reliability of *Plasmodium* detection in livestock populations.

Comprehensive surveillance studies

Conducting comprehensive surveillance studies in areas where livestock populations coexist with human malaria transmission hotspots is important for understanding the dynamics of *Plasmodium* infections, identifying potential reservoirs, and implementing effective control measures. These studies should include entomological, epidemiological, and genetic components to understand better the interaction between livestock, vectors, and human malaria transmission dynamics (Gueye et al., 2023). Understanding whether specific *Plasmodium* species are shared between the two populations is crucial. To determine the frequency of *Plasmodium* infections in humans and cattle, conducting epidemiological surveys and analyzing variables that might affect transmission, such as the closeness of habitats for humans and animals, patterns of land use, and environmental factors, are necessary (Castro, 2017). Also, it is mandatory to investigate the mosquito vectors responsible for transmitting malaria in humans and animals and determine the distribution and abundance of *Anopheles* mosquitoes and their feeding preferences. The most often used entomological metric to ascertain the correlation between malaria incidence and vectors is the number of mosquito species (Amaechi et al., 2018).

Furthermore, it is necessary to examine the genetic diversity of *Plasmodium* parasites in human and animal populations using genetic analysis methods, including high-throughput sequencing and molecular markers. Also, the similarities in parasite strains between animals and humans must be checked, and potential reservoir hosts among livestock species should be identified. In this regard, human and animal behavioral factors that may influence the risk of *Plasmodium* transmission should not be overlooked. These measures include human activities, livestock management practices, and movements of both populations. Human mobility and livelihood activities impact malaria risk in eradication settings and contribute to the epidemiology of vectorborne infections (Abdalal et al., 2023). Each newly developing zoonotic disease’s ecology must be evaluated to conduct a risk assessment, create response and control strategies, and adopt a collaborative, multidisciplinary strategy that transcends borders between animal, human, and environmental health (Mackenzie & Jeggo, 2019).

The early detection and treatment of malaria, together with an appropriate community understanding of the illness, are essential for its eradication. Engage with residents, livestock keepers, and healthcare providers to gather information on health-seeking behavior, livestock management practices, and assessments of malaria in humans and animals (Hasabo et al., 2022). Evaluate the effectiveness of malaria control interventions in both human and animal populations. This measure may include the usage of bed nets, insecticide-treated livestock, and other vector control measures. A current understanding of the essential epidemiological characteristics of each species is required to ensure that focused treatments and control measures are implemented to eradicate all *Plasmodium* species. Also, it is advisable to integrate data from human and veterinary health systems to comprehensively understand the epidemiology of *Plasmodium* infections in the area (Dao et al., 2023). Surveillance studies that adopt a comprehensive and interdisciplinary approach are critical for designing targeted interventions and reducing the overall burden of malaria in areas where humans and livestock coexist. The findings from such studies help advance knowledge of the intricate relationships between different hosts and the malaria parasite.

Future directions for research

Malaria research continues to be a dynamic and evolving field with ongoing efforts to understand the disease better, develop new tools for prevention and treatment, and ultimately work towards global malaria elimination. Further research is required to overcome the challenges mentioned above and advance our understanding of malaria reservoirs within livestock populations. The following are potential future directions for the investigation of malaria.
Antimalarial drug development

Further research into synthesizing antimalarial medications with novel mechanisms of action is crucial. This endeavor includes addressing drug resistance issues and improving the efficacy and safety of existing treatments. Most antimalarial medications focus on the blood stage of the parasite’s life cycle, and a few on the liver stage. Emerging resistance to blood-stage malaria medications, such as artemisinin, highlights the significance of potential new liver-stage medications (Stanway et al., 2019). Targeting distinct phases of the life cycle of parasites, including the liver stage, could provide new opportunities for drug development (Burns et al., 2019). Research to understand the mechanisms of drug resistance in malaria parasites and strategies to overcome resistance is essential. This research includes studying genetic and molecular factors associated with resistance. Combination therapies and drug regimens that minimize the risk of resistance development are areas of active investigation.

Genomic research

Advances in genomics and genetic epidemiology can provide insights into the genetic diversity of *Plasmodium* parasites and their vectors. This information is valuable for understanding transmission dynamics, drug resistance, and host-parasite interactions (Su et al., 2019). Recent developments in malaria parasite genetics and genomics have significantly improved our knowledge of the pathophysiology, treatment responses, population dynamics, and transmission of parasites. Studying the human genetic factors that influence susceptibility to malaria and the development of immunity is an important avenue for research. Our understanding of the biology, gene function, medication resistance, population dynamics, transmission, and molecular evolution of malaria parasites has significantly increased with the discovery of genetic variants and genomic diversity of malaria parasite populations (Su et al., 2019).

Point-of-care diagnostics

Developing and improving rapid and accurate point-of-care diagnostics is crucial for timely and effective case management. Advances in diagnostic technologies, including molecular and immunological assays, can enhance surveillance and monitoring efforts (Kazemi et al., 2005; Wang et al., 2021). WHO has set an objective of eradicating *Plasmodium* by 2030; however, achieving this goal would require accurate diagnosis and proper treatment (de Freitas Borges et al., 2021; Okyere et al., 2020). The effectiveness of various diagnostic technologies has to be regularly assessed and verified to achieve this objective. For afflicted individuals to receive focused therapy, more advanced diagnostic tools capable of detecting incredibly low parasite concentrations are required. It is predicted that the results of these tools will help doctors manage patients more effectively, leading to decreased death rates and improved quality of life (de Freitas Borges et al., 2021).

Vaccine development

Ongoing efforts to develop an effective malaria vaccine are a priority. Developing vaccines targeting different *Plasmodium* species and life stages is crucial for comprehensive malaria control. Research into optimizing existing vaccines, such as the RTS,S/AS01 vaccine, and the development of next-generation vaccines are essential areas of focus (Draper et al., 2018). *Plasmodium* exhibits a range of surface antigens throughout the pre-erythrocytic, erythrocytic, gametocyte/sexual, and mosquito phases of development. Many options for anti-malaria vaccines have been evaluated from different parasite stages during the last few decades (Figure 5). The high polymorphism linked to suggested vaccine candidates and their poor efficiency has likely contributed to the difficulty in developing a highly effective vaccination against malaria, even though there are several potential vaccines. Due to their efficiency, safety, and biocompatibility, novel nanoparticle-based immunization strategies may produce effective anti-malaria vaccines (Xu et al., 2022). Overall, alternative vaccination strategies based on complete sporozoites appear favorable for creating powerful, secure, and safe anti-malaria vaccines.

The four phases of the malaria parasite life cycle are depicted in steps 1 through 14 (Chandley et al., 2022).

Community engagement and behavioral research in malaria control

Community involvement and malaria prevention must go hand in hand. Even the best-planned preventive measures could not be implemented if people in the community do not recognize the benefits of preventing the sickness. Understanding a community’s perspective on febrile illness, its significance in people’s conceptions of sickness in general, and the practices that are currently in place that either support or contradict preventative efforts are all important (Zerdo et al., 2022). Research on community engagement and behavior change is vital for successfully implementing malaria control interventions. Understanding social, cultural, and economic factors influencing malaria prevention and treatment is essential (Whittaker & Smith, 2015).
Malaria elimination strategies

Priority should be given to research into malaria elimination strategies in specific regions and countries, including tools for surveillance, ACD, and population-wide interventions (Lourenço et al., 2019). These research directions are interconnected, and progress in one area frequently leads to advances in others. Create and implement vector control strategies that target mosquito vectors that feed on people and animals. This measure may include the application of insecticides, bed nets, and other interventions. Developing innovative vector control strategies, including new insecticides, bed net technologies, and spatial repellents, is critical for reducing malaria transmission (Gari & Lindtjorn, 2018; Lourenço et al., 2019). Understanding mosquito vectors’ behavior and ecology and developing interventions targeting specific vector species is essential for effective control. Addressing these challenges and pursuing future research directions requires a collaborative and multidisciplinary approach involving researchers, healthcare professionals, policymakers, and communities to develop effective strategies for malaria control in areas where humans and livestock coexist (Dhiman, 2019; Mackenzie & Jeggo; 2019).

Conclusion

While considering livestock populations as reservoirs for malaria presents various challenges, it is a topic that deserves significant attention. One of the main challenges is the lack of comprehensive data on malaria’s prevalence and transmission dynamics in livestock. Additionally, understanding the potential role of livestock in transmitting malaria to humans requires further research and investigation. However, given the potential impact on public health and disease control strategies, investing resources in studying this field and developing effective interventions is crucial. Enhanced diagnostic techniques, comprehensive surveillance studies, and
a thorough assessment of zoonotic transmission risks must be prioritized to shed light on the contribution of livestock populations to malaria transmission. Enriching our knowledge in this domain will contribute to a comprehensive and effective strategy for malaria control, potentially significantly reducing the burden of this devastating disease.

Raising awareness among communities about the potential role of livestock in malaria transmission is crucial. It is also necessary to promote good animal husbandry practices, educate communities about preventive measures, and implement monitoring and evaluation systems to assess the impact of livestock on malaria transmission dynamics. Regular assessments can guide adaptive management strategies. Building capacity in both human and veterinary healthcare systems to address the challenges and opportunities presented by the potential role of livestock as reservoirs for malaria is mandatory. Finally, training professionals in a one health approach is crucial.

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**Compliance with ethical guidelines**

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