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Research Article

Plasmodium vivax Transmission to Cattle in A Malaria Endemic Area in Jayapura Regency, Indonesia

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I N F O

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A B S T R A C T

Background: It is not enough to study malaria incidence in the community from a human perspective alone. It must involve environmental aspects and potential animal hosts for the *human-Plasmodium* (*h-Plasmodium)* parasite. The behaviour of some zoophilic *Anopheles* species that like to suck animal blood is a concern for all. Empirical evidence of parasite transmission from *Anopheles* to domestic animals is crucial to the study. Specific markers for the presence of *h-Plasmodium* in the erythrocytic phase are the appearance of the enzymes histidine-rich protein and parasite lactate dehydrogenase. This study aimed to track the presence of *h-Plasmodium* by detecting HRP-2 and pLDH in cattle.

Method: An exploratory observational study was conducted in Kemtuk Gresi District and Nimboran District in Jayapura Regency. Blood samples were taken from 30 cows from the jugular vein in the neck, and tested using StandaReagent™ RDT of malaria for *P. falciparum* and *P. vivax*.

Results: Most of the samples did not contain *h-Plasmodium* (93.33%), but two cows were found to be positively infected with *P. vivax* from both districts (6.67%). This suggests that the zoophilic *Anopheles* mosquito might have transmitted the parasite to the cattle.

Conclusion: Cattle can be infected with *h-Plasmodium* as evidenced by the detection of *P. vivax* lactate dehydrogenase (*Pv*LDH) in the samples and have the potential to be a reservoir for malaria transmission.

Keywords: Bovine Blood, *h-Plasmodium*, Malaria, *P. vivax*, RDT, StandaReagent™

Introduction

Malaria is still a health problem in Indonesia as well as in the world.[1] The difficulty of eliminating malaria is due to many variables that play a role in its transmission.[2-5] Malaria control programmes rely more on handling vectors and patient populations, previously believed to be the only reservoir and have not yet reached non-human reservoirs.[6-8] Recent studies in the last five years have found the presence of *human-Plasmodium (h-Plasmodium)* in several types of domestic livestock.[9-12]

The existence of *h-Plasmodium* that causes malaria in livestock still needs scientific strengthening because the findings are still very limited.[13,14] Evidence for the existence of this parasite can be seen from the various biomedical markers produced during its life activities.[15-17] Two markers that are believed to be the evidence of the activity of *Plasmodium* sp parasites are enzymes formed in the erythrocytic phase, namely histidine-rich protein 2 (HRP-2), and parasite lactate dehydrogenase (pLDH).[18-21]

The availability of diagnostic tools for malaria is still oriented toward detecting suspected human sufferers and has not been specifically designed for non-human samples. Advances in molecular diagnostic techniques are very helpful in tracking the presence of *h-Plasmodium* in various hosts, including suspicious domestic livestock.[22] Microscopic testing, which is the gold standard for diagnosis of malaria,[23] may differ in diagnosis due to the highly variable morphology of the parasites. The use of a rapid diagnostic test (RDT) for malaria screening in areas with high endemicity is more helpful in finding new cases quickly and easily.[24,25] The most valid marker for the presence of *h-Plasmodium* in patients is the appearance of the enzymes histidine-rich protein (HRP) and parasite lactate dehydrogenase (pLDH).[26] They are the most reliable indicators of *h-Plasmodium* infection in patients, however, they still have significant limitations.[27]

This study aims to trace the presence of HRP-2 and pLDH in domestic livestock as a marker of parasitic life processes in the host. The study focused on types of cattle that are frequently utilised as a barrier against *Anopheles (An.)* mosquito bites.

Material and Method

An exploratory observational design was chosen for the study in Kemtuk Gresi and Nimboran Districts in Jayapura Regency. The study was conducted from September to December 2022. Thirty cattle were chosen for the study by the saturated sampling technique. The owners had kept all cows for more than three months.

Material Collecting

Bovine blood specimens were collected from the jugular vein using an EDTA vacuum tube by trained personnel from the local Animal Husbandry Service. HRP-2 and pLDH testing was carried out using the Rapid Diagnostic Testing (RDT) of the StandaReagen™ malaria brand.

Protocol of the Testing

A sample loop was used to add 5 µL of whole blood into the sample well. Two drops (60 µL) of assay buffer were added to the buffer well. The test result was read within 20 minutes.

Interpretation of Result

The result was considered negative if only one pink or purple band appeared on the control region, and positive if in addition to a pink or purple coloured control band, a pink or purple coloured band appeared at the Pf and/ or Pv region (Figure 1).[28]

Ethical Approval

Ethical approval was issued by the Ethics Commission of the Faculty of Public Health, Universitas Muhammadiyah Semarang number 707/KEPK-FKM/UNIMUS/2022.

Results

The cattle population in the two districts was not large because the residents used to raise other livestock such as pigs which had a higher selling value. Most of the livestock (as much as 86.67%) were within a distance of fewer than 100 meters from the owner's house. None of the cattle discovered in the two regions were confined in proper cattle pens. Cattle pens discovered were simply enclosures with a border made of wood and a simple barrier to keep livestock from escaping. In fact, as many as 43.3% of the livestock were left unrestrained in the forest by their owners in Nimboran District. Almost all livestock owners had experienced malaria, but when the samples were taken, some had recovered from treatment, and only 16.67% were still sick with malaria and lived in Nimboran District. The positive cow from the two districts had its blood tested using the malaria RDT (Table 1).

P. falciparum was not found in cows, but *P vivax* was found in 2 cows (6.67%). A biomedical marker for the presence of *P. vivax* is indicated by a positive result for the *Pv*LDH enzyme (Figure 2). Two cows were detected to produce the enzyme lactate dehydrogenase. Although the proportion is relatively small, this shows the survival ability of *P. vivax* in bovine blood (Figure 3).

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Table 1.Maintenance and Cowshed Condition

Variable		District of Kemtuk Gresi	District of Nimboran
Number of cattle		12	18
Distance of cattle to house (m)			
	0-10	0	2
	10-50	12	9
	50-100	0	3
	± 1000	0	4
Cowshed condition			
	No shed	0	13
	No roof, no walls	12	5
Was the farmer suffering from malaria?			
	Yes	0	5
	No	12	13
StandaReagen™ RDT testing			
	Positive	1	1
	Negative	11	17

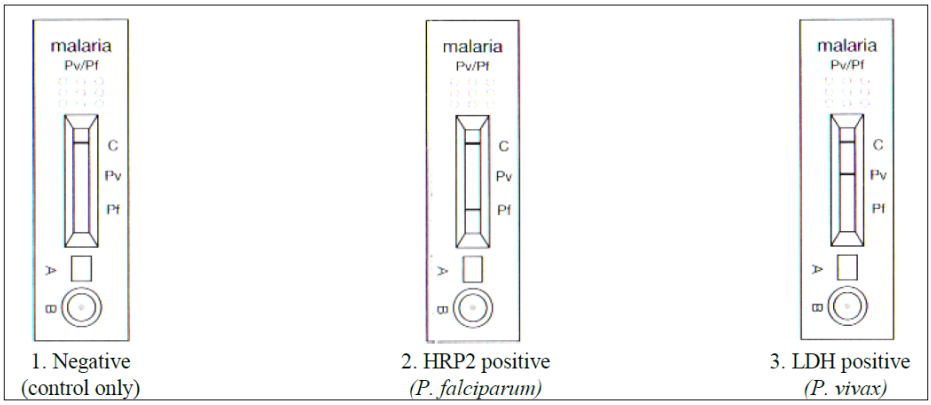

Figure 1.Interpretation of StandaReagen™ Malaria RDT

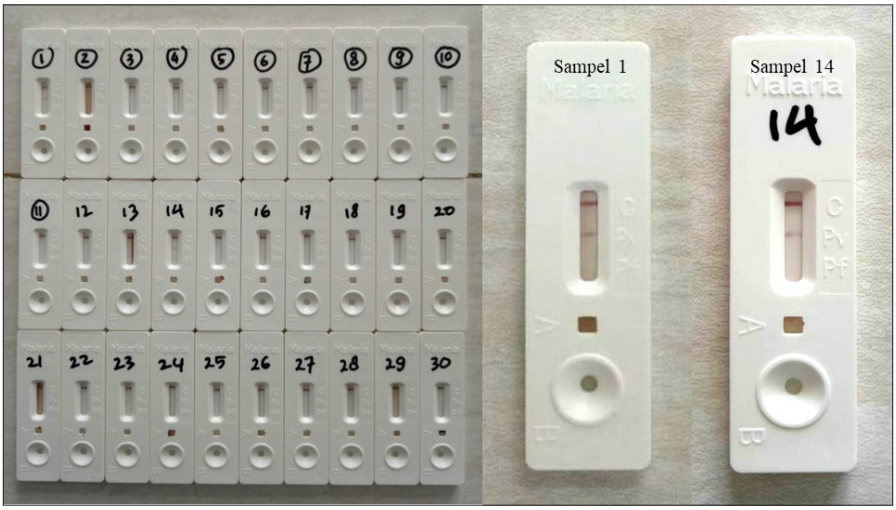

Figure 2.The StandaReagen™ RDT Test Results - Positive for P. vivax in Sample Numbers 1 and 14 indicated by the Appearance of a Reddish Antigen Band Line

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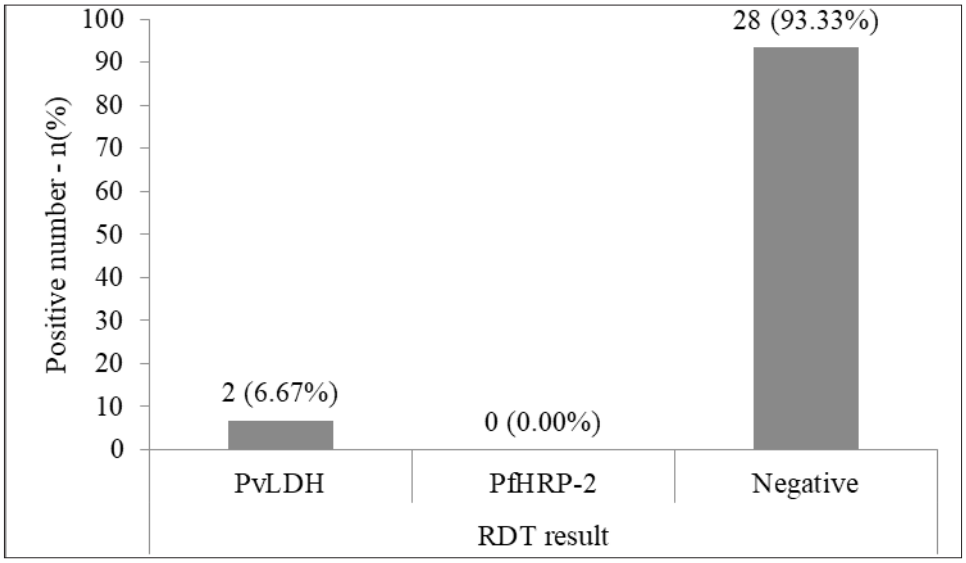

Figure 3.Results of the HRP-2 and pLDH Plasmodium sp by RDT

Discussion

Jayapura Regency is located between 2° and 3° South Latitude and between 139° and 140° East Longitude and has an area of 17,516.6 km^2 divided into 19 districts.[29] The topography of the area is mostly in the form of relatively steep slopes with a slope of 5%-30% and a height of 0.5 m-1500 m above sea level. The northern coastal area is in the form of undulating lowlands with a slope of 0%-10% which is covered with alluvial deposits and partly in the form of swamps covering an area of 13,700 ha. The majority of Jayapura Regency (72.09%) is above the slope of 41%, while the range of places with a slope of 0%-15% is approximately 23.74%.[30]

Kemtuk Gresi District and Nimboran District are two district areas that are located next to each other in the central area of Jayapura Regency. Most of the population here earns livelihood as farmers. Raising livestock, such as poultry and medium to large livestock, is common among the population. Home-scale pig farming seems to be a necessity for residents, while other large livestock are relatively rare. There are only a few people who raise cattle in the two districts, so the number of cattle-population is also not large.

Kemtuk Gresi District is an area directly adjacent to Keerom Regency which is the highest malaria endemic area in Indonesia.[1] Geographical conditions that are relatively same and continuous between regions are conducive for Anopheles vectors. There are reports of zoophilic *Anopheles* species in the area that prefer both human and animal blood.[31]

Several *Anopheles* species have been confirmed as vectors for malaria in Papua, Indonesia, viz., *An. farauti, An. bancroftii, An. punctulatus,* and *An. coliensis*.[32,33] The zoophilic *Anopheles* species found in Papua were *An. hinesorum, An. farauti, An. coliensis,* and *An. tessellatus*.[34] The existence of cattle in the open pen area is a source of blood feed for zoophilic *Anopheles*.[35,36] Female *Anopheles* mosquitoes need blood for their reproductive process to produce eggs.[37] The behaviour of female zoophilic *Anopheles* sucking the blood of livestock opens opportunities for the transfer of *Plasmodium* parasites to livestock.[38]

The important stage that causes *Anopheles* to become infectious is the gametocyte.[39] It is the sexual stage of *Plasmodium sp* which will continue the life cycle through mating.[40] The sexual cycle of *Plasmodium sp* will not occur without the gametocyte stage, and there will be no confirmed vector for malaria transmission.[41] Macrogametocytes are fertilised by microgametocytes in the stomach of the female *Anopheles*.[42] Furthermore, the development process from zygote to sporozoite occurs.[43]

The finding of gametocyte stages in the blood confirms the existence of *h-Plasmodium* transmission in domestic livestock. Unfortunately, there was no microscopic testing done in this study and the type of parasitic stage that had formed could not be known. The rapid diagnostic tool can only detect the presence of *Pf*HRP-2 and *Pv*LDH formed in the erythrocytic phase. However, the pLDH is a terminal enzyme produced by the *h-Plasmodium* parasite from the start of the erythrocytic phase to its peak at the gametocyte stage.[44]

There is not much known about the ability of *Plasmodium* to survive in animals. Several previous studies need attention in this regard. The finding of *h-Plasmodium* in Etawa crossbreed goats in Purworejo, Central Java, showed that the malarial parasite can live and develop up to the erythrocytic phase in the animal's body.[13] Similar findings were also reported from the Sumba and Fakfak areas where *Plasmodium vivax* was found in buffaloes, horses, goats, and

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dogs even up to the gametocyte stage.[14] The results of these two studies have actually answered doubts about the role of livestock as part of the chain of transmission of malaria so far.[45] The gametocyte stage proves that *Plasmodium* sp can really survive and is able to develop to the final stage, thus it has the potential to make its host a source of transmission or reservoir.

The detection of *Plasmodium vivax* in two cows from the two districts in the current study strengthens and complements the findings regarding the viability of *h-Plasmodium* in livestock. The findings from Jayapura Regency are based on an examination of the RDT method using StandaReagen™. The malaria RDT test kit uses the principle of a colour reaction on the formation of bonds between antigen and antibody.[46] RDT StandaReagen™ has coated the diagnostic tool membrane with 2 types of monoclonal antibodies, namely HRP-2 for the *Plasmodium falciparum* band line and pLDH for the *Plasmodium vivax* band line. A colour reaction in the form of a line is formed when the antigen from the blood sample reacts with specific monoclonal antibodies in the membrane of the device.[28]

The finding of *Pv*LDH in these cattle (Figure 2) is an improvement after the same method failed to detect the pLDH enzyme in the blood of Etawa crossbred goats[25], and other domestic animals[47] although finally *Pf*LDH was found using the polymerase chain reaction (PCR) method.[48] The finding of *Pv*LDH in this cow showed a parasite species different from the one in Etawa crossbred goats.[47] Both *P. vivax* and *P. falciparum* species produce LDH enzymes when they enter the erythrocytic phase of the schizogony cycle.

These two are terminal enzymes, namely the final metabolite products produced by *Plasmodium* sp, that can be detected and used as biomarkers for their presence in the host's body.[49,50] The pLDH was detected easily in blood samples with a parasitaemia level of 0.2%-10%.[51,52] The pLDH production from gametocyte stages in this asexual stage after treatment remains positive for several days.[53]

If the HRP-2 enzyme is not detected, it cannot automatically be concluded that *P. falciparum* cannot be transmitted and cannot thrive in cattle, considering that in other locations, it can be identified in several types of domestic animals.[13,14,48] The low level of parasitaemia that occurs can lead to the undetectable presence of parasites because it is beyond the capabilities of the diagnostic tools used.[25] *Pf*HRP-2 begins to be produced when merozoites invade erythrocytes and transform into young, ring-shaped trophozoites,[54] but is more dominantly produced by the mature stage of *Plasmodium*.[55] HRP-2 was also detected at the developmental stage of *P. falciparum* gametocytes in erythrocytes. *Pf*HRP-2 can be used as a marker for the presence of gametocyte stages in the erythrocytic phase because this protein is expressed from the membranes of erythrocytes invaded by *P. falciparum* and is also found in the cytosol.[56]

The detection of *h-Plasmodium*, especially *P. vivax* and *P. falciparum* in domestic livestock in several places in Indonesia shows that these parasites can live and develop in the bodies of domestic livestock.[45] These findings represent new scientific developments in terms of the transmission of malaria in society. The understanding of the transmission cycle of malaria must begin to shift, from only "humans - *Anopheles* - humans"[57] to "humans and livestock - *Anopheles* - humans and livestock". The emergence of domestic livestock as a non-human reservoir must receive serious attention because it will change efforts to control malaria in the community which has livestock in residential areas.

Conclusion

Cattle have the potential to become a reservoir of malaria transmission, as evidenced by the *Pv*LDH detected in the cow's blood. This finding is significant for the control of malaria transmitted by zoophilic vectors. The existence of livestock is vital to watch out for as it may be a source of infectious parasites.

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Conflict of Interest: None

References

1. Kementerian Kesehatan RI. Profil Kesehatan Indonesia Tahun 2020. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020. p. 200-4. Indonesian.
2. Kementerian Kesehatan RI [Internet]. Kejar target bebas malaria 2030, Kemenkes Tetapkan 5 regional target eliminasi. Sehat Negeriku; 2022 [cited 2023 Apr 10]. Available from: https://sehatnegeriku.kemkes.go.id/baca/rilis-media/20220422/1439692/kejar-target-bebas-malaria-2030-kemenkes-tetapkan-5-regional-target-eliminasi/#:~:text=Malaria%20adalah%20penyakit%20menular%20yang,tahun%202009%2C%20yaitu%20sebesar%20418.439. Indonesian.
3. Nisrina H, Sumanto D, Widodo S. Pengasapan kandang ternak: perilaku potensial peningkatan risiko gigitan Anopheles pada penduduk daerah endemik malaria. J Kesehatan Masyarakat Indonesia [Internet]. 2020 [cited 2023 Mar 20];15(1):35-41. Available from: https://doi.org/10.26714/jkmi.15.1.2020.35-41. Indonesian. [Google Scholar]

4. Lobo CA. *Babesia divergens* and *Plasmodium falciparum* use common receptors, glycophorins a and b, to invade the human red blood cell. Infect Immun [Internet]. 2005 [cited 2022 Dec 15];73(1):649-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15618210 [PubMed] [Google Scholar]
5. Lobo CA, Cursino-Santos JR, Rodriguez M, Ord R, Singh M. Receptor–ligand interactions underlying RBC invasion in Babesia. ISBT Sci Ser. 2015;10(S1):173-80. [Google Scholar]
6. Susanna D, Eryando T. Faktor dominan yang mempengaruhi kejadian malaria di perdesaan. J Kesehat Masy Nas. 2010;4(4):180-5. Indonesian. [Google Scholar]
7. Erdinal E, Susanna D, Wulandari RA. Faktor-faktor yang berhubungan dengan kejadian malaria di Kecamatan Kampar Kiri Tengah Kabupaten Kampar, 2005/2006. Makara Kesehat. 2006;10(2):64-70. Indonesian. [Google Scholar]
8. Donnelly B, Berrang-Ford L, Ross NA, Michel P. A systematic, realist review of zooprophylaxis for malaria control. Malar J [Internet]. 2015 [cited 2022 Dec 15];14(1):313. Available from: http://www.malariajournal.com/content/14/1/313 [PubMed] [Google Scholar]
9. Opara MN, Nwokedi CC. Occurrence of haemoparasites among small ruminants reared under traditional husbandry system in Owerri, Southeast Nigeria. Bull Anim Health Prod Afr [Internet]. 2011 [cited 2022 Dec 20];59(4):393-8. Available from: http://105.27.231.85/bitstream/handle/123456789/496/BAHPA_59-4.pdf?sequence=1&isAllowed=y#page=7 [Google Scholar]
10. Kaewthamasorn M, Takeda M, Saiwichai T, Gitaka JN, Tiawsirisup S, Imasato Y, Mossaad E, Sarani A, Kaewlamun W, Channumsin M, Chaiworakul S, Katepongpun W, Teeveerapunya S, Panthong J, Mureithi DK, Bawm S, Htun LL, Win MM, Ismail AA, Ibrahim AM, Suganuma K, Hakimi H, Nakao R, Katakura K, Asada M, Kaneko O. Genetic homogeneity of goat malaria parasites in Asia and Africa suggests their expansion with domestic goat host. Sci Rep. 2018;8(1):5827. [PubMed] [Google Scholar]
11. Aseme T, Robert B, Amuzie CC, Akani GC. Haematological parameters and haemoparasites of West African Dwarf goats sold at Trans-Amadi and Rumuokoro Abattoirs, Port Harcourt, Nigeria. Curr Trends Vet Dairy Res [Internet]. 2020 [cited 2022 Dec 19];1(1):14-20. Available from: https://www.researchgate.net/publication/346718018_Haematological_Parameters_and_Haemoparasites_of_West_African_Dwarf_Goats_Sold_at_Trans-Amadi_and_Rumuokoro_Abattoirs_Port_Harcourt_Nigeria_Aseme_T_Robert_B_Amuzie_CC_and_Akani_GC#fullTextFileContent [Google Scholar]
12. Al-Badrani BA, Alabadi BH. A preliminary study of malaria infection (Plasmodium spp.) in Iraqi livestock. Egypt J Vet Sci [Internet]. 2021 [cited 2022 Dec 23];51(1):97-111. Available from: https://doi.org/10.21608/ejvs.2020.46641.1195 [Google Scholar]
13. Sumanto D, Hadisaputro S, Adi MS, Susanti S, Sayono. Human-plasmodium like in domestic-goat blood in malaria endemic areas in Purworejo Indonesia. J Commun Dis [Internet]. 2021 [cited 2022 Dec 10];53(4):148-52. Available from: https://medical.advancedresearchpublications.com/index.php/Journal-CommunicableDiseases/article/view/794 [Google Scholar]
14. Yanmanee S, Seethamchai S, Kuamsab N, Karaphan S, Suwonkerd W, Jongwutiwes S, Putaporntip C. Natural vectors of *Plasmodium knowlesi* and other primate, avian and ungulate malaria parasites in Narathiwat Province, Southern Thailand. Sci Rep [Internet]. 2023 [cited 2023 Apr 10];13(1):8875. Available from: https://doi.org/10.1038/s41598-023-36017-3 [PubMed] [Google Scholar]
15. John CC, Tande AJ, Moormann AM, Sumba PO, Lanar DE, Min XM, Kazura JW. Antibodies to pre-erythrocytic Plasmodium falciparum antigens and risk of clinical malaria in Kenyan children. J Infect Dis. 2008;197(4):519-26. [PubMed] [Google Scholar]
16. Carrolo M, Giordano S, Cabrita-Santos L, Corso S, Vigario AM, Silva S, Leiriao P, Carapau D, Armas-Portela R, Comoglio PM, Rodriguez A, Mota MM. Hepatocyte growth factor and its receptor are required for malaria infection. Nat Med. 2003;9(11):1363-9. [PubMed] [Google Scholar]
17. Nakamura T, Mizuno S. The discovery of Hepatocyte Growth Factor (HGF) and its significance for cell biology, life sciences and clinical medicine. Proc Jpn Acad Ser B Phys Biol Sci. 2010;86(6):588-610. [PubMed] [Google Scholar]
18. Aley SB, Sherwood JA, Howard RJ. Knob-positive and knob-negative Plasmodium falciparum differ in expression of a strain-specific malarial antigen on the surface of infected erythrocytes. J Exp Med. 1984;160(5):1585-90. [PubMed] [Google Scholar]
19. Kilejian A. Characterization of a protein correlated with the production of knob-like protusions on membranes of erythrocytes infected with Plasmodium falciparum. Proc Natl Acad Sci USA. 1979;76(9):4650-3. [Google Scholar]
20. Hadley TJ, Leech JH, Green TJ, Daniel WA, Wahlgren M, Miller LH, Howard RJ. A comparison of knobby (K +) and knobless (K-) parasites from two strains of Plasmodium falciparum. Mol Biochem Parasitol. 1983;9(3):271-8. [PubMed]

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21. Vernot-Hernandez JP, Heidrich HG. The relationship to knobs of the 92,000 D protein specific for knob-by strains of Plasmodium falciparum. Z Parasitenkd. 1985;71(1):41-51. [PubMed] [Google Scholar]
22. Beck HP. Extraction and purification of Plasmodium parasite DNA. Methods Mol Med. 2002;72:159-63. [PubMed] [Google Scholar]
23. Centers for Disease Control and Prevention [Internet]. Malaria diagnosis (United States); 2015 [cited 2022 Dec 20]. Available from: https://www.cdc.gov/malaria/diagnosis_treatment/diagnosis.html
24. Laban NM, Kobayashi T, Hamapumbu H, Sullivan D, Mharakurwa S, Thuma PE, Shiff CJ, Moss WJ; Southern Africa International Centers of Excellence for Malaria Research. Comparison of a PfHRP2-based rapid diagnostic test and PCR for malaria in a low prevalence setting in rural southern Zambia: implications for elimination. Malar J. 2015;14:25. [PubMed] [Google Scholar]
25. Sumanto D, Hadisaputro S, Sakundarno Adi M, Susanti S, Sayono S. Human Plasmodium in livestock: the absence of PfHRP2 and pLDH among high parasitemia cases. Int J Med Parasitol Epidemiol Sci. 2021;2(2):35-41. [Google Scholar]
26. Jimenez A, Rees-Channer RR, Perera R, Gamboa D, Chiodini PL, González IJ, Mayor A, Ding XC. Analytical sensitivity of current best-in-class malaria rapid diagnostic tests. Malar J. 2017;16(1):128. [PubMed] [Google Scholar]
27. Koita OA, Doumbo OK, Ouattara A, Tall LK, Konaré A, Diakité M, Diallo M, Sagara I, Masinde GL, Doumbo SN, Dolo A, Tounkara A, Traoré I, Krogstad DJ. False-negative rapid diagnostic tests for malaria and deletion of the histidine-rich repeat region of the hrp2 gene. Am J Trop Med Hyg. 2012;86(2):194-8. [PubMed] [Google Scholar]
28. StandaReagen [Internet]. Diagnostic kit for malaria Pf/Pv antigen whole blood; 2022 [cited 2022 Dec 20]. Available from: https://e6mfzsx5bsk.exactdn.com/wp-content/uploads/2022/01/Malaria-SR-brochure.pdf
29. BPS Kabupaten Jayapura. Geografi dan Iklim. In: Kabupaten Jayapura Dalam Angka 2022. Jayapura: BPS Kabupaten Jayapura; 2002. p. 1-12. Indonesian.
30. Pemerintah Provinsi Papua [Internet]. Kondis Wilayah Menurut Distrik Kabupaten Jayapura; 2022 [cited 2022 Dec 15]. Available from: https://papua.go.id/view-detail-kabupaten-260/gambaran-umum.html. Indonesian.
31. Tedrow RE, Rakotomanga T, Nepomichene T, Howes RE, Ratovonjato J, Ratsimbasoa AC, Svenson GJ, Zimmerman PA. Anopheles mosquito surveillance in Madagascar reveals multiple blood feeding behavior and Plasmodium infection. PLoS Negl Trop Dis. 2019;13(7):1-21. [PubMed] [Google Scholar]
32. Balai Litbang B2P2VRP Salatiga. Laporan akhir riset khusus vektor dan reservoir Peyakit Provinsi Papua Barat 2017. Salatiga; 2017. Indonesian.
33. Hastuty HS, Kurniawan DA, Mofu RM. The diversity of Anopheles sp. in Kehiran Village Jayapura Regency, Papua. Proceeding of the 1st International Conference Health Polytechnic of Kupang [Internet]. 2018 [cited 2022 Dec 18];(1):800-9. Available from: https://proceeding.poltekeskupang.ac.id/index.php/ichpk/article/view/126 [Google Scholar]
34. Laurent B, Supratman S, Asih PB, Bretz D, Mueller J, Miller HC, Baharuddin A, Shinta, Surya A, Ngai M, Laihad F, Syafruddin D, Hawley WA, Collins FH, Lobo NF. Behaviour and molecular identification of Anopheles malaria vectors in Jayapura district, Papua province, Indonesia. Malar J. 2016;15(1):192. [PubMed] [Google Scholar]
35. Asale A, Duchateau L, Devleesschauwer B, Huisman G, Yewhalaw D. Zooprophylaxis as a control strategy for malaria caused by the vector Anopheles arabiensis (Diptera: Culicidae): a systematic review. Infect Dis Poverty. 2017;6(1):160. [PubMed] [Google Scholar]
36. World Health Organization [Internet]. Malaria; 2023 [cited 2023 Apr 14]. Available from: https://www.who.int/news-room/fact-sheets/detail/malaria
37. Thomas S, Ravishankaran S, Justin NA, Asokan A, Mathai MT, Valecha N, Montgomery J, Thomas MB, Eapen A. Resting and feeding preferences of Anopheles stephensi in an urban setting, perennial for malaria. Malar J. 2017;16(1):111. [PubMed] [Google Scholar]
38. Iwashita H, Dida GO, Sonye GO, Sunahara T, Futami K, Njenga SM, Chaves LF, Minakawa N. Push by a net, pull by a cow: can zooprophylaxis enhance the impact of insecticide treated bed nets on malaria control? Parasit Vectors [Internet]. 2014 [cited 2022 Dec 22];7(1):52. Available from: https://parasitesandvectors.biomedcentral.com/articles/10.1186/1756-3305-7-52 [PubMed] [Google Scholar]
39. Mayo Clinic. Malaria transmission cycle. Mayo Clinic Press; 2023.
40. Meibalan E, Marti M. Biology of malaria transmission. Cold Spring Harb Perspect Med. 2017;7(3):a025452. [PubMed] [Google Scholar]
41. Centers for Disease Control and Prevention [Internet]. Life cycle of Anopheles species mosquitoes; 2022 [cited 2022 Mar 19]. p. 1-4. Available from: https://www.cdc.gov/mosquitoes/about/life-cycles/anopheles.html
42. Medicines for Malaria Venture. Lifecycle of malaria parasite. Medicines for Malaria Venture. 2017.
43. Malaria Vaccine Initiative. Malaria parasite life cycle. PATH's Malaria Vaccine Initiative. 2023.
44. Markwalter CF, Davis KM, Wright DW. Immunomagnetic capture and colorimetric detection of malarial biomarker Plasmodium falciparum lactate dehydro-

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202329

genase. Anal Biochem [Internet]. 2016 [cited 2022 Dec 21];493:30-4. Available from: http://dx.doi.org/10.1016/j.ab.2015.10.003 [PubMed] [Google Scholar]
45. Hasyim H, Dhimal M, Bauer J, Montag D, Groneberg DA, Kuch U, Muller R. Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia. Malar J. 2018 Aug 20;17(1):302. [PubMed] [Google Scholar]
46. World Health Organization [Internet]. How to use a Rapid Diagnostic Test (RDT)? Geneva, Switzerland; 2010 [cited 2022 Oct 10]. Available from: https://www.who.int/docs/default-source/malaria/diagnosis/generic-pfpan-training-manual-web.pdf
47. Munirah M, Wahyuni S, Wahid I and Hamid F. The discovery of human *Plasmodium* among domestic animals in West Sumba and Fakfak, Indonesia [version 2; peer review: 2 not approved]. *F1000Research* 2023, 10:645 [cited 2023 August 13]. Available from: https://doi.org/10.12688/f1000research.53946.2
48. Sumanto D, Sayono S, Garedaghi Y, Martini M, Handoyo W, Kristini TD. PfLDH detected in Etawa crossbred goats using polymerase chain reaction methods. Int J Med Parasitol Epidemiol Sci [Internet]. 2021 [cited 2022 Dec 23];2(3):66-70. Available from: http://ijmpes.com/Article/ijmpes-3057 [Google Scholar]
49. Vander Jagt DL, Hunsaker LA, Heidrich JE. Partial purification and characterization of lactate dehydrogenase from Plasmodium falciparum. Mol Biochem Parasitol. 1981;4:255-64. [PubMed] [Google Scholar]
50. Makler MT, Piper RC, Milhous WK. Lactate dehydrogenase and the diagnosis of malaria. Parasitol Today. 1998;14(9):376-7. [PubMed] [Google Scholar]
51. Makler MT, Ries JM, Williams JA, Bancroft JE, Piper RC, Gibbins BL, Hinrichs DJ. Parasite lactate dehydrogenase as an assay for Plasmodium falciparum drug sensitivity. Am J Trop Med Hyg [Internet]. 1993 [cited 2022 Dec 20];48(6):739-41. Available from: https://doi.org/10.4269/ajtmh.1993.48.739 [PubMed] [Google Scholar]
52. Oduola AM, Omitowoju GO, Sowunmi A, Makler MT, Falade CO, Kyle DE, Fehintola FA, Ogundahunsi OA, Piper RC, Schuster BG, Milhous WK. Plasmodium falciparum: evaluation of lactate dehydrogenase in monitoring therapeutic response to standard antimalarial drugs in Nigeria. Exp Parasitol [Internet]. 1997 [cited 2022 Dec 19];87(3):283-9. Available from: https://doi.org/10.1006/expr.1997.4251 [PubMed] [Google Scholar]
53. Tjitra E, Suprianto S, McBroom J, Currie BJ, Anstey NM. Persistent ICT malaria P.f/P.v panmalarial and HRP2 antigen reactivity after treatment of Plasmodium falciparum malaria is associated with gametocytaemia and results in false-positive diagnosis of Plasmodium vivax in convalescence. J Clin Microbiol [Internet]. 2001 [cited 2022 Dec 21];39(3):1025-31. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC87868/ [PubMed] [Google Scholar]
54. Howard RJ, Uni S, Aikawa M, Aley SB, Leech JH, Lew AM, Wellems TE, Rener J, Taylor DW. Secretion of a malarial histidine-rich protein (Pf HRP II) from Plasmodium falciparum-infected erythrocytes. J Cell Biol. 1986;103(4):1269-77. [PubMed] [Google Scholar]
55. Dondorp AM, Desakom V, Pongtavornpinyo W, Sahassananda D, Silamut K, Chotivanich K, Newton PN, Pitisuttithum P, Smithyman AM, White NJ, Day NP. Estimation of the total parasite biomass in acute falciparum malaria from plasma PfHRP2. PLoS Med [Internet]. 2005 [cited 2022 Dec 23];2(8):e204. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0020204 [PubMed] [Google Scholar]
56. Ndour PA, Larréché S, Mouri O, Argy N, Gay F, Roussel C, Jauréguiberry S, Perillaud C, Langui D, Biligui S, Chartrel N, Mérens A, Kendjo E, Ghose A, Hassan MU, Hossain MA, Kingston HW, Plewes K, Dondorp AM, Danis M, Houzé S, Bonnefoy S, Thellier M, Woodrow CJ, Buffet PA; French Artesunate Working Group. Measuring the Plasmodium falciparum HRP2 protein in blood from artesunate-treated malaria patients predicts post-artesunate delayed hemolysis. Sci Transl Med [Internet]. 2017 [cited 2022 Dec 21];9(397):eaaf9377. Available from: https://www.science.org/doi/10.1126/scitranslmed.aaf9377?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub 0pubmed [PubMed] [Google Scholar]
57. Malaria Site [Internet]. Transmission of malaria; 2018 [cited 2022 Dec 24]. Available from: https://www.malariasite.com/transmission/

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202329