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Traditional Malaria Eye Drops Treatment Measures Based on Local Knowledge (Study in Manusa Village, Inamosol District)

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Abstract This study analyzed traditional eye drop treatment based on local knowledge in Manusa Village, West Seram Regency, which is known as a malaria endemic area. The research method used a descriptive design with a cross-sectional approach, the validity of the instrument showed a calculated r value > r table, and reliability showed a Cronbach's Alpha value = 0.754. The results of the study revealed that 81.4% of the community believed this treatment was safe and passed down from generation to generation, 95.1% did not report any dangerous reactions, and 100% believed Kenar leaves could cure malaria. As many as 48% of the community reported no longer being positive for malaria after using this method. This traditional treatment is considered effective, safe, and based on local resources.

Keywords: Eye drops; Katimaha; Kenar; Malaria; Traditional medicine

Introduction

Malaria is an infectious disease that is still a health problem in several regions of Indonesia, especially in Eastern Indonesia. The number of Malaria cases in Indonesia in 2021 was 304,607, but the number of infection cases decreased when compared to 2009, which was 418,439 positive cases of Malaria in Indonesia (Kleden et al., 2024). Based on the *World Health Organization* (WHO) report in *the World Malaria Report* 2020, Indonesia is the second highest country after India and Southeast Asia for the number of Malaria cases. Although Indonesia experienced a decrease in cases in 2010-2014, the trend of Malaria cases in Indonesia tended to stagnate from 2014-2019 (Watmanlusy et al., 2019).

Infectious diseases that are a priority for long-term national development 2005-2025 are Malaria, Dengue Fever, Diarrhea, Polio, Filarial, Leprosy, Pulmonary Tuberculosis, HIV/AIDS, Pneumonia and other diseases that can be prevented by immunization (Watmanlusy et al., 2019). Malaria is a priority health problem in Indonesia because its morbidity and mortality rates are still high, especially in areas outside Java and Bali. Transmigration areas that have a mixture of residents from endemic and non-endemic areas of Malaria, still often experience explosions of cases or outbreaks that cause many deaths (Aziz et al., 2018).

The trend of positive Malaria cases with the number of sufferers of *Annual Parasite Incidence* (API) indicates the highest endemic Malaria area in Eastern Indonesia. Based on data from the Ministry of Health in 2019 there were 86% of positive Malaria cases in Papua Province with a total of 216,380 cases, in East Nusa Tenggara (NTT) Province there were 12,909 positive Malaria cases and there were 7,079 positive Malaria cases in West Papua (Aziz et al., 2018).

The large number of moderate to high endemic areas in Eastern Indonesia is caused by climate factors. According to the Meteorology, Climatology and Geophysics Agency (BMKG) in the region, it explains that the five weather changes from rain to long dry seasons are sometimes difficult to interpret, causing changes in the body's stimulus for people in Eastern

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Indonesia to be very susceptible to positive Malaria (Bandzuh, 2023).

The achievement of Malaria-Free Indonesia in 2030 is carried out through the province first before moving on to the Regency/City to achieve the target of Malaria-Free Indonesia in 2030 (Yuliyanti, 2020). In order to achieve the above target, the regionalization area is made into 5 regions, namely, the first region consists of the Provinces of Java and Bali, the second region of the Provinces of Sumatra, Sulawesi, and West Nusa Tenggara, the third region of the Provinces of Kalimantan and North Maluku, the fourth region consists of the Provinces of Maluku and East Nusa Tenggara, and the fifth region of the Provinces of Papua and West Papua.

Based on data from the Indonesian Health Profile in 2014, *the Annual Parasite Incidence* (API) per 1,000 population in Indonesia was 1.0, when compared to *the Annual Parasite Incidence* (API) per 1,000 population in 2013, there was a decrease of 0.38. The five provinces with the highest *Annual Parasite Incidence* (API) per 1,000 population in 2014 were Papua Province (29.57%), West Papua (20.85%), East Nusa Tenggara (12.81%), Maluku (6.00%) and North Maluku (3.32%). Of the 34 provinces in Indonesia, there are eight provinces that have Malaria incidents above the national figure, most of which are in the eastern part of Indonesia (Yuliyanti, 2020).

Maluku is the fourth highest endemic area nationally. Reported cases of Malaria in the last five years have decreased significantly. API of 9.86%, in 2012, to 3.83% in 2016 (Faizah & Fibriana, 2016). The Anopheles sp. species found in Maluku are 24 species and have been confirmed as vectors are Anopheles Flavirotris, Puntulatus, Sbpictus, Barbirotris and Farauti. In West Seram there are 23 species but none have been confirmed as vectors, cases in this area are still high (Kleden et al., 2024).

Malaria cases in the last three years in West Seram Regency based on API in 2014 (20%), 2015 (10.87%), 2016 (8.42%). Although Malaria cases have decreased every year, it is still the third highest Malaria endemic area out of 11 regencies/cities in Maluku. West Seram Regency is one of the areas in Eastern Indonesia that is endemic to Falciparum Malaria and is categorized as high with an API indicator reaching 10.87 per 1000 population. Since 2013-2015, clinical malaria case data in West Seram Regency were 28,764 cases, of which 46.64% were positive cases and 80.97% were positive cases treated. In 2015, clinical malaria case data were 7,057, 57.03% were positive cases, and 70.01% were positive cases treated. The proportion of *P. Falciparum malaria cases* is higher than other Plasmodium malaria. The large number of malaria cases in the interior of West Seram that were not examined had a negative impact on the continuation of the malaria elimination program and breaking the chain of transmission. People in the interior usually treat malaria with traditional medicine.

Based on its geographical location, the Manusa area is a remote village in the middle of the forest which is very far from other villages, making it difficult for the West Seram district health team to reach Manusa village. Due to the lack of health infrastructure in Manusa village for Malaria control, the community seeks Malaria prevention based on local knowledge, namely the use of traditional medicine that has developed for a long time and is practiced from time to time by the community in Manusa village. An interesting thing found in this study is the traditional treatment method which is dripped directly into the eyes of sufferers or suspects suspected of suffering from Malaria. Almost all of the pre-elderly community have used traditional "eye drops" treatment for Malaria prevention.

Another interesting thing that was obtained was the traditional medicinal plant used leaves from the Kinar/Kenar tree (local name) or known as Katimaha. Katimaha itself is a family of *Malvales* genus *Kleinhovia L* from the species *K. Hospita* which is often found in mountainous areas. The Katimaha plant (*Kleinhovia Hospita L.*) is one of Indonesia's natural biological resources that needs to be scientifically empowered, because it contains natural compounds that are beneficial for human life needs. The Katimaha plant or also called Timah wood is one type of wood that is traditionally considered efficacious. The leaf water extract can be used in the health sector, for example in South Sulawesi, it is used as a traditional medicine for the treatment of hepatitis. While in South Kalimantan, empirically Katimaha leaves are used by the local community to prevent the growth of gray hair (whitening) on the hair by shampooing. However, there has been no study to prove the use of these leaves scientifically.

Based on one of the results of phytochemical screening conducted in Sabah, Malaysia, the local Katimaha leaf sample showed a very strong positive result for saponin content (+4), while for alkaloid and steroid/triterpenoid content it gave a negative result (Yunita et al., 2009). This plant has been used for a long time by the elders (ancestors) before until it was passed down to the present generation. If at first glance seen prevention of Malaria with traditional medicine based on local community knowledge so far has not been successfully tested clinically but the practice of this traditional medicine is still carried out by the community in Manusa village. Based on the description above, the researcher is interested in conducting descriptive research related to how traditional eye drop treatment

for Malaria based on local knowledge is carried out by the Manusa village community.

Method

The research method used is quantitative descriptive with cross-sectional design. This approach aims to describe the research variables at a certain time. The research instrument is a closed questionnaire that has been modified from previous research. This questionnaire was tested for validity by producing 23 valid statements (r count> 0.361, p < 0.005) and its reliability with a Cronbach Alpha value of 0.754, which indicates that the instrument is reliable.

The population of the study was the community of Manusa Village totaling 596 people, consisting of 318 men and 278 women, with an age range of early adulthood to early elderly. Based on the Slovin formula with a margin of error of 5%, the number of samples taken was 240 people. The sampling technique used *purposive sampling* with inclusion criteria including early adulthood to early elderly, having used traditional medicine for malaria, having the ability to read and write, and being willing to be interviewed.

This study has two main variables, namely the dependent variable in the form of treatment actions, and independent variables which include traditional medicine processing skills, driving factors for the use of traditional medicine, past treatment history, response to traditional medicine, social environmental influences, and consumers of traditional medicine. Each variable is defined operationally, with a measurement method using questionnaire-based interviews and nominal scales.

Data collection was conducted for one month in Manusa Village through direct observation and interviews using questionnaires as primary data. Secondary data were obtained from previous literature, sub-district health center data, assistant health center data, and district health portals. The collected data were processed through several stages, namely cleaning, editing, coding, and data entry using the SPSS version 22 and Microsoft Excel 2018 applications.

Data analysis was performed using univariate method to describe the frequency distribution of each variable, and bivariate to test the relationship between independent variables and dependent variables using Chi-square test or Fisher test if the test requirements are not met. The p value <0.05 is used as the basis for accepting or rejecting the hypothesis. The data from the analysis are presented in the form of a frequency distribution table equipped with a description to facilitate interpretation of the results.

Results and Discussion

Understanding Malaria

Malaria is an infectious disease caused by the Plasmodium sp parasite that lives and reproduces in human red blood cells (erythrocytes). Malaria is an infectious disease caused by plasmodium which is included in the protozoa group (Avichena & Anggriyani, 2023). Malaria has attacked 209 countries in the world based on the report from the World Malaria Report 2015 (La & Kurnianta, 2019).

Malaria is still an infectious disease caused by sporozoa of the genus Plasmodium and transmitted through mosquito bites. Nearly half of the world's population is at risk of contracting Malaria. In 2015, there were around 212 million cases of Malaria and it is estimated 429,000 cases of malaria deaths. Improved prevention and control measures have led to a 25% reduction in deaths globally since 2010.

Malaria cases in Indonesia are estimated at 4.9 million out of 262 million people. Malaria cases in 2017 were recorded at 261,617 cases which resulted in the deaths of at least 100 people. In Indonesia, half of the 514 districts/cities have reached the Malaria-free category. Malaria cases in Indonesia were confirmed in 2019, namely 250,644. This number has increased compared to 2018 which amounted to 222,065 cases.

Malaria is one of the indicators of the Millennium Development Goals (MDGs), namely to stop the spread and reduce the incidence of Malaria in 2015, seen from the indicator of decreasing morbidity and mortality due to Malaria. The national Annual Parasite Incidence (API) decreased from 2008-2009 from 2.47 per 1000 population to 1.85 per 1000 population. This still needs to be done to achieve the target of the Ministry of Health's 2010-2011 Renstra, namely that the API must be reduced to 1 per 1000 population in 2014 (Fabanjo & Loihala, 2017) .

Pathophysiology of Malaria

Malaria is a parasitic infectious disease caused by Plasmodium that attacks erythrocytes and is characterized by the discovery of asexual forms in the blood. Malaria is caused by 5 species of the genus Plasmodium, namely: Plasmodium Falciparum, Plasmodium Vivax, Plasmodium Ovale, Plasmodium Malariae, and Plasmodium Knowlesi (Karolina et al., 2018).

The life cycle of Plasmodium sp. begins when humans are bitten by Anopheles mosquitoes and release sporozoites. Sporozoites will enter the liver and turn into schizonts. The schizonts will rupture, release merozoites and begin to infect erythrocytes. In the erythrocyte cycle, Plasmodium sp. will degrade hemoglobin and cause changes in the shape of the invaded erythrocytes, thus triggering the spleen to destroy erythrocytes, which will

result in a decrease in hemoglobin levels (Stefani et al., 2019).

The causative organism of Malaria is a protozoa of the genus Plasmodium. There are four species of Plasmodium, namely Plasmodium Falciparum, Plasmodium Vivax, Plasmodium Malariae, and Plasmodium Ovale. Plasmodium Falciparum is the cause of Tropical Malaria which often occurs Severe Malaria or Brain Malaria with death (Manning et al., 2011). The incubation period is 9 to 14 days, an average of 12 days. Plasmodium Vivax which causes Tertian Malaria with an incubation period of 12 to 17 days, an average of 15 days. Plasmodium Ovale, this is very rare, generally occurs in Africa and the West Pacific with an incubation period of 16 to 18 days, an average of 17 days. Plasmodium Malariae which causes Quartana Malaria with an incubation period of 18 to 28 days (Aziz et al., 2018).

The parasite reproduces in red blood cells, causing *symptoms* including anemia (lightheadedness, shortness of breath), as well as other general *symptoms such as fever, chills, nausea, coma and death.* The spread of Malaria can be reduced by preventing mosquito bites through mosquito nets and insect barriers, or through mosquito control measures such as spraying insecticide in the house and drying out sheltered water areas where mosquitoes lay their eggs.

The decrease in hemoglobin levels can be influenced by the type of Plasmodium sp. that infects because each Plasmodium sp. has different characteristics in infecting erythrocytes (Karolina et al., 2018). The decrease in hemoglobin levels will be clearly seen in Malaria patients caused by Plasmodium Falciparum compared to that caused by Plasmodium Vivax, Plasmodium Ovale, and Plasmodium Malariae because Plasmodium Falciparum can infect erythrocytes of various ages (Sidik et al., 2022).

Malaria Situation Assessment

Annual Parasite Incidence (API)

Malaria morbidity is described by the incidence of Malaria, in this case the Annual Parasite Incidence (API). API is the number of morbidity per 1,000 population at risk in one year (Karolina et al., 2018). The number of positive Malaria cases divided by the number of population at risk in the same time period multiplied by 1,000 population.

Annual Blood Examination Rate (ABER)

Annual Blood Examination Rate, abbreviated as ABER, is the percentage of blood specimens or preparations taken and examined in the laboratory/microscopically from the total population in a certain area (Yuliyanti, 2020).

Annual Malaria Incidence (AMI)

The AMI indicator is the incidence of clinical Malaria cases divided by the population while the API indicator is the incidence of positive Malaria cases divided by the population (Yuliyanti, 2020). Both indicators are used to measure the trend of Malaria cases.

Etiology of Malaria

Etiology Malaria is a protozoan parasite Plasmodium. There are 5 species of Plasmodium that can infect humans.

Plasmodium falciparum

Plasmodium Falciparum (Tropical Malaria) is the most common Plasmodium species that causes severe Malaria to death. The incubation period ranges from 9–14 days, causing intermittent or continuous fever (Watmanlusy et al., 2019). In severe malaria caused by Plasmodium falciparum infection, pathogenesis is related to the ability of the parasite to change the structure and biomolecules of erythrocyte cells to maintain parasite life. These changes include the mechanisms of cell membrane transport, cytoadherence, sequestration, and resetting (Okagu et al., 2022).

Cytoadherence is the event of attachment of erythrocytes that have been infected with Plasmodium falciparum to receptors in the endothelial part of venules and capillaries. Cytoadherence is mediated by the Plasmodium Falciparum erythrocyte membrane protein (PfEMP1) which is produced from the transcription of the var gene and predominantly binds to the CD36 receptor and *intercellular adhesion molecule* -1 (ICAM-1) on endothelial cells (Sutjahjono & Ginanjar, 2016). In addition, erythrocytes infected with the parasite can also attach to uninfected erythrocytes, forming a flower-like structure (*rosette*) (La & Kurnianta, 2019).

Cytoadherence of erythrocytes on endothelium and normal erythrocytes causes sequestration in small blood vessels in various organs, causing microcirculation obstruction, tissue perfusion disorders, lactic acidosis, and in severe conditions causing *end-organ damage*. Sequestration in the placenta of pregnant women can cause complications, namely abortion, low birth weight, and Congenital Malaria (Djabanor et al., 2016).

Plasmodium Vivax

Plasmodium Vivax (Tertian malaria) has an incubation period of 12–18 days and causes recurrent fever with a fever-free interval of 2 days. This type can also cause severe malaria (Vanadis et al., 2013).

The hallmark of Plasmodium Vivax infection is a predominance of red blood cells with reticulocytes and Duffy antigens for parasite invasion. As a result, parasitemia is relatively low in Vivax Malaria. The size

of reticulocytes is larger than mature red blood cells, so that in the peripheral blood smear the infected cells will appear larger than the surrounding red blood cells. Fever in Plasmodium Vivax can reappear when hypnozoites release merozoites (Wells et al., 2010).

In patients without comorbid diseases, Plasmodium Vivax rarely causes death. However, Plasmodium Vivax can relapse and in patients with chronic diseases, this species can cause severe anemia, malnutrition, and poor immune response. Severe manifestations that can arise are *Acute Respiratory Distress Syndrome*, liver failure, kidney failure, and shock. Coma can occur although rarely because this species is not like Plasmodium Falciparum which can cause sequestration of parasites in the brain in large numbers (Akide Ndunge et al., 2022).

Plasmodium Ovale

The incubation period of Plasmodium Ovale is 12–18 days so that the fever pattern is the same as Malaria vivax, with mild clinical manifestations (Taek et al., 2018). There are 2 species of Plasmodium ovale, namely Plasmodium Ovale Curtisi and Plasmodium Ovale Wallikeri. Both species have the same clinical manifestations and management. Plasmodium Ovale is similar to Plasmodium vivax, but does not require the Duffy antigen to invade red blood cells (Awasthi et al., 2022).

On examination of peripheral blood smear, Plasmodium Ovale appears as comet-like trophozoites and red blood cells will appear Oval with fimbria (like fingers) on the cell membrane. The shape of the ring, schizont, and gametocytes of Plasmodium Ovale are the same as Plasmodium Vivax (Wu, 2023).

Plasmodium Malaria

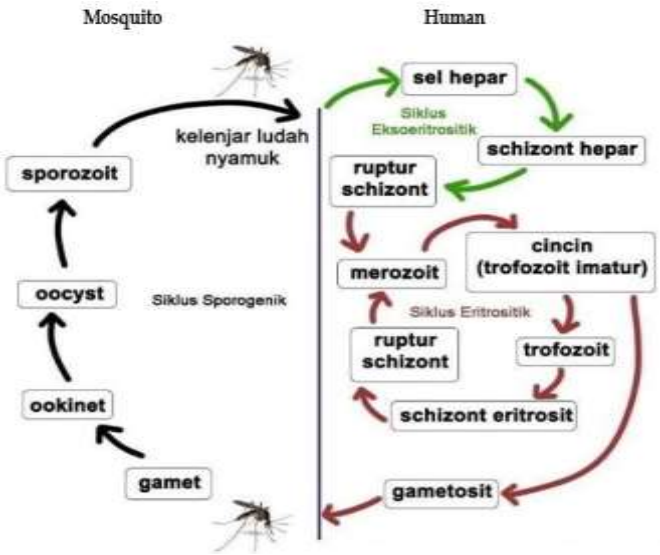

Figure 1. Life cycle of plasmodium

Plasmodium Malariae (Quartana Malaria) is Malaria with the mildest clinical manifestations. The incubation period is around 2–4 weeks with recurrent fever and a fever-free interval of 3 days (Meiyana & Sembiring, 2023).

The number of merozoites released during schizont rupture is much less, so parasitemia is lower compared to other types of Malaria. Plasmodium Malariae is also often referred to as chronic Malaria because it can last for decades. Plasmodium Malariae has a characteristic, namely immune complex deposits in the kidneys that can cause nephritis (Mishra & Das, 2008). In peripheral blood smears, parasites are found in the form of bands, schizonts with several merozoites, and globules with a golden pigment in the central part .

Plasmodium Knowlesi

Plasmodium Knowlesi has an incubation period of 9–12 days. The main clinical manifestations are fever and headache. The proportion of cases with severe complications due to Plasmodium Knowlesi is more common than Plasmodium Vivax and Plasmodium Falciparum. Severe manifestations of Plasmodium Knowlesi include hypotension, respiratory distress, acute renal failure, hyperbilirubinemia, and shock. Coma does not always occur in Plasmodium Knowlesi infection.

Severe manifestations occur due to an excessive immune response that occurs when treatment is delayed. Plasmodium Knowlesi shows a pathological picture similar to Plasmodium Falciparum in brain tissue, but with less ICAM-1. The mechanism by which Plasmodium Knowlesi interacts with the endothelium to create sequestration is still unknown.

Plasmodium Life Cycle

Cycle In Humans

The life cycle of Plasmodium has two developmental phases, one phase in the mosquito's body (sexual phase) and one phase in the human body (asexual phase). This parasite attacks red blood cells, causing fever, anemia, and *splenomegaly*. When an infective Anopheles mosquito sucks human blood, sporozoites in the mosquito's salivary glands will enter the bloodstream for about half an hour. After that, the sporozoites will enter the liver cells and become liver trophozoites. Then they develop into liver schizonts consisting of 10,000-30,000 liver merozoites (depending on the species).

This cycle is called the exo-erythrocytic cycle which lasts for approximately 2 weeks. In P. Vivax and P. Ovale, some liver trophozoites do not immediately develop into schizonts, but some become dormant forms called hypnozoites. These hypnozoites can live in liver cells for months to years. At some point when the body's

immunity decreases, they will become active so that they can cause relapse (relapse).

Merozoites originating from ruptured liver schizonts will enter the bloodstream and infect red blood cells. In red blood cells, the parasite develops from the trophozoite stage to the schizont (8-30 merozoites, depending on the species). This asexual development process is called schizogony. Furthermore, the infected erythrocytes (schizonts) rupture and the merozoites that come out will infect other red blood cells. This cycle is called the erythrocytic cycle.

In P. Falciparum after 2-3 cycles of blood schizogony, some merozoites infect red blood cells and form sexual stages (male and female gametocytes). In other species these cycles occur simultaneously. This is related to the time and type of treatment for eradication.

The cycle of P. Knowlesi in humans is still under study. The main reservoir of Plasmodium is the long-tailed macaque (Macaca sp). These long-tailed macaques are found in many forests in Asia, including Indonesia. Knowledge of the parasite cycle is better understood in macaques than in humans.

Cycle In Female Anopheles Mosquitoes
Exoerythrocytic Cycle

In the exoerythrocytic cycle, sporozoites will invade hepatocytes, replicate asexually and mature into schizonts. The schizonts then rupture releasing merozoites into the bloodstream. Patients are asymptomatic during the exoerythrocytic cycle. The exoerythrocytic cycle lasts for 8–25 days for Plasmodium Falciparum, 8–27 days for Plasmodium Vivax, 9–17 days for Plasmodium Ovale, and 15–30 days for Plasmodium Malariae.

Some sporozoites of Plasmodium Vivax and Plasmodium Ovale do not immediately develop into merozoites in the exoerythrocytic cycle, but instead become hypnozoites. Hypnozoites are able to survive (dormant) in hepatocytes for a long time, namely several weeks to several years. After the dormant phase, hypnozoites can become active again and produce merozoites to be released into the blood circulation. Hypnozoites that cause cases of Malaria Relapse (Traore et al., 2021).

Erythrocytic Cycle

Merozoites then infect erythrocytes which marks the beginning of the erythrocytic cycle. Merozoites then develop into immature trophozoites (rings), mature trophozoites, and finally into schizonts which when ruptured again release merozoites and re-infect normal erythrocytes (Traore et al., 2021).

Some parasites in the form of immature trophozoites differentiate into microgametocytes (male) or macrogametocytes (female). These gametocytes will enter the body of the Anopheles sp. mosquito when it bites humans [1,2] . The duration of the erythrocytic cycle varies depending on the Plasmodium species, which implies that fever symptoms occur every 24 or 48 hours (Traore et al., 2021).

Sporogenic Cycle

The sporogenic cycle occurs in the mosquito's body. The parasite reproduces sexually, which begins with a microgametocyte penetrating a macrogametocyte and producing a zygote. The zygote then transforms into a motile ookinete and invade the wall of the mosquito's midgut and develop into *oocysts* . *The oocysts* will then rupture and release sporozoites that will enter the mosquito's salivary glands. When a female Anopheles mosquito sucks blood containing gametocytes, in the mosquito's body the male and female gametes are fertilized into a zygote. The zygote develops into an ookinete and then penetrates the mosquito's stomach wall. On the outer wall of the mosquito's stomach the ookinete will become an oocyst and then become a sporozoite. These sporozoites are infectious and ready to be transmitted to humans.

The prepatent period is the time span from when sporozoites enter the human body until the parasite can be detected in red blood cells by microscopic examination.

Clinical Symptoms

In general, someone who experiences Malaria will experience symptoms of the disease such as fever, dizziness, weakness, paleness, muscle pain, temperature can reach 40˚C especially in Plasmodium Falciparum infection.

Shivering

The fever shivering stage or cold stage sufferers will feel very cold shivering, rapid and weak pulse, pale bluish lips and fingers, dry, pale skin, sometimes vomiting. In children, fever can cause seizures. This fever ranges from 15 minutes to 1 hour.

Fever

The peak stage of fever is the *hot stage* which lasts 2-6 hours, red face, dry skin, headache, strong pulse, very continuous thirst, nausea to vomiting. At this time, it is actually an event of rupture of mature schzon into merozoites that enter the bloodstream to attack red blood cells.

Sweating

Sweating stage. In this stage, the sufferer sweats a lot. This can last for 2 to 4 hours.

Splenomegaly (Enlarged Spleen)

The spleen is an organ located in the abdominal cavity, precisely under the left rib. This organ functions to filter and destroy damaged blood cells from healthy blood cells, store reserves of red blood cells and platelets, and prevent infection by producing white blood cells that can be the first line of defense against disease-causing organisms .

Normally, the spleen is only 11–20 centimeters in size and weighs up to 500 grams. However, in cases of splenomegaly, the spleen can enlarge to more than 20 centimeters and weigh up to 1 kilogram. This condition can disrupt the function of the spleen.

Anemia

Anemia in malaria occurs due to the process of hemolysis and phagocytosis of erythrocytes, both infected and normal, by the immune system.

Severe Malaria

Severe malaria due to P. Falciparum has a special pathogenesis. Erythrocytes infected with P. Falciparum will undergo a sequestration process, namely the spread of parasitized erythrocytes to the capillary vessels of the body's organs. In addition, on the surface of infected erythrocytes, *knobs* containing various P. Falciparum antigens will form. Cytokines (TNF, IL6 and others) produced by macrophages, monocytes, and lymphocytes will cause the expression of capillary endothelial receptors. When the knob binds to the capillary endothelial cell receptor, the cytoadherence process occurs. As a result of this process, obstruction (blockage) occurs in the capillary vessels which causes tissue ischemia. The occurrence of this blockage is also supported by the process of forming " *rosettes* ", namely clusters of parasitized red blood cells with other red blood cells.

Malaria Risk Factors

Host

It is known that there are more than 422 species of Anopheles in the world. In Indonesia there are only 80 species and 22 of them are determined to be Malaria vectors. There are 18 species confirmed as Malaria vectors and 4 species are suspected of playing a role in the transmission of Malaria in Indonesia. These mosquitoes live in certain areas with specific environmental habitat conditions such as coastal areas, swamps, rice fields, forests and mountains.

Anopheles is included in the Diptera order, *Nematoceera suborder, Culicidae* family, *Culicinae* subtribe and Anophelini tribe in zoological classification. In the *Anophelinie tribe,* the genus Anopheles has several subgenera. Mosquitoes have general characteristics, namely a relatively small body size (4 mm - 13 mm) and fragile. The head has a smooth proboscis and has a length that exceeds the length of the head. The proboscis and palpi are the same length, the scutellum is in one environment, the wing veins are pale and dark, the jumabi usually have pale stains, the palpi are pale or not at all banded, the legs are long and direct.

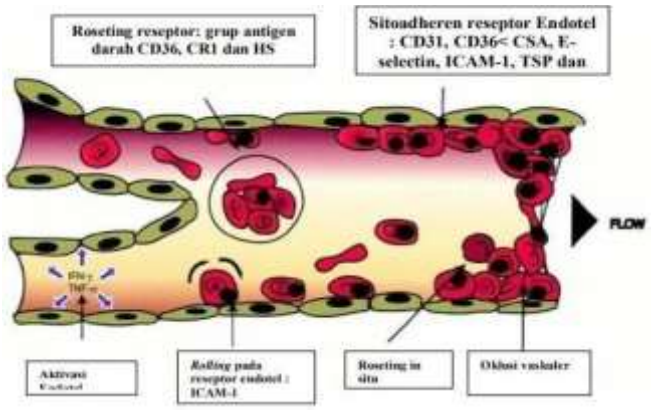

Figure 2. Pathophysiology of cytoaderene

Agent

Plasmodium known as the cause of Malaria disease (*agent*) is a single-celled animal (protozoa) belonging to the genus Plasmodia, family Plasmodiidae of the order *Coccidiidae* . When biting humans, female *Anopheles sp.* mosquitoes infected with Plasmodium will inoculate sporozoites from their saliva into human blood circulation.

Environment

Environmental factors in the home that have a significant influence are the condition of the house walls, indoor lighting, and hanging clothes, while those that do not have a significant influence are the use of wire mesh and the presence of a ceiling (Astria et al., 2021).

Malaria Prevention

Various efforts to control malaria according to WHO recommendations have been implemented globally, but the increase in the number and spread of parasites that are resistant to anti-Malaria drugs and vectors that are resistant to insecticides are one of the obstacles in themselves (Anyanwu et al., 2017). P. Falciparum parasites tend to be resistant to anti-Malaria drugs than other parasite species. In fact, P. Falciparum is likely to be resistant to almost all conventional Malaria drugs that have existed before, such as Chloroquine, Primaquine, Artemisinin and so on. This resistance event can have an impact on therapy failure, and cause high morbidity and mortality rates due to Malaria in several endemic areas. Research into the development of Malaria vaccines and other treatment innovations is still ongoing, so that research activities related to the

discovery of new drugs remain one of the important efforts in eliminating Malaria.

Eradication efforts made by the government have not yet achieved maximum results in reducing the incidence of Malaria because so far the community has only been the object of the program and the community has never realized that they are the ones who should be the subjects in the program. Active community participation is very important in the success of the Malaria control program. Community participation in Malaria control is effective in preventing Malaria. Efforts to break the chain of transmission between the host, agent and environment must be carried out by the community itself in an effort to control Malaria. For this reason, the community in this case the head of the family must have confidence and skills in implementing Malaria control (Saito et al., 2017).

Medical Treatment

The high prevalence of Malaria is caused by various factors, including plasmodium resistance to anti-Malaria drugs. In Indonesia, cases of Plasmodium Falciparum resistance to Chloroquine were first reported from Kalimantan in 1974 and spread throughout the provinces in Indonesia in 2000 for intraperitoneal P. Berghei infections. There are three factors that play a role in the emergence of this resistance, namely subtherapeutic factors, pharmacological factors and Malaria transmission factors, namely immunity, blood smear preparations, flat racks, droppers, aquades bottles, *drug pressure* and intensity. Malaria treatment is carried out by administering anti-Malaria drugs to kill the parasite. The type and duration of drug administration depend on the type of parasite that attacks, the severity of symptoms, and the patient's condition. To treat Malaria caused by Plasmodium Falciparum, the World Health Organization (WHO) has created a combination drug regimen called *Artemisinin-Based*.

Combination Therapies (ACT). The combination of drugs is: artemether and lumefantrine; artesunate and amodiaquine; dihydroartemisinin and piperaquine; and artesunate, sulfadoxine, and pyrimethamine. This drug is given for at least 3 days to adults and children. While for pregnant women in the first trimester, the drug given is quinine pills plus clindamycin for 7 days.

Chloroquine drugs can be given . In addition, to prevent recurrence of this type of Malaria, doctors can add *Primaquine*. For severe malaria, patients will be hospitalized and given medication by injection, at least for the first 24 hours. Later, the medication can be changed to tablets.

Traditional Medicine

Malaria is one of the infectious diseases with a fairly high prevalence rate. Malaria disease is becoming more serious due to the increasing number of Malaria parasites (Plasmodium) that are resistant to anti-Malaria drugs. The use of traditional plants as a treatment also needs to consider the safety and appropriateness of the use of traditional medicine as a therapy both in terms of the truth of the selected ingredients, the accuracy of the dosage, the method of use, the accuracy of the time of use, and the review of the information received (Nigussie & Wale, 2022). The use of traditional medicine tends to be based only on past experiences. The use of medicinal plants as anti-Malaria agents has been widely practiced and developed. The people in the Manusa village believe in the traditional Eye Drops treatment that has been passed down from generation to generation and has the effectiveness to overcome Malaria.

Prevention/Traditional Treatment

Many people believe that traditional medicine can cure all kinds of diseases. Both internal and external diseases, besides traditional medicine is known to be more natural without any serious side effects so that it can be done by anyone. There are two types of traditional medicine according to WHO, namely: treatment using spiritual methods, namely, related to supernatural matters; and treatment using medicines, namely herbal medicine or herbal remedies.

In the international world, the use of herbal medicine has been widely accepted in both developing and developed countries. Indonesia itself has a lot of natural biological potential, but its utilization is only done traditionally. Basically, humans have known the function of plants, especially as a way to overcome health problems. The discovery of medicinal plants by the community in general is due to intrinsic feelings that are passed down from generation to generation and maintained through oral narratives. Traditional medicine according to the Decree of the Minister of Health of the Republic of Indonesia No. 1076 / MENKES /SK/VII/2003 concerning the implementation of traditional medicine. Traditional medicine is treatment and / or care by means of drugs, and the treatment refers to experience, hereditary skills, and/or education and training and is applied in accordance with the norms prevailing in society. The use of herbal medicine as an alternative treatment has developed from generation to generation in Indonesia, this is supported because geographically Indonesia is a tropical country rich in medicinal plants. According to the results of basic health research in 2010, the use of herbal medicine by the community reached more than 50%.

Malaria is often considered a common disease in endemic areas. With this, there are differences in people's mindsets in seeking treatment for curing Malaria. Many factors influence the incidence of Malaria in the community. Individual factors, such as community behavior have a higher risk of transmission such as the habit of going out at night wearing short clothes, the habit of sleeping without using mosquito nets, not paying attention to puddles around the home environment, the habit of hanging clothes in the house in piles and work factors have a fairly large risk effect on the incidence of Malaria (Putro, 2021).

Efficacy of Traditional Medicine

Traditional medicine has many active ingredients, most of which have not been determined with certainty in their pharmacological effects, because the pharmacological effects of each substance contained in the plant have not been determined with certainty, so some medicinal plants tend to have more than one pharmacological effect. Only a few active compounds have been isolated for the development of new drug discoveries[12]. The use of traditional medicine for therapy should refer to scientific studies that have been carried out because the many active compounds in plants cause many pharmacological effects that will arise in their use.

Traditional medicine is also categorized as one of the branches of alternative medicine which can be defined as a treatment method chosen by someone if conventional treatment methods do not provide satisfactory results. Based on the elements of agents used in the process of providing treatment services/health services, alternative medicine is grouped as follows: h*erbal-agency*. Alternative medicine that uses plants, both natural and processed (herbal) as its medicinal ingredients; a*nimal-agency*. Alternative medicine that uses animals, either animal-based materials, products, or intermediaries as materials for the treatment service process; m*aterial-agency*. Alternative medicine that uses earth materials as alternative medicine services. For example, acupuncture, water and crystal therapy.

In Indonesia itself, there are many kinds of traditional medicine. The method of treatment has long been done. There are those that are original from the ancestral heritage that generally utilize the power of nature, human power, and there are also those that come from the Hindu era or the influence of India and China. Traditional medicine in Indonesia has developed for centuries so that it is a necessity for most of the Indonesian people. Seeing the reality around us by the existence of doctors as implementers of treatment and treatment from the west or traditional medicine must have a place in the hearts of the Indonesian people in general and the Javanese people in particular.

The traditional medical service personnel have their own patients and customers. There is a separate supporting community, there are also their own rules and requirements, there are also their own rules and requirements that they obey together. They are satisfied (some are also dissatisfied) with the reciprocal relationship of their supporting traditional health services. This is an element of culture and elements of humanity that also exist in nations in the world, no matter how modern (Djamaluddin et al., 2020).

Plants Used for Traditional Malaria Treatment

Indonesia with its tropical climate is one of the endemic areas of Malaria, especially in Eastern Indonesia. The problem that complicates the handling of Malaria is the emergence of cases of parasite resistance to antimalarial drugs.

Traditional medicine is often the forerunner to the discovery of new drugs. One type of plant that was later developed into a new Malaria drug comes from the bark of the cinchona tree (*Cinchona sucirubra, L*), where Cinchonine, which is an alkaloid, is able to become an anti-Malaria drug. Its mechanism of action suppresses the growth of protozoa in blood tissue. This discovery was not a coincidence, but was based on the traditional use of cinchona bark to overcome fever disorders by people in endemic Malaria areas (Kesetyaningsih & Sundari, 2013).

Sambiloto plant (*Andrographis Paniculata* (Burm. f.) *Wall. ex Nees*) is a plant originating from the *Acanthaceae family* . This plant originates from South Asia and China, known as Chuan Xin Lian. In Indonesia, sambiloto is known as bidara, sandilata, takila, ampadu tanah and pepaitan (Margarethy et al., 2019). This plant has been widely studied for its pharmacological effects. Sambiloto plants have morphological characteristics that are easy to recognize. This plant is an annual plant with a height that usually does not exceed one meter with single leaves that are pointed and crossed on the stem. The flowers are small, tubular in shape with a white color stained purple (Salami et al., 2022).

Mundu (*Garcinia dulcis Kurz*) is a plant that is included in the genus Garcinia which is closely related to mangosteen (*Garcinia Mangostana*) and kandis acid (*Garcinia Parvifolia*). Distribution starts from Southeast Asia then extends to New Caledonia, northern Australia, tropical Africa, Madagascar, Polynesia, Central America and South America. Mundu plants are already widely known in Indonesia. In some areas, mundu is called baros and kledeng (Javanese), jawura and golodog panto (Sundanese), and Patung (Makassar). Mundu grows wild in the eastern part of Java at a land height of less than 500 m above sea level and areas that are not too dry[15]. Adult mundu plants have a height of 10-12 meters,

a diameter of 0.20 meters, the main stem of the mundu plant is straight with angular branches, the leaves are arranged in pairs, oblong, narrow, the upper surface of the leaves is smooth with a length of 22-45 cm, and the root system is stronger than other types in the genus Garcinia[13]. Earrings (*Acalypha Indica L.*) showed anti-Malaria activity where the ethyl acetate extract of the earring plant was able to inhibit the growth of Plasmodium Berghei at a dose of 0.01 mg/g bb up to 87.19%, a dose of 0.1 mg / bb by 84.9% and a dose of 1 mg/g bb by 90.74%. The active compounds contained in the earring plant based on the results of phytochemical tests are tannins, alkaloids and steroids.

Johar plant which comes from the *Caesalpiniaceae family* has long been used as a traditional medicinal plant in Indonesia to treat Malaria. Research on this plant as an anti-Malaria in *vitro* and *in vivo* has been conducted. The results of *in-vitro testing* conducted on extracts to fractionation of alkaloids of johar leaves showed Malaria activity against P. falciparum. It was found that the water extract from C. Siamea leaves had the ability to inhibit the growth of P. Berghei in *vivo*.

The anti-Malaria activity of Pasak Bumi is widely known, but the active substance that has anti-Malaria ability as well as an immune response activator is not yet known for certain. Pasak Bumi plants contain active compounds called quassinoids which have the ability as antitumor, antiviral, antiamoeba and antiplasmodial. The activity test of Pasak Bumi extract (*Eurycoma longifolia jack*) can reduce the level of P. Berghei parasitemia which is accompanied by an increase in TNF-α expression in mice infected with P. Berghei.

Ketumpang herb with the name *Simplisia Tridax procumbens L* is the next plant that has activity as an anti-Malaria. Ethanol extract of ketumpang herb has activity as an anti-Malaria, with the concentration inhibition value 50 (IC50) of ethanol extract of ketumpang herb is 3 µg/mL. The active compounds contained in Ketumpang herb are alkaloids, saponins, flavonoids, steroids/triterpenoids, and polyphenols (Darmawan, 2014).

The active compounds contained in cocor bebek are bufadienolide and flavonoid compounds, which are abundant in the leaves. The anti-Malaria activity of Cocor Bebek leaves has extracting Cocor Bebek leaves using 96% ethanol solvent using the maceration extraction method. The ethanol extract of Cocor Bebek leaves was then tested to see the anti-Malarial activity determined by parasitemia, percent growth and parasite inhibition. The test results showed that the ethanol extract of cocor bebek leaves had an anti-Malaria effect with an IC50 value of 0.022 µg/mL.

The last plant is Talikuning (*Anamirta Cocculus*), which is one of the traditional herbal medicines commonly used in Papua empirically as an anti-Malaria. The stems and roots of Talikuning contain quaternary alkaloids which are considered to have physiological activity as an anti-Malaria. The extract of the parent Talikuning could inhibit the growth of Plasmodium Berghei significantly ($p<0.05$) against the control with an ED50 of 0.043 mg/g mouse BW which is equivalent to 4.7 mg/kg human BW.

Plants Used as Basic Ingredients for Malaria Treatment in Manusa Village

Katimaha, Timaha or Katimahar (*Kleinhovia hospita*) is a type of tree, the only species in the genus Kleinhovia, family *Malvaceae*. This wood grows naturally in Indonesia, Malaysia and other parts of the Asian continent. This tree with quite a lot of uses is known by various regional names such as Katimahar, Kinar/Kenar (Amb.); Tangkèlè, Tangkolo (Sd.); Katimåhå, Timåhå, Katimångå, Timångå, Kayu Tahun (Jw.); Mangar (Lamp.); Mangar (Md.); Katémaha (Kang.); Katimaha (Bl.); Nundang (Sumba); Bintangar, Bintanga, Bintang, Bitangal, Bintana, Wintangar (various languages in North Sulawesi); Ngědèdo, Ngědèdoro, Dèdoro, Ngaru (various languages in Malut); Paliasa Wood, Kauwasa (Mak.); Aju Pali, Wèu (Bug.); and others. While in English it is called *Guest Tree*.

Figure 3. Katimaha plants

Based on the results of phytochemical screening research on Katimaha plant leaves in 2009, it was shown that Katimaha has 3 (three) phytochemical contents, including: alkaloids which are a group (nitrogen-containing wet organic molecules) that have a structure similar to the structure of ephedrine and are now important as drugs, are found in a number of plants. Alkaloids that have pharmacological effects on humans and animals as antibacterial substances. This is because alkaloids have the ability to inhibit the work of enzymes to synthesize bacterial proteins. Based on the tests that have been conducted, positive results (+) were obtained for Flavonoid content in Katimaha leaves. There was a color change in the solution from dark green to blackish red. In addition to the various benefits above, there are a myriad of other benefits of flavonoids that are equally extraordinary for the body, including: Helping the body absorb vitamin C better. Helping prevent and/or treat

allergies, viral infections, arthritis, and certain inflammatory conditions (Budiarti et al., 2020). Flavonoid compounds in the pharmaceutical field function as strong antioxidants, as antimicrobials, antibacterials, antivirals, anti-inflammatory, antimutagenic, anticancer, antiplatelet and others, Flavonoids also function for Hypertension, atherosclerosis. The mechanism of action of flavonoids as antioxidants can be direct or indirect. Flavonoids as antioxidants directly are by donating hydrogen ions so that they can neutralize the toxic effects of free radicals. In the Katimaha leaf sample, after shaking very vigorously a stable foam was produced on the surface of the liquid and lasted for 15 minutes. This evidence shows that Katimaha leaves contain Saponin. The formation of a steady foam when extracting plants or concentrating plant extracts is evidence of the presence of saponins. Saponin is known to have an antimicrobial effect, inhibiting fungi and protecting plants from insect attacks. Saponins can reduce cholesterol, have antioxidant, antiviral and anti-carcinogenic properties and are manipulators of rumen fermentation.

Conclusion

The use of traditional medicine to treat malaria remains a primary option in many communities, especially in remote or poor areas with limited access to modern medicine. Factors such as belief in the effectiveness of traditional medicine, accessibility, and social and cultural influences play a major role in the decision to use these treatments. Positive family and community experiences also strengthen trust in traditional medicine, although challenges such as bitter taste and higher doses remain. Medical supervision and awareness of dosage and potential side effects are essential to ensure the safety of traditional medicine use, especially for vulnerable age groups.

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