Artikel Penelitian

Constant Malaria Transmission From Migrating Humans Residing In Low Endemic Areas

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Abstract

***Introduction**: Malaria is an infectious disease that continues to be a public health issue worldwide, including in Indonesia. This study aims to detect the presence of Plasmodium parasites among immigrants from malaria endemic areas.*
***Method**: The research was conducted from September until November 2019 in three regency/cities in South Sulawesi, namely Makassar City, Tana Toraja and North Toraja. The population in this study were immigrants from malaria endemic areas (native Papua and non-Papua) who lived in the area for at least 2 years before visiting the cities of Makassar, Tana Toraja, or North Toraja. All samples were examined for malaria parasites using Polymerase Chain Reaction (PCR).*
***Result**: The results of the PCR test on 256 samples of migrants (native Papuan and non-Papuan) detected 19.53% positive for malaria. This research showed that a high prevalence of malaria parasites was found among asymptomatic immigrants, both native Papuans and non-Papuans in South Sulawesi.*
***Conclusion**: It can be concluded that the asymptomatic immigrants from endemic areas such as Papua need to be screened early because they may still have malaria parasites in their blood and become carriers, leading potential to cause local transmission.*

***Keywords:** asymptomatic, endemic malaria, migrant, native-Papua, non-Papua*

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Transmisi Malaria Dari Penduduk yang Bermigrasi Ke Daerah Endemik Rendah

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Abstrak

***Pendahuluan**: Malaria merupakan salah satu penyakit menular yang masih menjadi masalah kesehatan masyarakat baik di dunia maupun di Indonesia. Penelitian ini bertujuan untuk mendeteksi keberadaan Plasmodium pada pendatang dari daerah endemis malaria.*
***Metode**: Penelitian ini dilakukan pada bulan September s.d November 2019 di tiga kabupaten/kota di Sulawesi Selatan yaitu Kota Makassar, Tana Toraja atau Toraja Utara. Populasi pada penelitian ini adalah pendatang dari daerah endemis Malaria (native Papua dan non-papua) yang menetap di daerah tersebut minimal selama 2 tahun dan berkunjung ke wilayah kota Makassar, Tana Toraja, atau Toraja Utara. Semua sampel dilakukan pemeriksaan parasit malaria dengan menggunakan. Hasil uji PCR dari 256 sampel pendatang (native Papua dan non-Papua) terdeteksi 19.53% positif malaria.*
***Hasil**: Hasil PCR menunjukkan bahwa keberadaan parasit Plasmodium dalam sampel darah pendatang lebih tinggi dibandingkan penduduk asli Papua yang sehat (asimtomatik). Penelitian ini menunjukkan bahwa prevalensi parasit malaria yang tinggi ditemukan pada pendatang asimtomatik, baik pada penduduk Papua asli maupun non-Papua di Sulawesi Selatan.*
***Kesimpulan**: Dapat disimpulkan bahwa pendatang asimtomatik dari daerah endemis seperti Papua perlu dilakukan skrining sejak dini karena kemungkinan masih memiliki parasit malaria dalam darahnya dan menjadi carrier sehingga berpotensi menyebabkan terjadinya penularan lokal.*

***Kata kunci:** asimtomatik, asli Papua, endemik malaria, non-Papua, pendatang*

Introduction

Malaria is an infectious disease that continues to be a public health issue worldwide, including in Indonesia. According to the World Health Organization's (WHO) 2018 World Malaria Report, there are approximately 219 million malaria cases worldwide, with approximately 435 thousand fatalities.[1] Malaria infections in Indonesia are widespread over the archipelago, with Papua, West Papua, Maluku, North Maluku, and East Nusa Tenggara accounting for 92.29 percent of all malaria cases in the country in 2018. Malaria cases decreased between 2010 and 2014, then were relatively stable between 2014 and 2018. Annual Parasite Incidence (API) was 0.99 in 2014, 0.85 in 2015, and 0.84 in 2016. However, it grew to 0.99 in 2017 before dropping to 0.84 in 2018.[2]

Since 2009, the Indonesian government has been working to eliminate malaria, as stated in the Minister of Health of the Republic of Indonesia's decree No. 293/MENKES/SK/IV/2019 concerning the elimination of malaria to create a healthy living community free of malaria transmission implemented in few stages until 2030. An area that is low endemic means entering the phase of release and maintenance by carrying out vigilance activities through intensive surveillance. However, malaria has continued to exist in low-endemic areas for the past five years. It may be due to the introduction of cases from high-endemic areas into non-endemic areas, contributing to this persistence. For example, after six years of malaria elimination, Karunasena et al. (2019) observed imported instances of malaria among foreign workers from malaria-endemic nations, resulting in introduced malaria

cases in Sri Lanka.[3]

The high mobility of the population from high-endemic areas, including migrants who stay in Papua for more than two years before returning to their hometowns and native Papua residents who travel to non-endemic or low-endemic areas, can result in imported malaria or even native transmission. For example, according to Yangzom et al. (2012), imported malaria cases occurred in Bhutan due to population mobility to and from endemic areas, resulting in native transmission.[4] Thus, due to the significant mobility of the population from malaria-endemic areas, native transmission may occur, posing a threat to Indonesia's goal of eliminating malaria by 2030. As a result, to meet the planned target, migration surveillance must be strengthened. Therefore, a surveillance test of native and migrant movements from endemic areas was conducted to determine the extent to which immigrants were the source of malaria infection.

Methods

Study Population

This research was conducted from September to November 2019. Makassar City, Tana Toraja, and North Toraja were the three districts/cities where sampling took place. Many native Papuans live in Makassar City. Meanwhile, many people of Tana Toraja and North Toraja participate in migration activity to malaria-endemic areas. People who have resided in Papua for more than two years since birth are considered native Papuans, while migrants are those who migrate to Papua and stay for at least two years. The Ethical Committee has approved the protocol of this study of the Faculty of Medicine Hasanuddin University (No. 173/UN4.6.4.5.31/PP36/2020).

Clinical Symptom Examination

Immigrants are scrutinised only based on their physical appearance. Therefore, anyone with fever, chills, sweating, or headaches was interviewed. Migrants presented with clinical symptoms were subjected to direct malaria screening and treatment but not collected as samples. Meanwhile, samples of healthy migrants (those with no clinical symptoms) were taken for PCR testing.

PCR Method

The extraction is done with an Instagene kit. A total of 100 ul of serum was diluted with 1 ml of distilled water, vortexed, and incubated at room temperature for 30 minutes before centrifuging for three minutes at 12,000 rotations per minute (rpm). Next, transfer the supernatant to a fresh tube, add 200 ul of instagene, and incubate for 30 minutes at 56°C (vortex every 15 minutes). After that, vortex for ten seconds before incubating at 95°C for eight minutes. Additionally, vortex for 10 seconds before centrifuging at 12,000 rpm for three minutes. Keep the DNA sample at -20°C.

The extracted DNA was amplified using the nested PCR (Applied Biosystems Veriti 96-Well Thermal Cycler) method. Nested 1 uses Primer rPLU1 and rPLU5 and the Supermix PCR kit. A total of 22.5 ul PCR Supermix, 10pmol rPLU1 0.5 ul, 10 pmol rPLU5 0.5 ul, and 2 ul DNA samples were polymerized at 94°C denaturation temperature for 15 seconds, 55°C annealings 1 minute, and 72°C extensions for 1 minute for 30 cycles. The nested 2 used KAPA 2G Fast kit and rPLU3 and rPLU4 primers for genus-specific primers. A total of 6.5 ul of KAPA 2G Fast enzyme, 10pmol primer F 0.5 ul, 10pmol R primer 0.5 ul, and DNA from nested 2 5 ul were polymerized at denaturation temperature 95 C for 30 seconds, genus-specific annealing primer 55°C for 1 minute, extension 72°C for 1 minute for 30 cycles.5 Electrophoresis: the sample was electrophoresed in 2% agarose solution and added with 5 ul of DNA stain, run for 2 hours at 100 volts. Agarose was imaged on a blue box and photographed using a camera.

Results

A total of 256 healthy people were including in the research (143 non-Papua and 113 native-Papua). PCR results showed non-Papua were 30.07% positive Plasmodium and native-Papua were 6.19% positive Plasmodium (Table 1). In Table 2 the study showed the malaria parasite was most common in males (13.67%) as compared to females (5.86%) in the study samples.

In the present study it was found that the most prevalent age group was group 20-45 years old (16.02% positive Plasmodium) follow by Group <20 years old (3.51% positive Plasmodium). The age wise distribution of positive Plasmodium has been shown in Table 3.

Table 1. Result Comparison of Non-Papua and Native-Papua Tested by PCR

	N	Positive Plasmodium	%
Non-Papua	143	43	30.07%
Native Papua	113	7	6.19%

Table 2. Malaria Parasites Distribution by Gender

Gender	Number Examinated	Number Positive
Male	128	35 (13.67%)
Female	128	15 (5.86%)
Total	256	50 (19.53%)

Table 3. Malaria Parasite Distribution by Age Groups

Age Group (years)	Number Examinated	Number Positive
<20	52	9 (3.51%)
20-45	202	41 (16.02%)
>45	2	0
total	256	50 (19.53%)

Discussion

Malaria transmitted from outside the city due to the migration of people from malaria-endemic areas is referred to as imported malaria.[6] Imported malaria is disseminated by the significant migration of malaria-endemic people to non-endemic locations. Yangzom et al. (2012), for example, indicated that imported malaria cases occurred in Bhutan as a result of population migration to endemic areas and that this case resulted in native transmission.[4] According to Smith et al. (2019), population migration to malaria-endemic locations such as India causes high imported malaria, which leads to native malaria in Nepal.[7]

Migrants exposed to malaria at work (in malaria-endemic areas) and subsequently returning to their original non-malaria-endemic locations are still at risk of contracting the disease. It will also have the potential for native transmission in the origin area, a non-endemic and receptive area (an environment conducive to supporting the proliferation of malaria vectors). Malaria-endemic residents who come to non-endemic areas also have a significant role in causing imported cases.

The study sample comprised 256 healthy individuals (143 non-Papua and 113 native-Papua) staying more than two years in the malaria-endemic area. In this study, non-Papua and native Papuan were screened for the presence or absence of clinical symptoms. Entrants with clinical symptoms were subjected to direct examination and treatment, but they were not used as study samples. Thus, all samples were 256 healthy/asymptomatic people from Papua (non-Papua and native-Papua). Papua has high endemicity and is one of Indonesia's five provinces, accounting for 95.05% of malaria cases in Indonesia in 2019.[8]

Out of the total 256 samples, 50 (19.53%) were positive for malaria, of which 35 (13.67%) were males, and 15 (5.86%) were females. This study showed males had a higher prevalence than females, which may be because males mostly go out and work in an open environment without covering their bodies. On the other hand, due to social costumes, females are limited at home, cover themselves well, and are not exposed to mosquito bites. A study conducted by Irshad et al. (2013) showed similar results higher prevalence of malaria in males (62.12%) than in females (37.88%).[20] Similarly, another report published in 2013 investigated that malaria is more common in males (58.70%) than females (41.27%).[21] Age group 20-45 years old had the highest prevalence rate of 16.02%. This high prevalence age group 20-45 years old can be attributed to the fact that persons in this age group are probably the most socially active and, as such spend longer hours outside their homes. Thus, they face a higher risk of exposure to the disease vector.

The results of PCR examination in this study found that 19.53% of malaria positive from asymptomatic samples. It shows that the prevalence of asymptomatic malaria is relatively high in immigrants from high-endemic malaria areas such as Papua. A high prevalence of asymptomatic malaria has also been reported in several countries, such as Bangladesh, Rondonia, Solomon, and Thailand.[9-12] This asymptomatic malaria is a source of malaria transmission in Southeast Asia.[13] Bousema et al. (2014) also reported that asymptomatic malaria is a reservoir of malaria parasites and carries parasites in the form of gametocytes which contribute to the persistence of malaria transmission.[14]

In this study, asymptomatic non-Papua and native Papua who come from high-en-

demic areas of malaria can act as a malaria reservoir and the cause of the high number of imported malaria cases that can even lead to introduced malaria cases in low or non-endemic areas. Karunasena et al. (2019) reported that many workers from high-endemic countries with malaria led to the introduction of malaria cases in Sri Lanka, which has eliminated malaria since 2012.[3] Residents from malaria-endemic countries who have lived permanently in non-endemic countries and then visit friends or family in their origin countries account for a high proportion of imported malaria in Europe.[15,16] In addition, residents of non-malaria endemic countries who travel to malaria-endemic countries for holidays or work reasons also contribute significantly to imported malaria cases in their origin countries.[16]

Healthy or asymptomatic people from Papua should be suspected because the area has high malaria endemicity, which allows their blood to contain malaria parasites and can be a transmission source in non-endemic areas. Asymptomatic malaria can maintain the chain of transmission because this malaria sufferer does not seek treatment because he does not feel sick. In addition, asymptomatic malaria tends to remain in the body for an average of six months.[17]

Malaria has a mild clinical percentage even in native Papuans and migrants who have lived in Papua for an extended period. It happens because malaria immunity develops over time due to constant and long-term exposure to the parasite. On the other hand, this immunity does not prevent a person from becoming infected with malaria; instead, it regulates the number of parasites in the blood.[14,18,19]

PCR results in migrant samples detected positive malaria samples in 43 samples (30,07%), while native samples were positive in seven samples (6.19%). The high positive PCR among migrants may be that the migrants lack a basic understanding of malaria transmission and prevention, rarely use insecticides, nets, or repellants while traveling, and fail to seek medication or treatment when sick. Smith et al. (2019) reported that high-risk migrant populations who travel to malaria-endemic areas lack a basic understanding of malaria transmission.[7] In addition, most travelers did not use any form of malaria prevention on their trips, like insecticide-treated bed nets or repellent, and tended not to seek treatment when sick. Therefore, surveillance should target migrants in order to contain the potential for vector transmission of malaria.

Conclusion

Migrants from a malaria-endemic area residing in the low-endemic area are a potential malaria transmission source.

Conflict of Interest

The authors declare that we have no competing interest of financial, professional, or personal interests that might affect the performance or presentation of this manuscript.

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