

Congenital Malaria Due to *Plasmodium vivax*: A Case Report

Anggia Rarasati Wardhana¹, Sukartini¹, Loly R.D. Siagian², Lily Pertiwi Kalalo²

¹Department of Child Health Faculty of Medicine, University of Mulawarman, Abdul Wahab Sjahranie Hospital, Samarinda, East Kalimantan, Indonesia

²Department of Clinical Pathology, Faculty of Medicine, University of Mulawarman, Abdul Wahab Sjahranie Hospital, Samarinda, East Kalimantan, Indonesia

Keyword:

Congenital malaria,
Plasmodium vivax,
Chloroquin, DHP

Abstract

Congenital malaria is an infectious disease caused by the malaria parasite that is transmitted from mother to child through placenta during pregnancy or at delivery. In areas where malaria is endemic, infants aged less than 3 months appear to be relatively protected from symptomatic and severe *Plasmodium falciparum* malaria, but less is known about the effect of *Plasmodium vivax* infection in this age group. Diagnosis of congenital malaria is difficult because of the similarity in clinical presentation with other infections. A 24-days old boy, hospitalized with repeated fever, intermittent, vomiting, and diarrhea with decreased appetite. Physical exams revealed pale conjunctiva, jaundice sclera and body, hepatosplenomegaly with dilatation of veins in the surface of abdomen. Mother had suffered from malaria at the 7 months of pregnancy and hospitalized. Parents were living in Papua for 2 years. Laboratory findings showed: peripheral blood smear showed gametocytes of *Plasmodium vivax* stadium trophozoite. His mother peripheral smear for malaria was positive. The patient was treated with chloroquin in doses of 10 mg/kgBW and followed by 5 mg/kgBW, but had no response, then replaced with dihydroartemisinin-piperaquine (DHP) for three days. After 19 days hospitalized, clinical symptoms were improved and repeated of peripheral smear was negative. In infants from mothers with any history of malaria fever at antenatal period, malaria should be suspected in any neonate with fever and anemia with hepatosplenomegaly. Early diagnosis and treatment could effectively prevent infant mortality.

Corresponding Author: anggiararasatiwardhana@gmail.com (Anggia Rarasati Wardhana)

INTRODUCTION

Malaria has always been the major parasite that causes death in human and spread throughout the world, especially in tropical regions such as Indonesia.^{2,3} Each year, there are 300-400 million new cases of malaria and 1.5 to 2.7 million of deaths, particularly in children under 5 years old.¹ According to WHO, there are 216 million cases of malaria in 2016 and 445,000 deaths in the world. Mortality caused by malaria reached around 3,000 deaths per year in Indonesia.² In children under 5 years old, the death rate of malaria is estimated to have decreased for 35% between 2010 and 2015.^{2,3}

Congenital malaria is established when malaria parasites are found in the peripheral blood smear of neonates aged 1 to 7 days of life.⁴ Congenital malaria is caused by malaria parasite transmitted from the mother to the child through the placenta during pregnancy or birth. The asexual form of malaria harbors in the peripheral blood of neonates aged 1-7 days without clinical symptoms.⁵ Symptomatic congenital malaria is rarely found in malaria endemic countries. The symptoms of congenital malaria is not specific and often diagnosed as neonatal sepsis.⁴

Globally, malaria is still a serious disease with quite high incidence.⁶ Most of the regions in Indonesia is still an endemic region of malaria infection, including West Indonesia such as Papua, Maluku, Nusa Tenggara, Sulawesi, Kalimantan and even several regions in Sumatra such as Lampung, Bengkulu, and Riau.⁷ API stratifies the regions in which West Indonesia is included in high malaria stratification, several regions in Kalimantan are included in moderate stratification even though several villages/foci of high malaria still exist. Every *Plasmodium* species have been documented in Indonesia, including a small number of *P. knowlesi* cases in human in Kalimantan and Sumatera. *Plasmodium falciparum* is slightly more common than *Plasmodium vivax*, with the proportion of 55% and 44%, respectively. However, in most regions excluding Papua, *P. vivax* is the dominant species. *P. malariae* and *P. ovale* spp. Are rarely documented and almost all cases are recorded in the east region of Indonesia.⁸

This report is a demonstration case thus is expected that it will not escape diagnosis in the future. Congenital malaria screening is needed for newborn babies especially in malaria and antenatal malaria endemic regions.

CASE REPORT

A 24-day-old infant was admitted to the hospital due to repeated fever for more than a week. The fever was intermittent followed by vomit, diarrhea, and decreased appetite. The mother had a history of malaria when she was 7 months pregnant. The parents of the patient lived in Papua, Indonesia for 2 years and affected by malaria for more than once. Physical examination showed anemic conjunctiva, icteric sclera and jaundice. Abdominal examination found hepatosplenomegaly accompanied by abdominal vein dilation, which was confirmed by abdominal ultrasound (Figure 1,2). Early laboratory examination showed 7.0 g/dl Hb, 21.8% hematocrit, 49,000 platelets, 17,320 leukocytes, and 4,070/ μ l parasites (Table 1). Thick and thin peripheral blood smear found gametocyte of *P. vivax* in trophozoite and advanced trophozoite stadium. The diagnosis of congenital malaria was established. The patient was treated by 10 mg/kg body weight chloroquine followed by 5 mg/kg body weight, however significant response was not shown. The therapy was replaced by 1 DHP tablet for three days combined with primaquine for 14 days. After 19 days of admittance, the patient showed improvement of clinical symptoms. Re-examination of peripheral blood smear showed no parasite.



Figure 1. Abdominal Physical Examination

Table 1. Laboratory Findings

Laboratory Results	18/04/25	18/04/30	18/05/03	18/05/07	18/05/11
Hemoglobin	7,0 g/dl	14,3 g/dl	12,0 g/dl	10,6 g/dl	
Hematocryte	21,8 %	44,6%	36,6%	32,5%	
Plt	49.000/ μ l	47.000/ μ l	61.000/ μ l	224.000/ μ l	
leukocytes	17.320/ml	11.390/ml	8.350/ml	7.680/ml	
Parasit Count	4.070/ μ l		423/ μ l	-	
Bilirubin Total		13,5 mg/dl			3,0 mg/dl
Bilirubin Direct		10,0 mg/dl			2,0 mg/dl
Bilirubin Indirect		3,5 mg/dl			1,0 mg/dl
Alkali Phosphatase		373 U/L			369 U/L
SGOT		108 U/L			95 U/L
SGPT		72 U/L			85 U/L
Gamma GT		158 U/L			156 U/L

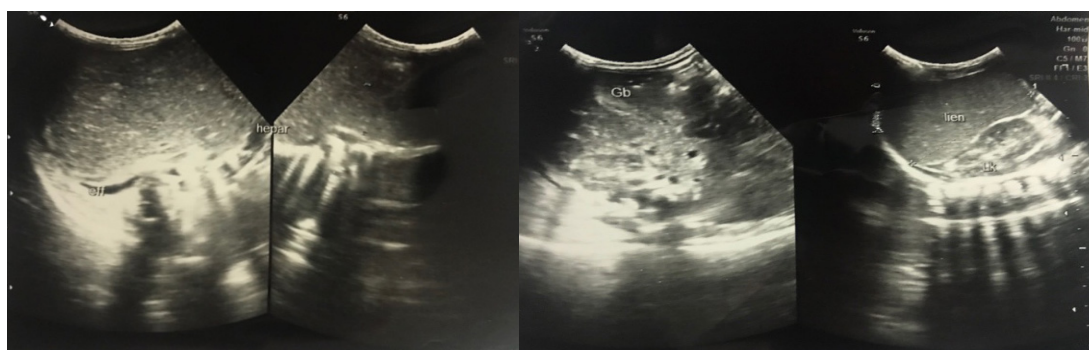


Figure 2. Ultrasonografia of abdomen: showed hepatomegali and aerofagia

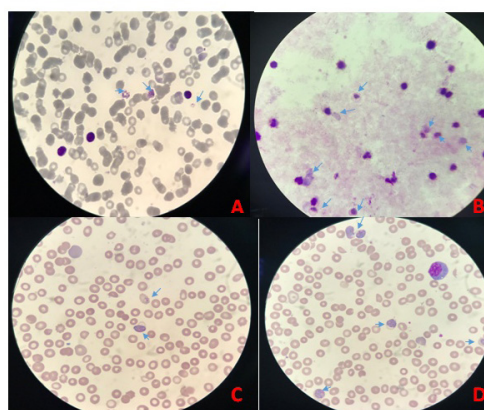


Figure 3. Peripheral blood smear examination: (A) gametosit P.vivax stadium trofozoite (Giemsa stain, 1000x); (B) Gametosit of P.vivax stadium trofozoite; (C) A thin blood smear showing ring-shaped P.vivax gametocytes; (D) Thin blood smear showing advanced trophozoite stage P. vivax gametocytes.

DISCUSSION

Malaria in pregnancy and neonates causes significant disease burden and estimated to cause more than 300,000 deaths in fetuses and infants and 2,500 deaths of pregnant women in the world every year.^{9,10} Regardless of serious health problem, only a few epidemiological studies were conducted to investigate disease burden, diagnostic approach, management and prevention of congenital malaria.

Congenital malaria is caused by the transmission of parasites from mother to child during pregnancy or during birth. Malaria infection to the placenta was marked by syncytiotrophoblast and villi abnormality, synchronous bond formation, and deposition of fibrinoid-type fibrin. Syncytial destruction can cause low birth weight and congenital infection.¹¹

Therefore, malaria during pregnancy can cause two extreme consequences in neonates. It can cause premature labor, intrauterine growth retardation, high perinatal death, anemia, miscarriage, low birth weight, and mother's death, both in cases infected by *P. vivax* and *P. falciparum*.¹⁰ On the other hand, malaria during pregnancy can protect infants from malaria infection and severe diseases through acquired immune system of the mother. Antimalaria IgG and IgM antibodies can be detected in the mother's blood, but only IgG flow through placenta which is often found in the infant's blood.¹²

Immunity from the mother's antibody acquired through the placenta can delay the appearance of symptoms to 3 to 6 weeks after birth. Literatures described the appearance of congenital malaria symptoms from 3-12 weeks after birth, coincide with the half-life of mother's IgG antibody in the infant. History and relevant investigation from the mother's side can help differentiate from malaria transmitted through vector in this situation. This differentiation is important because exoerythrocytic cycle does not exist, thus does not require radical treatment with antimalaria that has damaging potential such as primaquine.¹² Symptoms start to occur when mother's antibody passively decreases. Fever and accompanying symptoms should be considered, including irritability, hepatosplenomegaly, anorexia,

hemolytic anemia, icterus, and thrombocytopenia.¹²

Several studies have reported congenital malaria caused by *P. falciparum* infection in Africa.^{13,14} However, congenital malaria caused by *P. vivax* was also reported in several countries.^{15,16} This case showed that the diagnosis of congenital malaria should be considered as an important differential diagnosis from neonatal infection and sepsis in infants born from mothers from malaria endemic countries with or without history of malaria during pregnancy.¹⁷

The treatment of neonate vivax malaria includes blood schizonticides, such as 10 mg/kg base body weight chloroquine followed by 5 mg/kg base for on 6, 24, and 48 hours. Primaquine should not be given to congenital malaria because no exoerythrocytic phase is found from parasite.¹⁷ Primaquine is contraindicated in pregnant and nursing mothers and there is no strategy of radical malaria treatment for pregnant women with absolute safety for the fetus. High prevalence of multidrug resistance in *P. falciparum* and *P. vivax*, infants weighing less than 5 kg and pregnant women on their first trimester with malaria can be treated by oral quinine. Dihydroartemisinin-piperaquine can be used for malaria without complication in infants weighing more than 5 kg and in pregnant women during their second and third trimester. Neonates and pregnant women with severe malaria can be treated by intravenous artesunate.¹⁸

Reports of resistance to malaria treatment against old drugs (chloroquine, sulfadoxine-pyrimethamin and quinine) in the last 10 years are indeed worrying more than 25% of provinces in Indonesia.¹⁹ No response to early therapy of chloroquine in this case can be caused by resistance to antimalaria.

P. vivax congenital malaria is a condition that are relatively rare, thus should be considered as differential diagnosis in neonatal infection, sepsis, unexplainable fever or in infants with hemolytic anemia, jaundice and hepatosplenomegaly in malaria endemic zone. It has delayed clinical symptoms and can occur in infants with asymptomatic mother. Prompt diagnosis and intervention can prevent morbidity and mortality of mothers and newborns. The protocol of malaria treatment in pregnancy, nursing mothers

and congenital malaria is different than the usual recommendation and should be adjusted individually.

REFERENCES

1. Committee on Infectious Diseases AA of P. Malaria. In: Pickering L, editor. Red Book. 25th ed. Elk Grove Village; 2000. p. 381–5.
2. WHO. World malaria report 2017. Geneva; 2017. 1-196 p.
3. Ghanghoriya P et al. Study clinical response and parasite clearance response to Artemisinins in severe malaria in children. *Int J Contemp Pediatr*. 2018;5(3):905–11.
4. Bhatia R et al. Congenital Malaria due to Plasmodium Vivax Infection in a Neonate. *Case Rep Pediatr*. 2016;6(1):1–5.
5. Carlier Y et al. Congenital parasitic infections: A review. *Acta Trop*. 2012;121(2):55–70.
6. Harijanto P et al. Malaria pada Anak dalam Malaria dari Molekul ke Klinis. kedua. Jakarta: EGC; 2010. 158-90 p.
7. Poorwo S et al. Malaria pada Anak dalam Buku Ajar Infeksi dan Pediatri Tropis. kedua. Jakarta: Ikatan Dokter Anak Indonesia; 2010. 408-96 p.
8. Elyazar I et al. Malaria distribution, prevalence, drug resistance and control in Indonesia. *Adv Parasitol*. 2011;74:41–175.
9. Menendez C et al. Reducing the burden of malaria in pregnancy by preventive strategies. *Lancet Infect Dis*. 2007;7:126–35.
10. Rodriguez-Morales A et al. Malaria mortality in Venezuela: focus on deaths due to Plasmodium vivax in children. *J Trop Pediatr*. 2008;54:94–101.
11. Crocker I et al. Syncytiotrophoblast degradation and the pathophysiology of the malaria-infected placenta. *Placenta*. 2004;25:273–82.
12. Rai P et al. Congenital malaria in a neonate : case report with a comprehensive review on differential diagnosis , treatment and prevention in Indian perspective. *J Parasit Dis [Internet]*. 2015;39(June):345–8. Available from: <http://dx.doi.org/10.1007/s12639-013-0342-1>
13. Opare DA. Congenital malaria in newborn twins. *Ghana Med Jour*. 2010;44(2):76–8.
14. Olupot-Olupot P et al. Neonatal and congenital malaria: A case series in malaria endemic eastern Uganda. *Malar J [Internet]*. 2018;17(1):1–5. Available from: <https://doi.org/10.1186/s12936-018-2327-0>
15. Valecha N et al. Congenital malaria with atypical presentation: a case report from low transmission area in India. *Malar J*. 2007;6:43.
16. Wiwanitkit V. Congenital malaria in Thailand, an appraisal of previous cases. *Pediatr Int*. 2006;48:562–5.
17. Punta V Del et al. Congenital Plasmodium vivax malaria mimicking neonatal sepsis: a case report. *Malar J*. 2010;9:63.
18. Poespoprodjo J et al. Highly effective therapy for maternal malaria associated with a lower risk of vertical transmission. *J Infect Dis*. 2011;204:1613–1619.
19. Indonesia KKR. Buku Saku Penatalaksanaan Kasus Malaria. Jakarta: Ditjen Pengendalian Penyakit dan Penyehatan Lingkungan; 2017. 1-10 p.