

MANAGEMENT OF MALARIA IN PREGNANCY WITH COVID-19

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Abstract

Malaria is one of the most common diseases in the world. According to WHO in 2015 there were 214 million cases of malaria. In Indonesia, the percentage of positive cases of malaria in Papua Province in 2016 was 54.3%. The design of this research is descriptive with the type of descriptive research used is a case study. This study was conducted at the RSAL Dr. Soedibjo Sardadi Jayapura in August 2020 on a 37-year-old woman G3P2A0 who was 16 weeks pregnant at term, a single live intrauterine fetus with tropical malaria, reactive SARS CoV-2 IgG antibodies. Malaria in pregnancy can cause pathological conditions both in pregnant women and in fetuses. In pregnant women, such as fever, hypoglycemia, anemia, acute pulmonary edema, kidney failure can even cause death. In the fetus it causes abortion, premature delivery, low birth weight, and fetal death. Prevention of malaria in pregnancy using mosquito nets, prophylaxis, mosquito repellent, and gauze for ventilation, and not having a habit of going outside at night or going out at night with a frequency of <2 times. Prevention efforts against COVID-19 are to break the chain of transmission by isolation, early detection, and basic protection such as maintaining cleanliness (hygiene), washing hands, and disinfecting. Chloroquine is still the drug of choice for the treatment of malaria in pregnancy and quinine for the treatment of severe malaria.

Keywords: *malaria; pregnancy; covid-19, chloroquine, Jayapura*

Introduction

Malaria is one of the most common diseases in the world. According to WHO in 2015 there were 214 million cases of malaria and caused the death of 438,000 sufferers (Puasa, Asrul H and Kader, 2018).

Based on data from the 2014 Indonesian Health Profile, 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. Five Provinces with the highest Annual Parasite Incidence (API) per 1,000 population in 2014 were Papua (29.57%), West Papua (20.85%), East Nusa Tenggara (12.81%), Maluku (6.00 %) and North Maluku (3.32%) (Pilmeks D Layan, Rahayu H. Akili, Dina V. Rombot, 2016), while the prevalence of malaria based on a history of blood tests in Indonesia in 2018 was 0.4% (Risikesdas, 2018).

Based on data from Risikesdas in 2018, the prevalence of malaria based on a history of blood tests in Indonesia in 2018 was 0.4%. Of the 35 provinces, the highest prevalence is Papua (12%), West Papua (8%), East Nusa Tenggara (2%) (Risikesdas, 2018). The malaria morbidity rate was assessed using the annual parasite incidence (API) per 1,000 population in Papua Province, in 2016 it was 49.6 per 1,000 population, while the percentage of positive cases of malaria in Papua Province in 2016 was 54.3%. (Dinas Kesehatan Papua, 2016).

Malaria is a disease caused by infection with the Plasmodium parasite (Mawuntu, 2018). In Indonesia, the parasites that cause malaria are Plasmodium vivax which causes malaria tertiana and Plasmodium falciparum which causes tropical malaria. The location of the most widespread distribution is in the Lesser Sunda Islands or Nusa Tenggara and Papua (Junarli and Somia, 2017).

Factors related to the incidence of malaria in pregnant women are the level of knowledge, behavior patterns (Darmiah *et al.*, 2019), attitudes and actions to prevent malaria (Layan, Akili and Rombot, 2016), monitoring of the health of pregnant women by midwives which is manifested in the possession of a Maternal Child Health (KIA) book, the use of mosquito coils/electric when sleeping at night, the economic status of pregnant women, and the ease of access of pregnant women to the practice of midwives/maternity hospitals. (Budiyanto and Wuriastuti, 2017).

Malaria can be infected by everyone, including infants, toddlers, children and adults as well as pregnant women (Puasa, Asrul H and Kader, 2018). Pregnant women are more easily infected with malaria and are also easy to be infected again to severe complications (Rahmawaty, 2014). Malaria in pregnancy can cause pathological conditions both in pregnant women and in fetuses. In pregnant women, such as fever, hypoglycemia, anemia, acute pulmonary edema, kidney failure can even cause death. In the fetus it causes abortion, premature delivery, low birth weight, and fetal death (Rusjdi, 2012).

The process of pregnancy which is an individual factor will exacerbate malaria cases experienced by pregnant women, and a pregnant woman suffering from malaria will affect the pregnancy process and abnormalities in the newborn. Malaria infection in pregnant women can cause anemia in the mother and fetus, as well as babies with low birth weight. The risk of low birth weight infants (LBW) in mothers with malaria increased two times compared to pregnant women without malaria. This can increase maternal and infant mortality. Complications of malaria infection in pregnancy can include abortion, low birth weight babies, anemia, pulmonary edema (swelling or accumulation of fluid in the lung tissue), impaired kidney function, and congenital malaria (Budiyanto and Wuriastuti, 2017).

Pregnant women are susceptible to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can increase the risk for both pregnant women and their unborn babies. Pregnant women who experience COVID-19 are feared that there will be intrauterine transmission from mother to fetus. In addition, they can also have symptoms of pneumonia due to the Covid-19 virus, which is one of the main causes of death in pregnant women worldwide. In the fetus, fetal complications can occur in mothers infected with Covid-19, namely miscarriage (2%), Intra Uterine Growth Restriction (IUGR; 10%), and premature birth (39%). Fever with an average temperature of 38.1-39.0°C (Ramadhani *et al.*, 2020).

Malaria treatment in adult COVID-19 patients, including pregnant women, is given according to the patient's symptoms. In patients with mild Covid-19 symptoms with malaria infection, chloroquine/hydroxychloroquine, azithromycin, piperazine (one of the components of the DHP drug) and primaquine can prolong the QTc interval, therefore it is necessary to have an ECG examination to see the QTc interval before being given for treatment. If the patient with COVID-19 does not undergo an EKG examination and receives chloroquine/hydroxychloroquine and azithromycin, for the treatment of malaria, oral DHP is not given, but artesunate is injected for 7 days. Primaquine administration was postponed until the patient's condition improved and Covid-19 treatment was completed. If malaria complications occur, the patient is referred to the hospital. If the symptoms of COVID-19 are moderate and the symptoms are severe with malaria infection, then the malaria drug is given using artesunate injection for 7 days. And for malaria sufferers with COVID-19, primaquine administration is postponed until the patient's condition improves and Covid-19 treatment is completed (Ditjen P2P, 2020).

Methods

The design of this research is descriptive, namely research that aims to explain, give a name, situation or phenomenon in finding new ideas (Nursalam, 2013). The type of descriptive research used is a case study, namely examining a problem through a case study consisting of a single unit. Participants are objects that will be examined in the case study, namely pregnant women with malaria. The number of participants used is 1 person. This research was conducted at the RSAL Dr. Soedibjo Sardadi Jayapura in August 2020. The data collection methods in this case study were observation and physical examination, and a documentation study.

Result and Discussion

Kasus

A woman Mrs. X Age 37 years G3P2A0 14 weeks pregnant came to the RSAL dr. Soedibjo Sardadi Jayapura with complaints of fever accompanied by dizziness, nausea and vomiting since 3 days ago. The results of the anamnesis that the mother is a housewife, before being treated, the mother felt a fever that came and went with chills, bitter mouth, body aches, fever, sore throat and headache. The next day the fever went down after taking paracetamol but a few hours later it came back. On the third day, the patient complained of fever and chills as before and complained of nausea and vomiting, decreased appetite, felt weak and had aches and pains. The patient also complained of cough and runny nose.

On physical examination, the general condition appeared moderately ill, *compos mentis* consciousness, blood pressure 90/60 mmHg, pulse 80x/minute, breathing 18x/minute, temperature 37.9 °C. Eyes, ears and nose, impression within normal limits. On chest examination, chest movement and tactile fremitus were symmetrical, no rhonchi and wheezing were found, the impression was within normal limits. Cardiac examination found no abnormalities, the impression was within normal limits. Flat abdomen has *striae gravidarum*.

The patient had his first period at the age of 12 years with a regular 28-day cycle, for 5-7 days, 4 times changing pads, with the first day of last menstruation (HPHT) on May 08, 2020 and estimated delivery on February 15, 2021. The patient married the first and has been going on for 8 years.

Leopold's external inspection was still ballomen. On laboratory examination, Hb: 12.4 g/dl, leukocytes: 5,700/ μ l, erythrocytes: 3,800,000/ μ l, platelets: 76,000/ul and hematocrit: 29%. Serum bilirubin: Serum Glutamic Oxaloacetic Transaminase (SGOT) 47 u/L, Serum Glutamic Piruvic Transaminase (SGPT) 37 I/L and peripheral blood smear: *Plasmodium falcifarum* +4, rapid test antibody SARS CoV-2 IgM Ractif, Antibody SARS CoV- Reactive 2igG, positive swab examination, RO/thorax results: cast and pulmo, no abnormalities were seen, ultrasound examination at 14 weeks gestation, according to gestational age.

Based on the results of the examination, it was found that the diagnosis was Mrs. X G3P2A0 37 years old 14 weeks pregnant single live intrauterine with tropical malaria and covid-19.

The management carried out was hospitalization of the mother with infusion of RL drips NB 20 tts/min, injection of ranitidine 3x1, ondancetron 2x1, artesunate 0;12;24;36, goldrion oral medication 1x1, comvit C 1x1, education on sunbathing and light exercise every morning 09.00 for 15-30 minutes, giving green bean porridge every morning and evening, giving 1 can of bear milk every afternoon, observing mother's vital signs, reducing contact/bites of *Anopheles* mosquitoes by using mosquito nets and insect repellent, recommending adequate eating and drinking, recommending rest sufficient.

Discussion

Based on the data obtained from the results of the study on the patient, a woman Mrs. X Age 37 years G3P2A0 16 weeks pregnant preterm came with complaints of fever since 3 days before being treated. In this patient, the results of the anamnesis were fever accompanied by

dizziness, nausea and vomiting since 3 days ago. Before the patient was treated, the fever seemed to come and go. Fever accompanied by chills, bitter mouth, body aches all over, fever, sore throat and headache, The next day the fever went down after taking paracetamol but a few hours later it came back. On the third day, the patient complained of fever and chills as before and complained of nausea and vomiting, decreased appetite, felt weak and had aches and pains. The patient also complained of cough and runny nose. The most common symptoms in malaria patients are headache, nausea, muscle aches, vomiting, fever, chills, and sweating, which are the most common symptoms in malaria patients. (Sandy *et al.*, 2019). The characteristic features of malaria are periodic fever, anemia and splenomegaly. There are often prodromal symptoms such as malaise, headache, bone/muscle pain, anorexia and mild diarrhea (Rehana and Mutiara, 2017).

Laboratory results showed hemoglobin (Hb): Hb: 12.4 g/dl, leukocytes: 5,700/ μ l, erythrocytes: 3,800,000/ μ l, platelets: 76,000/ul and hematocrit: 29%. Serum bilirubin: Serum Glutamic Oxaloacetic Transaminase (SGOT) 47 u/L, Serum Glutamic Piruvic Transaminase (SGPT) 37 I/L and peripheral blood smear: Plasmodium falcifarum +4 Diagnosis of malaria in pregnancy can also be established based on microscopic examination of blood samples (Sandy *et al.*, 2019)

Malaria during pregnancy has consequences for morbidity, mortality, abortion, premature birth, low birth weight (referring to intra-uterine growth inhibition and prematurity) and transplacental transmission of the malaria parasite. Malaria infection in pregnant women can not only increase the risk of anemia which can increase the risk of bleeding during childbirth, but also increase the risk of infant mortality, prematurity and low birth weight. The risk of getting malaria increases, especially in the second trimester of pregnancy, pregnant women have a three times greater risk of suffering from other serious diseases when infected with malaria than women who are not pregnant. (Anggraeni *et al.*, 2017).

This patient was also diagnosed as positive for COVID-19, although without symptoms, it was seen from the laboratory results, namely a rapid test for the SARS CoV-2igG Reactive antibody, a positive swab examination. Patients infected with COVID-19 can show symptoms or no symptoms. Usually mild symptoms in patients infected with COVID-19 are patients with acute uncomplicated upper respiratory tract infections, which can be accompanied by fever, fatigue, cough (with or without sputum), anorexia, malaise, sore throat, nasal congestion, or headache. In this condition, the patient does not need oxygen supplementation (Susilo *et al.*, 2020).

Pregnant women are susceptible to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can increase the risk for both pregnant women and their unborn babies. Pregnant women who experience COVID-19 are feared that there will be intrauterine transmission from mother to fetus. In addition, they can also have symptoms of pneumonia due to the Covid-19 virus, which is one of the main causes of death in pregnant women worldwide. In the fetus, fetal complications can occur in mothers infected with Covid-19, namely miscarriage (2%), Intra Uterine Growth Restriction (IUGR; 10%), and premature birth (39%). Fever with an average temperature of 38.1-39.0oC (Ramadhani *et al.*, 2020).

Based on the diagnosis, G3P2A0 is 14 weeks pregnant single live intrauterine with tropical malaria and covid-19. Then the management of these patients was carried out, namely hospitalization of the mother with infusion of RL drips NB 20 tts/min, injection of ranitidine 3x1, ondancetron 2x1, artesunate 0;12;24;36, goldrion oral medication 1x1, comvit C 1x1, sunbathing education and exercise light every morning at 09.00 for 15-30 minutes, giving green bean porridge every morning and evening, giving 1 can of bear milk every afternoon, observing

mother's vital signs, reducing contact/bites of Anopheles mosquitoes by using mosquito nets and mosquito repellent, recommend eating and drinking healthy enough, recommend adequate rest.

In principle, malaria treatment in pregnant women is the same as treatment for other adults. Primaquine, tetracycline or doxycycline are not given to pregnant women. Treatment of falciparum malaria and vivax malaria in pregnant women in the I-III trimester (0-9 months) at the Puskesmas/Clinic Care or Hospital with intravenous Artesunate is the main choice. If not available, quinine drip can be given. Artesunate packaging and administration Parenteral artesunate is available in vials containing 60 mg dry powder of artesunic acid and solvent in ampoules containing 5% sodium bicarbonate. The two are mixed to make 1 ml of sodium artesunate solution. Then it was diluted with 5% Dextrose or 5 ml NaCL 0.9% to obtain a concentration of 60 mg/6ml (10mg/ml). The drug is given as a slow bolus. Artesunate is given at a dose of 2.4 mg/kg body weight intravenously 3 times in 0, 12, 24 hours on the first day. Subsequently, 2.4 mg/kg body weight was given intravenously every 24 hours a day until the patient was able to take oral medication (Kemenkes, 2017).

In the prevention of malaria, namely reducing the contact/bite of the Anopheles mosquito by using mosquito nets and mosquito repellent, encourage adequate eating and drinking, and encourage adequate rest. Prevention efforts for malaria include reducing the habit of being out of the house until late at night, carrying out environmental sanitation activities, using mosquito nets, using household insecticides, using repellents, using closed clothes, installing wire nets on doors and windows. (Alami and Adriyani, 2016).

Pharmacological interventions commonly given related to COVID-19 in pregnancy include antiviral therapy (remdesivir, lopinavir/ritonavir), antibiotics, corticosteroids (dexamethasone, betamethasone), thromboembolic (low molecular weight heparin/LMWH), and immunomodulators (convalescent plasma, tocilizumab, immunoglobulin). G, etc.) (Fatmawati, 2021). Guidelines for handling COVID-19 based on the severity of the disease, namely if asymptomatic, mild symptoms, aged <70 years without risk factors, namely clinical observation and supportive therapy. Mild symptoms, aged >70 years with risk factors and symptoms of fever, cough, shortness of breath, and x-rays showing pneumonia: LPV/r 200 mg/50 mg, 2 x 2 tablets per day; or Darunavir/ritonavir (DRV/r) 800 mg/100 mg, 1 x 1 tablet per day; or Darunavir/cobicistat 800 mg/150 mg, 1 x 1 tablet per day; AND chloroquine phosphate 2 x 500 mg/day or hydroxychloroquine (HCQ) 2 x 200 mg/day. Therapy is given for 5-20 days based on clinical changes (Susilo *et al.*, 2020). The handling of COVID-19 in these patients is clinical observation and supportive therapy because the patient does not show symptoms of Covid-19. In addition, continue to apply the Covid health protocol in providing treatment.

Besides being given drug therapy, they were also given education on sunbathing and light exercise every morning at 09.00 for 15-30 minutes, giving green bean porridge every morning and evening, giving 1 can of bear milk every afternoon, observing the mother's vital signs. According to Gonzalez et al, in Maulana in 2021, by basking in the morning sun, especially before 10:00 am, Vitamin D is obtained which can increase calcium and phosphorus levels in the body, maintain muscle and nerve function, and increase endurance or the body's immune system in controlling the body's immune system. fight infection. According to Alsary 2020 research, sunlight can maintain the health condition of Covid-19 patients so that they have a chance to recover from this disease (Maulana *et al.*, 2021). In addition to sunbathing in the morning to increase immunity by doing clean life such as getting used to washing hands.

Prevention efforts against COVID-19 are to break the chain of transmission by isolation, early detection, and basic protection such as maintaining hygiene, washing hands, disinfecting (Susilo *et al.*, 2020).

Treatment of malaria in adult COVID-19 patients including pregnant women is as follows, if symptoms of mild Covid-19 with malaria infection are given Chloroquine/hydroxychloroquine, azithromycin, piperazine (one of the components of the DHP drug) and primaquine can prolong the QTc interval, therefore it is necessary to do this ECG examination to see the QTc interval before being given for treatment. If the results of the ECG examination obtained $QTc > 500$ ms, then the administration of DHP is not allowed to be replaced with artesunate injection for 7 days. If the results of the ECG examination with $QTc > 500$ ms, then oral DHP is given for malaria treatment. If the patient with COVID-19 does not undergo an EKG examination and receives chloroquine/hydroxychloroquine and azithromycin, for the treatment of malaria, oral DHP is not given, but artesunate is injected for 7 days. Primaquine administration was postponed until the patient's condition improved and Covid-19 treatment was completed. If malaria complications occur, the patient is referred to the hospital. If the symptoms of COVID-19 are moderate and the symptoms are severe with malaria infection, then the malaria drug is given using artesunate injection for 7 days. And for malaria sufferers with COVID-19, primaquine administration is postponed until the patient's condition improves and Covid-19 treatment is completed (Ditjen P2P, 2020). It is important for pregnant women to take medication as one of the steps to minimize the worsening of the condition that arises. The drug chloroquine is the right option for the treatment of coronavirus infections in pregnant women. Chloroquine therapy does not cause serious side effects in pregnant women and newborns (Hidayah, Indriani and Rahmatika, 2021).

Conclusion and Suggestion

Malaria in pregnancy accompanied by COVID-19 is a serious problem considering its effects on the mother and fetus, if not treated quickly and appropriately, malaria can increase maternal and neonatal mortality. Malaria causes complications such as anemia, organomegaly, cerebral malaria, pulmonary edema and sepsis. In addition, it can cause problems for the fetus such as low birth weight, abortion, IUFD and IUGR. Covid-19 in pregnant women can cause symptoms of pneumonia in pregnant women and can cause fetal complications, namely miscarriage, IUGR, and premature birth. Chloroquine is still the drug of choice for the treatment of malaria accompanied by symptoms of COVID-19 in pregnancy. Malaria prevention is to reduce contact/bite by Anopheles mosquitoes by using mosquito nets and mosquito repellent, encourage adequate eating and drinking, and encourage adequate rest. Prevention efforts against COVID-19 are to break the chain of transmission by isolation, early detection, and basic protection such as maintaining hygiene, washing hands, disinfecting.

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