

Malaria in Neonates: Case series

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INTRODUCTION

Malaria is a parasitic infection caused by different plasmodium species. Plasmodium falciparum is the most prevalent species in Rwanda, but the cause of its transmission in neonates is unknown. Malaria is a major problem worldwide, especially in Sub-Saharan Africa, with significant health risks for infants and pregnant women [1], with 50 million women living in malaria-endemic areas becoming pregnant every year. Prevalence of maternal malaria is estimated at 28% with an incidence of congenital malaria of 0.3 to 10% [2][3]. Despite interventions such as distribution of mosquito nets and free rapid diagnostic tests for all age groups, cases are still being seen in hyper-endemic areas [4].

Newborns are known to rarely contract congenital malaria due to protection from passive maternal antibodies, high levels of fetal hemoglobin (which is resistant to *P. falciparum*), and the placental barrier [5]. However, its occurrence in neonates is not unusual [2]. It can be acquired from the mother prenatally or perinatally following a breach in the placental barrier, from mosquito bites, or by blood transfusions [6].

In this paper we describe clinical features of three cases of neonatal malaria treated successfully in the neonatal unit of the University Teaching Hospital of Butare (CHUB) from July to September 2014.

CASE PRESENTATIONS

Neonate 1

A preterm twin with estimated gestational age of 29 weeks, birth weight 1.098 kg, who received an empiric course of antibiotics due to maternal fever two days prior to delivery. The mother tested negative for malaria at delivery. On DOL 15, the infant presented with mild jaundice and respiratory distress but no fever was found. There was no history of blood transfusion. Blood smear for malaria was positive with 640/μl of *P. falciparum* parasites. The neonate was treated with intravenous Artesunate 2.4mg/kg/dose for 7 days and recovered fully.

Neonate 2

A term baby born to a mother with a history of a treated vaginal infection (not specified but without fever) and no other risk factors, who presented from home on DOL 8 with only fever and unremarkable systematic examination. There was no history of blood transfusion, mosquito-net was reported as being used and the mother was never tested for malaria. Blood smear for malaria was positive with 120/μl trophozoites of *P. falciparum*. The baby responded well to the treatment of intravenous Artesunate 2.4mg/kg/day for 7 days.

Neonate 3

This was a preterm infant of 31 weeks gestational age with Extremely Low Birth Weight (ELBW) of 700g and small for gestational age who had a prior history of receiving antibiotics for neonatal sepsis, as well as several blood transfusions due to recurrent anemia and thrombocytopenia. On day-of-life (DOL) 41 while he was not on any antibiotherapy and previous days of being clinically stable, he developed fever and was found to have grade II splenomegaly. Septic work up was performed and found to be negative for any bacterial sepsis; blood smear for malaria was negative once, no rapid diagnostic test for malaria was performed. This couldn't help in terms of final diagnosis as it requires both of RDT and series of blood smears done every 6 to 12 hours for 72 hours to exclude malaria in this neonate. The mother was tested and found to be negative for malaria on peripheral smear at delivery but placental testing was not done. This would have been helpful as it is known that blood smear can be negative while placenta histopathology is positive in infected mothers [7]. Empirical antimalarial agents were therefore given. This decision based on signs and symptoms of the patient, the fact that bacterial sepsis was excluded and on malaria endemicity in this location.

The only evidence of malarial infection was the improvement clinically after initiation of Artesunate 2.4mg/kg/dose without any given antibacterial agents. The neonate received a 7-day course. The full blood count (FBC) was in normal range after completion of antimalarial based treatment.

Noted that for the all above three cases, none received oral Coartem which is an ACT (Artemisinin-based Combined Therapy) to complete the Artesunate treatment course for resistance protection.

DISCUSSION

In the three described cases, the source of the malaria infection was difficult to determine as the mothers who were tested were negative for malaria on blood smear. None of the mothers had placenta histopathology testing performed which can reveal placental malaria in absence of peripheral parasitemia [8][7]. Placental histopathology testing is highly recommended in pregnant mother presenting with an acute fever or from hyper-endemic areas as it has been found that placental malaria is detectable in the absence of peripheral parasitemia [7].

In terms of diagnosis, the 2015 WHO malaria guidelines recommend either microscopy (to quantify level of parasitemia and for speciation), or rapid diagnostic tests (RDT). The RDT is simple to perform and to interpret without requiring electricity, special equipment, or specialized lab technicians. Both blood smear and RDT tests should be done for all patients suspected to have malaria as initial blood smear can be negative [9]. Malaria is excluded when the series of blood films, done every 6 to 12 hours for 72 hours, and RDT are both negative.

One neonate received blood transfusions; in this case the blood for transfusion was not tested for malaria. It is known that parasites can be detected in blood donors in malaria-endemic areas [10][11]. The World Health Organization (WHO) normally recommends screening blood donors for malaria, but methods used in malaria-endemic countries are not sensitive enough to be used by blood banks which lead to not systematically testing blood for malaria across African countries [6].

History of mosquito bites was unknown for the cases who were inpatients. However incubators in the unit are not contained in mosquito nets and do have entry points where mosquitoes can enter.

Treatment options for neonatal malaria include either Quinine or Artesunate intravenously, though Artesunate has been found to have fewer side effects and faster clearance of parasitemia [12]. The treatment chosen for these cases was based on the Rwanda National Protocol, which is intravenous Artesunate 2.4mg/kg/dose [13].

However, the 2015 WHO malaria guidelines recommend a higher dose of 3mg/kg/dose for children weighing less than 20kg [9]. All the described babies responded well to 7 days courses of Artesunate 2.4mg/kg/dose.

Despite the initial known protection against congenital malaria such as: Passive maternal antibody, High levels of fetal hemoglobin (resistant to *P. falciparum*) and Placental barrier [3]; published studies report that babies born from infected mothers during pregnancy are at high risk of congenital malaria [14], and most are due to materno-foetal transfusion during pregnancy or increased friability of placenta related to any maternal fever and at delivery direct penetration through the chorionic villi or through premature separation of the placenta [8][7]. But also infected mosquito bites and infected blood used for transfusion have been found to transmit malaria [10].

Infection can be asymptomatic, but can also present as: fever, poor feeding, vomiting, restlessness, drowsiness, apnea and respiratory distress, diarrhea, anemia, jaundice, cyanosis, hepatosplenomegaly and thrombocytopenia. These symptoms are often not specific and difficult to differentiate from neonatal sepsis, which creates a large challenge for care providers [15]. Diagnosis requires a high index of suspicion based on the history, physical exam, signs and residence in malaria endemic areas.

The exact prevalence of Neonatal Malaria is not known, though it may not be as rare as it was previously thought. The infection can be asymptomatic or with no specific symptoms. Providers should include neonatal malaria in the differential diagnosis of neonatal sepsis in hyper-endemic areas, placental histopathology testing at delivery is conclusive in pregnant mothers with negative peripheral smears, and blood should be tested before being used for transfusion. More studies are needed to ascertain the prevalence of neonatal malaria, and strategies for prevention of malaria in neonates in Rwanda.

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