INNOVARE JOURNAL OF MEDICAL SCIENCES

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 8, Issue 1, 2020

ISSN - 2321-4406

Review Article

SEVERE FALCIPARUM MALARIA – PATHOPHYSIOLOGY, CLINICAL MANIFESTATIONS/ COMPLICATIONS, AND MANAGEMENT CHALLENGES IN NIGERIA

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Received: 12 October 2019, Revised and Accepted: 01 January 2020

ABSTRACT

Severe falciparum malaria remains a common cause of death among the under-5 Nigerian children despite Nigerians having partial immunity arising from their residence in a hyperendemic region for malaria transmission. It is, also, being reported in clinical practice among adolescent and adult Nigerians. The objective of this narrative review is to highlight the pathophysiology of severe malaria and relate that to its clinical manifestations/ complications and to highlight the challenges of severe malaria management in Nigeria. With a good understanding of the pathophysiology of severe malaria as it relates to its clinical manifestations, one expects a favorable outcome from the current treatment protocol.

Keywords: Severe falciparum malaria, Pathophysiology and clinical manifestations of severe malaria, Nigeria, Management challenges of severe malaria.

INTRODUCTION

Malaria in man is an infection caused by any of the following malarial parasites of the plasmodium species – *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium vivax,* and *Plasmodium ovale* – which are spread to people through the bites of infected female *Anopheles* mosquitoes. *P. falciparum* is the most common of the parasites in most of the sub-Saharan Africa where it accounts for almost all the mortalities [1]. The global malaria burden is disproportionately borne by sub-Saharan Africa such that in 2015, the region had 90% of the global malaria cases and 92% of the malarial deaths [2].

Malaria can be severe or uncomplicated. According to the World Health Organization (WHO) [3], the criteria for severe malaria include that the malaria must be attributable to *P. falciparum*, the patient with the malaria is unable to swallow tablets, has evidence of, at least, one vital organ dysfunction or has a high malaria parasite count in his/her blood, and is at increased risk of dying. Additional WHO criteria [3] for the diagnosis of severe malaria from 2000 include impaired consciousness, prostration or general body weakness, hyperparasitemia (>5% parasitized erythrocytes), hyperpyrexia (core body temperature >40°C), and hyperbilirubinemia (total bilirubin >2.5 mg/dl). Severe malaria is a potentially fatal but treatable disease.

As regard to the risk of severe malaria [3], it has been shown that in parts of the world where malaria is endemic, transmission of falciparum malaria is stable such that severe malaria is mainly a disease of children from the first few months of life to the age of 5 years. It is less common in older children and adults in those regions because they have partial immunity. In their study in Jos [4], Nigeria, 71% of the children admitted for severe malaria were aged 5 years and below. Mortality in that study was associated with hypoglycemia, severe anemia, shock, and repeated prolonged seizures. Similarly, in their study in Enugu [5], Nigeria, 66.7% of the children treated for severe malaria were under the age of 5 years with 8.8% of them being 6 months and below. In areas of the world with lower endemicity, severe malaria occurs in both children and adults. Travelers and migrant workers who do not have malaria immunity are at increased risk for severe malaria.

In some other studies, risk factors for severe malaria and death noted included age >65 years, female sex (especially when associated with pregnancy), non-immune status, coexisting medical conditions, no antimalarial prophylaxis, delay in treatment, and severity of the illness at admission (coma, acute kidney injury [AKI], shock, pulmonary edema, or coagulation disorders) [6-8].

Severe malaria is a major cause of death among children and often the major reason for children hospital admissions in sub-Saharan Africa. In Nigeria, malaria is one of the most important health problems [9], accounting for 25% of infant mortality, 30% of under-5 mortality, and 11% of maternal mortality. Severe malaria is a medical emergency that is rapidly associated with complications and death if prompt and appropriate treatment is not given.

PATHOPHYSIOLOGY OF SEVERE MALARIA

P. falciparum [10] attacks red blood cells (RBCs) at all stages of development unlike *P. malaria* which preferentially attacks old RBCs or *P. ovale* and *P. vivax* which prefer to attack reticulocytes (developing RBCs). In severe malaria, there is heavy parasitemia, in which the proportion of parasitized RBCs increases to more than 3% of the total RBCs.

The heavy load of *P. falciparum* in the peripheral blood [10] consumes and degrades the hemoglobin in the RBCs, the RBCs become irregular in shape, less deformable, adhere to venule and capillary endothelium to form cytoadherence, adhere to uninfected RBCs to form rosettes, and to other parasitized RBCs to form agglutination. Consumption and degradation of the RBCs hemoglobin, hemolysis of parasitized RBCs, blackwater fever, hypersplenism, and nutrients deficiency all lead to the severe anemia in complicated malaria. With massive hemolysis, lots of hemoglobin are liberated into the peripheral blood, are filtered in the renal glomeruli to cause hemoglobinuria.

The process of cytoadherence, rosetting, and agglutination is central to severe malaria pathogenesis [10]. Reduced deformability of the RBCs (parasitized) compromises their passage through the microcirculation resulting in reduced RBCs survival or lifespan, causes ischemic changes in the affected organs/tissues such that ensuing peripheral vasodilatation which occurs in an attempt to correct ischemia leads to systemic hypotension (shock). Shock in severe malaria could, also, be from sepsis which is a common associated feature of severe malaria.

With shock, anaerobic glycolysis occurs at the cellular level resulting to increased production of lactic acid, thus, leading to increased anion gap