An Overview on Malaria and Its Complications in Patients

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ABSTRACT: ***Malaria is a life threatening emergency because it can quickly develop to complications and death if not treated promptly and effectively. Plasmodium falciparum is nearly often the cause of severe malaria. Despite advances in intensive care and antimalarial therapy, the prevalence of imported malaria is rising, and the case fatality rate remains high. Clinical worsening occurs 3–7 days following the start of the fever. The neurological, pulmonary, renal, and/or hematopoietic systems are all involved in complications. Systemic problems such as metabolic acidosis or hypoglycemia are frequent. In the first treatment of severe falciparum malaria, intravenous quinine as well as quinidine are the most often used medicines, but artemisinin derivatives are now indicated for quinine-resistant patients. Oral therapy should begin as soon as the patient is clinically strong and able to swallow. To avoid the establishment of acute respiratory distress syndrome, the intravascular volume should be kept at the lowest amount necessary for good systemic perfusion. Renal replacement treatment should be started as soon as possible. For the treatment of individuals with severe malaria and high parasitemia, an exchange blood transfusion has been proposed. Malaria should be considered in any feverish patient diagnosed of travel to a malaria-endemic region for early detection.***

KEYWORDS: Clinical, Malaria, Medicine, Renal, Plasmodium.

1. INTRODUCTION

Malaria continues to be a catastrophic worldwide health issue. Malaria affects an estimated 300–500 million people worldwide each year, causing 1.5–2.7 million fatalities. The incidence of import cases of malaria in affluent nations has increased as a result of increased worldwide travel to and immigration of individuals from malaria-endemic regions. Each year, malaria is anticipated to infect between 10,000 and 30,000 visitors from developed nations. Furthermore, drug-resistant Plasmodium falciparum malaria keeps spreading and now affects nearly every country on the planet. A growing number of visitors are coming into contact with drug-resistant plasmodia. Malaria is caused by Plasmodium genus obligate intraerythrocytic protozoa. Humans may be infected with one (or more) of the four parasitic species: Plasmodium falciparum, Plasmodium vivax, Plasmodium oval, and Plasmodium malaria. Plasmodia infections are spread mainly via the bites of infected female Anopheles mosquito, although infections may also be spread through contaminated blood products (transfusion malaria) and congenital transmission [1].

Most instances of malaria in developed nations occur in tourists, immigrants, or military personnel coming from malaria-endemic regions (imported malaria). Local transmission through mosquitoes happens on rare occasions (indigenous malaria). Malaria must be considered in the differential diagnosis of individuals with unexplained fever as well as clinical deterioration who have just returned from an endemic region. A thorough travel history should always be taken into account while evaluating such situations. Malaria morbidity and death rise as a result of delays in diagnosing and treating the disease. Severe malaria's clinical symptoms, laboratory results, diagnosis, and therapy are discussed in this article.

Malaria's characteristics Morphology and life cycle When a blood meal is taken by an infected anopheline mosquito, sporozoites are injected into the circulation. Sporozoites enter hepatocytes within an hour and proceed to divide into exoerythrocytic merozoites (tissue schizogony). P. vivax and P. ovale generate hypnozoites, which are latent forms that stay inactive in the liver until a later period; P. falciparum does

not generate hypnozoites. Merozoites attack erythrocytes and grow into early trophozoites, which are ring-shaped, vacuolated, but uninucleate after they leave the liver. The trophozoites, which are made up of numerous daughter merozoites, are termed schizonts after the parasite starts to split (blood schizogony). The merozoites eventually lyse the infected erythrocytes, which then enter other erythrocytes, resuming the schizogony cycle. Each cycle in P. falciparum lasts about 48 hours. Each cycle, the infection is increased 20-fold in nonimmune people. Some merozoites grow into gametocytes, the sexual stage of malaria, which produce no symptoms but are infective to mosquitos after many cycles [2], [3].

Periods of pre-patent and incubation The median pre-patent duration (time from sporozoite inoculation to detectable parasitemia) in nonimmune people with P. falciparum infection is 10 days (range 5–10 days), while the median incubation period (time from sporozoite inoculation to onset of symptoms) is 11 days (range 6–14 days). The degree of immunity gained from past exposures, preventive prophylaxis, or prior partial treatment, which may reduce but not prevent the illness, may all substantially lengthen the incubation time. The majority of nonimmune visitors acquire symptoms of falciparum malaria within a month of leaving a malaria-endemic region (median 10 days); nevertheless, falciparum malaria has been reported to show up to 4 years later. The incubation time for nonfalciparum malaria is typically prolonged (median 15–16 days), and owing to the presence of hypnozoites in the liver, both P. vivax and P. ovale malaria may recur months or years after infection. P. vivax has been known to incubate for up to 30 years [4].

Malaria symptoms or signs Malaria's clinical symptoms are mainly caused by schizont rupture and erythrocyte damage. Malaria may manifest itself in a variety of ways, including a progressive or a fulminant course with vague symptoms. Malaria frequently has symptoms that are similar to those of common viral illnesses, which may cause a delay in diagnosis. Fever (>92 percent of cases), chills (79 percent), headaches (70 percent), and diaphoresis (70 percent) affect the majority of patients (64 percent). Dizziness, lethargy, myalgia, stomach discomfort, nausea, vomiting, moderate diarrhea, and a dry cough are also frequent symptoms. Fever, tachycardia, jaundice, hepatomegaly, pallor, orthostatic hypotension, as well as splenomegaly are some of the physical symptoms. Even without a fever, a clinical examination in nonimmune people may be totally normal. Malaria diagnosis is a term that refers to the process of determining whether or not Microscopy as we know it [5].

The usual technique for diagnosing malaria is light microscopy of thick and thin stained blood smears. For Plasmodium parasite screening, thick smears are 20–40 times more sensitive than thin smears, with a detection limit of 10–50 trophozoites/l. Thin smears may be used to identify malaria species (including mixed infections), quantify parasitemia, and check for schizonts, gametocytes, and malarial pigment in neutrophils and monocytes, among other things. The diagnosis accuracy is dependent on the quality of the blood smear and the laboratory personnel's expertise. At least 200 oil immersion visual fields at a magnification of 1000 should be evaluated on both thick and thin smears before reporting a negative result, with a sensitivity of 90%.

The number of parasites per microliter of blood or the proportion of parasitized erythrocytes are two ways to measure parasitemia. In no falciparum malaria, parasitemia seldom surpasses 2%, while in falciparum malaria, parasitemia may be much greater (>50%). Hyper parasitemia (>5% parasitemia or >250 000 parasites/l) is usually linked with severe illness in nonimmune people. In the case of falciparum malaria, parasitized erythrocytes may get trapped in tissue capillaries, resulting in a deceptively low parasite count in the peripheral blood (‘visible' parasitemia). In such cases, the developmental stages of the parasite observed on a blood smear may be more useful than parasite count alone in determining illness severity. More developed parasite forms (> 20% of parasites as late trophozoites and schizonts) and more than 5%

of neutrophils carrying malarial pigment suggest advanced illness and a poor prognosis. A single negative blood smear renders the diagnosis of malaria extremely improbable (particularly the severe type); nevertheless, if malaria is still suspected, smears should be repeated every 6–12 hours for 48 hours.

1.1.Methods of alternative diagnosis:

Although the 'gold standard' for diagnosing malaria is examination of thick and thin blood smears, significant advances in diagnostic testing have been made, including fluorescence microscopy of parasite nuclei stained with acridine orange, rapid dipstick immunoassays, and polymerase chain reaction assays. Some of these techniques have sensitivity and specificity that are comparable to or even better than thin and thick smears. Antigens targeting the histidine-rich protein-2 of Plasmodium falciparum or a parasite-specific lactate dehydrogenase are detected using rapid dipstick immunoassays. Despite the fact that dipstick testing may speed up diagnosis, microscopic inspection is still required in patients with suspected malaria since dipstick tests can be negative in individuals with high parasitemia, and their sensitivity below 100 parasites/l is poor. Tests for species-specific Plasmodium genomes based on polymerase chain reaction are more sensitive and specific than previous tests, identifying as little as 10 parasites/l blood. The presence of antibodies has no bearing on the diagnosis of acute malaria. It is mostly utilized in epidemiological research[6].

1.2.Malaria-related complications in patients:

Malaria patients should be treated in an intensive care unit (ICU). Although there have been rare instances of nonimmune individuals dying within 24 hours of acquiring symptoms, clinical progression to severe malaria typically occurs 3–7 days following the start of symptoms. Due to delayed cytokine release, severe malaria may emerge even after an initial therapeutic response and full parasitemia clearance

1.2.1. Hypoglycemia:

In individuals with severe malaria, hypoglycemia is a frequent symptom. Because all of the symptoms of hypoglycemia (anxiety, dyspnea, tachycardia, sweating, coma, aberrant posture, and widespread convulsions) are also symptoms of severe malaria, it may be missed. Hyperinsulinemia produced by quinine or quinidine may cause hypoglycemia, although it can also occur in individuals with normal insulin levels [7].

1.2.2. Shock and hypotension:

The majority of shock patients have a low peripheral vascular resistance and a high cardiac output. Despite extensive sequestration of parasitized erythrocytes in the microvasculature of the myocardium, cardiac pump function seems to be surprisingly well maintained. Autonomic dysfunction may be the cause of postural hypotension. Severe hypotension may strike quickly, typically as a result of pulmonary edema, metabolic acidosis, sepsis, and/or severe bleeding from the spleen or gastrointestinal system.

1.2.3. Abnormalities of the blood:

Children in highly endemic regions are more likely to develop severe anemia as a result of recurrent or chronic Plasmodium infections. Thrombocytopenia is widespread, although it is seldom linked to bleeding. Only around 10% of individuals with severe malaria develop disseminated intravascular coagulation.

Treatment for severe malaria with antimalarials Regardless of the severity of the illness at the time of presentation, nonimmune individuals with P. falciparum malaria should be treated as a medical emergency

and admitted to the hospital. All patients with severe malaria, as well as those who are unable to take medicines orally, should undergo parenteral therapy and be sent to the ICU very away. The oral route of administration is problematic in these individuals due to gastrointestinal sensitivity and irregular intestinal absorption. To avoid prescription mistakes, double-check if the prescribed dosage is for a base or a salt. Patients with severe malaria, particularly those with breakthrough malaria and those who have previously taken antimalarial medicine, should always get the entire treatment dosage [8].

1.3.Oral therapy:

Patients with severe falciparum malaria who can take tablets and demonstrate substantial clinical improvement (after at least 24 hours of parenteral treatment) should be transferred to oral medicine. The susceptibility pattern of the plasmodia guides the selection of oral antimalarials. Compared to mefloquine or quinine, combined regimens such as artemether–lumefantrin or atovaquone–proguanil have a reduced chance of developing resistance. When oral antimalarials are taken with or after meals, higher blood levels are achieved.

1.4.Management of critical care patients:

The intravascular volume should be kept as low as possible to provide appropriate systemic perfusion. Rather than overhydration, inotropic support should be used early in the treatment of hypotension. Negative fluid balance is necessary to prevent acute lung damage from worsening, but it must be weighed against the danger of triggering acute renal failure. Because of decreased awareness or severe lung damage, the patient may need to be intubated. The clinical result is improved by mechanical ventilation with a reduced tidal volume. To maintain optimum arterial oxygenation, a greater positive end-expiratory pressure may be required. The plateau pressure in respiratory acidosis should be more than 25 cm H2O, and the ventilator rate should be raised. In patients with ARDS, surfactant treatment, inhaled nitric oxide, and corticosteroids had no impact on survival or ventilation duration. To minimize the danger of aspiration, comatose patients should be positioned in a semi recumbent posture. The concentrations of sodium in the blood, carbon dioxide in the blood, blood glucose, and lactate in the blood should all be checked on a regular basis. Anticonvulsants should be used as soon as possible to treat seizures, although their preventive usage is still debated. The effectiveness of hypertonic mannitol in the treatment of cerebral edema has yet to be established.

1.5.Antimicrobial treatment:

Bacterial infections often worsen the course of severe malaria patients. Aspiration pneumonia and sepsis are two common illnesses. The synthesis and release of cytokines such as tumor necrosis factor (TNF) and interleukin-1 by macrophages is stimulated by parasite substances, resulting in fever, chills, and hyperkinetic hemodynamic abnormalities. Severe malaria has clinical and laboratory features that are comparable to sepsis. As a result, a bacterial infection in a malaria patient may go undetected at first. Microbiologic sample of relevant bodily fluids such as blood, sputum, cerebrospinal fluid, and urine on a regular basis may aid in the early diagnosis and treatment of an infection.

1.6.Blood transfusions and red cell exchanges are two different types of blood transfusions:

The amount of parasitemia in malaria patients is linked to death, with substantial mortality when parasitemia reaches 5% despite adequate parenteral antimalarial treatment. Rapidly reducing parasitemia, lowering the risk of intravascular hemolysis, improving blood flow, lowering cytokines, and increasing oxygen-carrying capacity are all benefits of exchange transfusion. Exchange blood transfusion has been proposed in patients with severe malaria, particularly those with hyperparasitemia (> 5%), despite the lack

of adequately powered, randomized, controlled trials. Exchange transfusion is only recommended by certain writers in countries with well-equipped and staffed ICUs and safe blood supplies. The efficacy of this technique has been debated in the literature.

LITERATURE REVIEW

Tizifa et al. studied about Malaria is a worldwide burden contributing to morbidity and death particularly in children under 5 years of age. Despite the progress made towards malaria load reduction, attaining eradication in additional countries remains a major challenge. This article intends to examine the preventive and control methods for malaria, to assess their effectiveness towards decreasing the disease burden as well as to highlight the best practices identified. Recent Findings: Use of long-lasting pesticide nets and indoor residual spraying has produced a decrease in the incidence and prevalence of malaria in Sub-Saharan Africa. Other methods such as larval direction of the company have been proven to decrease mosquito density but need more study. New techniques in development such as home renovation have shown to reduce illness burden but need additional proof on effectiveness. Development of the RTS, S or AS01 malaria vaccine that offers protection in under-five children has given significant advance in attempts of malaria control. Summary: There has been a significant decrease in malaria burden in the last decade; nevertheless, additional effort is needed to address the essential gaps to eradicate malaria [9].

Narayani Prasad et al studied about Malaria continues to be a significant health issue in more than 100 endemic nations situated mainly in tropical or sub-tropical areas throughout the globe. Malaria transmission is a dynamic process that includes numerous interconnected variables, from uncontrolled natural environmental circumstances to man-made disruptions to nature. Almost half of the people at risk of malaria lives in forest regions. Forests are hot beds of malaria transmission since they offer circumstances such as plant cover, rainfall, temperature or humidity levels that are favorable to dispersion as well as survival of malaria vectors. Forests typically lack infrastructure & contain tribes with unique genetic characteristics, socio-cultural beliefs and behaviors that significantly affect malaria transmission dynamics. Here we outline the numerous topographical, entomological, parasitological, human ecological as well as socio-economic variables, which are important and influence malaria transmission in wooded regions. An in-depth knowledge and synthesis of the complex connection of these factors in attaining improved malaria control in different kinds of forest ecosystems is highlighted [10].

DISCUSSION

Malaria continues to be a devastating global health problem. Malaria affects an estimated 300–500 million people globally each year, inflicting 1.5–2.7 million deaths. The prevalence of import cases of malaria in wealthy countries has risen as a consequence of increasing global travel to and immigration of people from malaria-endemic areas. Malaria is a life threatening issue because it may rapidly progress to complications and death if not treated immediately and properly. P. falciparum is almost frequently the cause of severe malaria. Despite improvements in intensive care and antimalarial treatment, the incidence of imported malaria is increasing, and the case fatality rate remains high. Clinical deterioration happens 3–7 days after the onset of the fever. The neurological, pulmonary, renal, or hematopoietic systems are all implicated in complications. Systemic issues such as metabolic acidosis as well as hypoglycemia are common. In the initial treatment of severe falciparum malaria, intravenous quinine as well as quinidine are the most frequently used medications, although artemisinin derivatives are now recommended for quinine-resistant individuals. The major complications of p. falciparum malaria are cerebral malaria, respiratory failure, acute renal failure, severe anemia, and/or bleeding. Any of these issues may develop rapidly and lead to death within hours or days. Light microscopy of blood smears is the conventional

method for identifying malaria, however new and promising non microscopic diagnostic techniques are under research. All individuals with severe malaria should receive parenteral treatment immediately.

CONCLUSION

Malaria should indeed be considered in the differential diagnosis of any febrile illness in an individual with a history of travels to a malaria-endemic region. Delays in identification and proper treatment of malaria increase morbidity and death. The main consequences of p. falciparum malaria include cerebral malaria, respiratory failure, acute renal failure, severe anemia, and/or hemorrhage. Any of these problems may develop quickly and lead to death within hours or days. Light microscopy of blood smears is the traditional technique for detecting malaria, but novel and promising non microscopic diagnostic approaches are under development. All individuals with severe malaria should get parenteral therapy promptly. Currently, intravenous quinine as well as quinidine are the most frequently utilized medicines, while artemisinin derivatives in general are indicated for diagnosis of quinine-resistant P. falciparum infection. Several Internet sources with further and updated information about malaria are mentioned in the Appendix.

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