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Linking Malaria and Hypertension: Unveiling the Interconnected Pathophysiological Nexus

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ABSTRACT

Malaria, a devastating infectious disease caused by Plasmodium parasites, has long been recognized for its direct impact on global health. Recent studies have unveiled a potential connection between malaria infection and the development of hypertension, a prevalent cardiovascular disorder worldwide. Understanding the underlying pathophysiological mechanisms linking these seemingly disparate conditions is crucial for comprehensive disease management and prevention. The pathogenesis of malaria involves complex interactions between the parasite and the host immune system, resulting in systemic inflammation, endothelial dysfunction, and organ damage. Chronic exposure to Plasmodium infection induces alterations in vascular function, hemodynamics, and immune responses, potentially contributing to the development of hypertension. Several proposed mechanisms underscore the link between malaria and hypertension, including chronic inflammation, oxidative stress, endothelial dysfunction, and dysregulation of the renin-angiotensin-aldosterone system (RAAS). These mechanisms intertwine to disturb vascular homeostasis, leading to increased peripheral resistance and elevated blood pressure. Furthermore, the long-term consequences of repeated malaria episodes, especially in endemic regions, may potentiate vascular remodeling and contribute to the onset or exacerbation of hypertension in affected individuals. Genetic predispositions and environmental factors also play pivotal roles in modulating susceptibility to both malaria and hypertension. Recognition of this intricate association between malaria and hypertension prompts the necessity for integrated healthcare approaches encompassing effective malaria control strategies, early detection, and management of hypertension in endemic regions. Targeted interventions addressing common pathways, such as inflammation and endothelial dysfunction, may offer potential therapeutic avenues.

Keywords: Malaria, Hypertension, Pathophysiology, Inflammation, Endothelial Dysfunction, Plasmodium Parasites, Cardiovascular Disorders, Immune Response, Vascular Remodeling, Global Health.

INTRODUCTION

Hypertension is a medical condition where the pressure in blood vessels is too high (140/90 mmHg or higher). It is common but can be serious if not treated [1-4]. It is one of the most important risk factors for ischemic heart disease, stroke, other cardiovascular diseases, chronic kidney disease and dementia [5-8]. Estimates suggest that 31.1% of adults (1.39 billion) worldwide had hypertension in 2010. The prevalence of hypertension among adults was higher in low and middle-income countries (LMICs) (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people) [9-12]. Hypertension is also referred to as the "silent killer" as person with hypertension may not notice or

present any symptom [13-16]. Without detection, hypertension can damage the heart, blood vessels, and other organs, such as the kidneys. In rare and severe cases, hypertension can cause: sweating, anxiety, sleeping problems, blushing, headache, dizziness and heart palpitation [17-20]. Several studies have demonstrated links between infectious diseases and cardiovascular conditions. Malaria and hypertension are widespread in many low- and middle-income countries, but the possible link between them has not been opined [21]. Malaria is a severe disease caused by parasites of the genus Plasmodium, which is transmitted to humans by a bite of an infected female mosquito of the species Anophel in search for blood meal [22-27]. It remains a significant global health concern. In 2020 an estimated 241 million cases of malaria occurred worldwide and 627,000 people died, mostly children in sub-Saharan Africa [28-32]. Nineteen countries in sub-Saharan Africa and India carried almost 85% of the global malaria burden. Six countries accounted for more than half of all malaria cases worldwide: Nigeria (25%), the Democratic Republic of the Congo (12%), Uganda (5%), and Côte d'Ivoire, Mozambique and Niger [33-38]. From the statistics stated, Nigeria having the highest burden. The risk of transmission exists throughout the country, all year round. However, the incidence of malaria infection is highest in the northern and north-eastern parts of the country [39-44]. More commonly, the patient presents with a combination of the following symptoms ranging from fever, chills, sweats, headaches, nausea, vomiting, body aches, general malaise [45-49].

The purpose of this seminar is to bring enlightenment on malaria infection, hypertension, their epidemiology, their pathophysiology, signs, symptoms, the lifecycle of malaria parasite, treatments, prevention and the epidemiological link between link malaria and hypertension.

Epidemiology of malaria

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes [20]. The plasmodium species that naturally infect humans and cause malaria in large areas of the world are limited to five; P. falciparum, P. vivax, P. malariae, P. ovale and P. knowlesi [51-56] of which Plasmodium vivax and P. falciparum are the most important human malaria species. P. falciparum is considered the most virulent and widespread species in sub-Saharan Africa [57-65]. Plasmodium falciparum malaria still remains a major global public health challenge with over 220 million new cases and well over 400,000 deaths annually. Most of the deaths occur in sub-Saharan Africa which bears 90 % of the malaria cases [59 Children under the age 5 years and pregnant women bear the greatest risk of malaria mortality [66-75].

Epidemiology of hypertension

Hypertension is a medical condition where the pressure in blood vessels is too high (140/90 mmHg or higher) [61]. It is also referred to as a medical condition where the force of blood pushing against the artery walls is consistently too high. This damages your arteries over time and can lead to serious complications like heart attack and stroke [62]. It is a global health issue. Estimates suggest that 31.1% of adults (1.39 billion) worldwide had hypertension in 2010. The prevalence of hypertension among adults was higher in LMICs (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people) [9] In Africa, the cumulative estimated prevalence of hypertension is 30.8% [63]. A review estimated that prevalence of hypertension in Nigeria to be 31.2% (men 29.5%, women 31.1%) [76-86].The risk factors of hypertension are divided into two modifiable and non-modifiable risk factors.

- The modifiable risk factors include diet, physical activity, alcohol consumption and tobacco smoking, and obesity or overweight.
- The non-modifiable risk factors include family history of hypertension, age >65 years, and the presence of other comorbidities, including diabetes and chronic kidney diseases [65-75].

Epidemiology link between malaria and hypertension

Malaria is responsible for more deaths worldwide when compared with any other parasitic diseases [66-80]. Children under the age 5 years and pregnant women bear the greatest risk of malaria mortality. A marked correlation between the incidence of malaria and hypertension has been reported for several sub-Saharan, low- and middle-income country populations. These correlations often associate a higher mean blood pressure, as well as greater incidence of cardiovascular diseases with high-rise infectious diseases such as malaria [80-86]. In 2018, an estimated 228 million cases of malaria occurred worldwide (95% confidence interval [CI]: 206–258 million), compared with 251 million cases in 2010 (95% CI: 231–278 million) and 231 million cases in 2017 (95% CI: 211–259 million). Most malaria cases in 2018 were in the World Health Organization (WHO) African Region (213 million or 93%), followed by the WHO South-East Asia Region with 3.4% of the cases and the WHO Eastern Mediterranean Region with 2.1%. This link may depend on malaria parasitaemia symptomaticity or latency where individuals with more latent/asymptomatic malaria parasitaemia have lower risk of hypertension and those with more

acute/symptomatic malaria parasitaemia have a tendency toward higher blood pressure [70].

Mechanism of interaction

For decades, researchers have been fascinated by the idea of a causative connection between hypertension and malaria as the prevalence of hypertension is higher in populations who have been exposed to malaria for long periods.

Evidences that support the link between malaria and hypertension

The link between malaria and high blood pressure is currently a major subject of research as well as scientific reviews. The general view that malaria being endemic in the low-income countries, coupled with observations that non communicable diseases like hypertension are often associated with harsh economic and environmental conditions, have provided a basis for speculations for the possible linkage between malaria and hypertension.

1. Malaria in pregnancy leads to low birth weight through pathophysiologically connected mechanisms. In malaria-endemic regions, women with acquired immunity may experience fewer febrile episodes, yet low birth weight remains common due to fetal growth restriction from impaired uteroplacental blood flow and maternal anemia linked to malaria. Reduced immunity in women increases susceptibility to febrile malaria episodes, inducing uterine contractions and elevating tumor necrosis factor-α, potentially causing preterm birth. Malaria is also associated with hypertensive disorders of pregnancy, such as gestational hypertension and preeclampsia, particularly in young primigravid women, further increasing the risk of low birth weight. By virtue of its association with hypertensive disorders of pregnancy that are themselves risk factors for essential hypertension in women [71].
2. Malaria is associated with stunting and malnutrition in childhood [30-31] which predisposes to the development of hypertension in later life. The causes of hypertension following stunting and chronic malnutrition are not completely understood, but potential mechanisms include a decrease in nephron numbers and early aging in the kidney. Rapid weight gain after growth restriction may exacerbate these effects. A study on Jamaican individuals who experienced severe acute malnutrition in childhood revealed, at age 30, significantly smaller left ventricular outflow tracts, reduced cardiac output, elevated peripheral resistance, indicating a pattern that can contribute to hypertension later in life [72].
3. Malaria infection results in inflammation and studies have shown that inflammations are associated with the development of arterial stiffness which in consequence increased leads to increased blood pressure and hypertension.
4. An additional potential mechanism linking malaria to hypertension includes the supposed effect of angiotensin II (Ang II) in limiting erythrocyte invasion by Plasmodium. This concept seems to be supported by the results of epidemiological studies. Indeed, 2 polymorphisms of the angiotensin-converting enzyme and angiotensin-converting enzyme-2 leading to increased circulating Ang II levels have been associated with lower risk of cerebral malaria [73-86]. The renin-angiotensin-aldosterone system (RAAS) is one of the most important regulatory systems of blood volume, arterial pressure and cardiovascular homeostasis. Angiotensin II (Ang II) is the principal effector hormone of the RAAS in vascular biology, mediating effects via two main receptors: Angiotensin receptor type 1 (AT1) and type 2 (AT2). When Ang II binds to AT1 on vascular smooth muscle cells, it mobilizes intracellular Ca2+, leading to cellular contraction. Sustained cellular contraction increases peripheral vascular resistance, resulting in high blood pressure [74-86].

CONCLUSION

The emerging evidence linking malaria infection and hypertension unveils a complex interplay of pathophysiological mechanisms. Chronic inflammation, endothelial dysfunction, and dysregulated vascular responses induced by Plasmodium parasites appear to contribute to the development and exacerbation of hypertension. The intricate relationship between these conditions underscores the importance of a multifaceted approach that integrates malaria control measures with strategies for early detection and management of hypertension in endemic regions. Understanding the shared pathways and predisposing factors is crucial in developing targeted interventions and comprehensive healthcare policies. Further research endeavors are warranted to elucidate the specific molecular mechanisms underlying this association and to identify novel therapeutic targets for mitigating the burden of both malaria and hypertension on global health. Collaborative efforts across disciplines will be instrumental in addressing this intertwined health challenge and improving healthcare outcomes for affected populations worldwide.

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