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THE RELATIONSHIP BETWEEN MALNUTRITION, IMMUNITY AND MALARIA TRANSMISSION IN CHILDREN

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ABSTRACT: Malaria is one of the major causes of sickness and death in sub-Saharan Africa. It is responsible for 1·5–2·7 million deaths each year in sub-Saharan Africa, of which at least 0·7 million are among children aged under 5 years. Therefore, they continue to pose a serious public health problem throughout the world. Malnutrition is the condition that results from taking an unbalanced diet in which certain nutrients are lacking, in excess (too high an intake), or in the wrong proportions. Malnutrition increases the risk of infection and infectious disease, and moderate malnutrition weakens every part of the immune system subsequently making the body vulnerable to diseases. This paper therefore revealed the effect of malnutrition on malaria transmission in children.

KEYWORDS: Children, malaria, malnutrition, immune system

INTRODUCTION:

There is a strong relationship between malnutrition, infection and infant mortality because poor nutrition leaves children underweight, weakened and vulnerable to infections, primarily because of epithelial integrity and inflammation (Reuters, 2004). Five infectious diseases namely: pneumonia, diarrhea, malaria, measles and AIDS account for more than one-half of all deaths in children under five years of age (UNICEF, 2006). Malaria is a disease caused by *Plasmodium* species. Malaria is endemic in most African countries and one of the major causes of sickness and death in sub-Saharan Africa, and it continues to be a major public-health challenge. It is possibly the most serious vector-borne disease worldwide. Globally, 300 – 500 million cases of infections and over one million deaths are reported annually in which 90% of these occur in tropical Africa (WHO, 1996; Breman *et al*., 2004). Malaria is responsible for 1·5–2·7 million deaths each year in sub-Saharan Africa, of which at least 0·7 million are among children of under 5 years old (Snow *et al.*, 2003).

In Nigeria, malaria is endemic and constitutes the major cause of death in children. Although it affects all ages, cases in children under the age of five are commonly affected reflecting their relative low level of immunity to the disease compared with adults (Amodu *et al*., 2005). More than 80 percent of malaria cases are

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caused by *Plasmodium falciparum*, while the rest are caused by *P. malariae, P. ovale* or a combination. Severe falciparum malaria is the commonest cause of death in infants and children in endemic and hyperendemic areas for malaria.

Infection and malnutrition have always been intricately linked. Young children are more likely to fall victim to food shortages which results in malnutrition and thereby increases their susceptibility to malaria infection, leading to increase in mortality. Severely malnourished children with a malarial infection may have no fever and show few or none of the classic signs of the disease, making it much more difficult to diagnose and treat effectively. The World Health Organization suggests that all malnourished children in regions where malaria is endemic be screened proactively for malaria weekly even when they show no symptoms. Malnutrition increases the risk of infection and infectious disease; and moderate malnutrition weakens every part of the immune system (Stillwaggon, 2008). Protein and energy malnutrition and deficiencies of specific micronutrients (including iron, zinc, and vitamins) increase susceptibility to infection (Stillwaggon, 2008). Malnutrition affects infection transmission by increasing the risk of transmission from mother to child and also increasing replication of the etiologic agent (Stillwaggon, 2008). In communities or areas that lack access to safe drinking water, these additional health risks present a critical problem. Lower energy and impaired function of the brain also represent the downward spiral of malnutrition as victims are less able to perform the tasks they need to in order to acquire food, earn an income, or gain an education. This review focused specifically on the impact of malnutrition on prevention of malaria in children

Malaria and malnutrition as causes of mortality in children

According to Ziegler (2007), mortality due to malnutrition accounted for 58% of the total mortality in 2006: "In the world, approximately 62 million people die each year due to infectious diseases. One in twelve people worldwide is malnourished. In 2006, more than 36 million died of hunger or diseases due to deficiencies in micronutrients" (Ziegler, 2007). According to the World Health Organization, malnutrition is by far the biggest contributor to child mortality, present in half of all cases. Six million children die of hunger every year. Underweight births and intrauterine growth restrictions cause 2.2 million child deaths a year. Poor or non-existent breastfeeding causes another 1.4 million. Other deficiencies, such as lack of vitamin A or zinc, for example, account for 1 million. Malnourished children grow up with worse health and lower educational achievements. Malnutrition was previously seen as something that exacerbates the problems of diseases as measles, pneumonia and diarrhea.

The World Health Organization estimates that malnutrition accounts for 54% of child mortality worldwide. Even mild degrees of malnutrition double the risk of mortality for respiratory and diarrheal disease mortality and malaria. This risk is greatly increased in more severe cases of malnutrition. There are three commonly used measures for detecting malnutrition in children: stunting (extremely low height for age), underweight (extremely low weight for age), and wasting (extremely low weight for height) (Adams and Naoke, 1999). These measures of malnutrition are interrelated, but studies for the World Bank found that only 9% of children exhibit stunting, underweight, and wasting (Adams and Naoke, 1999). According to a 2008 review an estimated 178 million children under

age 5 are stunted, most of who live in sub-Saharan Africa (Bhutta *et al*., 2008). A 2008 review of malnutrition found that about 55 million children are wasted, including 19 million who have severe wasting or severe acute malnutrition (Bhutta *et al*., 2008). Measurements of a child's growth provide the key information for the presence of malnutrition, but weight and height measurements alone can lead to failure to recognize kwashiorkor and an underestimation of the severity of malnutrition in children.

Most of the 1-3 million who die each year from malaria are children, mainly in Africa, which is hyperendemic for malaria. In older children, malaria has a similar course as in adults. However, in children below the age of 5 years, particularly infants, the disease tends to be atypical and more severe. In the first two months of life, children may not contract malaria or the manifestations may be mild with low-grade parasitemia, due to the passive immunity offered by the maternal antibodies. In endemic and hyperendemic areas, the parasite rate increases with age from 0 to 10% during first three months of life to 80 to 90% by one year of age and the rate persists at a high level during early childhood. The mortality rate is highest during the first two years of life. By school age, a considerable degree of immunity would have developed and asymptomatic parasitemia can be as high as 75% in primary school children. In Africa, on an average about 1 in 20 children die from malaria and in worst affected areas, about 1 in 5 or 6 die from malaria and its related diseases (e.g., anemia). In areas of low endemicity, where the immunity is low, severe infection occurs in all age groups including adults. The morbidity and mortality due to malaria in children tends to be very high in these areas.

COMPLICATIONS OF SEVERE MALARIA IN CHILDREN:

Severe anemia: Anemia is the commonest complication of malaria in children. The rate of development and degree of anemia depend on the severity and duration of parasitemia. In some children, repeated untreated episodes of malaria can result in normocytic anemia. In these cases, bone marrow shows changes of dyserythropoeisis and peripheral blood shows low-grade parasitemia, sometimes with pigmented monocytes. In patients with high parasitemia, anemia may develop rapidly due to hemolysis of the parasitized red cells and this may worsen even after completion of antimalarial therapy. It can present with serious problems in children with pre-existing anemia. Anemia is as well common in malnourished children.

Children with severe anemia may present with symptoms and signs of cardiac failure-dyspnoea, tachycardia, gallop rhythm, basal crackles, hepatomegaly, raised jugular pressure etc. Severe anemia can also cause confusion, restlessness, retinal haemorrhages and even coma.

Renal failure: Renal failure is uncommon in children. A slight increase in urea and creatinine may sometimes occur due to dehydration and it returns to normal with rehydration.

Bleeding disorders: Bleeding tendencies with prolonged clotting time, thrombocytopenia and decreased coagulation factors may occur in falciparum malaria. Spontaneous bleeding from various sites, including the upper gastrointestinal tract may occur.

Pulmonary oedema: Children with cerebral malaria, severe anemia and high parasitemia

may develop acute pulmonary oedema. It may also be due to fluid overload. Tachypnoea is the earliest sign of impending pulmonary oedema.

Hypoglycemia: This is also less common in children compared to the adults. It may be associated with lactic acidosis in severe falciparum infections. It may present with convulsions, or impairment in the level of consciousness..

Fever: In children, high-grade fever itself can cause various problems and hence should be managed energetically. Fanning and tepid sponging should be used regularly. Paracetamol injection can be used in hyperpyrexia.

TYPES OF NUTRITIONAL ACQUIRED IMMUNE DEFICIENCY:

Malnutrition is considered to be the most common cause of immunodeficiency worldwide. Malnutrition, immune system and infectious diseases are interlocked in a complex negative cascade. Malnutrition elicits dysfunctions in the immune system and promotes increased vulnerability of the host to infections. These immune dysfunctions are referred to as nutritional-acquired immune deficiency syndrome (NAIDS). Every type of immunological deficiency induced by malnutrition can be included under the NAIDS umbrella.

Protein-energy malnutrition (PEM)

Now known as protein-energy under nutrition. It is an energy deficit due to chronic deficiency of all macronutrients (Wellman *et al*., 1997). In children, PEM causes widespread atrophy of lymphoid tissues, particularly T-lymphocyte areas. The thymus involutes causing a reduction in the thymus-derived lymphocyte growth and maturation factors, arrest of lymphocyte development, reduced numbers of circulating mature CD4 helper cells, and impairment of antibody production to T-dependent antigens. Imbalance in Th1-Th2 activation occurs depending on nature of stimuli and altered regulatory pathways, including responses mediated by the nuclear factor-kB (NF-kB) (Nikollaos, 2011), a major transcription factor involved in the development of innate and adaptive immunity. Hence the patient's ability to ward off infections and show recovery is compromised. However, CD8 suppressor cells are relatively preserved. The lymphocytes not only get reduced in blood, but also impaired show T-lymphocyte mitogenesis and diminished activity in response to mitogens (WHO, 2012). In malnourished children, changes such as dermal anergy, loss of delayed dermal hypersensitivity (DDH) reactions, and loss of the ability of killer lymphocytes to recognize and destroy foreign tissues were noted (Sue *et al.*, 2008).

Essential Fatty Acids

Particularly the omega-3 fatty acids, serve as the key precursors for the production of eicosanoids like prostaglandins, prostacyclins, thromboxanes, and leukotrines that play a variety of host defensive roles. Thus their deficiency in the diet can impair cytokine synthesis (Gueri *et al*., 1980)

Vitamins

Vitamin A has an important role in nucleic acid synthesis, and its deficiency is also characterized by lymphoid tissue atrophy, depressed cellular immunity, impaired IgG responses to protein antigens, and pathologic alterations of mucosal surfaces. Experimental animals with vitamin A

deficiency have decreased thymus and spleen sizes, reduced natural killer cell, macrophage and lymphocyte activity, lower production of interferon, and weak response to stimulation by mitogens (Waterlow, 1792). Until recently vitamin A deficiency was thought to be a problem only for the eye health and vision (night blindness). It is now clear, however, that vitamin A is also essential for the proper functioning of the immune system of the child and damage to the immune system occurs long before the damage to the eyes is apparent. Hence, the deficiency lowers children's resistance to common infections and results in increased levels of child's mortality. B-group vitamins like thiamin, riboflavin, pantothenic acid, biotin, folic acid, and cobalamin can influence humoral immunity by diminishing antibody production. Pyridoxine deficiency has also been associated with reduced cell-mediated immunity. Folic acid and vitamin B-12 are essential to cellular replication. Experimental deficiencies of these vitamins were shown to interfere with both replication of stimulated leukocytes and antibody formation. In anemia due to folic acid deficiency, cell-mediated immunity is depressed. In vitamin C deficiency, phagocytic cells cannot produce tubulin, therefore, with impaired chemotaxis, microorganisms cannot be engulfed and destroyed (Stillwaggon, 2008). Vitamin D acts as an immunoregulatory and a lymphocyte differentiation hormone (Schaible, and Kaufmann, 2007). In vitamin E deficiency, leukocyte especially lymphocyte killing power gets reduced. In animals it was shown to interfere with antibody formation, plaque-forming cells, and other aspects of cell-mediated immunity. At higher than recommended levels, it has been shown to enhance immune response and resistance to disease.

Minerals

Zinc is also the fundamental component of thymic hormones and shares a similar role as vitamin A in nucleic acid synthesis. Zinc deficiency influences both lymphocyte and phagocyte cell functions and affects more than 100 metalloenzymes that are zinc dependent. During infections, reticuloendothelial cells sequester iron from the blood and phagocytes release lactoferrin with a higher iron binding capacity than bacterial siderophores. The net effect is to deprive the infectious agent of iron for its replication and inhibit the spread of infection (Schaible and Kaufmann, 2007). Iron deficiency results in impaired phagocytic killing, less response to lymphocyte stimulation, fewer natural killer cells, and reduced interferon production. Selenium serves as an antioxidant and contributes to antibody responses and cytotoxicity of natural killer cells. In children with HIV infection, selenium concentration in plasma appeared to correlate with their immune functions. Similar changes were also seen in patients with copper deficiency (Laus *et al*., 2011). Copper concentrations often increase during infection as a result of stimulation of the hepatic production of ceruloplasmin. Conversely, plasma zinc concentration often declines due to internal redistribution to the liver. Antimicrobial systems in the neutrophils are affected by malnutrition. These include both oxygen-dependent systems responsible for the respiratory burst, and oxygen-independent systems, such as lactoferrin, lysozymes, hydrolase, and proteases (Schaible and Kaufmann, 2007).

Cytokine Abnormalities in Malnutrition

Cytokines are substances that play an important role in coordinating inflammatory response of the body to various external and internal stimuli. They may be proinflammatory, which are

essential to initiate defence against various pathogens, and anti-inflammatory, which down regulate the inflammatory process by suppressing production of the pro-inflammatory cytokines and balance the inflammatory

response. Excess production of both is counterproductive. The proinflammatory cytokines include IL-1β, IL-6, IL-8, TNF-α, and IL-2, and the anti-inflammatory cytokines include IL-1 receptor antagonist, IL-4, IL-10, and IL-13 (Lakhan, and Vieira, 2008). PEM diminishes immunoglobulin (IgA, IgM, and IgG) concentrations and cytokine production. Severe malnutrition alters the ability of T lymphocytes to respond appropriately to IL-1 rather than simply affecting synthesis of this monokine (Jere, 1996). During catabolic states, interleukin 1 is released by leukocytes which cause endocrine changes that lead to amino-acid mobilization, primarily from skeletal muscle. These amino acids are used for gluconeogenesis in the liver, and the nitrogen released is excreted in urine (Glewwe, 2001). Thus, a continual conversion of alanine carbon to glucose carbon occurs with acute infection. Benton and Sargent (1992) observed that the immunosuppressive PGE2 production was enhanced in malnutrition. In malnourished Africans without overt infections, increased circulating levels of inflammatory mediators (e.g., interleukin 6 (IL-6), the soluble receptors of tumor necrosis factor (sTNFR-p55 and sTNFR-p75), etc.) as well as C-reactive protein, were seen compared to healthy controls (Kanarek and Swinney, 1990)

CONCLUSION:

Since nutrient intake is an important factor in building the immune system of individual and subsequently plays a major role in the control of infection, an impaired immune system will readily increase the susceptibility of an individual to infection. Malnutrition does not increase susceptibility to severe falciparum malaria. However, when severe malaria does occur, a higher morbidity and mortality rates are most likely to occur in malnourished children as a result of low immunity. Malaria may cause malnutrition, whereas malnutrition itself may cause susceptibility to the disease.

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