

Concurrent giardiasis and amoebiasis infections in Nigerian children diagnosed with *Plasmodium falciparum* malaria: prevalence and pathophysiological implications.

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Citation

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Abstract

The prevalence of giardiasis and amoebiasis as concurrent infections in Nigerian children diagnosed with *Plasmodium falciparum* malaria was investigated. From the results, 69 (27.6%) of the 250 children diagnosed with malaria, were concurrently infected by amoebiasis, 13 (5.20%) were infected by giardiasis, while 38 (15.2%) were infected by both giardiasis and amoebiasis. In all, 119 (47.60%) of the test population were concurrently infected by either one or both protozoan infections. The prevalence of giardiasis and mixed giardiasis/amoebiasis infections was significantly ($p < .05$) higher in the malaria-positive subjects than in the malaria-free group. However, the prevalence of amoebiasis in the malaria-positive group (27.6%) was lower than the prevalence (37.14%) in the malaria-negative control. It is concluded that a relatively high percentage of cases of childhood malaria in Nigeria is confounded by giardiasis and amoebiasis with severe implications for severity, duration and eventual outcome of illness.

INTRODUCTION

Complicated childhood malaria, which remains a major cause of infant morbidity and mortality in the malaria endemic countries of the tropics(1), is associated with a number of metabolic and pathophysiological disorders including, anaemia, hypovolaemia, metabolic acidosis, hypoglycaemia, respiratory distress and a variety of neurological features, all of which contribute to the often undesirable outcome of malaria episodes in children(2, , 3, 4, 5, 6).

Contrary to the impression given by many studies on malaria (especially with laboratory-induced malaria), the prevailing climatic and socioeconomic conditions in the malaria - endemic countries of the tropics predispose affected populations to a number of other protozoan, bacterial and helminthic infections, which often confound episodes of malaria in these regions(7,8). When these diseases occur concurrently with malaria they have the ability to interfere with the immune responses to malaria(9, 10) and could also initiate (or aggravate) some of the life-threatening metabolic and pathophysiological disorders observed in childhood malaria. Thus, the severity, duration and eventual outcome of malaria episodes in children may depend on the absence

or presence of these concurrent infections. However, these infections are usually ignored during diagnosis and treatment of malaria both during home management and in clinical settings.

Children are often more vulnerable to these infections because they have a comparatively poorly developed immune system, which may not be sufficiently exposed to these infections to acquire the additional capability that sometimes renders the immune systems of adults impervious to these infections. In addition, children have a uniquely delicate physiology that increases their susceptibility to the life-threatening metabolic and pathophysiological disturbances and disorders associated with these infections.

In our opinion, the likely presence of these concurrent infections is one of the major causes of the rapid debilitation, symptom aggravation and delayed recovery typical of malaria episodes in children. Thus, the concomitant presence of these often neglected infections could contribute significantly to why malaria remains a major threat to the survival of young children in many endemic countries of the tropics, where annual deaths due to malaria have remained unacceptably high despite the availability of a wide range of relatively effective preventive, prophylactic and therapeutic

options (11, 12). There is need, therefore, to highlight the prevalence and possible pathophysiological implications of these concurrent infections in different populations of children as part of efforts to understand the complicated nature and unexpected outcomes of some episodes of childhood malaria.

In this study, stool samples from children presenting with signs of illness suspected to be due to malaria were examined for the presence of two protozoan parasites namely, *Giardia lamblia* and *Entamoeba histolytica*, which cause giardiasis and amoebiasis, respectively. Giardiasis and amoebiasis are potentially fatal protozoan infections, whose common clinical symptoms include diarrhoea, dysentery, vomiting, and headache and, to a less extent, fever (13, 14, 15). In addition, severe cases of amoebiasis may lead to intestinal colitis and abscesses of liver, spleen and brain (16). Our current interest in concurrent infections in malaria is necessitated by the many cases of childhood malaria characterised by rapid debilitation, the exaggeration of symptoms and delayed recovery, even after relatively effective antimalarial therapy.

MATERIALS AND METHODS

SUBJECTS AND LOCATION

The study was conducted in Nsukka - a semi-urban town in Enugu State located in South Eastern Nigeria. A total of 425 children aged between 6 and 60 months (5 years), presenting with symptoms of illness presumed to be malaria, who were referred to our laboratory for confirmatory diagnosis, were included in the study. The commonest signs were fever (characterised by body temperature higher than 38°C), vomiting and diarrhoea.

The test population was made up of 250 (58.82%) children who were diagnosed with *Plasmodium falciparum* malaria, while the remaining 175 (41.18%) children who tested negative to the malaria parasite test constituted the control group.

Following the explanation of the nature and purpose of the investigation, the consent of the accompanying parent/guardian was sought. Thereafter, consenting parents/guardian were requested to provide fresh stool samples of the children within 24 hours for examination. The test results were made available to the referring/consulting physician for the appropriate management. The experiment was conducted in consonance with the relevant guidelines for clinical research in the University of Nigeria, Nsukka.

DIAGNOSIS

Diagnosis of Malaria: Thick blood smears were prepared on glass slides within 6 hours of sample collection, and the malaria parasites were determined after staining with Giemsa buffer solution (17). Blood parasite density of over 5000 parasites per microlitre was taken as a confirmation of malaria.

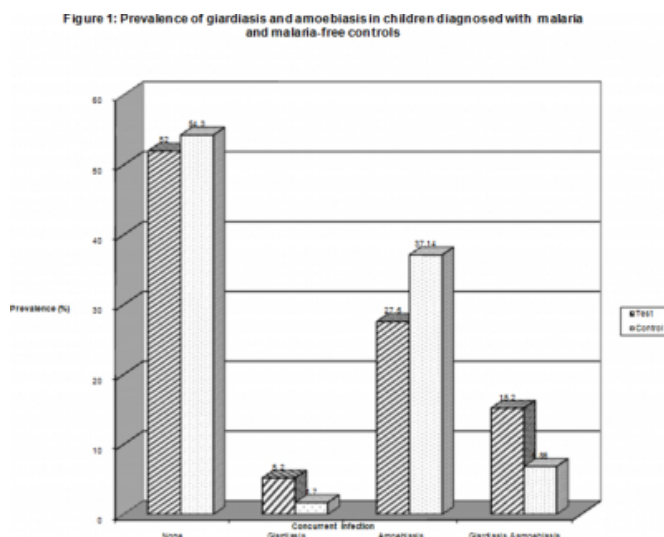
Diagnosis of giardiasis and amoebiasis: The presence of the protozoans, *Giardia lamblia* and *Entamoeba histolytica/dispar* were identified on fresh stool samples by light microscopy. Because light microscopy is unable to distinguish the two morphologically identical species of *Entamoeba* - *E. histolytica* (pathogenic) and *E. dispar* (non-pathogenic), the prevalence of the two species has been reported jointly as *E. histolytica/dispar* (EHD) complex (16).

RESULTS

Results of the study on the prevalence of *Giardia lamblia* and *Entamoeba histolytica/dispar* complex in malaria patients are presented in figure 1.

Out of 250 malaria-positive children in the test population, 13 (5.20%) were infected by GL alone, 69 (27.6%) were infected by EHD alone, while 38 (15.2%) had a mixed infection of both EHD and GL. Thus, 119 (47.60%) of the malaria-positive group were concurrently infected by one or both of the protozoan infections studied.

Figure 1



The prevalence of GL, EHD and mixed infections of GL and EHD in the malaria-free children were 3 (1.7%), 65 (37.14%) and 12 (6.86%), respectively.

DISCUSSION

PREVALENCE OF GIARDIASIS AND AMOEBIASIS IN CHILDHOOD MALARIA

Data on the prevalence of giardiasis and amoebiasis as concurrent infections in childhood malaria in Nigeria are lacking. The prevalence figures reported in this study for *G. lamblia* (GL) and *E. histolytica/dispar* (EHD) complex in both the malaria-infected and malaria-free patients (figure 1) are, however, a lot higher than the prevalence figures reported in school children in another part of Nigeria (19), but are comparable to prevalence values reported in a study conducted on subjects with symptoms of gastroenteritis in the same town almost two decades ago (20). Because of the oral-faecal route of transmission of both organisms, the prevalence figures, which could vary with seasons, reflect the sanitary conditions, especially the quality of drinking water and methods of sewage disposal in the geographical location of the study (21).

EHD was the more common infection and had a higher prevalence than GL in both children with a positive blood smear and the malaria-free subjects. However, because the microscopic method used in the diagnosis of amoebiasis is unable to distinguish the 2 morphologically identical species of *Entamoeba*, namely, *E. lamblia* and *E. histolytica*, we were unable to determine the relative prevalence of the two species.

The prevalence of GL in the malaria-infected children (5.20%) was significantly ($p < 0.05$) higher than the prevalence in the malaria-free controls (1.7%), but the prevalence of EHD in the malaria-infected children (27.6%) was lower than the prevalence in the malaria-free controls (37.14%). These observations are somewhat suggestive of an increased risk of giardiasis infection in children with malaria, but not amoebiasis. The suspicion of a predisposing effect by malaria on giardiasis alone or as mixed infection is strengthened by the observation that the prevalence of the mixed GL and EHD infections in the malaria-infected children (15.2%) was significantly ($p < 0.05$) higher than the prevalence in the malaria-free children (6.86%). Such an observation if proven could be attributed to the ability of *Plasmodium falciparum* to impair both mediated and humoral immunities of victims (22, 23), thereby making them more vulnerable to other infections. However, the existence of such a predisposing or protective interaction between these infections deserves further investigations as we could not establish which of the infections pre-existed

before the other.

The prevalence of GL (1.7%) and EHD (37.14%) in the malaria – free children, all of whom presented with signs of illness initially presumed to be due to malaria, further highlights the significant contributions of these often neglected diseases to the debilitation of children in Nigeria.

Beyond mere prevalence, the concurrent occurrence of one or both GL and EHD infections with malaria is likely to predispose the patients to more severe forms of illness, with equally severe implications for recovery. Since the severity of giardiasis and amoebiasis in a symptomatic patient is determined largely by the immune status of the host (24, 25), the concomitant existence of malaria could predispose to severe illness. This can be likened to the scenario described by Hocqueloux et al.(26), in which malaria-induced immunosuppression allowed an overgrowth of pre-existing *Aspergillus* leading to a rare case of fatal aspergillosis.

PATHOPHYSIOLOGICAL IMPLICATIONS OF CONCURRENT GIARDIASIS AND AMOEBIASIS IN CHILDHOOD MALARIA.

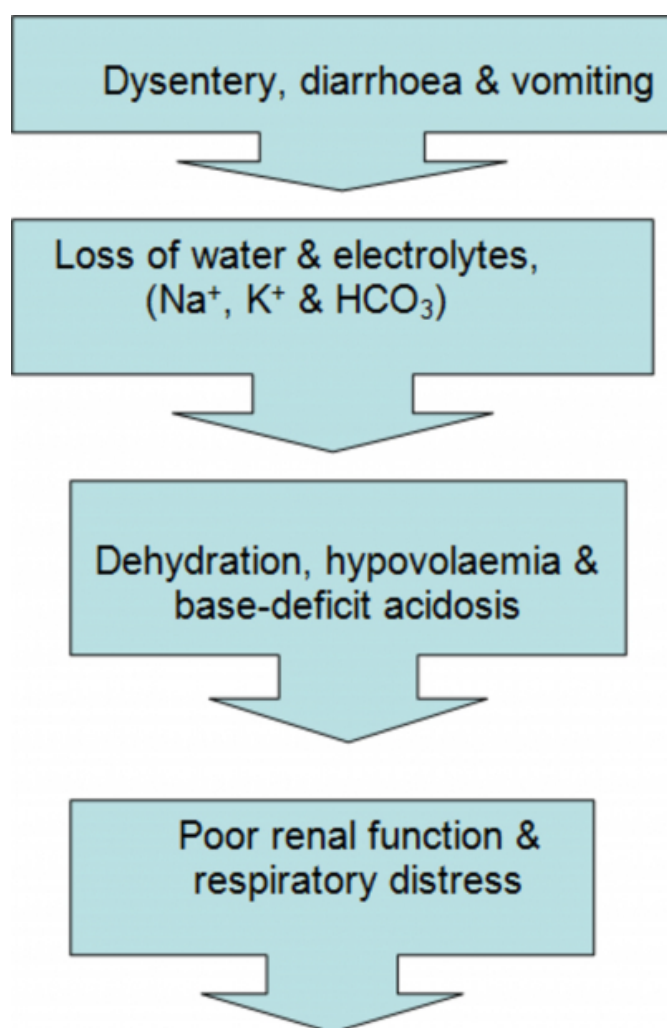
In our experience, whereas the life-threatening disorders associated with childhood malaria appear quite mild in some children, they appear so severe in others. In the later group, the occurrence of severe symptoms often results in the rapid debilitation of the patients as-well-as their delayed recovery. One possible cause of such rapid debilitation in childhood malaria is the existence of one or more concomitant illnesses. The pathophysiological complications of childhood malaria which are most likely to be initiated or aggravated by concurrent giardiasis and/or amoebiasis, include metabolic acidosis, hypovolaemia, respiratory distress and hypoglycaemia.

Figure 2 is a representation of how some of the pathophysiological disorders often implicated in malaria-associated morbidity and mortality in children(27), could be initiated or potentiated by concurrent giardiasis and/or amoebiasis. As shown in figure 2, diarrhoea and vomiting - the commonest symptoms of giardiasis and amoebiasis – predispose to dehydration because they cause the excessive loss of body fluid and electrolytes, namely sodium, chloride, bicarbonate and potassium. In malaria patients, the risk of dehydration is increased by additional water losses through evaporation and vomiting due to fever and nausea, respectively. If the excessive loss of water and electrolytes is not promptly compensated for, the resulting dehydration

could lead to a significant drop in blood volume (hypovolaemia), while the continued loss of bicarbonate could lead to metabolic or base-deficit acidosis. Ideally, the kidneys should quickly compensate for the loss of bicarbonate, but the ability of the kidneys to perform this function would be impaired by the reduction in renal blood flow caused by the drop in blood volume due to dehydration. As a consequence, the pH of arterial blood could fall below physiologically normal values leading to acidosis. In the absence of proper renal function (due to reduction of blood volume), respiratory distress or acidotic breathing, characterised by deep and rapid breathing is then initiated as a physiological compensatory mechanism intended to raise blood pH through respiratory alkalosis.

Figure 2

Figure 2: Proposed mechanism by which Giardiasis and Amoebiasis could lead to hypovolaemia, metabolic acidosis and respiratory distress in childhood malaria.



Giardiasis could also potentiate or aggravate the problem of

energy metabolism, which often manifests partly as hypoglycaemia in childhood malaria (28). Because *G. lamblia* colonises and proliferates in the upper region of the small intestine, where it damages the mucosal surface of the small intestine, it reduces the surface area available for nutrient absorption. Carbohydrates, especially disaccharides, including lactose - the main energy nutrient in milk - are the main nutrients whose absorption are usually affected (28, 29). Since giardiasis also affects the activity of lactase (30), the combined effect on lactose absorption and lactase activity will adversely affect the energy metabolism of children, especially those below 2 years, who depend on lactose in milk as a major source of energy. It is noteworthy that not all patients infected by both pathogens show signs of damage to the intestines and malabsorption, and in some cases the infections, especially giardiasis, could be self-resolving. In addition, the recent separation of what used to be known simply as *Entamoeba histolytica* into 2 morphologically identical species – *E. histolytica* (pathogenic) and *E. dispar* (non-pathogenic) - which cannot be distinguished by light microscopy (16), has settled part of the confusion over why some people infected with *Entamoeba* remained asymptomatic while others showed symptoms of severe illness.

In conclusion, a relatively high proportion of children infected with malaria in the rural areas of Nigeria are also concurrently infected by *Giardia lamblia* and *Entamoeba histolytica/dispar*, especially in populations living under poor hygienic conditions. Both infections are capable of initiating and/or aggravating some of the life-threatening pathophysiological disorders observed in childhood malaria resulting in rapid debilitation, delayed recovery and increased risk of death if not promptly diagnosed and managed. These concurrent infections could be a major problem for the many families who manage malaria episodes at home. There is, therefore, an urgent need for health promotion policies of government to address this risk when designing strategies for management of malaria in endemic areas. For example, in areas of high prevalence of concurrent giardiasis and amoebiasis, antimalarial drugs like chloroquine and quinacrine, which are also effective against *G. lamblia* and *E. Histolytica* (31, 32), could be considered the first line drugs for treating malaria in children.

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