

Malaria Among Refugee Children at Arrival in the United States

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Background: Malaria infects >70% of children at any given time in highly disease-endemic areas, such as parts of West Africa. Many infected children are asymptomatic. There are no published data regarding the prevalence of malaria among refugee children arriving in the United States from highly disease-endemic areas. This study was performed to determine the prevalence of malaria among asymptomatic children from West Africa.

Methods: A retrospective chart review for Liberian refugee children arriving in the United States was conducted from 1997 to 2000.

Results: Fifty-seven charts were reviewed. There were 28 (64%) positive thick and thin blood smears among the 44 children who had malaria smears performed during refugee medical screening examinations. There were 3 children who had been treated recently for malaria. An additional 3 children had splenomegaly and were treated for presumed malaria. Overall, the prevalence rate was 60% (34 of 57 cases). No sign or symptom, singly or in combination, was sufficient to predict the presence or absence of malaria. However, splenomegaly, fever and thrombocytopenia were highly specific for malaria and should alert clinicians to the likelihood of the diagnosis. Twenty-nine percent of children with malaria were asymptomatic.

Conclusion: The results of this study suggest that refugee children arriving from West Africa have a significant burden of malaria. It is recommended that children who arrive in the United States as refugees from West Africa be subjected to a thorough physical examination, complete blood count and malaria blood smear.

Key Words: malaria, refugee, medical screening, Liberia, West Africa

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An estimated 500 million cases of malaria cause 2.5 million deaths annually throughout the world.¹ Morbidity and mortality rates for children are disproportionately high,^{2,3}

and rates are particularly excessive in sub-Saharan African refugee populations.^{4–7} Furthermore, autochthonous transmission of malaria in non-disease-endemic areas such as the United States occurs,^{8,9} and minimally symptomatic or asymptomatic refugees may act as potential reservoirs.⁵ The Centers for Disease Control and Prevention (CDC) currently recommends consideration of screening of refugees and immigrants from highly disease-endemic countries for malaria and stresses that screening is most important when hemoglobin values are >30% below normal values for age.¹⁰ Despite this suggestion, very few eligible immigrants to the United States are subject to malaria laboratory screening. This is exemplified by the rates of screening in Minnesota, where <2% of eligible refugees were screened in 2003.¹¹ The 2004 ceiling for new U.S. refugee arrivals was set at 70,000. West Africa, the predominant area for highly endemic *Plasmodium falciparum* malaria, is the fastest growing origin for new U.S. refugee arrivals.¹²

To our knowledge, there are no data on the prevalence of malaria in new refugee populations arriving in the United States. The Hennepin County Medical Center (HCMC) Pediatric Clinic recommends performing one thick and thin blood smear during refugee medical screening for refugees arriving from highly malaria-endemic areas. A retrospective investigation of the prevalence of malaria among children of Liberian descent was conducted. These children accounted for a majority of the refugees arriving in Minnesota from a highly malaria-endemic area during the study period.

METHODS

This study was a retrospective chart review involving Liberian refugee children, conducted at the HCMC Pediatric Clinic in Minneapolis, Minnesota. The HCMC is a large, urban, inner city, teaching hospital that cares for a large immigrant population. During periods of high refugee influx, such as during the study period, the HCMC Pediatric Clinic performs refugee screening examinations as contracted with the Hennepin County Health Department. Study participants were identified by searching outpatient records for International Classification of Diseases, 9th revision, code V70.5, for

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the period January 1, 1997, through December 31, 2000. All refugee screening examinations performed for Liberian children 0 to 18 years of age during the study period were selected for review. A standardized data collection form was used to extract data from the patient records. Data were extracted and reviewed by 3 physicians familiar with tropical medicine and infectious diseases. The prevalence of common symptoms of malaria, including anemia, fever, splenomegaly and thrombocytopenia, was noted. The study protocol was reviewed and approved by the appropriate institutional review board.

RESULTS

A total of 57 children (40 male and 17 female) of Liberian descent who had undergone refugee screening medical examinations were identified. The records of both the group for which malaria smears had been obtained ($n = 44$) and the group for which malaria smears had not been obtained ($n = 13$) were reviewed. Among those with screening thick and thin smear results, the prevalence of malaria diagnosed with a single thick and thin blood smear was 64% (28 of 44 cases). The most common species identified was *Plasmodium falciparum* (53.6%, 15 of 28 cases), followed by *Plasmodium vivax* (7.2%, 2 of 28 cases) and single cases of *Plasmodium ovale* (3.5%, 1 of 28 cases) and *Plasmodium malariae* (3.6%, 1 of 28 cases). In addition, a total of 10 (35.7%) of 28 cases had only ring forms on smears and were classified as malaria species.

Of the group not subjected to malaria smears, several had received malaria treatment before arrival ($n = 3$), others were presumed to have malaria because of detected splenomegaly and were treated empirically ($n = 3$) and the remainder failed to have smears performed ($n = 7$). The groups did not significantly differ according to age or rate of anemia. There were lower frequencies of splenomegaly (25% versus 42%, $P < 0.002$), thrombocytopenia (8% versus 16%, $P < 0.011$) and previous or current fever (8% versus 27%, $P < 0.005$) in the group without malaria smears. Therefore, when all cases of known and presumed malaria were included,

there were a total of 34 cases (60%) among the 57 Liberian children examined during the study period.

Of the children with a single thick and thin malaria smear, the most common sign was age-adjusted anemia (with American standards), affecting 84% (37 of 44 children). However, anemia was a nonspecific sign, because many children who did not have positive malaria smear results also had anemia ($P > 0.05$). Infants <2 years of age with malaria had more severe anemia (3.1 g/dL below age-adjusted lower limit of normal range; 95% confidence interval, 2.6–3.6 g/dL; $n = 6$), compared with infants without malaria (1.6 g/dL below age-adjusted lower limit of normal range; 95% confidence interval, 1.2–3.0 g/dL; $n = 6$; $P < 0.05$). Although 96% of children (27 of 28 children) with malaria in smears had anemia (positive predictive value, 96%), 63% of children (10 of 16 children) with negative malaria smear results also had anemia (negative predictive value, 38%).

The most specific signs of malaria were splenomegaly, fever and thrombocytopenia. All 3 signs were highly specific (94% for each) and were associated with positive malaria smear results (Table 1). Although the presence of these signs possessed high positive predictive value, consistently predicting the presence of disease, lack of any of these signs did not reliably eliminate the possibility of malaria. The presence of any of the 3 signs identified only 72% of the children (20 of 28 children) with positive malaria smears. If anemia were eliminated as a sign of malaria, because of lack of specificity, 29% of children (8 of 28 children) with malaria would be considered asymptomatic. It is interesting to note that, although it was highly predictive of malaria, thrombocytopenia was not commonly or significantly associated with positive smears, as would be expected to be found with acute malaria.^{13,14}

DISCUSSION

Malaria was the most common infectious disease identified in this cohort of Liberian refugee children. The high prevalence of malaria (60%) may not be surprising, because Liberia and the countries of transit where refugee camps are located (eg, Ivory Coast, Ghana and Sierra Leone) frequently reach malaria-

TABLE 1. Prevalence of Common Signs of Malaria and Associated Malaria Thick and Thin Smear Results

	Anemia*†	Thrombocytopenia*	Splenomegaly	Fever	T/S/F
Prevalence of sign (N = 44) (%)	84 (n = 37)	16 (n = 7)	41 (n = 18)	27 (n = 12)	50 (n = 22)
Sensitivity (%)	96	21	61	39	71
Specificity (%)	38	94	94	94	88
PPV (%)	73	86	94	92	91
NPV (%)	86	41	58	47	64
Significant risk of sign (P)	0.004	0.031	<0.001	<0.001	<0.001
Significant risk of sign among malaria patients (P)	<0.001	<0.999	0.168	0.832	0.004
Significant risk of sign versus those without sign (P)	0.011	0.352	0.001	0.036	<0.001

*Adjusted for age.

†Children with malaria had a mean hemoglobin value 2.3 g/dL (95% confidence interval, 2.1–2.6 g/dL) below the normal limits for age, whereas children without malaria had a mean hemoglobin value 2.1 g/dL (95% confidence interval, 1.9–2.4 g/dL) below the lower limits of the normal range for age.

T/S/F indicates thrombocytopenia, splenomegaly and fever; PPV, positive predictive value; NPV, negative predictive value.

holoendemic status. An area is considered malaria holoendemic when >80% of children between the ages of 2 and 12 years are infected with malaria, as determined in a cross-sectional survey.¹⁵ In addition, refugee screening generally occurs within 3 months after arrival in the United States, and children may continue to have detectable parasitemia for months after the last exposure to *P. falciparum* malaria. This is particularly relevant because West Africa represents the fastest growing population of new refugee arrivals to the United States, with up to 6000 Liberian refugees being considered for relocation to the United States in 2004.⁶

Ideal malaria screening consists of a minimum of 3 sets of thick and thin blood smears performed at least 8 hours apart.^{2,11} Because of the cost and inconvenience, this suggestion is rarely followed in the clinical setting for asymptomatic individuals. One set of thick and thin smears, as used at the HCMC Pediatric Clinic, is inadequate to eliminate malaria as a diagnosis. Therefore, it is assumed that the 60% prevalence in this study was an underestimation of the true prevalence among these children. The clinical findings of splenomegaly, thrombocytopenia and/or fever had high positive predictive value and were significantly associated with positive malaria smears. Therefore, we recommend that children with any of these clinical findings be subjected to additional investigation for malaria if original blood smear results are negative. Anemia was common among children with or without malaria, and the degree of anemia did not facilitate differentiation of the 2 groups, with the exception of children <2 years of age. Therefore, no signs or symptoms eliminated the diagnosis of malaria and malaria smears would be necessary to establish the diagnosis for at least 29% of children.

There are currently no standards for either empiric treatment of malaria before departure or medical screening of refugees upon arrival in the United States. Since the data collection for this study, it has become common, during mass resettlements from malaria-endemic areas to the United States, for the CDC to recommend empiric treatment before departure. The most common medication used for this purpose is sulfadoxine-pyrimethamine. Relapsing malaria (*P. vivax* or *P. ovale*) may not be adequately treated with this regimen, because of the persistence of liver hypnozoites. At least 10% of malaria in this study was *P. vivax* or *P. ovale*, which is approximately the underlying rate of non-*P. falciparum* malaria in Liberia. Therefore, sulfadoxine-pyrimethamine would be considered inadequate treatment, because it lacks causal effect (treatment of liver hypnozoites). Furthermore, it is now clear that *P. falciparum* resistance to sulfadoxine-pyrimethamine may be high, and resistance was shown to lead to clinical failure for up to 50% of treated patients in one area of Liberia.¹⁶ In response to these shortfalls with sulfadoxine-pyrimethamine monotherapy, the CDC recently initiated combination empiric therapy with artesunate and sulfadoxine-pyrimethamine.

Malaria detection and treatment among refugee children assist the children and protect public health. The ideal method for limiting malaria imported into the United States through refugee resettlement is being debated currently. Malaria smears and rapid malaria tests have been found to be insensitive in this setting, compared with polymerase chain reaction assays.⁵ However, the utility of polymerase chain reaction assays is limited by availability and cost. A new study would be of particular interest because of the CDC's new approach of empiric treatment before resettlement, instituted since these data were collected. Although a single blood smear is suboptimal, when it is performed in conjunction with a thorough history and physical examination, most children with malaria may be diagnosed and treated.

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