Clinical Impact of Malaria Rapid Diagnostic Testing at a US Children's Hospital

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Background. Children who develop malaria after returning to a setting in which the disease is not endemic are at high risk for critical delays in diagnosis and initiation of antimalarial therapy. We assessed the clinical impact of the implementation of malaria rapid diagnostic testing (RDT) on the management of children with malaria at an urban US children's hospital that serves a large immigrant population.

Methods. This was a retrospective cohort study of all children diagnosed with laboratory-confirmed malaria at the Children's Hospital of Philadelphia (CHOP) between 2000 and 2014. RDT using a US Food and Drug Administration–approved immunochromatographic assay was introduced at CHOP on August 1, 2007. We compared clinical management and outcomes of patients with malaria diagnosed before and after RDT introduction.

Results. We analyzed 82 pediatric malaria cases (32 before and 50 after RDT implementation). The majority of these patients had traveled to West Africa (91.5%) and were infected with *Plasmodium falciparum* (80.5%). The mean time to a positive result decreased from 10.4 to 0.9 hours ($P < .001$) after the introduction of RDT for patients with *P falciparum*. The mean time to antimalarial therapy decreased from 13.1 to 6.9 hours ($P = .023$) in hospitalized patients. We found no significant reduction in the mean number of clinical signs of severe malaria between 0 and 48 hours of hospitalization and no difference in the need for exchange transfusion, time to resolution of parasitemia, or length of hospital stay.

Conclusions. Implementation of RDT for malaria was associated with shorter times to malaria diagnosis and initiation of antimalarial therapy. The results of this study support RDT in the optimal management of patients with malaria who present in settings in which the disease is not endemic.

Keywords. children; international travel; malaria; rapid diagnostic test.

Malaria continues to be a major global health threat, particularly for children [1]. In 2017, approximately 219 million cases of malaria were documented, and an estimated 435 000 deaths occurred; 93% of these deaths occurred in Africa, and the majority of them were among children younger than 5 years [2].

Although endemic transmission of malaria has been eliminated in the United States for more than 50 years, an increasing number of malaria cases have been diagnosed in the United States since the early 1970s [3]. Malaria cases treated in the United States reached a 40-year peak in 2011, and in 2015, 1517 cases (including 1 congenital case) were confirmed [3]. The majority of these cases (68.4%) were among returning travelers who had been visiting friends and relatives in a region in which malaria is endemic [3].

Children who develop malaria after returning to a setting in which the disease is not endemic are at high risk for critical delays in having their condition diagnosed and initiating appropriate antimalarial therapy. In regions of nonendemicity, malarial infection might not be considered at the initial presentation [4]. When malaria is considered, there can be additional delays in care related to the processes of performing blood smears and having them read by a capable reader [5].

Laboratory diagnosis of malaria traditionally depends on thick and thin Giemsa smears, which require highly trained laboratory personnel to perform them, and might nevertheless result in either a false-negative or false-positive reading [6, 7]. As an alternative, rapid diagnostic testing (RDT) has been found to have excellent sensitivity and negative predictive value, superior to those of blood smears performed in routine US laboratory settings, and does not require specific expertise [5]. Yet, most US clinical laboratories have not adopted malaria RDT [8].

The Children's Hospital of Philadelphia (CHOP) is an urban tertiary children's hospital serving a large immigrant population, including a large West African community, and therefore sees a substantial number of children with imported malaria. A US Food and Drug Administration–approved

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immunochromatographic assay for the rapid detection of *Plasmodium* antigens (BinaxNOW Malaria [Alere, Scarborough, Maine]) was introduced at CHOP on August 1, 2007. RDT, in addition to a routine blood smear, is performed for all patients suspected to have malaria. The BinaxNOW Malaria assay qualitatively detects the histidine-rich protein 2 antigen specific to *Plasmodium falciparum* and aldolase, a panmalarial antigen common to all *Plasmodium* species, and results are reported according to the antigens identified (Table 1) [9, 10].

We investigated the effect of RDT implementation on clinical outcomes for children presenting to CHOP with malaria. To date, the clinical effect of RDT for malaria in a US setting had not been documented. It is important to measure the impact of RDT on clinical outcomes to support decisions regarding procurement at clinical laboratories.

METHODS

This was a retrospective cohort study of all pediatric patients diagnosed with malaria at CHOP (at either the main hospital or outpatient locations in the CHOP network). Throughout the study period, microscopy was performed immediately after receipt of the blood specimen (24 hours/day, 7 days/week). After RDT was implemented, RDT was always performed at the same time as the preparation of the slides. (Typically, slides were prepared, and RDT was performed while the slides were drying; after the RDT returned a result, the slides were stained and read).

Patients were included in this retrospective study if they had a CHOP laboratory result that was positive for malaria (according to blood smear and/or RDT) between January 1, 2000, and December 31, 2014, and if they were between 0 and 18 years of age at the time of the test. The clinical chart associated with that episode of malarial infection was reviewed. Patients were excluded from the analysis if they were treated before presentation to CHOP or if the providers did not treat for malaria when a false-positive result was suspected. Patient demographics, travel history, comorbidities, clinical variables, malaria test results, and outcome variables were abstracted from the medical charts and entered into a REDCap database [11]. Clinical variables included the following documented signs of severe malarial infection (according to Centers for Disease Control and Prevention criteria): signs of cerebral malaria (including

altered mental status, impaired consciousness, and seizures), anemia, hemoglobinuria, acute respiratory distress syndrome, coagulopathy, hypotension, acute kidney injury, metabolic acidosis, and hypoglycemia, as well as the level of parasitemia [12]. Outcome variables included time to first report of a positive malaria test result, time to initiation of antimalarial therapy, clinical indicators of disease severity 24 and 48 hours after presentation, need for exchange transfusion, time to resolution of parasitemia, and length of hospital stay. Clinical variables of disease severity were reviewed and adjudicated as necessary by 2 investigators.

This study was reviewed and approved by the CHOP Institutional Review Board.

Data Analysis

Demographic and clinical variables at presentation were summarized by standard descriptive statistics. Clinical outcomes were analyzed before and after the implementation of RDT. The primary outcomes of interest were time to first report of a positive malaria test result and time to initiation of antimalarial therapy. Secondary outcomes included number of signs of disease severity 24 and 48 hours after presentation, need for admission to an intensive care unit or exchange transfusion, time to resolution of parasitemia, and length of hospital stay. We measured the association between the use of RDT for diagnosis and all primary and secondary outcomes described earlier using χ^2 analysis for categorical variables and the Student *t* test for continuous variables. Any 2-sided *P* value of $<.05$ was considered statistically significant. Data were analyzed using Stata 13.1 (Stata Corp, College Station, Texas). We also adjusted for clinical covariates using multivariable linear regression.

We estimated that a sample size of at least 16 patients would be required in each group (ie, the pre-RDT and post-RDT groups) to detect a 20% difference in the mean time to initiation of antimalarial therapy with 80% power. Other clinical outcomes required greater numbers; we estimated that a sample size of at least 63 would be required in each group to detect a 20% difference in length of hospital stay with 80% power.

RESULTS

We identified 90 patients with laboratory-confirmed malaria who were seen at CHOP during the study period. RDT was performed for 55 patients. The sensitivity of the RDT was 98.1% and the positive predictive value was 96.3% compared with microscopy (Table 2). RDT had a sensitivity of 100% for detecting malaria in patients with *P falciparum* infection; a false-negative result occurred in 1 patient with non-*falciparum Plasmodium* malaria identified by blood smear. Treatment was initiated before arrival to CHOP for 5 patients, and 3 patients with a positive test result were not treated for malaria (including 2 patients with a false-positive RDT result with a concurrent negative

Table 1. Results Reported by the BinaxNOW Malaria Test

Test or Control Bands Detected	Test Result
C, T1, T2	<i>P falciparum</i> or mixed infection
C, T1	<i>P falciparum</i>
C, T2	<i>P vivax</i> , <i>P ovale</i> , or <i>P malariae</i>
C	Negative

Abbreviations: C, Control; T1, target 1 (histidine-rich protein 2); T2, target 2 (aldolase).

Table 2. Comparison of Malaria RDT Results With Those of Microscopy During the Post-RDT-Implementation Period

RDT Result	Microscopy-Positive Results (n)				Microscopy-Negative Results (n)	Total (n)
	<i>P falciparum</i> or mixed	<i>P vivax</i>	<i>P ovale</i>	Unable to Determine Species		
Positive						
<i>P falciparum</i>	45	0	0	0	2	47
Non- <i>falciparum Plasmodium</i> sp	1	3	2	1	0	7
Negative	0	0	0	1	0	1
Total	46	3	2	2	2	55

Abbreviation: RDT, rapid diagnostic testing.

microscopy result and 1 patient with a positive result by blood smear; the blood smear was repeated and returned a negative result, and the patient was not treated by the medical team [this patient had no further malaria testing or subsequent medical records at CHOP]). These patients were excluded from further analysis. Therefore, the final sample included 82 children, 32 of

whom presented with malaria before RDT implementation and 50 of whom presented after RDT implementation.

The 2 groups were generally similar with respect to their demographic and clinical characteristics (Table 3). Among all patients who presented with malaria, 52.4% were female, and the mean age was 8.2 years; patients in the RDT group were slightly

Table 3. Comparison of Patient Characteristics at Presentation Before and After Implementation of Malaria RDT*

Patient Characteristic at Presentation	Data for Patients With Malaria			<i>P</i> ^b
	All Patients with Malaria (n = 82)	Pre-RDT Group (n = 32)	Post-RDT Group (n = 50)	
Sex, female	43 (52.4)	14 (43.8)	29 (58.0)	.21
Age (mean [SD]) (years)	8.2 (4.9)	7.0 (4.9)	9.0 (4.7)	.06
Region of travel ^c				
West Africa	75 (91.5)	30 (93.8)	45 (90.0)	.69
East Africa	1 (1.2)	0	1 (2.0)	
Asia	6 (7.3)	2 (6.3)	4 (8.0)	
Definite <i>P falciparum</i> ^d malaria	66 (80.5)	22 (68.8)	44 (88.0)	.032 ^e
<i>Plasmodium</i> species				
<i>P falciparum</i>	66 (80.5)	22 (68.8)	44 (88.0)	.06
<i>Plasmodium</i> sp, unable to determine species	5 (6.1)	4 (12.5)	1 (2.0)	
Non- <i>falciparum Plasmodium</i> sp only	11 (13.4)	6 (18.8)	5 (10.0)	
<i>P vivax</i>	5 (6.1)	2 (6.3)	3 (6.0)	
<i>P ovale</i>	4 (4.9)	2 (6.3)	2 (4.0)	
<i>P malariae</i>	1 (1.2)	1 (3.1)	0	
Non- <i>falciparum Plasmodium</i> , unable to determine species	1 (1.2)	1 (3.1)	0	
Presence of clinical comorbidity ^f	15 (18.3)	6 (18.8)	9 (18.0)	.93
Parasitemia on initial smear				
Negative or <1.0%	44 (53.7)	16 (50.0)	28 (56.0)	.71
1.0%–4.9%	18 (22.0)	9 (28.1)	9 (18.0)	
5.0%–9.9%	10 (12.2)	4 (12.5)	6 (12.0)	
≥10.0%	10 (12.2)	3 (9.4)	7 (14.0)	
Admitted to hospital	72 (87.8)	27 (84.4)	45 (90.0)	.45
Admitted to ICU	25 (30.5)	7 (21.9)	18 (36.0)	.18
Severe malaria ^g	39 (47.6)	13 (40.6)	26 (52.0)	.31
Signs of severe malaria at presentation (mean [SD])	1.1 (1.6)	0.9 (1.3)	1.2 (1.7)	.33
Signs of severe malaria at presentation				
0 or 1	57 (69.5)	23 (71.9)	34 (68.0)	.90
2	13 (15.9)	5 (15.6)	8 (16.0)	
≥3	12 (14.6)	4 (12.5)	8 (16.0)	

Abbreviations: ICU, intensive care unit; RDT, rapid diagnostic testing; SD, standard deviation.

^a Values are number (percentage) unless otherwise indicated.

^b Using χ^2 or the Student *t* test, where appropriate.

^c Not documented for 1 patient.

^d Including mixed infections.

^e Significant result.

^f Including asthma (n = 8), sickle cell anemia (n = 4), latent tuberculosis infection (n = 2), and malignancy (n = 1).

^g As defined by the Centers for Disease Control and Prevention, at least 1 of the following signs of severe malaria: signs of cerebral malaria, anemia, hemoglobinuria, acute respiratory distress syndrome, coagulopathy, hypotension, acute kidney injury, metabolic acidosis, hypoglycemia, or a parasitemia level of ≥5%.

older (mean, 9.0 years) than those in the pre-RDT group (mean, 7.0 years) ($P = .06$). A large majority of the patients had traveled to West Africa (91.5%), and the most frequently documented country of travel was Liberia (36.6% [30 of 82]). One patient had traveled to East Africa, and 6 (7.3%) had traveled to Asia. Most (80.5%) of the patients were infected with *Plasmodium falciparum*. This proportion was higher in the post-RDT group (88.0% [44 of 50]) than in the pre-RDT group (68.8% [22 of 32]) ($P = .032$). The proportions of patients for whom the *Plasmodium* species could not be determined definitively were 4 of 32 (12.5%) in the pre-RDT group and 1 of 50 in the post-RDT group (2.0%) ($P = .053$). Other patients were infected with *P. vivax* (6.1%), *P. ovale* (4.9%), or *P. malariae* (1.2%). Clinical comorbidities included asthma (9.8%), sickle cell anemia (4.9%), latent tuberculosis infection (2.4%), and malignancy (1.2%). Twenty (24.4%) patients had a $\geq 5\%$ parasitemia level, and 10 (12.2%) had a $\geq 10\%$ parasitemia level. The majority (87.8%) of the patients were treated in an inpatient setting, and 25 (30.5%) patients required admission to an intensive care unit.

After implementation of RDT, the mean time to report of a positive malaria result was reduced dramatically, particularly among those with *P. falciparum* infection, from 10.4 to 0.9 hours ($P < .001$) (Table 4). The mean time to initiation of (or discharge from hospital on) antimalarial therapy was reduced from 13.1 to 6.9 hours among hospitalized patients ($P = .023$). We found no difference in the mean length of hospital stay (3.3 vs 3.6 days; P

$= .75$). We also found no significant difference in the change in the number of signs of severe malaria from presentation to 24 or 48 hours after presentation. Among the patients with an initial parasitemia level of $\geq 5\%$, the times to resolution of parasitemia were similar before and after RDT implementation (42.9 and 39.3 hours, respectively; $P = .59$).

In multivariable analyses, we constructed 3 separate models to evaluate the following outcomes: time to initiation of antimalarial therapy, length of stay, and mean reduction in number of clinical signs of severe malaria 48 hours after presentation (Table 5). The primary predictor was RDT use. Covariates were selected for their clinical significance and were consistent across each model; these covariates included disease severity at admission, presence of comorbidities, and patient age. An interrupted time series analysis was incorporated into each model, but it did not affect the overall findings. In the adjusted model, time to antimalarial treatment was reduced with the use of RDT, although statistical significance was not reached (coefficient, -3.923 ; $P = .47$). Nonsignificant variables ($P > .20$) were then removed from each model. Length of stay was not associated with the use of RDT, but it was positively associated with disease severity and the presence of clinical comorbidities. Mean reduction in signs of severe malaria from 0 to 48 hours after presentation also was not associated with RDT; it was associated only with the number of signs of severe malaria documented at presentation.

Table 4. Comparison of Clinical Outcomes Before and After Implementation of Malaria RDT

Clinical Outcome	Data for Patients With Malaria			P^a
	All Patients With Malaria (n = 82) (%)	Pre-RDT Group (n = 32) (%)	Post-RDT Group (n = 50) (%)	
Malaria result reporting (n)	81	31 ^b	50	
Time to a positive result (mean [SD]) (hours)	4.9 (7.0)	10.7 (7.9)	1.3 (2.7)	<.001 ^c
Patients with <i>P. falciparum</i> infection (n)	65	21	44	
Time to a positive result (mean [SD]) (hours)	4.0 (6.5)	10.4 (8.2)	0.9 (0.5)	<.001 ^c
Treatment end points (n)	81	31 ^d	50	
Time to initiation of antimalarial treatment or discharge with a prescription (mean [SD]) (hours)	9.3 (11.1)	12.6 (10.9)	7.3 (10.9)	.039 ^e
Hospitalized patients (n)	72	27	45	
Time to initiation of antimalarial treatment (mean [SD]) (hours)	9.2 (11.3)	13.1 (10.9)	6.9 (11.0)	.023 ^e
Need for exchange transfusion	4 (5.6)	2 (7.4)	2 (4.4)	.60
Length of hospital stay (mean [SD]) (days)	3.5 (4.0)	3.3 (3.8)	3.6 (4.2)	.75
Decrease in number of signs of severe malaria (mean [SD]) (hours)				
Presentation to 24 hours	0.7 (1.1)	0.8 (1.1)	0.7 (1.1)	.68
Presentation to 48 hours	1.1 (1.3)	0.9 (1.1)	1.2 (1.4)	.31
Patients with initial parasitemia level of $\geq 5\%$	20	7	13	
Time to resolution of parasitemia (mean [SD]) (hours)	40.5 (13.8)	42.9 (14.1)	39.3 (14.0)	.59
Decrease in number of signs of severe malaria (mean [SD])				
Presentation to 24 hours	1.4 (1.3)	1.7 (1.1)	1.2 (1.4)	.45
Presentation to 48 hours	2.4 (1.4)	1.9 (1.1)	2.6 (1.5)	.25

Abbreviations: RDT, rapid diagnostic testing; SD, standard deviation.

^a Using χ^2 or the Student t test, where appropriate.

^b Excluded from this analysis was 1 patient in the pre-RDT group who required confirmation by the Centers for Disease Control and Prevention (result reported >600 hours after presentation).

^c Significant result.

^d Treatment information on 1 patient in the pre-RDT group was missing.

Table 5. Multivariable Linear Regression Analyses for Key Indicators: Time to Antimalarial Treatment, Length of Stay, and Change in Signs of Severe Malaria From 0 to 48 Hours After Presentation

Analysis and Dependent Variables	Coefficient (95% CI)	P
Time to antimalarial treatment		
Model incorporating key clinical variables of interest		
Use of RDT	-3.923 (-14.670 to 6.824)	.469
Presence of clinical comorbidities	4.996 (-5.573 to 15.565)	.349
No. of signs of severe malaria at presentation	0.694 (-1.023 to 2.411)	.423
Age	-0.625 (-1.193 to 0.057)	.032
Time variable (months)	-0.031 (-0.231 to 0.169)	.759
Shifted time variable (months)	0.033 (-0.203 to 0.270)	.780
Constant	17.884 (4.687 to 31.082)	.009
R ²	0.147	
Model incorporating only those variables above with a P value of <.20		
Age	-0.642 (-1.177 to -0.107)	.019
Constant	14.381 (9.369 to 19.392)	<.001
R ²	0.0756	
Length of stay ^a		
Model incorporating key clinical variables of interest		
Use of RDT	0.025 (-0.266 to 0.316)	.866
Presence of clinical comorbidities	0.217 (-0.070 to 0.503)	.136
No. of signs of severe malaria at presentation	0.111 (0.064 to 0.158)	<.001
Age	-0.009 (-0.025 to 0.006)	.237
Time variable (months)	0.001 (-0.004 to 0.007)	.663
Shifted time variable (months)	-0.001 (-0.008 to 0.005)	.711
Constant	0.212 (-0.145 to 0.570)	.240
R ²	0.272	
Model incorporating only those variables above with a P value of <.20		
Presence of clinical comorbidities	0.184 (-0.090 to 0.458)	.186
No. of signs of severe malaria at presentation	0.104 (0.060 to 0.148)	<.001
Constant	0.259 (0.168 to 0.351)	<.001
R ²	0.248	
Decrease in signs of severe malaria from 0 to 48 hours after presentation ^b		
Model incorporating key clinical variables of interest		
Use of RDT	-0.056 (-0.165 to 0.052)	.303
Presence of clinical comorbidities	-0.031 (-0.138 to 0.076)	.569
No. of signs of severe malaria at presentation	0.138 (0.120 to 0.155)	<.001
Age	0.002 (-0.004 to 0.008)	.534
Time variable (months)	0.000 (-0.002 to 0.002)	.853
Shifted time variable (months)	0.001 (-0.002 to 0.003)	.458
Constant	0.041 (-0.092 to 0.175)	.537
R ²	0.823	
Model incorporating only those variables above with a P value of <.20		
No. of signs of severe malaria at presentation	0.141 (0.125 to 0.157)	<.001
Constant	0.063 (0.030 to 0.095)	<.001
R ²	0.814	

Abbreviations: CI, confidence interval; RDT, rapid diagnostic testing.

^a Length of stay was logarithmically transformed.

^b Decrease in signs of severe malaria was transformed by uniformly adding 1 and then performing logarithmic transformation.

DISCUSSION

At our center, malaria is encountered relatively commonly, given the frequent travel of families between Philadelphia and West Africa. We found a significant reduction in time to diagnosis and initiation of antimalarial treatment since the introduction of RDT. RDT did not seem to have a significant effect on our secondary clinical outcomes of interest (such as length of hospital stay or signs of clinical severity 48 hours

after presentation). These outcomes seemed to be driven by disease severity at the time of presentation rather than by access to RDT.

At our center, the post-RDT-implementation period saw a greater frequency of malaria cases and a greater proportion of infections attributable to *P falciparum*. Both trends also were observed nationally over the same time period [3]. It is possible that the identification of *P falciparum* was facilitated better by RDT than by microscopy. Although the greater proportion of

severe malaria cases at our center in recent years did not reach statistical significance, it did emerge as the primary driver of clinical outcomes as measured by our analysis.

Although we did not detect a change in secondary clinical outcomes after the implementation of RDT, this result did not rule out a true clinical benefit of the test. The greater proportion of *P falciparum*-attributable cases of malaria in the post-RDT-implementation period at our center might have biased against detecting an effect of RDT on secondary clinical outcomes because *P falciparum* is associated with more severe disease. Length of hospital stay might not have been a precise representation of clinical improvement, given that this outcome can be affected also by timing of the performance of follow-up blood smears. Likewise, the number of signs of severe malaria might not have been an optimal measure of clinical improvement. In addition, it is likely that our sample size was not sufficient to detect modest improvements in secondary clinical outcomes. It is not clear why time to antimalarial treatment was not significantly associated with RDT in multivariable analysis, but it might have been related to the large standard error of this outcome and the addition of multiple covariates to the model, which reduced our ability to detect a significant difference.

To our knowledge, ours is the first study to have examined the clinical effect of malaria RDT at a children's hospital in a region in which malaria is not endemic and the first to evaluate the clinical impact of RDT in the US. RDT for malaria was developed primarily to improve diagnosis where malaria is most prevalent. In such settings, the tests might be particularly useful for their negative predictive value, which prompts consideration of other diagnoses [13]. At our children's hospital in a region of nonendemicity, RDT enables rapid identification of children with malaria who present with nonspecific symptoms and for whom urgent diagnosis and treatment are critical. Indeed, we found in this study that children with malaria were diagnosed with malaria and started on treatment more quickly when RDT was used than when microscopy was used alone.

Two false-positive RDT results were identified by care providers. One false-negative RDT result was returned for a patient with malaria; the species could not be determined by microscopy. The malaria RDT is known to have decreased sensitivity for detecting non-*falciparum* *Plasmodium* species and cannot identify malaria infection that involves more than 1 *Plasmodium* species [5, 14]. Because of these observed limitations, RDT always must be combined with the examination of a Giemsa-stained blood smear [6, 15]. When RDT is implemented in a setting in which malaria is not endemic, it should not replace smear microscopy, which provides confirmation of RDT results, species identification (particularly for non-*falciparum* *Plasmodium* species not differentiated by RDT), and estimation of parasitemia [15]. Indeed, after initial RDT, only blood smears should be repeated in subsequent testing to monitor parasite load in response to therapy. As shown in this study, the critical

benefit of also performing RDT in the initial laboratory evaluation is that it provides more rapid identification of malaria infection while definitive smear microscopy results are pending. This utility might be particularly beneficial when expertise in the examination of blood smears for diagnosing malaria is more limited.

According to the most recent review available, the majority of US clinical laboratories have not implemented malaria RDT [8]. Although malaria remains an infrequent diagnosis in this setting, its incidence in the United States is increasing, and this trend is expected to continue given the increasing pace of global travel and migration [16]. Several studies have pointed to the risk of misdiagnosing or delaying diagnosis for children who present with malaria in a setting in which it is not endemic [4, 17, 18]. Furthermore, when malaria is seen infrequently, there might be a lack of experienced laboratory staff available to readily identify *Plasmodium* species on blood smears, particularly if a child presents at an off-hour or overnight [6]. Therefore, the reduced times to diagnosis and initiation of treatment observed at our center after implementation of malaria RDT should inform other clinical centers (particularly those that serve large immigrant populations) considering adopting the test. The potential usefulness of the test to effectively rule out *P falciparum* malaria also should be considered in such settings, although we did not evaluate this aspect in our study.

There are limitations to this study. Its retrospective design depended on chart review and might have limited our ability to characterize clinical outcomes. Although we used objective criteria for our clinical signs of interest, the measurement or documentation of each of these factors over the study time period might have been different. Our study population was derived from 1 pediatric center, which might have affected the generalizability of our results. It is possible that unrelated trends at our center resulted in the more rapid initiation of antimalarial medication concurrent with the implementation of RDT; however, we found the abrupt and marked reduction in the time to initiation of antimalarial treatment to be compelling evidence of its impact. We evaluated multiple measures of clinical improvement (time to resolution of parasitemia, length of hospital stay, total clinical signs of severe disease), but we might have missed other important clinical outcomes, such as changes in antibiotic use for presumptive bacterial infection while awaiting results of malaria test results.

In conclusion, the results of this study indicate that the implementation of malaria RDT in a US children's hospital resulted in shorter time to malaria diagnosis and more timely initiation of antimalarial treatment. When coupled with a high index of suspicion for malaria in children who present with fever, gastrointestinal symptoms, or nonspecific symptoms and have a history of travel to a region of malaria risk, RDT can help to

optimize the care of children with malaria in settings in which the disease is not endemic.

Notes

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