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Screening for Chronic Infectious Diseases by Serology in Those Presenting with Malaria in London, United Kingdom

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Abstract. The United Kingdom's cases of malaria infection are primarily acquired in sub-Saharan Africa, with the majority of infections presenting in London.[1] When patients go to a hospital with malaria, there is a screening opportunity for other geographically associated chronic infections. We identified patients who were diagnosed with malaria after presenting to our emergency department in London over a 2-year period, to assess whether there may be clinical benefit in screening for chronic viral (hepatitis B, hepatitis C, HIV) or parasitic (schistosomiasis, strongyloidiasis) infection in this cohort. Over this period, 131 patients were diagnosed with malaria. Crude seropositivity rates for HIV, hepatitis B, and strongyloidiasis were higher than expected compared with local population estimates, 7 and 28 times higher for HIV and hepatitis B, respectively. Those patients with previously unidentified cases were offered appropriate treatment. These findings support the potential clinical and public health benefits of screening for other infectious diseases in the context of a malaria diagnosis.

BACKGROUND

Malaria is one of the most commonly diagnosed imported infections in the United Kingdom,[2] with 85% of cases acquired through travel to Africa, predominantly among people visiting friends and relatives (VFR).[1] These cases can be an opportunity to screen for other treatable infectious diseases that are endemic in the same geographical areas. This general approach is broadly endorsed in the British Infection Association malaria guidelines, which advise to "consider other travel-related infections" when assessing a patient with possible malaria.[2]

Currently there is no standardized screening program or guideline in place for those patients presenting with malaria in the United Kingdom. However, there is a significant body of work exploring the feasibility and cost-effectiveness of opportunistic infectious disease screening in other groups associated with travel, most commonly in migrant groups at a point of entry into a country. A systematic review of infectious disease screening for migrants to Europe[3] concluded that there is reasonable evidence for the cost-effectiveness of such screening programs, though this is likely to vary depending on which migrant groups and diseases are targeted. Guidelines from the European Centre for Disease Control in relation to newly arrived migrants (i.e., those within 5 years of arrival into a country) recommend screening for TB/latent TB, HIV, hepatitis B, hepatitis C, strongyloidiasis, and schistosomiasis, as they conclude that this is likely to be cost-effective.[4] United Kingdom guidance[5] highlights the need to consider infectious disease testing in migrants, though it is not prescriptive about what form this surveying should take.

Those people presenting with malaria in the United Kingdom tend to be VFR travelers.[6] Of all United Kingdom malaria cases in travelers in 2018 whose country of origin was known, over two-thirds were born in Africa,[1] and this proportion is even higher in London.[6] This group clearly shares risk factors for some endemic infectious diseases with newly arrived migrants. We therefore sought to explore whether testing malaria patients for treatable infectious diseases that are endemic in regions of malaria transmission might represent a valuable screening opportunity.

STUDY FINDINGS

Cases of malaria diagnosed between January 2017 and December 2018 at Guy's and St. Thomas' NHS Foundation Hospital Trust were identified retrospectively and records examined for serological test results for hepatitis B, hepatitis C, HIV, *Strongyloides.* and schistosomiasis during the same presentation. For cases with positive test results, clinical notes were reviewed to determine the clinical impact of this diagnosis. Data were made anonymous for processing and analysis. Local audit approval processes were completed prior to data collection (audit approval reference number 10748).

Over the 2-year study period, 131 patients were diagnosed with malaria after presenting to the emergency department. Details of the age, ethnic background, and travel destination of these patients are summarized in Table 1. Table 2 illustrates the number of patients tested for each condition, and the number and proportion of positive test results.

Most cases of malaria were reported following travel to Africa, predominantly West Africa (89%). We did not capture their reason for travel in our cohort.

Of the 14 patients aged under 16 years, two (14%) were tested for blood-borne viruses, and one (7%) for strongyloidiasis and schistosomiasis. All test results in this age group were negative.

Four patients had positive HIV serology; all were known to be HIV-positive. In two cases the results were indeterminate or the sample insufficient; these tests were not repeated (lost to follow up). Of the seven patients with positive hepatitis B surface antigen (HBsAg), two were new diagnoses. Unfortunately, both patients were lost to follow up. One-third of the patients with malaria were screened for hepatitis C, and none had hepatitis C IgG detected. All three of the patients with positive *Strongyloides* serology attended follow up and were treated for the condition. Two patients had indeterminate *Strongyloides* tests, which were negative on repeat testing. Of the four patients with positive *Schistosoma* serology, two were treated and two were lost to follow up without having received treatment. Two patients had indeterminate schistosomiasis tests, which were negative on repeat testing. These false

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TABLE 1
Age, ethnicity, and travel destination of patients presenting with malaria between January 2017 and December 2018 (n = 131)

Age, median (interquartile range)	45 (31–57)
Ethnicity, *n* (%)	
Black African	125 (95)
Asian	2 (2)
White British	2 (2)
Other white background	2 (2)
Travel destination, *n* (%)	
Ghana	16 (12)
Ivory Coast	14 (11)
Nigeria	51 (39)
Sierra Leone	27 (21)
Other West Africa	8 (6)
Other Africa	11 (8)
India	2 (2)
Not specified	2 (2)

positives are a foreseeable risk of screening programs, particularly in the context of malaria where false positive serological tests are not uncommon in the acute stage of the illness.[7]

Our data show a high rate of testing for HIV (85%), likely driven by knowledge of local disease prevalence (extremely high prevalence at more than five people per 1,000)[8] and by hospital policy (since 2015, all adult patients having blood tests in the emergency department are tested for HIV on an "opt out" basis). There were lower testing rates for the other blood-borne viruses (despite a routine hepatitis B and C testing protocol in the emergency department during 7 months of our 2-year study period), and far lower rates for strongyloidiasis and schistosomiasis, presumably reflecting a lower index of clinical suspicion for these conditions in patients presenting with malaria. The retrospective nature of this study limits evaluation of the rationale for testing strategy in each patient, particularly in the absence of an existing screening policy for the population in question.

Despite the relatively low rate of testing for some conditions, we nonetheless found crude rates of seropositivity in our sample that were higher than estimates for these diseases in the local population. In our sample, 4% of those tested for HIV (or 3% of all malaria diagnoses) had a positive result, which would represent a prevalence seven times higher than the London average of 0.57% among those aged 15–59.[8] However, prevalence in the hospital's surrounding area is higher than the London average.[8] Selection bias could also have led to an overestimate in HIV prevalence because of the hospital's specialist HIV center, as it is likely that people in our sample with known HIV were already attendees at the hospital and therefore likely to present there with other medical problems.

TABLE 2
Serological test results for patients presenting with malaria between January 2017 and December 2018 (n = 131)

Serological test	Tested, *n* (% of all malaria cases)	Positive tests, *n* (% of those tested)	Positive tests, % of malaria cases	Indeterminate result or sample insufficient, *n*
HIV	111 (85%)	4 (4%)	3%	2*
Hepatitis B	49 (37%)	7 (14%)	5%	0
Hepatitis C	44 (34%)	0	–	0
Strongyloidiasis	37 (28%)	3 (8%)	2%	2†
Schistosomiasis	27 (21%)	4 (15%)	3%	2†

* Test not repeated (lost to follow up).
† Negative on repeat testing.

Hepatitis B prevalence in our hospital trust's population was recently estimated at 0.5% based on weighted prevalence of HBsAg positivity.[9] In our cohort 14% of those tested (or 5% of all malaria diagnoses) were HBsAg positive—a finding 28 times higher than the population estimate. The crude prevalence of positive hepatitis C serology in the same population has been estimated as 2.0%,[9] though we identified no positive cases in our cohort, which may be related to the small sample size.

We did not discover any recent studies providing directly comparable prevalence estimates for the parasitic infectious diseases in those presenting to secondary care. In a study undertaken in an acute care setting in the same city as our hospital,[10] returning travelers had positive *Strongyloides* serology in 31 of 3,306 attendances (0.94% proportionate morbidity). However, the study does not report what proportion of attendees were tested for *Strongyloides* to yield this rate of seropositivity, and a far lower proportion of cases were in VFR travelers compared with our sample. A recent systematic review[11] cites prevalence estimates of strongyloidiasis in European countries as ranging widely from 0.8–77%, depending on the population in question and the detection methods used. Our study's estimate of 8% (or 2% of all malaria diagnoses) appears reasonable, in the context of this heterogeneous data.

Similarly, we could not identify any directly comparable studies to help evaluate our findings regarding schistosomiasis. A longitudinal observational study from the Hospital for Tropical Diseases (HTD) in London found that people diagnosed with schistosomiasis made up approximately 4.2% of all patients presenting to their outpatient department between 2000 and 2012, and the majority of those were returning travelers rather than migrants entering the country. [12] This is similar to the 3% of malaria patients who tested positive for schistosomiasis in our sample. However, these groups (those presenting to secondary care with malaria versus those presenting to a specialist tropical diseases hospital outpatient department) are likely to be significantly different, and in neither setting was schistosomiasis screening routine so we cannot infer prevalence in either population. Notably, the HTD study[12] found that the most common presentation of schistosomiasis was asymptomatic (36.1%), with cases diagnosed incidentally or following routine post-travel screening, which highlights a potential benefit of screening.

Risk-based screening involves screening a population with one illness based on increased odds of shared risk factors for other illnesses. For example, a sexual health clinic will routinely test for a range of sexually transmitted infections, while clinicians may be prompted to consider viral hemorrhagic fever risk when testing for malaria because of the overlapping geography. This approach can be beneficial for the individual as well as for public health, but these benefits must be balanced against the acceptability of risk-based screening to patients. An ongoing large study of community-based testing of migrants for infectious diseases in Leicester (United Kingdom)[13] aims to contribute some valuable data to this question through a qualitative sub-study that will specifically examine the acceptability of screening among target groups.

To further explore the potential for screening for infectious diseases among those presenting to hospital with malaria, a

prospective study with a defined opt-out screening protocol would be of benefit. This should include assessment of participants' migration status and purpose for travel as well as an evaluation of the acceptability of screening based on these factors. Screening protocols should incorporate potential mitigation of the risk of patients being lost to follow up, which may limit the otherwise potentially significant clinical and public health benefits of screening for infectious diseases in this context.

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