Prevalence of Malaria and Covid-19 in Febrile Patients in Lomé, Togo in 2020

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Abstract
Purpose The objective of this study was to estimate the prevalence of malaria and Covid-19 by PCR and serological tests in febrile patients in Lomé.
Methods A cross-sectional study was conducted from September 1 to October 31, 2020 in febrile patients ≥ 10 years in three health facilities in Lomé. Finger stick blood was collected to detect Plasmodium spp. using thin/thick smear and venous blood on EDTA tubes to test for malaria Histidin-Rich-Protein-2 antigen using rapid diagnostic tests (RDT) and SARS-CoV-2 antibodies specific immunoglobulin (Ig) M and G. Detection of SARS-CoV-2 in nasopharyngeal samples was performed by rRT-PCR using GeneXpert.
Results A total of 243 participants (61.7% of female) with median age 28 years (IQR 18–41) were included in the study. Prevalence of malaria was 25.1%, 95% CI [19.8–31.0] and 30.4%, 95% CI [24.7–36.7] for thin/thick smear and rapid malaria test, respectively. Eighteen patients (7.4%, 95% CI [4.4–11.5]) were positive for SARS-CoV-2 and forty-two (17.3%, 95% CI [12.8–22.6]) were positive for IgM and/or IgG against SARS-CoV-2. SARS-CoV-2 IgM seroprevalence was significantly higher in malaria RDT positive participants (33.8% vs. 10.1%, \( p < 0.001 \)).
Conclusion This study confirms a possible cross-reactivity between Covid-19 and malaria in case of single use of rapid tests, suggesting a possible past contamination. In case of clinical signs related to Covid-19 in malaria-endemic areas, PCR screening should be requested in order to identify and isolate patients.
Keywords Prevalence · Covid-19 · Malaria · Febrile patients · Togo

Introduction
Despite several decades of malaria control efforts, malaria-related mortality and morbidity remain a public health problem in the world. Indeed, more than half of the population in the world, living in 100 countries, is exposed to malaria and the World Health Organization (WHO) African region carries a disproportionate burden of this disease. In fact, every year, 93% of malaria cases are notified in Sub-Saharan Africa (SSA), with 213 million cases in 2018 and 1.5–2.7 million deaths. Over 99% of malaria cases in Africa are attributed to Plasmodium falciparum [1].

In December 2019, a rapidly increasing number of patients presenting with fever and respiratory symptoms including cough and shortness of breath was observed in China [2]. This outbreak of pneumonia was caused by a "new virus" (SARS-CoV-2) and this ailment would later
be called coronavirus disease 2019 (COVID-19) [3]. This outbreak had spread rapidly to all continents and on March 11th, 2020, the WHO declared the outbreak of Covid-19 to be a pandemic. As of April 30th, 2022, more than 510 million cases of Covid-19 have been reported worldwide with more than 6 million deaths [4]. In the WHO African region, most affected with malaria, nearly 8.5 million cases of Covid-19 with more than 1.6 million deaths have been reported [4]. The possible devastating consequences of the association Malaria–Covid-19 in these countries should be considered [5, 6]. Malaria and Covid-19 present similar symptoms such as fever, asthenia and myalgia. This represents a diagnosis challenge for healthcare workers to distinguish between Covid-19 and malaria.

In Togo, the first positive case of Covid-19 was notified on March 05, 2020 and since then, all 39 districts in the country have reported confirmed cases. As of April, 30th, 2022, nearly 37,000 cases had been confirmed including 273 deaths in Togo [7].

In August 2020, with the beginning of the rainy season which is the rainy season characterized by a recrudescence of malaria cases, there was also an increase in the number of Covid-19 cases in Togo. As the majority of local communities have a denial of the Covid-19, in the presence of the signs common to malaria and Covid-19, the first reflex of the populations and health workers was to use an antimalarial drug. This has been exacerbated by the fact that the initial therapeutic protocol adopted by Togo to treat Covid-19 cases is the combination Hydroxychloroquine–Azithromycin [8].

In order to improve the management of febrile diseases in the context of Covid-19 and since antibody-based serologic diagnostics reveal unspecific reactivity in up to 25% [9] of febrile patients, possibly due to acute malaria, this study was carried to estimate the prevalence of malaria and Covid-19 in febrile patients in Lomé.

Study Design
A cross-sectional study was conducted from September 1st to October 31st, 2020 in Lomé, capital of Togo. Togo is West African country where malaria is endemic and stable with seasonal recrudescence. The country is characterized by two types of climates: a sub-equatorial one in the south and a tropical one in the northern part. Malaria remains a major public health problem in the country, with 2.4 million estimated cases of malaria in 2019 nationwide and a 3.2% mortality rate. Children under 5 years and pregnant women are the most affected, representing 58.0% and 4.0% of confirmed cases, respectively [10].

The study was conducted in three health structures: the community health center of Legbassito (CHC Legbassito), the Hospital of Bè, and the teaching hospital “Centre Hospitalier Universitaire Campus” (CHU Campus), which represent the first, second and third levels of the Togolese health pyramid, respectively. The three health facilities are located in the health region of Grand-Lomé which represents the capital city of Lomé and its suburbs. The CHU Campus and Hospital of Bè are located in urban area while the CHC Legbassito is in a semi-urban area. In 2019, there were 532 malaria cases and 24 deaths reported in CHU Campus while 388 cases and 42 deaths in the Hospital of Bè. In the CHC Legbassito which is a health facility of first contact with patients and where patients are not hospitalized, 6460 malaria cases were reported in 2019.

Study Population and Sampling
The target population included all febrile patients in Lomé. Inclusion criteria were: (a) consulting in one of the three participating health facilities; (b) being at least 10 years old, regardless of sex; (c) having febrile syndrome with high suspicion of malaria; and (d) giving an informed consent, signed by adults or, in the case of children, by their guardians or parents. Recruitment was carried out based on convenience sampling and all patients meeting inclusion criteria were approached to participate in the study.

For an expected proportion of Covid-19 cases among all included patients (p) of 25%, a precision of 5%, a risk of error (α) of 5% and a 10% non-response rate, based on the single proportion population formula, the minimum sample size was 217.

Data Collection
Questionnaire
A structured questionnaire was used to collect information on sociodemographic characteristics, clinical signs presented, history of the disease, existence of other diseases and current treatments if applicable.

Laboratory Testing
Each patient had a capillary blood sampling for a thick/thin blood smear to test for Plasmodium spp. infection and a nasopharyngeal swab for SARS-CoV-2 infection. Molecular research for SARS-CoV-2 was performed at the Mycobacteria Laboratory of the teaching hospital ‘Centre Hospitalier Universitaire Sylvanus Olympio’ by GeneXpert (Cepheid®, CA, USA) and the reading of a blood smear slides for the identification of plasmodial species and the estimation of the parasite density (PD) was performed at the laboratory.
of the National Malaria Control Program (NMCP). Also, for each patient included in the study, venous blood samples were collected on EDTA tubes for the detection of malaria Histidine-Rich-Protein-2 (HRP2) antigen by rapid diagnostic tests (RDT) for malaria (SD Bioline® Malaria Ag Pf RDT, Republic of Korea) and for the detection of SARS-CoV-2 specific immunoglobulin (Ig) M and G (Clungène Rapid Test Covid IgM/IgG test®, Republic of China). Malaria RDTs used in this study were those validated by the NMCP and the SARS-CoV-2 RDTs used were evaluated and validated by the Togolese regulatory authorities with a sensitivity of 77% and a specificity of 95%. All tests and the interpretation of their results were carried out according to the instructions of the manufacturers.

Data Management and Statistical Analysis

Data were entered into a computerized database while maintaining confidentiality, in accordance with Togo’s data protection legislation. Statistical analyses were performed using R software version 1.3.959 and prevalence were presented as proportions with their 95% confidence interval (95% CI). The prevalence of each infection (SARS-CoV-2, malaria) was defined as the ratio of the number of participants tested positive for one of the markers tested to the total number of patients tested. Comparison of categorical variables was performed with Chi-square test or Fisher’s exact test.

Results

Sociodemographic Characteristics

A total of 243 participants with a median age of 28 years (IQR 18–41) were included in the study. Women represented 61.7% (n=150) of the sample. The majority of study participants were Togolese (n=236; 97.1%), more than half (n=127; 52.3%) were married, and a fifth (n=48; 19.8%) of participants had university level education. The sociodemographic characteristics of participants are summarized in Table 1.

Prevalence of Malaria

The overall prevalence of malaria was 25.1%, 95% CI [19.8–31.0] and 30.4%, 95% CI [24.7–36.7] for thick smear and rapid malaria test, respectively (Table 2). P. falciparum and P. malariae were the species identified in 95.1% and 1.6% % of cases, respectively. The association P. falciparum + P. malariae was found in 3.2% and the mean of parasitemia (geometric mean) was 6176.93 /µL with extremes of 16/µL and 464,727/µL.

Table 1 Sociodemographic characteristics of patients (N=243)

| Frequency (n) | Proportion (%) |
|--------------|---------------|
| Age (years)  |               |
| 10–19        | 68            | 28.0 |
| 20–29        | 62            | 25.5 |
| 30–39        | 42            | 17.3 |
| 40–49        | 40            | 16.5 |
| ≥ 50         | 31            | 12.7 |
| Sex          |               |
| Female       | 150           | 61.7 |
| Male         | 93            | 38.3 |
| Nationality  |               |
| Other        | 7             | 2.9  |
| Togolese     | 236           | 97.1 |
| Marital status|              |
| Single/divorced/widowed | 116 | 47.7 |
| Married      | 127           | 52.3 |
| Education level|            |
| None         | 20            | 8.2  |
| Primary      | 58            | 23.9 |
| Secondary    | 117           | 48.1 |
| University   | 48            | 19.8 |
| Type of residence|       |
| Common courtyard | 131 | 53.9 |
| Individual court | 112 | 46.1 |
| Type of symptoms presented | |
| Fever        | 241           | 99.2 |
| Headache     | 169           | 69.5 |
| Tiredness    | 123           | 50.6 |
| Myalgia      | 94            | 38.7 |
| Cough        | 32            | 13.2 |
| Rhinorrhea   | 21            | 8.6  |
| Number of symptoms | |
| 1            | 34            | 14.0 |
| 2            | 74            | 30.5 |
| 3            | 57            | 23.5 |
| ≥ 4          | 78            | 32.0 |

Malaria and Covid-19 results, according to sociodemographic characteristics, are presented in Table 3. There was no difference of malaria prevalence according to sex. There was a statistically significant decrease in malaria prevalence with age: it varied from 41.2 in 10–19 years old to 12.9% in 50 years old and over using thick/thin smear (p=0.002) and from 57.4 to 9.7% (p < 0.001) using the RDT (Table 3).

Prevalence of Current SARS-CoV-2 Infection

Eighteen patients (7.4%, 95% CI [4.4–11.5]) had a positive rRT-PCR test for SARS-CoV-2 at the time of recruitment. Forty-two patients (17.3%, 95% CI [12.8–22.6])
were positive for IgM or IgG against SARS-CoV-2 (Table 2). SARS-CoV-2 rRT-PCR was more positive in malaria negative participants especially when diagnosed by malaria RDT (10.1% vs. 1.4%, \( p = 0.034 \)). In addition, the SARS-CoV-2 IgM seroprevalence was significantly higher in malaria RDT positive participants (33.8% vs. 10.1%, \( p < 0.001 \)). Highest prevalence of SARS-CoV-2’s IgM and malaria (both thin smear and RDT) in the community health center of Legbassito recorded. Prevalence of Covid-19 based on rRT-PCR was higher in patients aged 40–49 years and \( \geq 50 \) years with 15.0% and 12.9%, respectively.

### Discussion

This study, which was conducted in the context of a Covid-19 pandemic in febrile patients seen in health facilities in the capital of Togo, reported a prevalence of malaria of 25.1% using Thick/Thin smear and a prevalence of SARS-CoV-2 of

| Table 2 | Thick/thin smear and Malaria rapid diagnostic test results according to Covid-19 results |
|---------|-----------------------------------------------------------------------------------------|
| SARS-CoV-2 | Thick/thin smear for malaria | p* | RDT for malaria | p* |
|          | Negative | Positive | Total | Negative | Positive | Total |
| rRT-PCR  | (n = 182) | (n = 61) | (n = 243) | (n = 169) | (n = 74) | (n = 243) |
| Negative | 166 (91.2) | 59 (96.7) | 225 (92.6) | 152 (89.9) | 73 (98.6) | 225 (92.6) |
| Positive | 16 (8.8) | 2 (3.3) | 18 (7.4) | 17 (10.1) | 1 (1.4) | 18 (7.4) |
| IgG      | 0.531 | 0.181 |
| Negative | 173 (95.1) | 56 (91.8) | 229 (94.2) | 162 (95.9) | 67 (90.5) | 229 (94.2) |
| Positive | 9 (4.9) | 5 (8.2) | 14 (5.8) | 7 (4.1) | 7 (9.5) | 14 (5.8) |
| IgM      | 0.247 | <0.001 |
| Negative | 154 (84.6) | 47 (77.0) | 201 (82.7) | 152 (89.9) | 49 (66.2) | 201 (82.7) |
| Positive | 28 (15.4) | 14 (23.0) | 42 (17.3) | 17 (10.1) | 25 (33.8) | 42 (17.3) |
| IgM and/or IgG | 0.247 | <0.001 |
| Negative | 154 (84.6) | 47 (77.0) | 201 (82.7) | 152 (89.9) | 49 (66.2) | 201 (82.7) |
| Positive | 28 (15.4) | 14 (23.0) | 42 (17.3) | 17 (10.1) | 25 (33.8) | 42 (17.3) |

*Chi-square or Fisher test; RDT for Malaria: Malaria rapid diagnostic test

| Table 3 | Malaria and Covid-19 results according to sociodemographic characteristics |
|---------|--------------------------------------------------------------------------------|
| N       | Malaria | SARS-CoV-2 |
|         | Thick/thin smear+ | RDT+ | IgM+ | IgG+ | rT-PCR+ |
| Sex     | n | % | p* | N | % | p* | N | % | p* | N | % | p* | n | % | p* |
| Female  | 150 | 26.0 | 29.3 | 0.797 | 0.735 | 0.882 | 1.000 | 0.845 |
| Male    | 93  | 23.7 | 30.3 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| Age (years) | n | % | p* | n | % | p* | n | % | p* | n | % | p* |
| 10–19   | 68  | 41.2 | 39.7 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| 20–29   | 62  | 27.4 | 30.6 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| 30–39   | 42  | 14.3 | 16.7 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| 40–49   | 40  | 15.0 | 15.0 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| \( \geq 50 \) | 31  | 12.9 | 9.7 | 0.002 | <0.001 | <0.001 | 0.089 | 0.059 |
| Location | Campus | HBE | LEG | n | % | p* | n | % | p* | n | % | p* | n | % | p* |
| Campus  | 32  | 3.1 | 3.1 | <0.001 | <0.001 | <0.001 | 0.315 | 0.025 |
| HBE     | 66  | 9.1 | 10.6 | 0.002 | <0.001 | <0.001 | 0.315 | 0.025 |
| LEG     | 145 | 37.2 | 45.5 | 0.002 | <0.001 | <0.001 | 0.315 | 0.025 |

*Chi-square or Fisher test; RDT for Malaria: Malaria rapid diagnostic test

were positive for IgM or IgG against SARS-CoV-2 (Table 2). SARS-CoV-2 rRT-PCR was more positive in malaria negative participants especially when diagnosed by malaria RDT (10.1% vs. 1.4%, \( p = 0.034 \)). In addition, the SARS-CoV-2 IgM seroprevalence was significantly higher in malaria RDT positive participants (33.8% vs. 10.1%, \( p < 0.001 \)). Highest prevalence of SARS-CoV-2’s IgM and malaria (both thin smear and RDT) in the community health center of Legbassito recorded. Prevalence of Covid-19 based on rRT-PCR was higher in patients aged 40–49 years and \( \geq 50 \) years with 15.0% and 12.9%, respectively.

### Discussion

This study, which was conducted in the context of a Covid-19 pandemic in febrile patients seen in health facilities in the capital of Togo, reported a prevalence of malaria of 25.1% using Thick/Thin smear and a prevalence of SARS-CoV-2 of
7.4% using rRT-PCR. The prevalence of Covid-19 specific IgM/IgG was higher for IgM than for IgG (17.3% vs. 5.8%). The prevalence of malaria and parasite density decreased with age while that of SARS-CoV-2 increased with age, and the prevalence was highest in patients 40 years and older. This high prevalence of malaria found in our study shows that malaria remains highly endemic in Togo despite the control activities implemented for several years. Indeed, in our study all age groups were affected. The highest prevalence of malaria (41.2%) was observed in patients aged 10–19 years. This prevalence is high compared to that prevalence (28%) reported in the malaria indicator survey conducted among children aged 06–59 months in Togo in 2017 [11]. In fact, our study focused on febrile cases and on malaria disease cases while the malaria indicator survey assessed malaria infestation. In addition, the semi-urban location of CMS Legbassito on the outskirts of the capital city is another factor that may explain the high prevalence in this structure. The prevalence of malaria estimated using RDT confirmed this trend, with a relatively higher proportion than that by Thick/Thin smear (30.4% vs. 25.1% for Thick/Thin smear).

In a study conducted in Togo in 2020, two months after the first confirmed case of Covid-19 in high-risk patients in Lomé, a prevalence of SARS-CoV-2 of 0.7% [12] was reported. In febrile patients included in our study, six months after the first case reported in Togo, the prevalence was 10 times higher than that observed in high-risk patients, indicating the important evolution of the pandemic in Togo. This difference could also be due to the type of sampling and the PCR platform used. In our study, we used nasopharyngeal swab and the GeneXpert platform for the diagnosis of SARS-CoV-2, whereas Halatoko et al. used oropharyngeal swab and the classical PCR platform. Indeed, several studies have reported that the sensitivity of viral genome detection is significantly better with GeneXpert and nasopharyngeal swabs [13, 14]. However, the hospital prevalence observed in our study remains lower than that reported in countries where malaria is not endemic [15, 16].

Indeed, there is a hypothesis that the circulation of SARS-CoV-2 is lower in malaria-endemic areas [17]. For example, in the Italian population, the spread of SARS-CoV-2 in the first wave (until mid-July 2020) was more limited in provinces where malaria was endemic in the early twentieth century. Some genetic variants, including ACE2, which are thought to be protective against malaria could also play a protective role against SARS-CoV-2, explaining the low spread of the Covid-19 infection in some region in Italy with history of high prevalence of malaria, similar to Togo [17]. The identification of genes known to be associated with malaria or COVID-19 is necessary. This knowledge of common genes would allow the identification or proposal of new molecules, or even the repositioning of existing drugs in the management of COVID-19 [18].

Performing thick/thin smear in the presence of a febrile syndrome is almost systematic in the health structures of Togo. This is not the case for SARS-CoV-2 screening despite a pandemic context in the country since March 2020. The high prevalence of SARS-CoV-2 found in our study should lead to a change in the diagnostic approach to any febrile case received in consultation. Currently in Togo, the diagnosis of Covid-19 is focused on the screening of patients with respiratory symptoms such as cough in a febrile context or people who have been contacts of a confirmed case [19]. However, this approach would miss more than half of the people infected with SARS-CoV-2 [20], especially since there is variability and evolution of the clinical signs of this virosis and the respiratory signs are not necessarily the main clinical features [21]. Although the patients included in our study were febrile, testing for SARS-CoV-2 was not routinely prescribed. This readjustment of the diagnostic approach is necessary for patients aged 40 years and older, since in our study, the prevalence of SARS-CoV-2 by rRT-PCR increased with age. Furthermore, a systematic review on fever in Covid-19 patients showed that the likelihood of fever increases with age, whereas fever due to malaria decreases with age [22].

In our study, the prevalence of SARS-CoV-2 in the age group 10–19 years is similar to that reported in a study in China with 1% in the same age group [23] and in the USA for the age group 5–17 years with 1.3%. In the latter study, the average positivity rate was 14.4% [24]. Most studies have shown that children and adolescents are less likely to be infected with SARS-CoV-2, with a mean probability of death of 0.2%, while older people would develop a severe form of the disease [25]. It is therefore necessary that any febrile syndrome with or without respiratory signs in older patients be tested for SARS-CoV-2 by PCR or by antigenic RDT, especially in countries with limited resources where access to PCR is often limited. Indeed, antigenic RDTs have the advantage of similar sensitivity to PCR in symptomatic individuals [26].

While the use of malaria thin/thick smear and RDT provides information on the same indicator, the presence of immunological markers of SARS-CoV-2 allows for an assessment of the level of virus circulation in the community. In our study, the prevalence of IgM was higher than that of IgG (17.3% vs. 5.8%) and all IgM positive cases were also IgG positive. Our prevalence is very high compared to that reported in high-risk populations in Togo with 0.2% and 0.8% for IgM and IgG, respectively [12]. In another study conducted in China by Xie et al., in 2020, prevalence of IgM and IgG was higher with 87.5% and 100%, respectively, in patients with fever or respiratory symptoms [26].
In our study, IgM was three times more frequent in patients with positive thin/thick smear and/or RDT than in patients with negative thin/thick smear and/or RDT and IgG was twice as frequent \( (p < 0.001) \). This high prevalence of IgM could be due to possible cross reactions with other infectious diseases such as HIV infection, leishmaniasis, arboviruses, malaria which are endemic in SSA, according to studies by Cota et al. \[25\]. Pending further studies to investigate the issue of possible cross reactions between SARS-CoV-2 and these infectious agents, the use and interpretation of RDT results in areas endemic for these diseases should be done with caution.

Many studies have evaluated the performance of serological tests for the diagnosis of Covid-19. A study conducted in Brazil on the performance of Covid-19 serological tests showed high levels of sensitivity for tests based on lateral flow immunoassays and enzyme-linked immunosorbent assays (ELISA) but better specificity for lateral flow tests than ELISA \[27\]. Another study by Sethuraman et al., in 2020 of IgM and IgG antibody assays using ELISA showed specificity greater than 95% for the diagnosis of Covid-19 \[28\]. This suggests that for Covid-19 seroprevalence studies, tests based on lateral flow immunoassays should be coupled with those using enzyme immunoassays. However, this approach cannot be applied to low-income countries because of the limited technical resources available for ELISA and especially with the availability of antigenic RDTs, which provide better information on the active phase of transmission of the disease.

In order to address these limitations, it would be valuable to develop new RDTs that would not only minimize interferences that biomarkers of other endemic infections in SSA could have on the detection of Covid-19 specific antibodies but would also allow a combined detection of SARS-CoV-2 and some pathogens such as plasmodial species in malaria-endemic areas.

In our study, only two cases (0.8%) of SARS-CoV-2 and malaria co-infection were reported based on reference tests. Similar cases with low prevalence have been described in Qatar \[29\]. Also, diagnosis and/or treatment of one may lead to failure to identify the other disease \[19\] resulting in dissemination of confirmed Covid-19 cases. This is highly concerning since the objective of epidemiological surveillance of this virus is to detect, isolate and treat the patient early if he is symptomatic. Therefore, it is important to provide primary health care providers with a decision algorithm that includes the screening of Covid-19 in febrile patients.

Our study has some limitations. A selection bias could not be excluded given the mode of recruitment and the recruitment sites. Only febrile patients who came for consultation in selected health facilities in Lomé were included. Thus, the results obtained cannot be extrapolated to the general population of Togo. However, this study provided useful information on the diagnosis of Covid-19 and malaria in health facilities of Lomé in febrile patients. Indeed, the public health consequences of Covid-19 and malaria described by Sherrard-Smith et al. could be catastrophic for fragile health care systems, as is the case in SSA countries, if appropriate measures are not taken in terms of availability and accessibility of diagnostic tests for these two diseases \[21\].

In addition, other vector-borne diseases such as dengue, Zika and Chikungunya closely share common symptoms with Covid-19 and malaria, including fever; there is an urgent need to initiate other studies in Togo to determine the share of these conditions in febrile patients beside the two diseases that we have studied. The results would help to equip health structures to detect other arbovirus epidemics such as dengue on time in order to avoid possible cases of double outbreak of Covid-19 and dengue as it has occurred in Singapore in 2020 \[27\].

**Conclusion**

This study confirms a possible cross-reactivity between Covid-19 and malaria in case of single use of rapid tests, suggesting a possible past contamination. PCR test should remain the reference test. In case of clinical signs related to Covid-19, even in malaria areas, PCR screening should be requested in order to identify and isolate patients. Malaria control activities should also be continued in the country.

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**Author Contributions** Ameyo Monique DORKENOO, Didier Koumavi EKOUVEI, Komivi GBADA and Anoumou Claver DAGNRA conceived the study protocol. Ameyo Monique DORKENOO, Didier Koumavi EKOUVEI, Fifonsi Adjidossi GBEASOR-KOMLANVI, Yao Rodion KONU, Arnold Junior SADIO and Wendpouiré Ida Carine ZIDA-COMPAORE drafted the analysis plan and wrote the first draft of the manuscript. Martin Kouame TCHANKONI performed the statistical analysis. Wendpouiré Ida Carine ZIDA-COMPAORE, Komivi GBADA, Diwaba TEOU and Fiali LACK supervised the data collection. All authors contributed to data analysis through review and interpretation of the results. All authors read, revised and approved the final manuscript.
Availability of Data and Materials  The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest  The authors declare that they have no competing interests.

Consent to Participate  Written informed consent was obtained from every adult enrolled and from the parent or guardian of each child enrolled in this study.

Consent for Publication  All authors gave final approval for publication.

Ethics Approval  The protocol for this study was approved by the Bioethics Committee for Health Research of the Togo Ministry of Health (No. 006/2020/CBRS). In addition, written informed consent was obtained from every adult enrolled and from the parent or guardian of each child enrolled in this study. Data collected are kept secured with a password and only the investigation team has access to this. No personal identification information has been reported. All patients tested positive by thick/thin blood smear or malaria RDT received artemether–lumefantrine fixed-dose combination tablets (Coartem®, Novartis Pharma, Switzerland) at no cost during 3 days in case of uncomplicated malaria according to Togo’s NMCP recommendations. However, treatment of severe malaria was at the patients’ charge. Patients tested positive for SARS-CoV-2 with PCR were notified to the surveillance division and referred to dedicated management centers in Lomé to benefit from the therapeutic protocol free of charge recommended in Togo.

References

1. WHO (2020) World malaria report. 20 years of global progress and challenges. https://apps.who.int/iris/bitstream/handle/10665/337660/9789240015791-eng.pdf. Accessed 5 May 2022
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-3
3. Lu H, Stratton CW, Tang YW (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. J Med Virol 92(4):401. https://doi.org/10.1002/jmv.25678
4. WHO (2020) Coronavirus (COVID-19) Dashboard. World Health Organization https://covid19.who.int/. Accessed 5 May 2022
5. Haakenstad A, Harle AC, Tsakalos G, Micah AE, Tao T, Anjomshoa M, Cohen J, Fullman N, Hay SI, Mestrovic T (2019) Tracking spending on malaria by source in 106 countries, 2000–16: an economic modelling study. Lancet Infect Dis 19(7):703–716. https://doi.org/10.1016/S1473-3099(19)30165-3
6. Chanda-Kapata P, Kapata N, Zumla A (2020) COVID-19 and malaria: a symptom screening challenge for malaria endemic countries. Int J Infect Dis 94:151–153. https://doi.org/10.1016/j.ijid.2020.1004.1007
7. République Togolaise (2020) Courbe épidémique COVID-19, Togo. https://covid19.gov.tg/. Accessed 5 May 2022
8. Conseil Scientifique pour la Gestion de la pandémie Covid-19 au Togo (2020) Protocole de prise en charge thérapeutique des cas de Covid-19 confirmés au Togo. http://news.alome.com/documents/docs/Covid-Protocole-therapeutique-Togo.pdf. Accessed 5 May 2022
9. Yadouleton A, Sander A-L, Moreira-Soto A, Tchibozi C, Hounkainn G, Badou Y, Fischer C, Krause N, Akogbeto P, de Oliveira Filho EF (2021) Limited specificity of serologic tests for SARS-CoV-2 antibody detection, Benin. J Emerg Infect Dis 27(1):233. https://doi.org/10.3201/eid2701.203281
10. Programme National de Lutte contre le Paludisme (2020) Rapport annuel 2020. Ministère de la Santé, de l’Hygiène Publique et de l’Accès Universel aux Soins du Togo
11. Ministère de la Santé et de la Protection Sociale (2017) Enquête sur les Indicateurs du Paludisme au Togo. The Demographic and Health Surveys Program 2018. https://www.dhsprogram.com/pubs/pdf/MIS29/MIS29.pdf. Accessed 5 May 2022
12. Halatoko WA, Konu YR, Gbeasor-Komlanvi FA, Sadio AJ, Tchankoni MK, Komlanvi KS, Salou M, Dorkenoo AM, Maman I, Agbobli A (2020) Prevalence of SARS-CoV-2 among high-risk populations in Lomé (Togo) in 2020. J PLoS One 15(11):e0242124
13. Wang H, Liu Q, Hu J, Zhou M, Yu M-Q, Li K-Y, Xu D, Xiao Y, Yang J-J, Yu Y-J (2020) Nonpharyngeal swabs are more sensitive than oropharyngeal swabs for COVID-19 diagnosis and monitoring the SARS-CoV-2 load. Front Med 7:334. https://doi.org/10.3389/fmed.2020.00334
14. Rakotosaminanana N, Randrianirina F, Randremanan R, Raherison MS, Rasolofo Ala, Sosofomalala GD, Spiegel A, Herald J-M (2020) GeneXpert for the diagnosis of COVID-19 in LMICs. Lancet Glob Health 8(12):e1457–e1458. https://doi.org/10.1016/S2214-110X(20)30428-30429
15. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, Spijker R, Hooft L, Emperador D, Van der Bruel A, Cochrane COVID-19 Diagnostic Test Accuracy Group (2021) Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. Cochrane Database Syst Rev 2(2):CD013665. https://doi.org/10.1002/14651858.CD013665
16. Scheier T, Schibli A, Eich G, Rüegg C, Kube F, Schmid A, Karrer U, Wolfensberger A, Sax H, Schreiber PW (2021) Universal admission screening for SARS-CoV-2 infections among hospitalized patients, Switzerland. 2020. J Emerg Infect Dis 27(2):404. https://doi.org/10.3201/eid2702.202318
17. Rusmini M, Uva P, Amoroso A, Tolomeo M, Cavalli A (2021) How genetics might explain the unusual link between malaria and COVID-19. Front Med (Lausanne) 8:650231. https://doi.org/10.3389/fmed.2021.650231
18. Gaziano L, Giambartolomei C, Pereira AC, Gaulton A, Posetti N, Oliveira Filho EF (2021) Limited specificity of serologic tests for SARS-CoV-2 antibody detection, Benin. J Emerg Infect Dis 27(1):233. https://doi.org/10.3201/eid2701.203281
19. Scherhage F, Schibli A, Eich G, Rüegg C, Kube F, Schmid A, Karrer U, Wolfensberger A, Sax H, Schreiber PW (2021) Universal admission screening for SARS-CoV-2 infections among hospitalized patients, Switzerland. 2020. J Emerg Infect Dis 27(2):404. https://doi.org/10.3201/eid2702.202318
20. Rusmini M, Uva P, Amoroso A, Tolomeo M, Cavalli A (2021) How genetics might explain the unusual link between malaria and COVID-19. Front Med (Lausanne) 8:650231. https://doi.org/10.3389/fmed.2021.650231
21. Gazzano L, Giambartolomei C, Pereira AC, Gaulton A, Posetti N, Oliveira Filho EF (2021) Limited specificity of serologic tests for SARS-CoV-2 antibody detection, Benin. J Emerg Infect Dis 27(1):233. https://doi.org/10.3201/eid2701.203281
22. Scherhage F, Schibli A, Eich G, Rüegg C, Kube F, Schmid A, Karrer U, Wolfensberger A, Sax H, Schreiber PW (2021) Universal admission screening for SARS-CoV-2 infections among hospitalized patients, Switzerland. 2020. J Emerg Infect Dis 27(2):404. https://doi.org/10.3201/eid2702.202318
23. Rusmini M, Uva P, Amoroso A, Tolomeo M, Cavalli A (2021) How genetics might explain the unusual link between malaria and COVID-19. Front Med (Lausanne) 8:650231. https://doi.org/10.3389/fmed.2021.650231
malaria in Africa. J Nat Med 26(9):1411–1416. https://doi.org/10.1038/s41591-41020-41025-y

22. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention. JAMA 323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648

23. Prevention CDCa (2020) Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/04102020/labs-regions.html. Accessed 04 October 2022

24. Saghazadeh A, Rezaei N (2020) Immune-epidemiological parameters of the novel coronavirus—a perspective. Expert Rev Clin Immunol 16(5):465–470. https://doi.org/10.1080/1744666X.1742020.1750954

25. Cota G, Freire ML, de Souza CS, Pedras MJ, Saliba JW, Faria V, Alves LL, Rabello A, Avelar DM (2020) Diagnostic performance of commercially available COVID-19 serology tests in Brazil. Int J Infect Dis 101:382–390. https://doi.org/10.1016/j.ijid.2020.1010.1008

26. Xie J, Ding C, Li J, Wang Y, Guo H, Lu Z, Wang J, Zheng C, Jin T, Gao Y (2020) Characteristics of patients with coronavirus disease (COVID-19) confirmed using an IgM–IgG antibody test. J Med Virol 92(10):2004–2010. https://doi.org/10.1002/jmv.25930

27. Lam LT, Chua YX, Tan DH (2020) Roles and challenges of primary care physicians facing a dual outbreak of COVID-19 and dengue in Singapore. J Fam Pract 37(4):578–579. https://doi.org/10.1093/jamapractice/cmaa1047

28. Sethuraman N, Jeremiah SS, Ryo A (2020) Interpreting diagnostic tests for SARS-CoV-2. JAMA 323(22):2249–2251. https://doi.org/10.1001/jama.2020.8259

29. Sardar S, Sharma R, Alyamani TYM, Aboukamar M (2020) COVID-19 and Plasmodium vivax malaria co-infection. J InfectCases. 21:e00879

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