RE: Final Technical Report

Project Title

Assessment of the burden of concurrent infections with malaria and dengue among febrile patients in Hodeidah governorate, Yemen

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SUMMARY

Concurrent infection with malaria and dengue is an emerging health problem that is often misdiagnosed as a mono-infection. Therefore, this study aimed to determine the prevalence of malaria, dengue and their concurrence in relation to sociodemographic and clinical characteristics among febrile outpatients seeking healthcare in Hodeidah city, west of Yemen. This cross-sectional study was conducted among 355 febrile outpatients seeking healthcare in hospitals of Hodeidah during malaria transmission season (November 2018 - April 2019). Sociodemographic and clinical data were collected using a pre-designed structured questionnaire. NSI antigen and IgM and IgG antibodies against dengue as well as antigens of falciparum and non-falciparum species were detected in sera using rapid diagnostic tests (RDTs). Thick and thin smears were prepared, stained with Giemsa and examined for malaria parasites. Data were double-entered, validated and analyzed using appropriate statistical tests. Of the 355 febrile patients, 32.4% had microscopy- and/or RDT-confirmed falciparum malaria and 35.2% had RDT-confirmed dengue. *Plasmodium vivax* and *P. falciparum*/*P. vivax* were detected among 3.1% and 1.1% of febrile patients, respectively. RDTs detected non-falciparum species and falciparum/non-falciparum mixed species among 3.4% and 2.5% of febrile patients, respectively. Of dengue patients, recent probable dengue was detected among about two-thirds of patients. Concurrent infection with falciparum malaria and recent probable dengue was detected among 4.8% of febrile cases. Patients mono-infected with malaria had a significantly higher frequency of sweating than those concurrently infected with dengue (78.6% versus 35.3%, respectively; P <0.001). On the other hand, those concurrently infected with malaria and dengue had a significantly higher frequency of vomiting than those mono-infected with dengue (47.1% versus 20.4%, respectively; P = 0.17). Malaria and dengue are concurrent among approximately 5% of febrile patients in Hodeidah. Therefore, their detection is critically needed, preferably using RDTs after assessing their diagnostic accuracy. Sociodemographic characteristics of febrile patients cannot be used to predict the concurrence of infections, and clinical differentiation of concurrent infection from mono-infections with either type can be rather challenging to physicians. Further large-scale studies are recommended to investigate the concurrence of malaria and dengue among febrile using more robust diagnostic tools.

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1. Background and rationale

Malaria and dengue are major mosquito-borne diseases in terms of morbidity and mortality in tropical and subtropical countries. The global prevalence of malaria was estimated to be 219 million cases and contributed to 435,000 deaths in 2017 across 87 countries (1). On the other hand, the global burden of dengue is increasing, with an annual incidence estimate of about 50–100 million infections across 100 countries, and about a half of the world's population in endemic areas is at disease risk (2, 3). These diseases are often co-endemic with overlapping existence and share similar clinical manifestations, with febrility being the most common symptom (4). Concurrent infections with these two diseases among febrile patients are often overlooked and misdiagnosed as being a mono-infection with either type as result of clinical similarities (5-7). Such concurrence is an emerging health issue after the increase in dengue cases in malaria-endemic areas in various parts of the world (6, 8-15). A systematic review reveals the concurrence of malaria and dengue in 20 countries in 2018 (4). In previously published reports, concurrent infections with malaria and dengue among febrile patients ranged from 0.2% in Sierra Leone (16) to 23.0% among dengue-positive febrile patients in Pakistan (17).

In Yemen, malaria accounts for more than 114,000 confirmed cases and 37 deaths as reported by health facilities in 2017 (1). *P. falciparum* is the predominant malaria parasite in the country, responsible for 99% of malaria infections (1). Furthermore, dengue cases have escalated, where several outbreaks caused by dengue virus (DENV) serotypes 2 and 3 have been reported between 2010 and 2012 (18-20). DENV serotype 2 has been reported among about a third of febrile patients with dengue-like illnesses in Hodeidah city in 2012 (20). An increase of about six times in the number of suspected cases of dengue was reported in 2016 compared to 2015 (21).

Diagnosis, care and control of malaria and dengue in Yemen have probably been affected by the unstable political situation and wars since 2012, where only half of the health facilities in Yemen are functional as of December 2018 (22). A major reason for deterioration of care could be linked to lack of available diagnostic tests, which led physicians to commonly treat malaria presumptively, which may lead to unnecessary treatment of malaria in patients with other febrile diseases, including dengue. It is well known that inappropriate malaria treatment can lead to severe complications or even death (11, 15, 23-26). It may also

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contribute to the emergence and spread of drug resistance (27). Diagnosis of malaria depends mainly on the examination of stained blood smears, while RDTs are recommended in remote areas with no facilities for light microscopy. Similarly, a large number of sub-clinical dengue cases may not be detected. These may lead to an underestimation of malaria and dengue, respectively.

Similar to other endemic countries, concurrent infections with malaria and dengue may exit in Yemen, and is yet to be reported. Therefore, there is a need to assess the proportion of malaria and dengue, as mono-infections and as a concurrent infection, among febrile patients in Yemen. Therefore, we determined the prevalence of malaria, dengue and concurrent malaria-dengue infections in relation to sociodemographic and clinical characteristics among febrile outpatients seeking healthcare and undergoing laboratory investigations for fever in hospitals of Hodeidah city, west of Yemen - during malaria transmission season (November 2018 to April 2019).

1. Methods

1.1. Study design

A cross-sectional study based on primary laboratory data.

1.2. Study setting

This study was conducted in Hodeidah city, which is the capital of the governorate most afflicted with malaria in the country and comprises three districts; namely, Al Mina, Al Hali and Al Hawak (Figure 1) and has witnessed several dengue outbreaks as well as a recently reported increase in the number of suspected dengue cases. It is located on the Red Sea at 14°46' north latitude and 42°15' east longitude. It is inhabited by about 2.3 million people according to the latest population census (29).

1.3. Study subjects

Febrile patients seeking healthcare in hospitals of Hodeidah city and referred from the outpatient departments to undergo laboratory investigations for fever in six hospitals in the period from November 2018 to April 2019 were included. Outpatients of any gender and age were included if having a an axillary temperature of ≥37.5 ^{o}C at presentation and referred to

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the medical laboratories of the hospitals provided that they gave informed consent to voluntarily participate and were residents of Hodeidah for at least six months before the study. We excluded patients who or whose guardians refused to give informed consent, reported antimalarial drug intake within the past six months or were admitted to hospitals as inpatients or with severe complications.

For the purpose of this study, concurrent infection was defined as an infection with malaria based on microscopy and/or RDT and recent probable dengue based on RDT [non-structural antigen 1 (NS1) and/or IgM-positive] on the same day of taking blood samples from the patient at presentation in the laboratory.

Figure 1. Map of Hodeidah showing the three study districts

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1.4. Sample size and sampling strategy

The minimum required sample size was calculated as 273 based on an expected concurrent infection prevalence of 23.0% (based on the highest prevalence of malaria-dengue concurrent infection found elsewhere [17], to be conservative on the calculation) at a confidence level of 95%, a precision of 5%. However, 355 patients were included in the study. The three districts of Hodeidah city were included in the study. Febrile patients referred to the laboratories of the hospitals of each district were invited to voluntarily participate in the study over the transmission season period until the required total sample size was attained.

Note:
The sample size in the original proposal application was 384 subjects. However, we re-calculated it based on a reasonable expected concurrent infection rate as in the paragraph above.

1.5. Data and sample collection

Once at the laboratory, patients were informed about the objective of the study and their consent for participation was sought before data and sample collection. Laboratory technicians were trained on the study recruitment, informed consent and data collection and supervised by a co-investigator of the study. Data on gender, age, temperature and clinical manifestations were collected using a paper-based, pre-designed structured questionnaire in Arabic by the laboratory technicians. About 3-5 ml of whole blood samples were collected into pre-labeled plain test tubes. Then, blood samples were left to clot, and sera were separated by centrifugation at 3000 rpm for 5 minutes. Sera were then used for performing rapid testing for malaria and dengue, and the remaining was transferred into Eppendorf tubes and stored at -20 ºC if needed later.

1.6. Laboratory investigations

1.6.1. Rapid diagnostic testing for malaria and dengue

Blood samples were screened for anti-DENV antibodies using CareStart™ Dengue Combo RDTs, a brand of dengue point-of-care diagnostics currently marketed in Yemen. It is noteworthy that the CareStart™ Dengue Combo RDT detects NS1 antigen that is used as a basis for enzyme-linked immunosorbent assay (ELISA) in addition to the detection of IgM and

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IgG antibodies. According to the guidelines of the Centres for Disease Prevention and Control (30), the NS1 antigen of the dengue viral genome has been proven to be a useful tool for the diagnosis of acute dengue and can be detected in the serum of DENV-infected patients as early as one day after the start of symptoms and up to 18 days. Blood drops were also screened for malaria parasites using CareStart™ Malaria HRP2/pLDH (Pf/PAN) Combo RDTs to detect *P. falciparum* and non-falciparum species (AccessBio, New Jersey, USA). This test kit has been listed among the latest updated version of prequalified in vitro diagnostic products by the WHO (31). It is one of the commonly used RDTs for malaria diagnosis in Yemen. RDTs for malaria and dengue diagnosis were used and checked for performance quality according to the manufacturer's instructions.

1.6.2. Blood film microscopy

Duplicate thick and thin blood films will be prepared, stained with Giemsa for 20 minutes and examined under the oil-immersion lens of a light microscope by qualified microscopists according to standard procedures (32).

1.7. Data analysis

Data were double-entered and validated using EpiData software, version 3.1 (EpiData Association, Odense, Denmark) and transferred for analysis in IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA) by the Principal Investigator. Categorical variables were statistically compared using chi-square or Fisher's exact tests, whichever suitable, and considered statistically significant at *P* values <0.05.

2. Results

2.1. Characteristics of the study population

Table (1) shows that the majority of the febrile patients were males (63.1%) and aged between 20 and 40 years (54.0%), with median age of 28.0 years (interquartile range: 21.0) and a mean temperature of 38.8 ± 0.7. The majority of the patients were private sector employees (33.2%), living in separate houses (58.5%) and within households of more than four members (64.5%).

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Table 1. Characteristics of febrile patients attending the outpatient clinics in Hodeidah city, Yemen in 2018-2019*

Characteristic		*n*	(%)
Gender			
	Male	224	(**63.1**)
	Female	131	(**39.9**)
Age (years) [a]			
	<20	92	(**26.1**)
	20–40	190	(**54.0**)
	>40	70	(**19.9**)
	Median ± IQR: 28.0 ± 21.0		
Temperature			
	Mean ± SD: 38.8 ± 0.7		
District [b]			
	Al Mina	129	(**37.8**)
	Al Hali	119	(**34.9**)
	Al Hawak	93	(**27.3**)
Education status [c]			
	No formal education	50	(**14.7**)
	Primary education	75	(**22.0**)
	Secondary education or above	216	(**63.3**)
Occupation [d]			
	Unemployed	92	(**31.8**)
	Public service employee	51	(**17.6**)
	Private service employee	96	(**33.2**)
	Other	50	(**17.3**)
House type [e]			
	Separate house	200	(**58.5**)
	Apartment within a house	125	(**36.5**)
	Slum	12	(**3.5**)
	Hut	5	(**1.5**)
Household size (members) [f]			
	≤4	102	(**35.5**)
	>4	185	(**64.5**)

* Total number of patients was 355; ** [a] 3 missing cases; [b] 8 missing cases; [c] 14 missing or non-applicable cases; [d] 66 missing or non-applicable cases; [e]13 missing cases; [f] 68 missing cases; IQR, interquartile range.

2.2. Prevalence of malaria, dengue and their concurrence

Of the 355 febrile patients, 32.4% had falciparum malaria as confirmed by microscopy and/or RDTs, where 29.0 % of patients were confirmed positive by microscopy while 28.7% were confirmed positive by RDTs. Microscopy revealed *P. vivax* among 3.1% of patients and mixed infection with *P. falciparum* and *P. vivax* among 1.1% of patients. On the other hand, non-falciparum species were detected among 3.4% of the patients while falciparum and non-falciparum species were detected among 2.5% of the patients using RDTs (Table 2).

Of the 355 febrile patients, 35.2% were tested positive for dengue using RDTs. The majority of patients were IgG-positive (13.0%) followed by those positive for IgM and IgG (9.6%) and NS1 (8.2%). Recent probable dengue was detected among approximately two-

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thirds of the patients, while 36.8% of patients had past infections as revealed by IgG positivity. On the other hand, concurrent infection with falciparum malaria and recent probable dengue infection was detected among 4.8% of febrile cases (Table 2). Figures (2) and (3) show representative results of the RDTs.

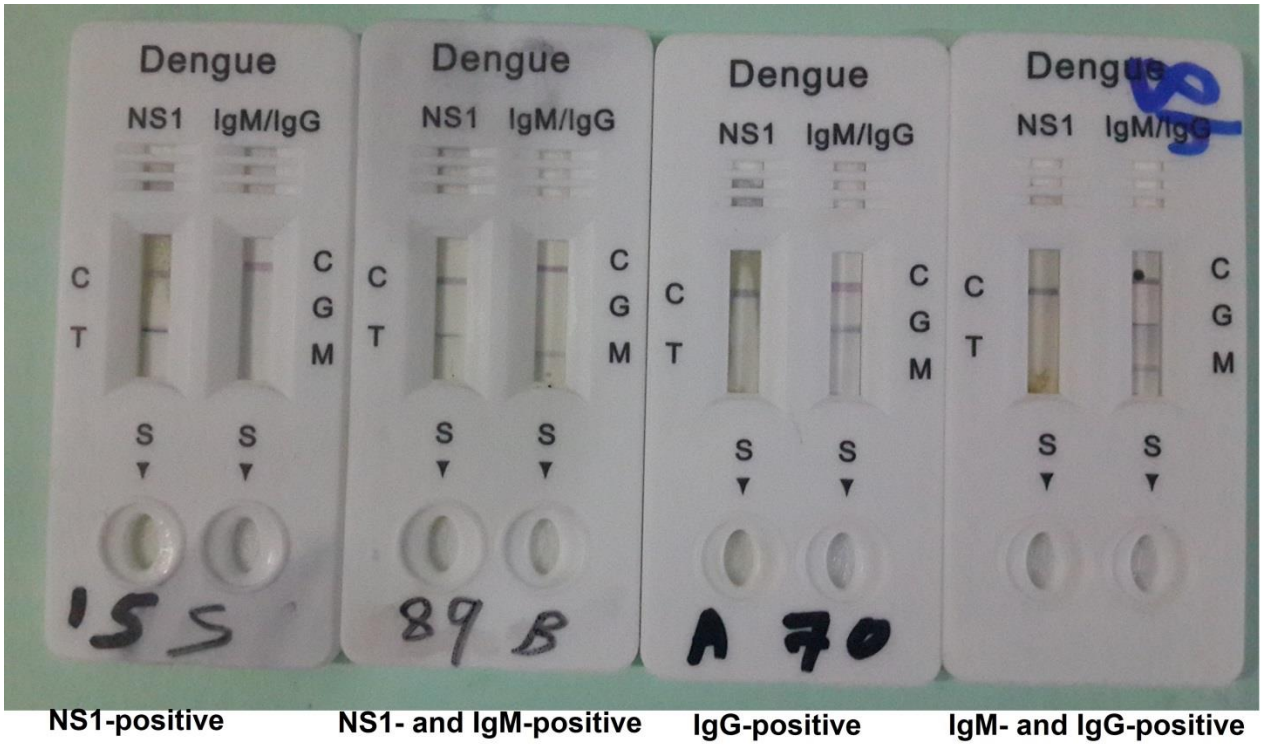

Figure (2): Representation of some results of Dengue Combo RDTs

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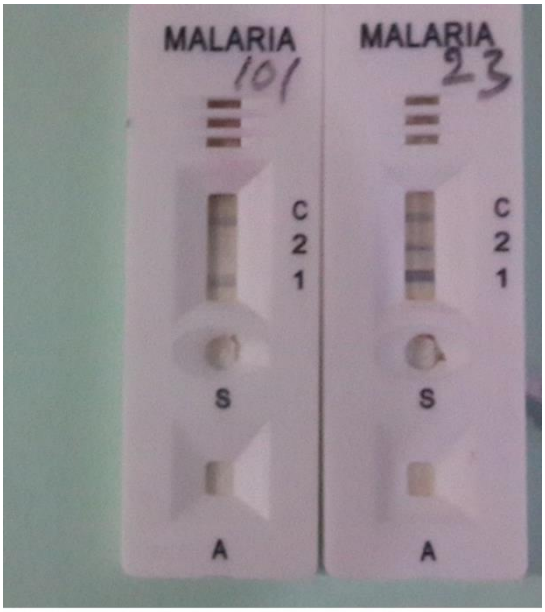

P. falciparum | **Falciparum & non-falciparum spp.**

Figure (3): Representation of some results of malaria RDTs

Table 2. Positivity of malaria and dengue among febrile patients in Hodeidah city, Yemen (2018–2019)*

Infection status		*n*	(%)
Microscopy-confirmed malaria			
	P. falciparum	103	(**29.0**)
	P. vivax	11	(**3.1**)
	Concurrent infection	4	(**1.1**)
RDT-confirmed malaria			
	P. falciparum	102	(**28.7**)
	Non-falciparum species	12	(**3.4**)
	Falciparum and non-falciparum species	9	(**2.5**)
Total confirmed falciparum malaria (microscopy and/or RDT)		115	(**32.4**)
Dengue RDT result			
	IgM-positive	11	(**3.1**)
	IgG-positive	46	(**13.0**)
	IgM- and IgG-positive	34	(**9.6**)
	NS1-positive	29	(**8.2**)
	NS1- and IgM- and/or IgG-positive	5	(**1.4**)
	Total	125	**(35.2)**
RDT-confirmed dengue [a]			
	Recent probable (positive for IgM and/or NS1 irrespective of IgG)	79	(**63.2**)
	Past (positive for IgG only)	46	(**36.8**)
Malaria-dengue concurrent infection [b]		17	(**4.8**)

* Total number of patients was 355; RDT, rapid diagnostic test; IgM, immunoglobulin M; IgG, immunoglobulin G; NS1, Non-structural protein 1; [a] Calculated from dengue-positive cases; *b* Cases co-infected with recent probable dengue and confirmed falciparum malaria.

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2.3. Frequency distribution of malaria and/or dengue in relation to sociodemographic factors

Table (3) shows that there were no statistically significant differences between mono-infection with malaria or dengue and concurrent infection with both types of diseases among febrile patients with respect to the studied sociodemographic factors.

Table 3. Frequency distribution of malaria and/or dengue among febrile patients in Hodeidah city, Yemen (2018–2019)

Characteristic	Malaria (M) *n* = 98	Dengue (D) *n* = 108	Concurrent infection (C) *n* = 17	M *versus* C	D *versus* C
	n (%)	*n* (%)	*n* (%)	*P*-value)	*P*-value
Gender					
Male	65 (66.3)	65 (60.2)	14 (82.4)		
Female	33 (33.7)	43 (39.8)	3 (17.6)	0.188	0.078
Age (years)					
<20	22 (22.9)	30 (28.3)	3 (17.7)		
≥20	74 (77.1)	76 (71.7)	14 (82.3)	0.629	0.357
Education status [c]					
No formal education	17 (17.9)	16 (15.2)	2 (13.3)		
Primary education	15 (15.8)	29 (27.6)	3 (20.0)	0.860	0.770
Secondary education or above	63 (66.3)	60 (57.2)	10 (66.7)		
Occupation status [d]					
Unemployed	30 (35.7)	26 (29.9)	5 (33.3)		
Public service employee	13 (15.5)	16 (18.4)	2 (13.3)	0.706	0.311
Private service employee	28 (33.3)	24 (27.6)	7 (46.7)		
Other	13 (15.5)	21 (24.1)	1 (6.7)		
Type of house [f]					
Separate house	58 (61.7)	55 (54.4)	9 (60.0)		
Apartment within a house	34 (36.2)	40 (39.6)	6 (40.0)	0.945	0.810
Slum	1 (1.1)	4 (4.0)	0 (0.0)		
Hut	1 (1.1)	2 (2.0)	0 (0.0)		
Household size [f]					
≤4	28 (34.6)	29 (31.9)	3 (18.7)		
>4	53 (65.4)	62 (68.1)	13 (81.3)	0.215	0.291

[a] Missing cases: 2 for malaria and dengue; [b] Missing cases: 3 for malaria and 1 for dengue; [c] missing cases: 3 for malaria and dengue, and 2 for concurrent infection; [d] missing cases: 4 for malaria, 21 for dengue and 2 for concurrent infection; [e] missing cases: 4 for malaria, 7 for dengue and 2 for concurrent infections; [f] missing cases: 17 for malaria, 17 for dengue and one for concurrent infection.

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2.4. Comparison between mono- and concurrent infections with respect to clinical features

Table (4) shows that febrile patients mono-infected with malaria had a significantly higher frequency of sweating than those concurrently infected with dengue (78.6% *versus* 35.3%, respectively; *P* <0.001). On the other hand, those concurrently infected with malaria and dengue had a significantly higher frequency of vomiting than those mono-infected with dengue (47.1% *versus* 20.4%, respectively; *P* = 0.17). In contrast, there were no statistically significant differences between mono-infections with malaria or dengue and concurrent infection with both types of diseases.

Table 4. Clinical characteristics of febrile patients with malaria, dengue or concurrent infection in Hodeidah city, Yemen (2018–2019)

Clinical characteristic		Malaria (M) *n* = 98	Dengue (D) *n* = 108	Concurrent infection (C) *n* = 17	M *versus* C	D *versus* C
		n (%)	*n* (%)	*n* (%)	*P*-value)	*P*-value
Sweating						
	Yes	77 (78.6)	59 (54.6)	6 (35.3)		
	No	21 (21.4)	49 (45.4)	11 (64.7)	<0.001	< 0.138
Chills						
	Yes	75 (76.5)	65 (60.2)	14 (82.3)		
	No	23 (23.5)	43 (39.8)	3 (17.7)	0.596	0.078
Headache						
	Yes	90 (91.8)	98 (90.7)	15 (88.2)		
	No	8 (8.2)	10 (9.3)	2 (11.8)	0.627	0.744
Muscle pain						
	Yes	25 (25.5)	31 (28.7)	6 (35.3)		
	No	75 (74.5)	77 (71.3)	11 (64.7)	0.401	0.580
Joint pain						
	Yes	81 (82.7)	97 (89.8)	13 (76.5)		
	No	17 (17.3)	11 (10.2)	4 (23.5)	0.542	0.116
Retro-orbital or ocular pain						
	Yes	20 (20.4)	49 (45.4)	5 (29.4)		
	No	78 (79.6)	59 (54.6)	12 (70.6)	0.406	0.217
Skin rash						
	Yes	2 (2.0)	2 (1.9)	0 (0.0)		
	No	96 (98.0)	106 (98.1)	17 (100.0)	0.552	0.572
Vomiting						
	Yes	33 (33.7)	22 (20.4)	8 (47.1)		
	No	65 (66.3)	86 (79.6)	9 (52.9)	0.287	0.017

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3. Discussion

The overall decline in malaria incidence has raised the significance of detecting non-malarial causes of febrile illnesses. Up to the best of our knowledge, this is the first study to report on concurrent infection with malaria and dengue among febrile patients seeking healthcare in Yemen. About one third of febrile patients in Hodeidah city were positive for falciparum malaria as confirmed by microscopy and/or RDTs. Similarly, about one third of patients were confirmed to be positive for dengue by RDTs; one third with past infections as revealed by IgG positivity and the other two-thirds with recent probable infections as revealed by NS1 and/or IgM positivity. This finding supports what had already been published in Hodeidah in 2012 (20), where about one third of febrile patients with dengue-like illnesses were confirmed to be acutely infected with dengue using IgM ELISA and reverse-transcription-polymerase chain reaction (RT-PCR).

The concurrent infection with malaria and dengue among 4.8% of febrile cases in the present study indicates that the concurrence of mosquito-borne diseases is not uncommon in Hodeidah, even though co-circulation of dengue and chikungunya was reported in Hodeidah in 2012 (20). The co-existence of malaria and dengue had been already evidenced during the outbreak of malaria and dengue among prisoners in Hodeidah in May 2018 (33). The prevalence of concurrent infection in the present study is lower than that (7.2%; 27/ 367) reported among febrile patients confirmed to be infected with dengue by the detection of NS1 antigen and IgM antibodies using RDTs during a dengue outbreak in Odisha state of India in 2011 (24). However, it is higher than that (0.2%; 3/1260) reported among febrile patients from Sierra Leone in 2012-13 based on the detection of both infection types with RDTs (16). Concurrent infection varies in different endemic and may not be found in certain populations. For instance, concurrent infection among febrile patients was reported to be absent elsewhere (34, 35).

In contrast to rapid testing adopted in the present study, ELISA was the most frequently used method for the detection of dengue NS1, IgM and/or IgG followed by the detection of virus ribonucleic acid by RT-PCR in studies from other regions of the world. This makes it inappropriate to compare concurrent infection in Hodeidah with such studies. Moreover, the study population categories are different. Against this background, concurrent infection with microscopy-confirmed *P. vivax*/*P. falciparum* and ELISA-confirmed dengue was

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reported among 23.0% of dengue-positive febrile patients in Karachi, Pakistan in 2007-2008 (17). However, lower prevalence rates were reported from Punjab province of Pakistan (1.1% in 2003-04 and 2.0% in 2012) for concurrent infection with microscopy-confirmed *Plasmodium* species and ELISA-confirmed dengue (14, 36). Lower concurrent infection rates were also reported among febrile Indian patients from Chandigarh 2011-2012 (0.3%), Uttarakhand 2012-13 (0.3-3.8%) (37-40), Odisha 2013 (1.0%) (41), Kolkata 2005-10 (1.5%) (12) and Chennai 2013-2014 (3.0%) (42) based on microscopy for malaria and ELISA for dengue. In contrast, higher concurrent infection rates were reported among febrile patients from Mumbai, being 10.3% and 6.7% during monsoons in 2014 and 2015, respectively, based on malaria microscopy and dengue ELISA (43). In Africa, concurrent infections with malaria and dengue were reported among 2.0-6.0% of febrile patients from Nigeria in the period from 2008-2016 (44-47), 3.0% (7/218) of Ghanaian patients with confirmed malaria (48) and 8.5% of febrile patients from Tanzania in 2013 (49). In South America, concurrent infection with malaria and dengue ranged from 1.0% (17/1723) among febrile patients from French Guiana (11) to 2.8% (44/1578) among patients with acute febrile syndrome in the Brazilian Amazon (50).

Quite similar clinical manifestations of malaria and dengue usually lead to ignore the concurrent infection among febrile patients once a mono-infection with either type is confirmed. In the present study, sweating was significantly more frequent among febrile patients mono-infected with malaria, while vomiting was significantly more frequent among concurrently infected patients. In another context, vomiting was found to be significantly more frequent among febrile patients co-infected with dengue and vivax malaria than those mono-infected with dengue in the Brazilian Amazon (50). The lack of differences in other signs and symptoms, such as joint pain, retro-orbital pain and skin rash, makes it difficult to predict the concurrent infection among patients with acute febrile illnesses in Hodeidah. In line with this, Abbasi et al. (17) and Mohapatra et al. (24) found a clinical similarity between concurrent malaria-dengue and dengue among Pakistani and Indian febrile patient, respectively. Because the present study was limited to outpatients not presenting with severe complications, the impact of concurrent infection on the severity of illness needs to be investigated among febrile patients admitted to hospital in Hodeidah. In a retrospective matched-pair study in French Guiana, more severe clinical presentations were found in

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patients concurrently infected with malaria and dengue and admitted to hospital compared with those mono-infected with either type of disease (23).

It is noteworthy that Yemeni physicians usually depend on platelet count as an indication for the presence of dengue among patients with acute febrile illnesses wherever diagnostics for dengue are not easily available. In addition, they have no knowledge about the frequency of concurrence between both types of infections and may consider it as an uncommon finding. Despite being one of the indicators for dengue infection (51), thrombocytopenia can also be present in malaria (52, 53). Therefore, laboratory confirmation of dengue and malaria is crucial to avoid unnecessary treatment with antimalarial drugs in case of dengue mono-infection. Although no specific medication for dengue currently exists, supportive treatment with antipyretics, analgesics and fluid replacement in case of dehydration is recommended (54).

This study is limited by the fact that it was hospital-based recruiting symptomatic patients and may not reflect the epidemiologic status of concurrent infections at community level. Despite the non-generalizability of the study findings, this study is the first ever to unveil the concurrence of malaria and dengue in Yemen and can be a basis for further large-scale studies in areas of the country co-endemic for both infections. Moreover, the outcomes of this study can help the National Malaria Control Programme in orienting its efforts to prevent and control mosquito-borne diseases. In addition, these will contribute to guide healthcare personnel about potential malaria-dengue concurrent infection, which is usually ignored once either of the diseases is already diagnosed. Because this study might not be powered enough to assess the differences between mono-infections and their concurrence in relation to sociodemographic and clinical characteristics, more extensive studies should build on its findings to further investigate such differences. Another limitation of this study is the adoption of RDTs for dengue diagnosis. However, such rapid tests detect NS1 antigen besides the detection of IgM and IgG, which is a useful marker of acute dengue (30). In Yemen, a resource-limited country, there is a demanding need to evaluate the accuracy of point-of-care diagnostics for malaria and dengue in light of their co-existence in endemic areas.

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4. Conclusions

This study highlights the concurrence of malaria and dengue among approximately 5% of febrile patients in Hodeidah. Therefore, diagnosis of one type of infections should not preclude the presence of the other until having been screened. Sociodemographic characteristics of febrile patients cannot be used to predict the concurrence of infections, and clinical differentiation of concurrent infection from mono-infections with either type can be rather challenging to physicians. Further large-scale studies are recommended to investigate the concurrence of malaria and dengue among febrile patients using more robust diagnostic tools. In addition, evaluation of the diagnostic accuracy of RDTs for the diagnosis of both types of infections is highly recommended to broaden the accessibility and affordability of diagnostic tools in such a resource-limited country.

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Note:

The above report is already drafted as a manuscript to be submitted to the open access journal BMC Infectious Diseases within the next two weeks.

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