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Malaria and Typhoid Fever Coinfection in the Hospital University of Bobo-Dioulasso, Burkina Faso

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Abstract

Malaria and typhoid fever are two endemic infectious diseases in developing tropical countries including Burkina Faso. There are two distinct infectious diseases with many similar clinical signs. In each sanitary area, it is important to describe the "typhomalaria" epidemiology to elaborate adequate diagnosis algorithm and efficient treatment protocol. A cross-sectional study was carried out from July to October 2014 in the lab department of University Hospital Souro SANOU, Bobo-Dioulasso. All microscopy positive malaria during the study period was included. Serodiagnosis of Widal and Felix was performed systematically in all *Plasmodium sp* malaria cases. Titers of antibodies anti-agglutinin O equal or higher than 1/400 and/or 1/800 for anti-agglutinin H antibodies were considered positive for *Salmonella sp.* A total of 283 malaria cases were included in this study, majority falciparum malaria. In this malaria cases, 91 patients were seropositive for *Salmonella sp*. "Typhomalaria" co-infection prevalence was 34.3% (CI 95% [28.8%; 40.1%]). The patient with the normal hemoglobin rate had the highest prevalence of co-infection (46.7% *versus* 30.9; p=0.02). Malaria and typhoid fever co-infection was high (approximately 1/3 of malaria cases) in University hospital of Bobo-Dioulasso. This study revealed the need to explore typhoid fever in malaria confirmed cases, especially in persistent fevers and non-anemic situation despite adapting antimalarial treatment.

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Introduction

Malaria and typhoid fever (TF) are the endemic infectious diseases in tropical areas. Both diseases have been considered as poverty related diseases and cause high morbidity and mortality mainly in sub-Saharan Africa [1–5]. Malaria and TF coinfection has been described in the medical literature in the mid-19th century and named "typhomalaria" [6].

Malaria and TF, whose clinical sign dominating is the fever, are due to two distinct pathogens, with different transmission modes. In fact, human malaria is caused by 5 haematozoa parasite species, *Plasmodium* genus and transmitted actively by *Anopheles* female mosquito infecting bite [7]. *Salmonella* TF is due to invasive enteric bacteria, *Salmonella* genus and transmitted through the oral route consuming water and food contaminated by infected faeces [8]. Thus, malaria is vector borne diseases and TF food borne diseases.

Although TF and malaria are caused by distinct microorganisms (Gram-negative bacillus *versus* hematozoa protozoan parasite for malaria) and transmitted *via* different mechanisms. The two diseases have many similar clinical signs such as fever, headache and abdominal pain [1]. Differential diagnosis between malaria and TF are essential for treatment and co-infection care management is a challenge for clinicians.

In the biological profile, the previous study has reported a false positive malaria rapid diagnostic test (RDT) (BinaxNOW® malaria) result for *P. falciparum* in *Salmonella typhi* bacteremia case without rheumatoid or autoimmune factors due to an immunological disorder [9]. In addition, it was also reported that *Plasmodium* infections increase, *Salmonella spp* infection susceptibility. In fact, haemolysis during malaria, releases heme oxygenase, which is an enzyme that demobilizes the granulocytes involved in anti-*Salmonella* cellular immunity [10].

In Africa, few epidemiology studies have shown that the prevalence of "typhomalaria" is not negligible. In Ethiopia, 6.5% of prevalence was reported [11] and 5% to 40% in Nigeria [10,12,13]. In Burkina Faso, to our best knowledge, no data on "typhomalaria" was published. We performed this study to analyze the epidemiological profile of co-infection malaria-typhoid fever at the University Hospital Sourô SANOU of Bobo-Dioulasso.

Materials and Methods

Study Design

A cross-sectional prospective study was carried out from July to October 2014 in the lab department of University Hospital Souro SANOU of Bobo-Dioulasso, Burkina Faso. All positive *Plasmodium sp.* cases diagnosis by microscopy were included after their consent. In a brief interview with the patient or legal guardian for children, we have explained the aim of the additional medical analyzes. Three to four milliliter of venous blood was collected in anticoagulant EDTA tubes and non-anticoagulant tubes. Patient age, sex and clinical informations were registered on the data collection sheet.

Malaria Diagnosis

Microscopy technique was used for the diagnosis of malaria cases. Thick and thin blood films were performed from anticoagulant EDTA venous blood, stained with Giemsa 10% solution and were examined by microscopy.

Salmonella Typhoid Fever Diagnosis

Serodiagnosis test of Widal and Felix (SDWF) was performed on the plasma after non-anticoagulant venous blood centrifugation according to the manufacturer's instructions of Febrile Antigens Widal (Quimica Clinican Aplicada S.A., Spain). It is an antigen-antibody agglutination test for *Salmonella sp* O and H agglutinins detection. Titers of anti-agglutinin O antibodies equal or higher than 1:400 and / or 1:800 for anti-agglutinin H antibodies after plasma dilution using saline water 0.9% were considered positive for *Salmonella sp*.

Data Analysis

Data were double entered based on EpiData 3.1. Statistical analysis was performed with SPSS Statistics 17.0 (SPSS Inc., Chicago, IL). The Chi-square test was used to compare the categorical variables. Fisher's exact test was used when the expected value in any cell was less than 5. The tests were considered significant with a *p*-value inferior to 0.05. For analytical purposes, the study participants were subdivided into the age group, according to the risk of infection with salmonellosis (autonomy to ensure food hygiene by itself) and malaria. For blood parameters, the following definition

have been used: anemia is defined by the hemoglobin rate inferior and/or equal to 11 g/dL; leukocytosis by the number of WBC superior and/or equal to 11000/dL; leukopenia by the number of WBC inferior and/or equal to 4000/dL; eosinophilia by the number of eosinophil superior and/or equal to 500/dL; neutrophilia by the number of neutrophil superior and/or equal to 8000/dL and neutropenia by the number of neutrophil inferior and/or equal to 1500/dL.

Ethics Statement

Included patients have given consent and their parents or legal guardian for minors before. Personal data form and all diagnostic results were kept strictly confidential. Results of participants with parasitic infections were sent as soon as possible to clinicians for care management.

Results

Characteristics of the Study Population

From July to October 2014, 283 malaria cases were diagnosed in our laboratory and have been included. Among the 283 patients, 49.5% were male and 50.5% were female. The mean age of the participants was 21.8 years and the median 18 years (ranged 0–85 years). The prevalence of anemia was 78.8%. Leukocytosis was found in 36.4% of participants and 25.4% had neutropenia (Table 1).

Parasitological Results

Plasmodium falciparum was the most species found (98.9%). Three cases of *P. malaria* were diagnosed (1.1%). The parasitemia geometric mean was 549.2 ranged between 8 to 1000000.

Prevalence of Co-Infection Malaria and Typhoid Fever

The SDWF test was positive for agglutinins O and/or H in 97 patients. Thus, the co-infection prevalence was 34.3%, IC95% [28.8; 40.1%]. The prevalence of co-infection increase with age, but the association was not statistically significant ($p=0.23$) as reported in table 2. The patient with the normal hemoglobin rate had the highest prevalence of co-infection (46.7%; $p=0.02$) (Table 2). The WBC parameters were not associated to co-infection.

Discussion

Malaria and typhoid fever are the major public health problem in sub-Saharan African countries including Burkina Faso. Here, we analyzed epidemiology of concomitant infection of these two diseases. The prevalence of "typhomalaria" was high (34.28%). Similar prevalence has been found in Cameroon (32.5%) and in Nigeria (20-40%) [13-14]. Our high prevalence could be explained by the conditions of sanitation, food hygiene and the rainy season favorable to these diseases. Our study has been carried out during the rainy season in Burkina Faso. The peak of malaria transmission in Burkina Faso was September to October [15]. In addition many studies have indicated that the high prevalence of TF during rainy seasons [16].

The co-infection increased with age, but the difference between the age groups was not significant ($p = 0.32$). Identical observations had been made in Nigeria [12-16]. This result could be explained by the eating behavior. Usually, in our developing countries, adults eat in public restaurants where hygiene can be lacking [17]. Any association was not found between male and female concerning "typhomalaria ($p = 0.46$). However, the "typhomalaria" prevalence was higher in women, according with one study in Ethiopia [11]. Thus, women could be contaminated by Salmonella during food preparation and other maternal activities such childcare. Concerning blood parameters, hemoglobin rate was significantly associated to co-infection with the highest prevalence in non-anemic patient compared to anemic patient. The lack of anemia in malaria cases would be an indicator for co-infection exploration.

The major limitation of this study was the use of SDWF only for the TF diagnosis. The cross-reaction of SDWF with many non-pathogen *Salmonella*, *Brucella* and *Proteus* OX-19 have been notified [18]. In addition, SDFW cannot be discriminated between *Salmonella* carriage and infection. Thus, TF false positive has been reported using SDWF [19]. Accurate typhoid fever diagnosis needs to use hemoculture and/or coproculture. To limit the number of false positive, we have considered only titers of anti-agglutinin O antibodies higher than 1/400 and / or anti-agglutinin H higher than 1/800 positive for *Salmonella sp*. And also, *Andualem et al*, have shown a good negative predictive value of SDWF test indicating that negative SDWF results have a good indication for the absence of the disease [19].

Yet, our study has important implication for public health. The high prevalence of "typhomalaria

Table 1. Biological profile of study participants

Blood parameters	Criteria	Value	Percent (%)
Hemoglobin (g/dL)	**Minimum**	1.7	
	Median	8.2	
	Mean	8.1	
	Maximum	17.6	
	Normal	60	21.2%
	Anemia	223	78.8
White Blood cell (cell/mm^3)	Minimum	1000	
	Median	8000	
	Mean	10643	
	Maximum	71000	
	normal	163	57.6%
	Leukocytosis	103	36.4%
	Leukopenia	17	6.0%
Eosinophil (cell/mm^3)	Minimum	0	
	Median	133	
	Mean	215	
	Maximum	4499	
	Normal	267	94.3%
	Eosinophilia	16	5.7%
Neutrophil (cell/mm^3)	Minimum	112	
	Median	3606	
	Mean	4890	
	Maximum	27230	
	Normal	184	65.0%
	Neutrophilia	27	9.6%
	Neutropenia	72	25.4%

Table 2. Prevalence of typhomalaria according age, sex and biological parameters

Parameters	Criteria	Positive	Total tested	Prevalence	Khi2	*P*-value
Age (year)	1	4	25	16.0		
	1 to 5	24	65	36.0	4.3	0.23
	6 to 13	14	36	38.9		
	Up to13	55	157	35.0		
Sex	Male	47	140	33.5	0,1	0.8
	Female	50	143	35.0		
Hemoglobin (g/dL)	Normal	28	60	46.7	5,2	**0.02 ***
	Anemia	69	223	30.9		
WBC (cell/mm^3)	Normal	54	163	33.1		
	Leukopenia	7	17	41.2	0.5	0.79
	Leukocytosis	36	103	34.9		
Eosinophil ((cell/mm^3)	Normal	91	267	34.1	0.01	0.8
	Eosinophilia	6	16	37.5		
Neutrophil (cell/mm^3)	Normal	54	163	33.1		
	Neutropenia	7	17	41.2	0.5	0.8
	Neutrophilia	36	103	34.9		

** p < 0.05*

"found in our study raises the question of malaria care management in Burkina Faso. The national malaria management guidelines did not mention other infectious diseases exploration in positive malaria cases using microscopy or RDT associated with clinical signs. Malaria concomitant infection with other infectious fever diseases having similar clinical signs could be omitted. It is important to mention in this national guideline to explore other fever diseases, mainly TF focused on non-anemia malaria cases almost clinical signs do not improve 48h after an adapted treatment.

For future research, it would important to determine the potential impact of "typhomalaria" on malaria RDT diagnosis performance in Burkina Faso.

Conclusion

Epidemiological profile of typhomalaria in Bobo-Dioulasso indicated that in 1/3 of malaria cases, we have a *Salmonella* concomitant infection. Typhomalaria is thus a serious public health problem in Burkina Faso and must be integrate in the malaria diagnosis algorithm therefore to non-anemic cases. Interesting research perspective of our study would be to explore the epidemiology of other fever diseases associated to malaria and or not in order to elaborate adapted recommendations for fever etiological diagnosis in Burkina Faso.

Conflicting of Interest

None has been declared as far as it was ascertained

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