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The Prevalence of Salmonellosis in Patients with Malaria Attending an Urban Hospital in Douala, Littoral Region, Cameroon

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study was carried out to determine the rate of co-infection of Malaria/typhoid fever among patients attending the hospital.
Study Design: The study was a hospital based cross-sectional.
Place and Duration of Study: The study was carried out at the Centre Medical Camrail, de Bassa (CMCD), Douala, Littoral Region, Cameroon, from April to May 2015.
Methods: One hundred and sixty (160) blood and stool Samples were collected. Blood samples were subjected to microscopic examination used for the malaria parasite. Widal agglutination slide

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and tube test were performed for the identification of antibodies to *Salmonella typhi* and stool culture used for isolation of *Salmonella species*.
Results: Overall malaria prevalence was 19.4% (31/160) with a geometric mean parasite density (GMPD) of 788.62±1945.763 parasites/µL of blood. The overall prevalence of typhoid fever by stool culture was 32.5% (52/160) while malaria/typhoid fever and malaria/non-typhoidal salmonella co-infection rates were 29% (9) and 7% (3) respectively. Of the positive malaria samples, 03 (4%) were identified as *Salmonella typhi,* 4 (5.3%) as *S. typhimirium,* 02 (2.6%) as *S. paratyphi A* and 03 (4%) as *S. paratyphi B*. They were no significant relationship between malaria and typhoid fever ($\chi 2$=.609; p= .738). Typhoid fever was grossly under diagnosed by Widal test 1.25% (2/160) compared to stool culture 34.4% (55/160).
Conclusion: The study showed the rate of co-infections of malaria and typhoid fever is relatively high. Malaria was the most prevalent disease among febrile patients in the study area. There was a substantial result discrepancy between Widal test and stool culture for the diagnosis of typhoid fever.

Keywords: Widal; malaria; Salmonella typhi; co-infection; Camrail; Douala; Cameroon.

1. INTRODUCTION

Owing to the movement of the population due to wars and arms conflicts, lack of drinkable water, widespread misuse of the Widal agglutination test for diagnosing typhoid fever, compounded by increasing resistance of malaria parasites to antimalarial drug, malaria and typhoid co-infection remain a menace to many people in sub-Saharan Africa.

Nearly 214 million malaria cases are reported annually worldwide with 88% occurring in Africa. While the MDG Target 6C that is “to have halted and begun to reverse the incidence of malaria”, is estimated to have been met, malaria remains a major killer of children, taking the life of a child every 2 minutes [1]. The first symptoms of malaria are non-specific, and include a vague absence of wellbeing, headache, fatigue, muscle aches, and abdominal discomfort, which are followed by irregular fever. Nausea, vomiting, and hypotension occur frequently. Generalized seizures are associated specifically with *Plasmodium falciparum* infection and might be followed by cerebral malaria [2].

In Cameroon, the entire inhabitants of the country are at risk for malaria, meanwhile, pregnant women and children under the age of five are the most vulnerable groups. According to the Cameroon's National Malaria Control Programme [3], malaria caused 30% of all medical consultations, 48% of all hospital admissions, and 19% of deaths in health facilities.

Salmonellosis is an important global public health problem causing substantial morbidity and mortality [4]. Typhoid fever is caused by *Salmonella enterica* serovar *Typhi* (*Salmonella typhi*). Salmonella is named after an American Veterinary Bacteriologist, D.E. Salmon who first isolated *Salmonella Cholerasuis* from porcine intestine in 1884 [5]. *Salmonella typhi* is a Gram-negative, short bacillus that is motile due to its peritrichous flagella. *Salmonella enterica* subspecies enterica serovar Typhi (*Salmonella typhi*) caused typhoid fever, whereas paratyphoid fever is caused by any of the three serovars of *Salmonella enterica* subspecies enterica, namely *S. paratyphi A, S. schottmuelleri* (also called *S. paratyphi B)*, and *S . hirschfeldii* (also called *S. paratyphi C*). The overall ratio of the disease caused by *S. typhi* to that caused by *S. paratyphi* is about 10 to 1 [6]. The bacterium grows best at 37°C (human body temperature). Human beings are the only reservoir and host for typhoid fever. The infection is transmitted by the ingestion of food or water contaminated with the faeces of an infected person, which contains the bacterium *Salmonella typhi* enteric *serovar* [4].

Both typhoid and malaria share identical social millieu which are imperative to their transmission. Therefore, a person living in such an environment is at risk of contracting both diseases [7]. Although, the two infections are caused by different agents and transmitted via different modes, both diseases share similar symptoms [8] and are of public health importance [2,8].

Typhoid fever causes an overwhelming burden in many tropical countries, with an estimated 212 million cases occurring worldwide leading to 129 000 deaths annually [9]. The global estimate of invasive non-typhoidal salmonella (iNTS) burden

is approximately 3.4 million cases and the most vulnerable groups (1.9 million cases and 380,000 deaths) being children and young adults in sub-Saharan Africa. It is difficult to estimate the real burden of typhoid fever in the world because the clinical picture is confused with many other febrile infections, and the disease is underestimated because of the lack of laboratory resources in most areas in sub-Saharan Africa. In the rural areas, where trained personnel and well-equipped laboratory are lacking, patients are administered with both malaria and typhoid treatment even in the absence of confirmed laboratory cases. Without effective treatment, typhoid fever has a case-fatality rate of 10–30% [10].

Three typhoid vaccines are currently recommended by WHO for used: an injectable polysaccharide vaccine on the purified Vi antigen (aka ViPS vaccine) licensed in 1994, the live attenuated oral Ty21a vaccine first licensed in 1983 and the newest generation typhoid conjugate vaccine (TCV) prequalified for intramuscular administration in 2018. However, till date, vaccines against paratyphoid fever and iNTS diseases are yet to be licensed [8].

The clinical presentation of typhoid fever varies from a mild illness with low grade fever, to general malaise and fatigue, pain in the bone joints and severe abdominal discomfort. Despite the availability of recent data on enteric fevers, additional research is needed in many regions, particularly sub-Saharan Africa [10]. There is a paucity of information pertaining to the prevalence of malaria-typhoid fever co-infection in most regions of Cameroon. This survey was, therefore, aimed at determining the prevalence of malaria and typhoid fever co-infection among febrile patients attending CMCB in Douala, Cameroon. The data generated from the study will help in the management of the co-infections, which will consequently, mitigate the burden of the disease.

2. MATERIALS AND METHODS

2.1 Study Design

This was a hospital based cross-sectional study conducted from April to May 2015 aiming to determine the prevalence of co-infection malaria typhoid in patients attending CMCB. Blood and stool samples collected and structured questionnaires were administered to patients.

2.2 Study Area

The study took place at the CMCB, Douala, Littoral Region, Cameroon. This health facility is intended to cater for Camrail ' workers, worker's relatives and the general public. The hospital is situated at the highly populated and urbanized areas of Douala II Subdivision (261.407 inhabitants). Douala (3°48'N 10°08'E) is the economic capital and the most populated town (2.5 million inhabitants) in Cameroon [11]. The city is situated near the Atlantic coast and 1 m above sea level. The climate is a typical wet equatorial with the rainy seasons extending from April to November followed by a short dry season occurring between December and March. The annual total rainfall ranged from 754.6 mm in August to 34.8 mm in December and the temperatures varied between 24°C and 27°C [12]. Malaria transmission in Douala is considered holoendemic and seasonal with *Anopheles gambiae* as the main vector [13]. Water supply by national water supply company through the distribution system is inadequate and erratic.

2.3 Study Participants

Patients attending the CMCB, upon request by Clinicians of blood smears and Widal agglutination tests, were recruited in the study. A total of 160 blood and stool samples were collected. Prior to blood and stool collection, a written informed consent was obtained from all the subjects.

2.4 Sample Collection

Five (5) milliliters of whole blood was collected from each patient by venipuncture into a clean dry glass tube. On the other hand, stool samples were collected in universal (plastic) disposable bottles with screw cap. Thick and thin films for malaria parasites were carried out alongside Widal agglutination test and tube for Salmonella antibody. Structured questionnaires were also administered in order to obtain socio-demographic information of each patient.

2.5 Laboratory Analysis

2.5.1 Malaria parasite density

Thin and thick blood films were stained with 3% May-Grünwald-Giemsa for 30 minutes and observed microscopically under the 100x

objective. Malaria parasites were counted against 200 leucocytes in thick films to obtain the parasite density. This was expressed as the number of parasites per microlitre (µL) of blood assuming an average leucocyte count of 8000 cells per µL of blood. Slides were considered positive when asexual forms of any *Plasmodium species* were observed on the thick blood film. A slide was declared negative only after having examined at least 100 high power fields [14].

2.5.2 Widal test (Slide agglutination)

Widal agglutination test was performed on each blood sample using the rapid slide titration method using the febrile antigen kit (BIOREX Diagnostics Ltd, Northern Island) and carried out in accordance to manufacturer's instruction. The reagents contain somatic (O) and flagella (H) antigens of *Salmonella typhi and Salmonella paratyphi A-C.* A negative saline control was introduced in each batch of test. Fifty ml of the blood serum was placed on eight rows of circles on the test cards and a drop of positive and negative serum suspension were placed beside each sample on the test slide. Each contains on the slide were mixed thoroughly and spread over the entire circle and the slide was rocked gently for a minute and was observed for agglutination. A positive widal test was considered for any given serum sample with antibody titer of 1: 80 to the O antigen of *S. typhi* [15].

2.5.3 Widal test (tube agglutination)

Zero point One millilitre (0.1 ml) of serum sample was diluted in 1.9 ml of normal saline to get a dilution of 1:20,1:40, 1:80, 1:160, 1:320 and 1:640 using Accucare Widal Tube Tests (Lab Care Diagnostics (India) Pvt. Ltd, Dist Valsad, Gujarat, India) containing somatic (O) and flagella (H) antigens of *Salmonella typhi and Salmonella paratyphi A-B*. Zero point One ml of appropriately well shaken suspension was added to each test tube. The test tubes were incubated for 24 h à 37°C after which the tubes were examined for agglutination reaction [16]. Agglutination titre of 1:80 or more was significant for both typhi O and H.

2.5.4 Stool culture

All the samples were processed within 2 h of collection. A small portion of each stool sample was inoculated into selenite broth and incubated at 37°C for 24 hours. Then sub-cultured onto *Salmonella Shigella* agar (SSA) and incubated at 37°C for 24 hours. Colonies were later identified by inoculating on Kliglar Ion Agar (KIA), and Urea Broth [15]. Stool culture was carried out at the Laboratoire Sainte-Anne of New-bell, Douala.

2.6 Statistical Analysis

The data generated in this study were analyzed using SPSS 20.0. The association between malaria and typhoid/paratyphoid co-infections was determined by Pearson correlation and Chi-square. Pvalue<0.05 was considered statistically significant.

3. RESULTS

3.1 Demographic and Clinical Presentation of the Participants

Out of the 160 patients recruited for this study, 81 (50.6%) were females while 79 (49.4%) were males with a sex ratio of 0.98. Participants' age ranges from 18 months to 60 years (mean age of 28.46 ±19.095). Most of respondents 81 (52.6%) have attended secondary school while 27 (16.8%) have primary school level. Eighty-four 84 (52.5%) subjects held a bachelor degree and the vast majority 154 (96.3%) were residents of Douala city. With regards to the hygienic characteristics of the participants, 109(68.1%) use municipal tap water, 105 (65.6%) preferred eating at home and 128(80%) had flush toilet as toilet facilities (Table 1).

Table 1. Hygienic characteristics of the participants

Variables	Number	Percentage
Source of water		
Tap	109	68.1
Borehole	32	20.0
Bottle water	08	5.0
Tap/ borehole	11	6.9
Place of eating		
Home	105	65.6
Restaurant	04	2.5
Street	10	6.3
Home / Restaurant	11	6.9
Home/ street	30	18.7
Toilet facilities		
Flush toilet	128	80
Cesspit	14	09
Flush toilet / Cesspit	14	09
Others	04	02

Table 2. Prevalence of malaria and typhoid fever and their coinfection in relation to socio-demographic characteristics among febrile patients at CMCB Douala, Cameroon

Variables	Number examined (n)	Malaria % (n)		χ^2	p-value	Typhoid fever % (n)			χ^2	p-value	Co-infection			χ^2	p-value
		Positive	Negative			Typhoidal	Non-typhoidal	Negative			Typhoidal	Non-typhoidal	Negative		
Sex															
Male	79	20.3(16)	79.7(63)	0.077	0.781	31.6(25)	16.5(13)	51.9(41)			37.5(6)	12.5(2)	50(8)		
Female	81	18.5(15)	81.5(66)			37(30)	13.6(11)	49.4(40)			20(3)	6.7(1)	73.3(11)		
Total	160	19.4(31)	80.6(129)			34.4(55)	15(24)	50.6(81)	0.609	0.738	29(9)	9.7(3)	61.3(19)	1.777	0.411
Age group															
<10	44	22.7(10)	77.3(34)			22.7(10)	11.4(5)	65.9(29)			30(3)	0(0)	70(7)		
11-20	27	25.9(7)	74.1(20)			48.1(13)	18.5(5)	33.3(9)			57.1(4)	28.6(2)	42.9(3)		
21-30	8	12.5(1)	87.5(7)	7.849	0.165	37.5(3)	25(2)	37.5(3)	13.077	0.219	0(0)	0(0)	100(1)	11.054	0.353
31-40	30	30(9)	70(21)			23.3(7)	20(6)	56.7(17)			22.2(2)	11.1(1)	66.7(6)		
41-50	22	9.1(2)	90.9(20)			50(11)	13.6(3)	36.4(8)			10(2)	0(0)	0(0)		
>50	29	6.9(2)	93.1 (27)			37.9(11)	10.3(3)	51.7(15)			0(0)	0(0)	100(2)		
Total	160	19.4(31)	80.6(129)			34.4(55)	15(24)	50.6(81)			29(9)	9.7(3)	61.3(19)		

Table 3. Prevalence of malaria and typhoid fever and their coinfection in relation to educational level of febrile patients at CMCB Douala, Cameroon

Variables	Number examined (n)	Malaria % (n)		χ^2	p-value	Typhoid fever % (n)			χ^2	p- value	Co-infection			χ^2	p- value
		Positive	Negative			Typhoidal	Non-typhoidal	Negative			Typhoidal	Non-typhoidal	Negative		
Education															
Nursery	21	9.5(2)	90.5(19)			23.8(5)	4.8(1)	71.4(15)			0(0)	50(1)	50(1)		
Primary	27	33.3(9)	66.7(18)			33.3(9)	14.8(4)	51.9(14)			0(0)	33.3(3)	66.7(6)		
Secondary	81	19.8(16)	80.2(65)	5.511	0.138	40.7(33)	19.8(16)	39.5(32)	10.544	0.104	6.2(1)	31.2(5)	62.5(10)	6.254	0.395
University	31	12.9(4)	87.1(27)			25.8(8)	9.7(3)	64.5(20)			25(1)	25(1)	50(2)		
Total	160	19.4(31)	80.6(129)			34.4(55)	15(24)	50.6(81)			29(9)	9.7(3)	61.3(19)		

3.2 Malaria Prevalence

Malaria parasites were detected in 19.4% (31/160) of participants after examining blood films (Table 2). The prevalence of malaria was higher in male 16 (20.3%) than in females 15(18.5%), but the difference was not significant (χ^2= .077; P= .781). The mean parasite density was higher in the < 5 years' age group (Table 4). There were no significant association of malaria with sex, age (Table 2) and educational background (P > 0.05) (Table 3).

3.3 Prevalence of Typhoid Fever

Of the total study subjects, 04/160 (2.5%) were positive for various salmonella antibodies (Widal slide test) and only 1/160 (0.6%) positive case by Widal agglutination tube test. Of the 160 stool samples cultured, 79/160 (49.4%) isolates were presumptively identified as *Salmonella species* based on their morphological, cultural and biochemical characteristics: 24 (15%) *S. typhimirium,* 24 (13.8%) *S. typhi,* 11 (6.9%) *S. paratyphi A*, 18 (11.3%) S. *paratyphi B*, *and 01* (0.625%), *S. paratyphi C* (Fig. 1). Thus, a prevalence of 34.4% (55/160) was recorded for typhoidal salmonella and 24 (15%) for iNTS. More females 50% (41/81) than males 48.1% (38/79) were positive for salmonellosis by stool culture. There was no significant difference between both groups. Although, the age distribution pattern indicated that 41-50 age group has the highest number of cases of typhoid 11/22 (50%), this was not significantly different from the other age groups (χ^2=13.077; p=0.219). While 33 (40.7%) typhoidal salmonella and 16 (19.8%) iNTS (out of 79 presumptively identified *Salmonella species* were isolated from participants with secondary school level of education, there was no significant difference in typhoid infection between various levels of education (χ^2=10.544; *P*=0.104).

3.4 Prevalence of Malaria and Typhoid Fever Co-infection

Of the 31 patients who were positive for malaria parasite, no co-infection with typhoid fever by Widal agglutination slide test was observed. However, 12 (38.7%) co-infection by stool culture was recorded. Of the positive malaria samples: *S. typhimirium* were 04 (5.3%)*, S.typhi* 03 (4%), *S. paratyphi A* 02 (2.6%). *S. paratyphi B* 03 (4%). Male to female ratio was 0.92. This data indicated that the prevalence of 5.3% (04) of coinfection malaria and iNTS. There was not significant relationship between malaria and *salmonella species* with regards to sex (p=0.411), age groups (0.353) and educational levels (0.395) (Table 2).

3.5 Clinical Signs and Symptoms of Participants

The most common signs and symptoms presented by the patients (Fig. 2) were fever (66.9%), followed in decreasing order by asthenia (57.5%), headache (52.5%), abdominal pain (51.2%), anorexia (25%) and vomiting (20.6%). Although, all the patients complained of fever, only 107 (66.8%) had temperature ≥ 37.5ºC. Some patients indicated that they had taken fever reducing medications prior to consultations. Vomiting (Table 6) was the clinical feature significantly associated with concurrent malaria and typhoid fever infections (P = 0.025). However**,** fever and vomiting were significantly associated with malaria infection (P = 0.002; P = 0.023).

Table 4. Mean parasite density of malaria in relation to sex and age groups

Variables	Number examined	Mean parasite density ±SD	Fisher's test	P- value
Sex				
Male	79	829.29±2084.092		
Female	81	748.95±1812.893	0.068	0.795
Total	160	788.62±1945.763		
Age group				
<10	44	1194.48±2493.864		
11-20	27	1050.15±2038.097		
21-30	8	546.88±1546.796		
31-40	30	1151.27±2356.050	1.959	0.088
41-50	22	138.50±472.756		
>50	29	114.07±538.513		
Total	160	788.62±1945.763		

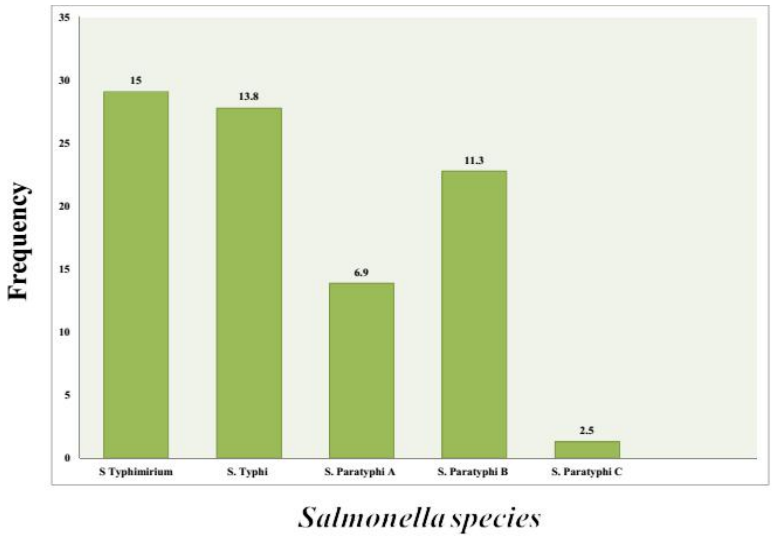

Fig. 1. Frequency of *Salmonella* species

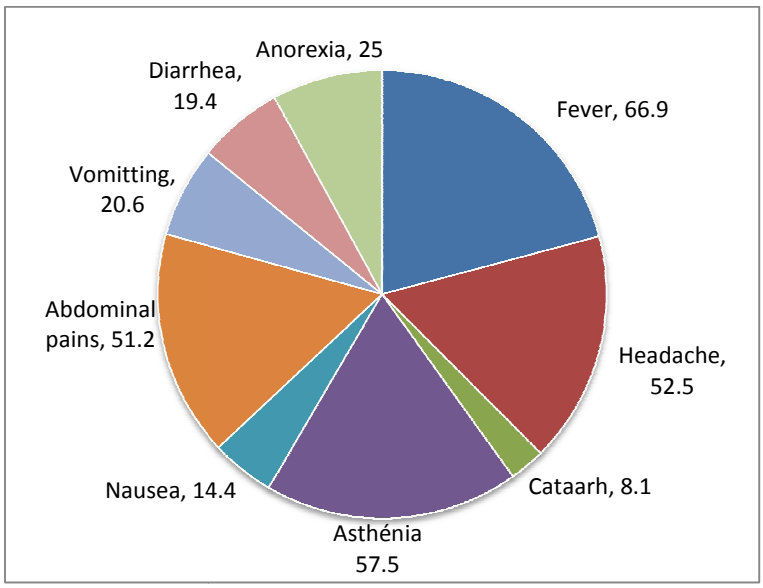

Fig. 2. Distribution of clinical signs and symptoms among study participants

3.6 Determinants of Typhoid Fever in Febrile Patients

There was not significant relationship between the source of drinking water (χ^2=14.968; *P*=0.454), the eating places (χ^2=20.004; *P* =0.458), types of toilet facilities (χ^2=13.573; *P* =.558) and the *Salmonella species* isolated (Table 5).

4. DISCUSSION

Malaria and Typhoid fever have been associated with poverty and underdevelopment with significant morbidity and mortality. In general, multiple parasitic infections in single host tend to cause more severe morbidities as compared to single infection. Even though parasitic co-infections are known to occur and cause multiple morbidities, yet most parasitic diseases are still studied individually [17]. Surprisingly, even the planning for prevention and control activities are designed to focus on single infection. The paucity of research information on parasitic co-infection hinders the ability to accurately assess the disease burden attributable to individual infections and impedes development of informed policy decisions [18]. Cameroon, like other

tropical countries, is an area of high endemicity for both infections. As a result, people living in Cameron are at risk of contracting both diseases either concurrently or as an acute infection superimposed on a chronic one [19]. Differentiation of infections causing febrile illnesses in patients presenting to hospitals in sub-Saharan Africa is a challenge for Clinicians, particularly in co-infections [20]. Consequently, the diagnosis of febrile patients based on clinical signs and symptoms is difficult to distinguish between malaria and typhoid fever [21].

The prevalence of malaria in the present study is relatively high (19.4%) compared to 10.92% [22] in West Region, but lower than the 90.3% [17] reported in Southwest Region of Cameroon. Though, the risk of contracting malaria in Douala is very high (1 m above the sea, swampy area), filthy environment, and the entomological inoculation rate estimated at 31 infective bites per annum [13], the present study showed a declining incidence rate. This reduction might be attributed to interventions put in place since 2008 consisting of the mass distribution of long lasting insecticide treated nets (LLINs), prompt treatment with ACT (Artemisinin Based Combination Therapy) and IPTp-SP in pregnancy (Intermittent Preventive Treatment-Sulphadoxine Pyrimethamine) among others. The prevalence of malaria was higher in females 16 (51.6%) than males 15(48.4%) but this was no statistically significant (P = 0.337). This is lower than report from 85.8%vs76.6% [23] and 64.4% vs 35.6% [24]. The present data are rather comparable with other studies in Sierra Leone which showed more females (53.4%) infected than (46.6%) males [25].

The distribution of malaria parasites, with respect to age pattern indicated those <10 years had the highest mean parasite density 1194.48± 2493.864 parasites/µL of blood whereas the age group 21-30 years had the lowest. The picture that emerges from this study is in agreement with reports in Nigeria [23,26]. This might be due to the fact that natural acquired immunity to malaria infection is relatively slow to develop, incomplete, and its protective efficacy varies depending on the characteristics of the host, place of stay, number of infections suffered [27].

A prevalence rate of 32.5% recorded for typhoidal Salmonella in the study, this calls for the need to strengthen typhoid control protocols in the study areas. Out of the 79 presumptive identified *Salmonella species*, 24(15%) were iNTS using stool culture, thus, highlighting the need to complete characterized Salmonella from stool samples to avoid treatment of iNTS as typhoid fever. More females 50% (41/81) than males 48.1% (38/79) were positive for salmonellosis by stool culture. The slight difference may be due to the fact that females may acquire infection during food preparation, child care, and other household activities, that put them at risk**.** The highest prevalence of *Salmonella species* found among the age group of 41-50 years (working age) is in agreement with previous studies [28] and could be due to poor hand hygiene, improper sanitation or as a result of eating and drinking any available food especially during work breaks.

The present study indicated that the prevalence of co-infection malaria/ typhoid fever (1.25% Widal vs 5% stool culture) is in contrast with studies by (42% Widal vs 5.6% stool culture) [28] and (21.2% Widal vs 0.8% stool culture) [16]. This substantial discrepancy between Widal test and stool culture for the diagnosis of typhoid might be due difference in Widal test kits. Widal agglutination slide test is the preferred technique used in most health care facilities in the study area. The reasons been that, the method is affordable, fast and easier to perform [17]. However, it has been reported to be unreliable for diagnosis of typhoid fever because of high incidence of false negative or false positive results especially in malaria endemic areas [29]. The low rate of typhoid and malaria co-infection using Widal test may be responsible for the under-diagnosis and clinical mismanagement of mixed infections. Poor diagnosis of typhoid fever could lead to the development of complications such as ulceration of Peyers's patches in the ileum causing intestinal haemorrhage or perforation. Consequently, this could give rise to the appearance of chronic carrier, development of resistance and sustained transmission of typhoid fever.

Surprising, of the 31 patients who were positive for malaria parasite, no co-infection with typhoid fever by Widal agglutination slide test was observed. However, 12 (38.7%) co-infection by stool culture was recorded. This is contrary to report by [30] where 6.5% malaria /typhoid by widal test in febrile patients was observed. This could be attributed to the use of poor quality of Widal agglutination slide test kits used in the CMCB.

Among patients with positive malarial parasitemia, 5.3% were co-infected with iNTS serotypes isolated by stool culture. The incidence of iNTS among patients with positive malarial parasitemia was recorded elsewhere. In Ghana, Nelsen [31] found that 6% of *P. falciparum* parasitemic positive children were co-infected with iNTS while in Kenya, Berkley [32] found that 3,0% of children had iNTS and malaria co-infection. However, our findings are consistent with study by Chakrabart [33] that showed that iNTS is more likely to occur in children than in adult's population. In response to the relative lack of sound epidemiological data for invasive Salmonellosis in sub-Saharan, in 2009, the Bill & Melinda Gates Foundation funded the International Vaccine Institute to conduct the Typhoid Surveillance in Africa Program (TSAP); a multicountry surveillance study aimed at bridging knowledge gaps on the population incidence of typhoid and iNTS infections in sub-Saharan Africa [9]. INTS serotypes cause a self-limited gastroenteritis in immunocompetent individuals, while children with severe *Plasmodium falciparum* malaria can develop a life-threatening infection. Takem [34] had hypothesized that malaria increases the risk of iNTS bacteraemia in those who are already infected (carriers).

The predominant symptoms found in the present study were fever (65.6%), headache (52.5%), asthenia (57.5%), abdominal pain (51.3%) which are common to both diseases. These data are similar to reports by [35,28]. These results also pointed out that, there was a significant association between the febrile cases and malaria (p=0.002). Although, malaria and typhoid fever are said to be endemic to Cameroon, this study showed that malaria is far more likely to cause fever than typhoid. The proportion of fever attributable to malaria in the present study is in line with the contribution of malaria to the febrile illnesses whose prevalence remains high ([36,28], but in contrast to studies by Mbah and Agu [37] and D'Acremon [38], in which a decrease in the attributable fraction of fever to malaria have been observed. Factors such as, dirty environment, filthy, pestiferous and foul-smelling gutters shouldering the roads, absence of functional public toilets, poor hand washing habit could have been the reasons why a higher rates of typhoid fever than malaria infections were observed in the study area. This showed a considerable similarity of signs and symptoms of malaria and typhoid fever. With regard to symptomology, malaria fever consists of structural paroxysms, against the stepwise pattern of fever accompanying with severe headaches and gastro-intestinal tract symptoms of typhoid fever which is more consistent when compared to malaria [39,40]. The major management challenges found in malaria and typhoid fever stems from the fact that they often occur in the same patient either at the same time or in sequence to each other. One of the hand, challenge in managing malaria and typhoid fever in CMCB, is the inherent problem of misdiagnosis and confusion in the symptomology of the two distinct etiological infections. Furthermore, most of the patients had the tendency to erroneously conclude that they have malaria when they have typhoid fever vice versa. Consequently, they resort to self-medication, which could put them at risk of more adverse outcomes. Iheukwumere [41] recommended that appropriate confirmatory tests should be used whenever patients present with either malaria or typhoid fever in order to minimize the mix up between the two febrile conditions. Our data suggested that the actual incidence of the typhoid fever will be obtained if stool culture technique is routinely adopted as a baseline for the diagnosis of typhoid fever in our health facilities. This would also reduce indiscriminate use of antibiotics without laboratory evidence that leads to the emergence of antibacterial drug resistance. Using a mathematical model of malaria/ typhoid, Akinyi [42] has predicted that misdiagnosis of typhoid and malaria will enhance malaria infection and lead to high endemicity for typhoid.

Nearly half of the participants using flushing toilet were infected with *salmonella spp*. This could have been as a result of participants practicing poor hand washing system thereby promoting transmission. However, the type of toilets facilities, water supply to house, and place of eating used by the subjects were no associated with the risk of contracting *Salmonella*. The vast majority of participants (75%) acknowledged to be connected to National Water Supply Company (Camwater). However, the water supply did not meet the domestic use both in terms of quantity and quality. About 50% of the Cameroonian population does not have access to safe drinking water [43]. The case of Douala is particularly unfathomable to inhabitants, since water can be found everywhere, however, safe drinking water is scarce.

Table 5. Prevalence of malaria and typhoid fever infection in relation to clinical features of patients

Variables	Number examined (n)	Malaria % (n)		χ^2	P-value	Typhoid fever % (n)			χ^2	P-value	Co-infection %(n)			χ^2	P-value
		Positive	Negative			Typhoidal	Non-typhoidal	Negative			Typhoidal	Non-typhoidal	Negative		
Fever															
Yes	107	26.2(28)	73.8(79)			33.6(36)	13.1(14)	53.3(57)			28.6(8)	10.7(3)	60.7(17)		
No	53	5.7(3)	94.3(50)	9.543	0.002	35.8(19)	18.9(10)	45.3(24)	1.287	0.525	33.3(1)	0.0(0)	66.7(2)	0.358	0.816
Total	160	19.4(31)	80.6(129)			34.4(55)	15.0(24)	50.6(86)			29(9)	9.7(3)	61.3(19)		
Asthenia															
Yes	92	17.4(16)	82.6(76)			34.8(32)	16.3(15)	48.9(45)			25.0(4)	12.5(2)	62.5(10)		
No	68	22.1(15)	77.9(53)	0.545	0.460	33.8(23)	13.2(9)	52.9(36)	0.381	0.826	33.3(5)	6.7(1)	60.0(9)	0.465	0.792
Total	160	19.4(31)	50.6(129)			34.4(55)	15.0(24)	50.6(86)			29.0(9)	9.7(3)	61.3(19)		
Vomiting															
Yes	33	33.3(11)	66.7(22)			18.2(6)	15.2(5)	66.8(22)	5.285	0.071	9.1(1)	0.0(0)	90.9(10)		
No	127	15.7(20)	84.3(107)	5.185	0.023	38.6(49)	15(19)	46.5(59)			45(9)	10(2)	45(9)	7.396	0.025
Total	160	19.4(31)	80.6(129)			49.4(79)	15(24)	50.6(80)			29(9)	9.7(3)	61.3(19)		
Anorexia															
Yes	40	275(11)	72.5(29)			30(12)	10(4)	60(24)			27.3(3)	9.1(1)	63.6(7)		
No	120	16.7(20)	83.3(100)	2.254	0.133	35.8(43)	16.7(20)	47.5(57)	2.112	0.348	30(6)10	10(2)	60(12)	0.040	0.980
Total	160	19.4(31)	80.6(129)			49.4(75)	15(24)	50.6(81)			29(9)	9.7(3)	61.3(19)		
Diarrhoea															
Yes	31	9.7(3)	90.3(28)			25.8(8)	19.4(6)	54.8(17)			33.3(1)	0.0(0)	66.7(2)		
No	129	21.7(28)	78.3(129)	2.315	0.128	36.4(47)	14(18)	49.6(64)	1.442	0.486	28.6(8)	10.7(3)	60.7(17)	0.358	0.836
Total	160	19.4(31)	80.6(129)			49.4(79)	15(24)	50.6(81)			29(9)	9.7(3)	61.3(19)		

Table 6. Determinants associated with typhoid fever in febrile patients

Variables	Number examined	Typhoid fever %(n)			χ^2	P-value
		Typhoidal	Non-typhoidal	Negative		
Water supply of house						
Municipal water supply	109	36.7(40)	13.8(15)	49.5(54)		
Borehole	32	31.2(10)	25(8)	43.8(14)		
Bottled water	8	12.5(1)	12.5(1)	75(6)		
Municipal water supply/Borehole	11	36.4(4)	0(0)	63.6(7)		
Total	160	34.4(55)	15(24)	50.6(81)	6.947	0.326
Place of eating						
House	105	30.5(32)	15.2(16)	54.3(57)		
Restaurant	4	25(1)	0(0)	75(3)		
Street food stall	10	50(5)	10(1)	40(4)		
House / Restaurant	11	36.4(4)	9.1(1)	54.5(6)	**5.675**	**0.684**
House / Street food stall	30	43.3(13)	20(6)	36.7(11)		
Total	160	34.4(55)	15(24)	50.6(81)		
Type of toilet						
Flush toilet	128	36.7(47)	14.8(19)	48.4(62)		
Cesspit	14	35.7(5)	28.6(4)	35.7(5)		
Flush toilet /Cesspit	4	25(1)	0(0)	75(3)	**8.220**	**0.222**
Others	14	14.3(2)	7.1(1)	78.6(11)		
Total	160	34.4(55)	15(24)	50.6(81)		

The principal limitation of the study was, the lower sample size that prevents us to draw a definitive conclusion. In parallel to the isolation of *salmonella species* by stool culture, the use molecular techniques involving PCR could have giving us more accurate results. The data were collected by cross sectional method from patients attending a single healthcare facility. Though this method is cost effective, it does not give a clear epidemiological and clinical panorama of these infections.

5. CONCLUSION

The study indicated no co-infection of typhoid fever by Widal agglutination slide test with malaria positive patients. However, 38.7% co-infection by blood culture was recorded. Thus, there was a substantial discrepancy between Widal test and stool culture for the diagnosis of typhoid fever in the participants. Typhoid fever was the most prevalent disease among febrile patients in the study area. Community should be educated on the importance of hand washing system to reduce the burden of typhoid fever infection in the area. The disease burden of *Plasmodium falciparum* malaria is decreasing with successful control measures in many countries in sub-Saharan Africa (WHO, 2015). Meanwhile, febrile disease is still commonly misdiagnosed as malaria without ruling out other potential causes of fever, including bacteraemia.

CONSENT AND ETHICAL APPROVAL

An ethical clearance was obtained from the Institutional Review Board of University of Douala (N^O CEI-UD/373 /01/2015/M) while administrative authorization was obtained from the Camrail management through Responsable Gestion Santé du CMCB. The consenting process involved the explanation of the content of the information sheets to parents or guardians by a research team member in the language (French/English) the participant best understood and opportunities were given for questions/clarifications. Emphasis was laid on the voluntary nature of participation and that participants could withdraw at any time without any explanation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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