



Co-infection of Malaria and Typhoid Fever in Feverish Patients in the Kumba Health District, Southwest Cameroon: Public Health Implications

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Authors' contributions

This work was carried out in collaboration between all authors. Author LMN designed the study, carried out field work and wrote the first draft of the manuscript. Author FNE designed the study, carried out field work, performed the statistical analysis and corrected the manuscript. Author HKK designed the study, wrote the protocol, did literature searches and thoroughly edited the manuscript, author HAN carried out field and laboratory work as well as literature searches. Author RNN designed the work, supervised it and corrected the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study was aimed at generating updated baseline data on co-infection of malaria and typhoid fever and finding out the implications of these co-infections in disease severity.

Study Design: The study was cross-sectional.

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Place and Duration of Study: The study was carried out in Kumba, Southwest Cameroon from May to July, 2010.

Methodology: Venous blood was collected from 206 febrile patients of both sexes aged 4-80 years old at the Kumba District Hospital. Malaria parasite density and speciation were determined using Giemsa-stained thick and thin blood films respectively. Typhoid fever was diagnosed by isolation and characterisation of the aetiological agent from stool samples in 178/206 patients. Antimicrobial susceptibility of recovered isolates was determined by the disc diffusion method. Anaemia status, Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) values were determined.

Results: Overall malaria prevalence was 90.3% (186/206) while geometric mean parasite density (GMPD) was 866 (range: 40 – 64880) parasites/ μ L of blood. *Plasmodium falciparum* was the most prevalent *Plasmodium* species. Overall prevalence of typhoid fever was 7.9% (14/178) while malaria/typhoid fever co-infection rate was 6.74% (12). Of the 14 typhoidal *Salmonella* isolates recovered, 6 were identified as *Salmonella typhi* and 8 as *S. paratyphi*. The *Salmonella* isolates were all susceptible to ciprofloxacin and gentamycin. Patients co-infected with malaria/typhoid fever had a significantly higher ($P = .007$) GMPD (1203, range: 100-64880 parasites/ μ L) when compared to patients with mono-infections of malaria (774, range: 40-18660 parasites/ μ L). Abnormal ALT and anorexia prevalence values were significantly higher ($P=.01$ and $P =.045$ respectively) in patients with only typhoid fever than their counterparts. The values of anaemia and AST were comparable in all groups of patients.

Conclusion: This study confirms that co-infections of malaria and typhoid fever are common and may exacerbate malaria intensity.

Keywords: Malaria; typhoid fever; co-infection; diagnosis; prevalence; severity; Cameroon.

1. INTRODUCTION

Malaria and typhoid fever are well known undifferentiated febrile illnesses which could be responsible for varying degrees of morbidity and mortality in developing sub-Saharan countries including Cameroon [1-4]. Despite the known clinical presentations of these infections and their response to treatment options, concomitant infections with malaria and typhoid fever or with other tropical diseases could affect the clinical course of the disease(s), leading to misdiagnosis and treatment failures. Therefore, in a country like Cameroon where malaria and typhoid fever are considered endemic, individuals are at substantial risks of contracting both diseases either concurrently or as an acute infection superimposed on a chronic one. As such, malaria and typhoid fever continue to be of major public health importance.

Malaria is caused by parasites of the genus *Plasmodium* with its initial symptoms varying particularly in children and may include irregular fever, malaise, headache, muscular pain, sweating, chills, nausea, vomiting and some diarrhoea and most of these symptoms are induced by the release of cytokines by the host's immune system [5]. About 207 million malaria cases and nearly 627 000 deaths are reported annually with more than 80% occurring in sub-

Saharan Africa and affecting mostly children under five years of age and pregnant women [6]. Like other sub-Saharan countries, it still remains a major cause of morbidity and mortality in Cameroon [3]. About 31% of consultations in hospitals are due to malaria; and approximately 44% of these patients are hospitalised with a resulting 18% deaths [7].

On the other hand, typhoid fever is a systemic infection characterized by a persistently high fever, headache, malaise, lethargy, skin rash, loss of appetite, constipation more often than diarrhoea, hepatosplenomegaly and bradycardia. Although widely recognized as a major public health problem in most developing sub-Saharan African countries, only 2.5% of febrile patients with symptoms clinically compatible with typhoid fever were actually confirmed as typhoid fever cases in one locality in Cameroon [2]. However, it is an important cause of morbidity in many regions of the world, with estimated 22 million new cases and 600,000 deaths registered annually [8].

Although co-infections of malaria and typhoid fever have been reported in some parts of Cameroon [1,2] and in many other countries such as Nigeria [9-12] and India [13,14], continuous monitoring and epidemiologic enquiry is quite essential because disease pattern or

trend does not only vary with geographical location but seems to change overtime with changes in global climatic conditions. Both malaria and typhoid fever usually lead to liver injury and this leads to an increase in serum levels of intracellular enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) above the normal ranges. Liver injury and severity of infections due to both diseases can thus be indirectly quantified by measuring the levels of these intracellular enzymes. ALT is usually present mainly in the liver while AST is found in many organs like kidney, liver, cardiac and skeletal muscles, brain, pancreas, white blood cells and red blood cells. An increase in the serum levels of these enzymes above the normal ranges could be due to the lysing of injured cells which leads to leakage of the enzymes into the blood stream thereby increasing the concentration above normal range.

Like many other developing countries, accurate diagnosis of infectious diseases remains a challenge due to lack of skilled man-power and equipment making clinical diagnosis a common practice. It is therefore very important that clinical diagnosis be informed by appropriate epidemiologic data. Accurate diagnosis of a disease needs to be followed by appropriate treatment. Due to drug resistance, it is usually necessary to carry out sensitivity tests before making an informed choice of an antibiotic for treatment. The purpose of this study was therefore to generate updated baseline data on co-infection of malaria and typhoid fever for clinico-epidemiologic purposes which will enhance better management and control; in addition to trying to understand the implications of these co-infections in disease severity.

2. MATERIALS AND METHODS

2.1 Study Population

The study population comprised febrile patients who presented at the Kumba District Hospital and were referred to the laboratory for malaria and/or typhoid fever investigations by the consulting physicians. After obtaining an informed consent, a structured questionnaire approach was used to record demographic and clinical data. Participation in the study was voluntary and those who refused to take part in the study were still given due attention without any bias. Patients were free to refuse to answer any question if they choose to do so. A total of

206 patients, all residents of Kumba (4°38'N; 9°27'E) and aged between 4 to 80 years were recruited in the study.

2.2 Collection of Blood and Stool Samples

Five (5) milliliters of whole blood was collected from each patient by venipuncture into a clean dry glass tube. The blood was smeared immediately onto a clean grease-free slide for preparations of thick and thin blood films, while some was used to fill a heparinized capillary tube. The rest of the blood was allowed to clot and serum was separated from blood cells and used (serum) to quantify ALT and AST enzymes. A total of 178 stool samples were also collected from the patients who could provide the specimen and preserved in Amies transport medium. All samples (serum and stool) were kept at 4°C until transported at the same temperature to the Laboratory for Emerging Infectious Diseases, University of Buea for analysis.

2.3 Staining of Blood Films and Determination of Malaria Parasitaemia as Well as Speciation

Thick and thin blood films were stained with 10% Giemsa for 20 minutes for the detection of *Plasmodium* parasites and speciation respectively. The slides were then observed microscopically under the x100 (oil immersion) objective of an Olympus® BX 40F light microscope (Olympus optical Co. Ltd., Japan). Parasite density was done by counting the number of parasites (asexual forms and gametocytes) against 200 white blood cells on thick films assuming a total leucocyte count of 8,000 / μ L of blood [15]. At least 100 high power microscopic fields were examined before declaring a slide negative. The presence of any parasite (at least one parasite per 100 thick fields) was considered significant since all the patients presented with fever. Species identification was done on thin blood films (when the thick-smear was positive) with the aid of identification tables as described by Cheesbrough [15]. Those found positive for malaria were referred to the consulting clinician of the hospital for appropriate treatment.

2.4 Measurement of Packed Cell Volume (PCV)

This was done by the method described by Chessbrough [15] in order to assess the anaemic

status of the recruited patients. The blood-filled heparinized capillary tube was centrifuged at 12,000 g for five minutes using a Haematocrit Centrifuge (Hettich Zentrifugen, Tuttlingen, Germany). PCV values of $\geq 33\%$ were considered to be normal while values between 24%–32% and $< 23\%$ were considered to be mild to moderately and severely anaemic respectively.

2.5 Measurement of Liver Function Tests (ALT and AST Values)

These assays were performed to measure the severity of infections since destruction of cells that contain these enzymes by any of the pathogens will lead to an increase in serum levels of ALT and AST above normal range. The ALT and AST values of the patients were measured using a test kit (Fortress Diagnostics Limited, UK) following the manufacturer's instructions using a BA-88 Semi-Auto Chemistry Analyzer (Shenzhen Mindray Bio-Medical Electronics Co, Limited, China) as the spectrophotometer to quantify the enzymes. ALT values ≤ 31 U/L and ≤ 39 U/L were considered normal values for females and males respectively, while AST values ≤ 33 U/L and ≤ 39 U/L were considered normal values for females and males respectively.

2.6 Isolation and Identification of Salmonella from Stool

Isolation of Salmonella from stool samples was done following standard microbiological practices [15]. Each stool sample was enriched in Selenite F broth (Pronadisa Laboratories, Spain) overnight and a loopfull streaked on salmonella-shigella medium (Pronadisa Laboratories, Spain) the next day and incubated aerobically at 37°C overnight. Suspected colonies (colourless colonies) were sub-cultured on fresh salmonella-shigella medium and incubated as reported above. The colonies were further streaked on nutrient agar to obtain pure isolates. Colonies were subjected to gram staining, motility, hydrogen sulphide production and oxidase tests [15,16]. Gram negative short motile rods that were oxidase negative with characteristic red slope/yellow butt reaction on Triple Sugar Iron (TSI) agar either with or without production of H₂S were confirmed as Salmonella species based on the API 20-E (BioMérieux, Marcy-l'Etoile, France) kit reactions. The tests were

performed as per manufacturer's instructions for use and data interpretation was performed using the Analytical profile index (API) database (V4.1) with the apiweb™ identification software. Polyvalent antisera were used for speciation [16].

2.7 Antimicrobial Susceptibility Test

The susceptibility of the Salmonella isolates to antimicrobial agents was determined using the Kirby-Bauer disk diffusion method [17,18]. A bacterial lawn was prepared by transferring 4 - 5 colonies of the same morphological type in 2.5 mL sterile normal saline using a sterile Pasteur pipette. The suspension was vortexed and its turbidity compared with Barium chloride (0.5 McFarland Turbidity Standard; 1.0×10^8 CFU/ μ L). One hundred microlitre of the inoculum was spread onto Iso-Sensitivity test agar plates. The excess inoculum was siphoned with sterile Pasteur pipettes. Plates were allowed to dry at room temperature in a laminar flow. Disks containing predetermined amounts of antibiotics were then dispensed onto the bacterial lawn using a sterile forceps. The disks were placed 15 mm away from the edge of the plate and 25 mm away from each other. Within 15 minutes after the disks were dispensed, the plates were inverted and incubated at 37°C for 16 - 18 hrs. After incubation, they were examined and diameters of the inhibition zones were read and interpreted in accordance with guidelines provided by the National Committee for Clinical Laboratory Standards, NCCLS (1999). The following commercially available antibiotics were used: streptomycin (25 μ g), gentamycin (10 μ g), kanamycin (30 μ g), ampicillin (10 μ g), chloramphenicol (30 μ g), ciprofloxacin (5 μ g) and nalidixic acid (30 μ g) (Mast Group Ltd, Merseyside, UK). These antibiotics are commonly prescribed in the study area as previously reported [16].

2.8 Data Analysis

All data was recorded and analyzed using statistical software (SPSS Version 11.0 SPSS Inc.). Differences between group means were compared using the Student's T-test or analysis of variance (ANOVA). Categorical data was compared using Pearson's Chi-Square test. The level of significance was set at $P < .05$. Regression was performed between clinical parameters.

3. RESULTS

3.1 Demographic and Clinical Presentation of the Study Population

Out of the 206 patients recruited for this study 137 (66.5%) were females while 69 (33.5%) were males, with their ages ranging from 4–80 years (mean age of 34.2±17.5 years). The most common signs and symptoms presented by the patients were fever (100%), followed in decreasing order by headache (62.6%), fatigue (50.5%), abdominal pain (48.1%), joint pain (45.7%), anorexia (28.2%) and diarrhoea (9.2%). Although all the patients complained of fever, only 27 (13.11%) had temperature $\geq 37.5^{\circ}\text{C}$, which is definitive of fever. Some patients indicated that they had taken fever reducing medications prior to consultations.

3.2 Malaria Prevalence, Intensity and Speciation

After examining blood films, malaria parasites were detected in 90.3% (186/206) of the participants. The prevalence of malaria was higher in males (91.3%, 63/69) than in females (89.8%, 123/137), but the difference was not significant ($\chi^2 = 0.121$; $P = .73$). The highest prevalence (100%) was recorded in the 71 - 80 years age group and the least (79.2%) in the 51 - 60 years age group, but the difference was insignificant ($\chi^2 = 7.093$; $P = .42$).

The geometric mean parasite density (GMPD) of the population was 866 (range: 40 – 64880) parasites/ μL of blood and the density was higher in males (943, range: 40 – 64880 parasites/ μL blood) than females (829, range: 40 – 23720 parasites/ μL blood) but the difference was not significant ($t = -0.66$; $P = .51$). The highest GMPD (1151, range: 40 - 64880 parasites/ μL blood) was recorded in the 11 – 20 years age group while the lowest (355, range: 40 - 17560, parasites/ μL blood) was recorded in the 71 – 80 years age group, but the difference between age groups was insignificant ($F = 0.571$; $P = .78$).

Three *Plasmodium* species were identified, with *P. falciparum* as the most prevalent (95.6%), *P. malariae* (15.6%) and *P. ovale* (1.0%). A total of 88.1% (164/186) had single infections while 11.8% (22/186) had mixed infections [*P. falciparum*/*P. malariae*; 21 (11.3%) and *P. falciparum*/*P. ovale*; 1 (0.5%)]. There was no case of *P. vivax*.

3.3 Identification of Salmonella from Stool and Prevalence of Typhoid Fever

Of the 178 stool samples collected and processed, 52 isolates were presumptively identified as *Salmonella* species based on their morphological, cultural and biochemical characteristics. Out of the 52 presumptive *Salmonella* isolates, 6 (11.5%) were identified as *Salmonella typhi* and 8 (15.3%) as *S. paratyphi*. Thus a prevalence of 7.9% (14) was recorded for typhoid fever. The infection was more prevalent in females (9.7%) than males (4.7%), but the difference was not significant ($P = .25$). The highest prevalence (13.3%) was observed in the 61 - 70 years age group, while no cases were reported for the age groups 41 - 50 and 71 – 80 years. However, the difference was not significant ($P = .66$). All patients with typhoid fever complained of abdominal pain and/or diarrhoea, while seven of them complained of anorexia. Of the 14 infected typhoid patients, 11 (78.6%) indicated that they used pipe borne water, 2 (14.3%) used well water, while 1 (7.1%) used a spring as their sources of portable water.

3.4 Antimicrobial Susceptibility Test of Salmonella Isolates

The isolates were markedly susceptible to ciprofloxacin and gentamycin (100%), and least to streptomycin (3, 21.4%). Three of the isolates showed resistance to more than one antibiotic, while five were not totally resistant to any but were intermediate to one or more antibiotics.

3.5 Co-infection of Malaria and Typhoid Fever and Severity of Disease in the Study Population

Out of the 178 patients that provided both blood and stool samples, 160 (89.9%) had either malaria and/or typhoid fever. One hundred and forty-six (82.0%) patients had only malaria, 2 (1.12%) had mono-infections of typhoid fever and 12 (6.74%) had co-infections of malaria/typhoid fever (Table 1).

Patients co-infected with malaria and typhoid fever had a higher GMDP (1203, range: 100 – 64880 parasites/ μL), when compared with patients that had mono-infections of malaria (774, range: 40 – 18660 parasites/ μL) and the difference was significant ($F = 5.038$, $P = .01$) as shown in Table 1. Although there was no

significant difference ($\chi^2 = 0.559$, $P = .62$) in anaemic status, prevalence of anaemia was however higher in patients with mono-infections of malaria (19.9%, 29) than those who were co-infected (16.7%, 2) (Table 1).

None of the two patients diagnosed with typhoid fever only was anaemic. However, these two patients had abnormal ALT and AST values when compared with the other patients. The prevalence of abnormal ALT was significantly highest ($P = .01$) in patients who had only typhoid fever (100%, 2) when compared with those who had only malaria (17.8%, 26) and those who were co-infected (16.7%, 2). The prevalence of abnormal AST was highest in participants who had only typhoid fever (100%, 2) when compared with those who were co-infected with malaria/typhoid fever (41.7%, 5) and those who had only malaria (27.4%, 40), but the difference was insignificant. The highest mean ALT value (35.5 ± 0.7) was recorded in those with mono-infections of typhoid fever and least in those infected with malaria/typhoid fever (23.167 ± 8.7) but the difference was insignificant ($F = 0.847$, $P = .430$) while the highest mean AST (36.43 ± 19.9) value was recorded in those with mono-infection of malaria and the least (26.80 ± 16.8) was in those co-infected with malaria and typhoid fever but the difference was not significant ($P = .63$) as indicated in Table 1.

All the infected patients, that is, those with mono-infections of malaria and typhoid fever as well as co-infections of malaria/typhoid fever had fever (temperature $\geq 37.5^\circ\text{C}$). Other signs and symptoms such as headache, abdominal pain, joint pains and diarrhoea were experienced by the patients, but their prevalence values were comparable in patients of all disease types. Only the prevalence of anorexia was significantly highest ($\chi^2 = 6.194$, $P = .045$) in patients who had only typhoid fever (100%, 2) and lowest in those who had malaria mono-infections (27%, 47) as shown in Table 2.

Co-infections of malaria and typhoid fever were similar in the females (7.8%, 9) and males (4.8%, 3). Age did not also influence the prevalence of malaria and typhoid fever co-infection although it was most prevalent in the 61-70 years age group (13.3%) and lowest in the 70-80 years age group as indicated in Table 3.

4. DISCUSSION

The circulation of infections of different aetiologies with similar differential clinical diagnosis and their implication in disease course remain a major concern especially in developing tropical countries where factors (such as vectors and poverty) that enhance their spread abound [19]. This study suggests that malaria-typhoid co-infections are not uncommon and further strengthens previous reports that malaria is highly prevalent (90.3%) in Kumba [20]. Furthermore, we observed that patients with dual infections of malaria and typhoid fever had an increased level of parasitaemia when compared to patients with only malaria infections.

Many infectious diseases of bacterial, viral and parasitic origin which are common in tropical and sub-tropical countries present as febrile illnesses with similar differential clinical diagnosis. Although in Cameroon several reports suggest or indicate that majority of the patients who present with a febrile illness are likely suffering from malaria [2], laboratory investigations to simultaneously detect the malaria parasite or anti-salmonella antibodies are quite random because the risks of contracting either or both infections are high.

Interestingly, these infections are caused by two completely different organisms (a parasite for malaria and a bacterium for typhoid fever), but they share a lot in common in their symptomatology. It is worth noting that in Kumba, the risk of contracting malaria is highly associated with the prevalence of the vector, *Anopheles* mosquitoes because the geographical location of Kumba (low altitude 258 meters a.s.l.) does not only favour the survival of the vector but the mosquitoes have been observed to have a high man-biting rate and consequently high malaria transmission rates [21,22]. On the other hand, poor water quality and hygienic conditions are risk factors for typhoid fever and these are conditions commonly encountered in the Kumba municipality as many households rely on well water especially as the pipe-borne water supply was declared unfit for drinking in 2010 (personal observation). These conditions expose individuals to dual infections with malaria and typhoid fever but the outcome of such dual infections especially as it concerns disease severity is obscured. This is in line with the reports of Ukaegbu et al. [4] and Snehanshu et al. [13] in Nigeria and India respectively.

Table 1. Variation in haematological and parasitological parameters in patients presenting with different disease types

Disease status	Number of patients (%) N = 178	PCV ^a		AST ^b		ALT ^c		Parasitaemia in parasites/ μ l blood (range)
		Mean \pm SD	Anaemic (%)	Mean \pm SD	Abnormal AST (%)	Mean \pm SD	Abnormal ALT (%)	
Malaria (only)	146 (82.0)	41.04 \pm 10.4	29 (19.9)	36.4 \pm 19.9	40 (27.4)	26.82 \pm 13.7	26 (17.8)	774(40 – 18660)
Malaria/typhoid	12 (6.7)	39.3 \pm 10.1	2 (16.7)	26.8 \pm 16.8	5 (41.7)	23.2 \pm 8.7	2 (16.7)	1203(100 - 64880)
Typhoid (only)	2 (1.12)	53.0 \pm 25.4	0 (0)	28 \pm 17.0	2 (100)	35.5 \pm 0.7	2 (100)	0
Total	160 (89.9)	41.0 \pm 10.5	31 (19.4)	35.6 \pm 18.8	47(29.4)	26.7 \pm 13.4	30 (18.8)	889(40 - 18660)
Level of significance		F = 1.446 P = .24	χ^2 = 0.559 P = .62	F = 0.463 P = .63	χ^2 = 5.958 P = .05	F = 0.847 P = .43	χ^2 = 8.786 P = .01	F = 5.038 P = .007

a Normal PCV \geq 34%

b Normal AST Females: \leq 32U/L males: \leq 38U/L

c ALT Females: \leq 30U/L males: \leq 38U/L

Table 2. Relationship between disease occurrence and clinical presentation in patients

Prevalence	Malaria	Malaria/typhoid	Typhoid	Level of significance
	n (%)	n (%)	n (%)	
Signs and symptoms				
Fever	174 (100%)	12 (100%)	2 (100)	$\chi^2 = 0.514$ P = .36
Headache	105 (60.3%)	7 (58.3%)	2 (100)	
Fatigue	91 (52.3%)	7 (58.3%)	0 (0)	$\chi^2 = 2.365$ P = .31
Abdominal pain	82 (47.13%)	9 (75.0%)	2 (100)	$\chi^2 = 5.554$ P = .06
Joint pain	75 (43.1%)	5 (41.7%)	2 (100)	$\chi^2 = 2.623$ P = .27
Anorexia	47 (27.0%)	5 (41.7%)	2 (100)	$\chi^2 = 6.194$ P = .045
Diarrhoea	16 (9.2%)	2 (16.7%)	1 (50)	$\chi^2 = 4.231$ P = .12

Table 3. Variation in co-infection of malaria and typhoid fever with respect to gender and age

	Number examined	Malaria/typhoid positive (%)	Level of significance
Sex			
Male	63	3 (4.8)	$\chi^2 = 0.608$, P = .44
Female	115	9 (7.8)	
Total	178	12 (6.7)	
Age group			
1 – 10	13	1 (7.7)	$\chi^2 = 3.393$, P = .846
11 – 20	23	2 (8.7)	
21 – 30	58	4 (6.9)	
31 – 40	26	1 (3.8)	
41 – 50	17	0 (0.0)	
51 – 60	21	2 (9.5)	
61 – 70	15	2 (13.3)	
71 -80	5	0 (0.0)	
Total	178	12 (6.7)	

Malaria and typhoid co-infections were observed in 6.7% of the patients and the clinical manifestations presented by the patients were quite similar to those who were diagnosed with either malaria or typhoid. However, it was observed that the level of parasitaemia in patients with malaria/typhoid infections were significantly higher than was observed for patients with only malaria. This finding is quite significant because according to the WHO definition of severity, parasitemia is indicated as a possible predictor of disease severity which may influence the outcome of a malaria infection. Identifying the relative importance of these and other factors likely to exacerbate disease severity in a resource poor setting is very important in order to develop evidence-based strategies for the prevention of deaths from malaria in malaria-endemic areas plagued with other tropical infectious diseases. Interestingly, anaemia and

elevated hepatic aminotransferase levels which are laboratory findings that could also serve as pointers for disease severity, were not significantly different from what was observed in patients with mono-infections.

Ammah and colleagues [1] reported a malaria/typhoid co-infection rate of 17% in Buea, another locality in Cameroon. We note that their data presented has quite a wide margin from what is reported here but our results are closely related to earlier findings by Nsutebu et al. [2], who reported a prevalence of 2.5% for typhoid fever. The prevalence value reported in various parts of Cameroon seems to be directly related to the method of diagnosis. Nsutebu et al. [2], confirmed typhoid fever in only 2.5% of clinical cases compatible with typhoid when the pathogen(s) were recovered from blood of febrile patients. Methods to diagnose typhoid fever

include cultures from blood and stool as well as detection of anti-salmonella antibodies by the Widal test.

In Cameroon like in most developing countries, the Widal test is the method usually used to diagnose typhoid fever in most health centres because it is cheap, fast and easier to perform. However, the use of this test suggests a high prevalence of typhoid fever or puts the prevalence of typhoid fever at an alarming rate, which clearly contradicts the results obtained from most research studies that have been based on isolation of the pathogenic agent from stool and/or blood. In this study, only 7.9% of the febrile cases investigated were indicative of typhoid fever. Attempts were made to recover Salmonella isolates from stool samples and our results suggest that even recovery of Salmonella by stool culture should be treated with caution because in addition to the fact that the isolation of Salmonella from stool could indicate a carrier state, out of the 52 presumptive isolates recovered from the stool samples, only 14 were identified as typhoidal Salmonella. Therefore, emphasis needs to be placed on complete characterisation of Salmonella isolates recovered from stool samples to avoid treatment of non-typhoidal salmonellosis as typhoid fever [4,13]. It should also be noted that these individuals from whom typhoid fever was diagnosed presented with clinical manifestations suggestive of typhoid fever and therefore isolation of Salmonella from their stool is indicative of current infection and not a carrier state.

In this study, gentamycin and ciprofloxacin were the best drugs of choice for the treatment of typhoid fever. Currently the quinolones are the drugs of choice for the treatment of salmonellosis. However, our study revealed that one *S. typhi* isolate was resistant to nalidixic acid and three others showed intermediate activity indicating that some Salmonella strains are acquiring resistance to this agent in the Kumba Health District. This is in line with a report by Nkemngu et al. [23] who indicated a case of typhoid fever treatment failure with nalidixic acid in Kumba. This suggests that resistant strains to the best drugs used in typhoid fever treatment could be emerging and therefore epidemiologic monitoring of susceptibility to the drugs of choice should be a routine activity especially as majority of our patients (54%) indicated that they do self-prescription (results not shown) and may indiscriminately use antibiotics without prescription.

As previously reported in other areas in Cameroon, the most prevalent *Plasmodium* species observed in Kumba was *P. falciparum* although a few mixed infections were also recorded [1,24,25]. The highest prevalence and intensity of malaria was recorded in the aged (71–80 years age group) and children (1–10 years age group) respectively. This is probably due to the ageing of the immune system of the aged and immature immune system of children as immunity to malaria requires repeated exposure to malaria attacks [25]. It has been established that children <5 years constitute a high risk group and this falls within the 1–10 years age group in our study [25-27].

5. CONCLUSION

Co-infections of malaria and typhoid fever exist in Kumba but not as common as previously thought thus, clinicians should not rely on clinical diagnosis alone; accurate laboratory diagnosis of febrile patients should be done for better management/treatment of these patients. Malaria is hyper-endemic in Kumba with *Plasmodium falciparum* being the most prevalent species.

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CONSENT

After explaining the potential benefits of the study to the patients they were requested to participate in the study by signing informed consent forms. Participation in the study was voluntary and those who refused to take part in the study were still given due attention without any bias. Patients were free to refuse to answer any question if they choose to do so.

ETHICAL APPROVAL

An ethical clearance for this study was obtained from the Ethics Committee of the South West Regional Delegation of Public Health, Cameroon while an administrative clearance was obtained from the Director of the Kumba District Hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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