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Practices Regarding the Use of Antimalarial Medications among Inhabitants of the Buea Health District, Southwestern Cameroon: Implications for Malaria Treatment Policy

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Abstract

Background: Malaria treatment policy recommends continuous monitoring and reporting of therapeutic efficacy of antimalarial medications for early detection of resistant strains. Patient adherence to policies regarding the use of antimalarial medications is critical to success of global malaria elimination. This study assessed the practices regarding the use of antimalarial medications in the Buea Health District, Southwest Cameroon.

Methods: A descriptive cross-sectional survey of a random sample of 495 people living in the district with episodes of malaria in the last one year prior to the study was conducted between February and August, 2015. Questionnaire was designed to obtain information from participants on the general knowledge of malaria and practices regarding to the use of antimalarial medications.

Results: Knowledge on malaria symptoms, transmission and prevention was reasonable among 80.6% (399) of the respondents ($p < 0.07$). Only 31.3% (155) of the respondent could attribute cause of malaria to protozoan of genus *Plasmodium species*. Majority of the respondents 56.9% (283) frequently treat malaria with ACT, 32.4% (161) with monotherapy, < 15% with other non-ACTs. Presumptive diagnosis was commonly practiced by 67.3% (333) of the respondents. The prevalence of self-medication in the study population was 18.4%. Only 57.2% (283) of respondents took prescribed antimalarials. Majority of self-medicated respondents (63%) obtained antimalarials from drugstores and friends. About 50.9% (252) of the respondents took medications regularly and 57.6% (258) completed the treatment regimen. Respondents whose treatments were based on laboratory diagnosis adhered better than those on self-medication or recommended at the pharmacy ($p < 0.02$).

Conclusion: The findings revealed a high knowledge of malaria with poor practices regarding the use of antimalarials. Efforts are needed to educate inhabitants of the district on practices regarding the use of antimalarials to prevent early emergence of drug resistance.

Keywords: Antimalarials, Drug resistance, Presumptive diagnosis, Self-medication, Adherence

1.0 Introduction

Malaria due to *Plasmodium falciparum* is the leading cause of morbidity and mortality in Africa, especially in children under the age of five years. The global malaria burden is disproportionately high in Sub-Saharan Africa which accounts for 89% of malaria cases and 91% of malaria deaths (WHO 2015). In Cameroon, over 90% of the population is at risk of malaria infection and approximately 41% have at least one episode of malaria each year (Mbenda *et al.* 2014). Moreover, malaria accounts for 50–56% of morbidity and 40% of the annual mortality among less than five years of age (NMCP 2008; WHO 2013). Malaria also imposes a heavy economic burden on both individuals and governments, with estimated direct costs of at least US $12 billion per year (CDC 2015). Between 2000 and 2015, control interventions have recorded a significant progress, resulting in 37% and 60% global decrease in incidence malaria and death rates respectively among all age groups (WHO 2015).

In spite of the global progress recorded in control interventions, the emergence and spread of resistant strains to antimalarial medications and insecticides has been an impediment to the management of malaria especially in endemic areas (WHO 2015). Resistance to traditional antimalarials, particularly chloroquine (CQ), the mainstay of 20th century malaria eradication (Attaran *et al.* 2004) and sulfadoxine-pyrimethamine (SP), the only alternative available for large scale implementation (WHO, 2006) lead to sweeping changes in antimalarial treatment recommendations. However, there are reports of a declining efficacy of Artemisinin–based combination therapies (ACTs), the recommended first-line treatment regimen for uncomplicated malaria in some endemic regions (White, 2011; Cui *et al.* 2012; Witkowski *et al.* 2013) suggesting that resistant parasite strains have emerged. There are fears that these resistant parasite strains may spread over to other endemic regions especially in Africa as was the case with chloroquine (Payne 1987).

Evidently, changing antimalarial treatment policy is not enough to ensure proper treatment of the disease. In fact, improving access to effective medications does not guarantee patient acceptability and ultimately adherence to the treatment regimen (WHO 2001). Appropriate disease management in part requires a critical review of individual factors related to patient acceptance and adherence, access to quality medications, perception regarding diagnosis and treatment recommendation. Accurate diagnosis is critical to malaria case management and may be compromised by the use of presumptive diagnosis, a practice which relies on clinical manifestations (Graz *et al.* 2011). A major setback in this method is that symptoms may be indistinguishable from many other infections including viral illness viral illness or dengue fever (Bloland 2001). WHO recommends that antimalarials should not be given to febrile patients unless the presence of malaria parasites has been confirmed by laboratory or rapid diagnostic testing (WHO 2010). Nevertheless, the proportion of people treated for malaria who have a confirmed diagnosis is low in the African Region compared with other regions of the world (WHO 2008).

Patient adherence is a major determinant of the therapeutic response to antimalarial medications (Yeung & White 2005). Poor adherence, the inability of patients to take their medications at the right dose, correct dosing frequency and recommended treatment frequency (Van den Bemt *et al*. 2012; Bruxvoort *et al*. 2014) is a common practice in endemic regions (Depoortere *et al*. 2004; Fogg *et al*. 2004). Factors related to poor patient acceptance and adherence not only result to treatment failure, but may lead to higher treatment costs and even resistance (Yeung and White, 2005; Banek *et al.* 2014). In populations with inadequate access to health services, self-medicating with poor quality drugs purchased at retail locations (drugstores) is a common practice (Sapkota *et al*. 2010; Chuma *et al*. 2010).

To complement efforts aimed at eradicating malaria, there is need to integrate individual factors that are related to the development of drug resistance such as patient acceptance and adherence, access to quality medications, and perception regarding diagnosis and treatment with the current treatment plan. This study was aimed at assessing the practices of inhabitants of Buea health district regarding the use of antimalarial medications.

2.0 Materials and Methods

2.1 The Study Area

The study was conducted in Buea Health District (BHD) of the Southwest region, of Cameroon. According to the 2015 census, BHD has a population of about 147842 inhabitants distributed over seven health areas namely: Bokwango, Bova, Buea Road, Muea and Tole with a total of seventy-six communities. About 58% of the population constitute people of age >17 years old (BHD 2015). Indigenes of the district are of the Bakweri tribe and part of the Bantu ethnic group (Achidi *et al*. 2012; Kimbi *et al*. 2014). However, the area attracts individuals from other tribes and ethnic groups including the Semi-Bantu and Foulbe from all over the country for farming, business and studies. Also present in the BHD is Mt. Cameroon, the highest mountain in west and central Africa and served as a touristic site for most foreigners visiting Cameroon (Kinge *et al*. 2013).

Buea has a Cameroon- type equatorial climate characterized by fairly constant temperatures ranging from 18°C-29°C annually with average humidity of 80% and two seasons: a short dry season (November–March) and a long rainy season (March-November). Malaria transmission occurs all year round with two peak periods, the first in April and May and the second in October and November. The prevalence of malaria parasitaemia in the low-altitude areas ranges from 30% in the dry season to 84% in the rainy season (Achidi *et al*. 2008) *P. falciparum* is the main species accounting for up to 96% of malaria infections in the area *Anopheles gambiae* is the dominant (most aggressive and most active of the three malaria vectors (*An. gambiae, An. funestus and Anopheles nili*), accounting for up to 72.7% of transmission Infection rates by (Wanji *et al*. 2012). An. gambiae are as high as 287 infective bites/ person/year and overall EIR estimated recently at 3.93 infective bites/person/night (Wanji *et al*. 2003; Bigoga *et al*. 2007).

2.2 Study Design, Population and Data Acquisition

This cross-sectional survey study was conducted between February-August, 2015 among randomly selected inhabitants within households of the seven health areas of the BHD. Individuals aged 17 years and above who had experienced at least an episode of malaria within the last one year were eligible of inclusion. Participants of this age should be sufficiently knowledgeable about the causative agent, signs and symptoms, mode of transmission and preventive methods of malaria. Participants' demographic data and information relating to their knowledge, attitudes and practice of malaria case management was captured using a pre-tested structured questionnaire.

2.3 Data Entry and Analysis

Data was double entered in Microsoft Excel and analyzed using SPSS Statistics 20.0 (IBM Corp, Atlanta, GA, USA). Relationship between qualitative variables, such as practices regarding the use of antimalarial medications and knowledge of malaria were assessed using the Pearson's Chi-Squared (χ^2) test. Statistical significance level

was set at $p \leq 0.05$.

2.4 Ethical Considerations

Ethical clearance was obtained from the Institutional Review Board of the Faculty of Health Sciences, University of Buea. Administrative authorization was sort from South West Regional Delegation of Public Health and the Buea District Health Service. Only individuals who volunteered to participate by signing a written informed consent, after adequate sensitization on the project objectives were enrolled.

3.0 Results

3.1 Demographic Characteristics and Knowledge of Malaria

A total of 495 participants were enrolled in the study. Most of the respondents were males (51.7%), aged 17-25 (52.7%), students (53.1%) and at tertiary level of education (66.5%) {Table 1). The majority of respondents knew the signs and symptoms [490 (99%)], mode of transmission [450 (90.9%)] and methods of prevention [399 (80.6%)] of malaria. However, only 155 respondents (31.3%) could attribute the cause of malaria to protozoans of genus Plasmodium species (Figure 1).

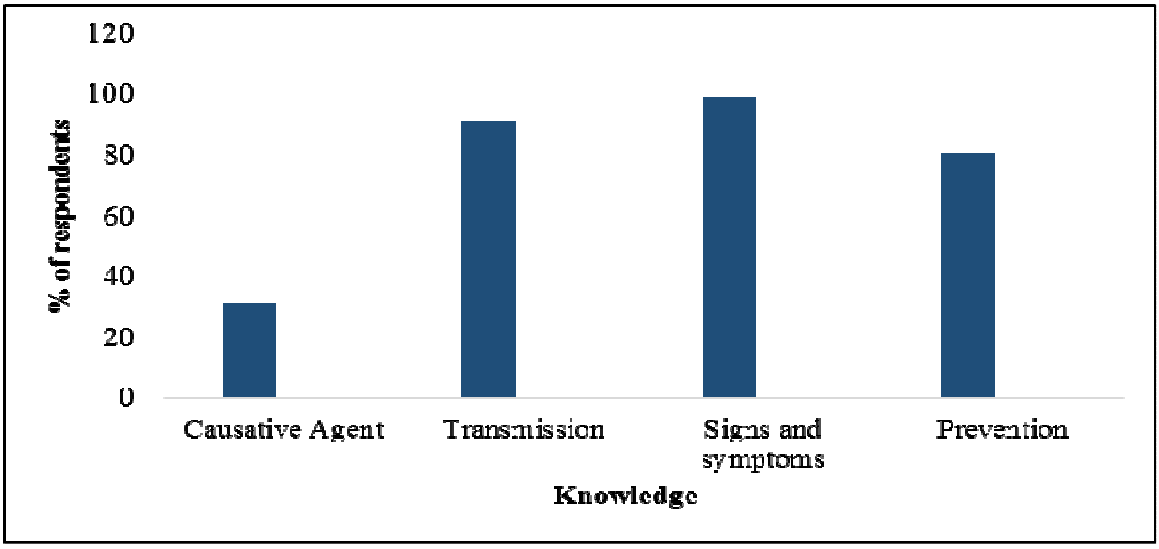

Figure 1: Knowledge of Respondents Regarding Malaria

The categories of correct and wrong/no responses for all four aspects of knowledge of malaria discussed above (causative agent, mode of transmission, signs and symptoms and methods of prevention) were put together to assess the level of knowledge of malaria among the participants. A participant with correct responses for at least three of the aspects was considered to have a good level of knowledge, those with correct responses to two or less responses were considered to have average and poor levels of knowledge respectively. Majority [399(80.6%)] of respondents had good, while 76(15.4%) and 20(4.0%) had average and poor levels of knowledge on malaria respectively.

Table1. Demographic Factors and Knowledge of Malaria.

Demographic variable		proportion n=495 (%)	Good knowledge n(%)	Statistics Chi-Square	P-value
Gender	Male	256 (51.7)	200(78.1)		
	Female	239(48.3)	199(83.3)		
	Total	**495(100)**	**399(80.6)**	2.573	0.281
Age group	17-25	26 0(52.7)	214(82.3)		
	26-34	165 (33.1)	133 (80.6)		
	35-43	35 (7.1)	27(77.1)		
	≥44	35 (7.1)	25(71.4)		
	Total	**495(100)**	**399(80.6)**	10.294	0.113
Level of Education	Tertiary	329 (66.5)	287(87.2)		
	High/secondary	113 (22.8)	80(70.8)		
	Primary	28 (5.7)	14(50.0)		
	None	25 (5.1)	18(72.0)		
	Total	**495(100)**	**399(80.6)**	35.659	0.000
Occupation	Student	263 (53.1)	219(83.3)		
	Civil servant	89 (18.0)	75(84.3)		
	Self employed	106 (21.4)	77(72.6)		
	None	37 (7.5)	28(75.7)		
	Total	**495(100)**	**399(80.6)**	12.401	0.054

Table 1 summarizes the association of demographic factors with good knowledge of malaria. Although there was no significant difference between good knowledge of malaria and sex of respondents ($p > 0.28$), they were higher in female (83.3%) than males (78.1%). The proportion decreased with and increased in age from 82.3% in the 17-25 years to 71.4% in ≥ 44 years old participants ($p > 0.11$). Moreover, good knowledge of malaria in tertiary level respondents (87.2%) was significantly higher ($p = 0.00$) than in high/secondary level respondents (70.8%), or primary level respondents (50.0%). Stratification by occupation revealed that civil servants (84.3%) were more knowledgeable regarding malaria than students (83.3%) or self-employed respondents (72.6%) though with no significant difference ($P > 0.05$)

3.2 Practices regarding the use of antimalarial medications

Table 2 summarizes the practices of respondents regarding the use of antimalarial medications. Majority of respondents [306 (67.2%)] knew they had malaria through presumptive diagnosis either determined by themselves 259 (52.3%) or by healthworkers or friends [74 (14.9%)]. Only [162 (32.7%)] of the respondent actually detect the presence of malaria through laboratory diagnosis by microscopy or rapid diagnostic test (RDT). Though there was no association between sex and practices regarding diagnosis ($P > 0.07$), it was better in females than males. Self-presumptive diagnosis was higher in males [145 (56.6%)] than females [114(47.7%)]. Moreover, most of the females [88 (36.8%)] took medication prior to confirmed laboratory diagnosis than males [74(28.9%)]. With regards to age group, medication based on confirmed diagnosis was higher (34.3%) in respondent of age group > 44 years and lower in respondents on age group 26-24 years. There was no significant difference between level of education and practices regarding diagnosis ($P > 0.15$). Presumptive diagnosis was higher among civil servant (59.6%), this was followed by people who were self-employed (53.8%), students (49.8%) and lower in people who were not employed (48.6%).

It was also observed that majority of the respondents [283 (57.2%)] took antimalarial based on recommendations from doctors or nurses, this was followed by [91 (18.4%)] who treated the disease based on self-prescription. 79 (16%) of the respondents got their recommended medications from pharmacies or drugstores whereas 42 (8.5%) of the respondents relied on friends' recommendations. Females adhered to good practices regarding treatment recommendations than males ($p < 0.042$). Self-prescription was generally higher in males (61.5%) and lower in females (38.5%) whereas prescription based on recommendations was higher in females (53.7%) and lower in males (46.3%). Treatment recommendation was not significantly different with age ($p > 0.23$). Self-prescription and treatment recommendations were higher in people of age group between 17-25 years and lower in people of age group > 44 years. There was no association between treatment recommendation and level of education or occupation ($p > 0.65$).

Table 2. Practices Regarding the Use of Antimalarials

		Parameter	Total population n=495 (%)
1	**Diagnosis**	Self (presumptive)	259 (52.3)
		Laboratory diagnosis	162 (32.7)
		Healthworker or friend (presumptive)	47 (14.9)
2	**Treatment recommendation**	Physician or Nurse	283 (57.2)
		Self	91 (18.4)
		Pharmacy or drugstore	79 (16)
		Friend	42 (8.5)
3	**Place of drug purchase**	Hospital	135 (27.3)
		Drugstore	146(29.5)
		Community pharmacy	232(46.9)
		Friend	10 (2.0)
4	**Adherence (regular dosage)**	Yes	252(50.9)
		No	243 (49.1)
	(treatment completion)	Yes	283 (57.2)
		No	212 (42.8)

Regarding the source of medication, the highest number of respondents [42(8.5%)] purchased antimalarials from community pharmacy, this was followed by 146 (27.9%) from drugstores, [135 (25.8%)] from hospital pharmacy and 10 (1.9%) took the antimalarials from friends. It was observed that most of those who used self-prescribed antimalarial medications obtained them from drugstore, some of them relied on leftover from previous malaria episodes, others obtained their medications from neighbors or friends whereas those who used medication prescribed based on laboratory findings obtained them from either hospital pharmacy or community pharmacy (Figure 2), 27.7% of respondents who bought drugs at the pharmacy were recommended at the pharmacy.

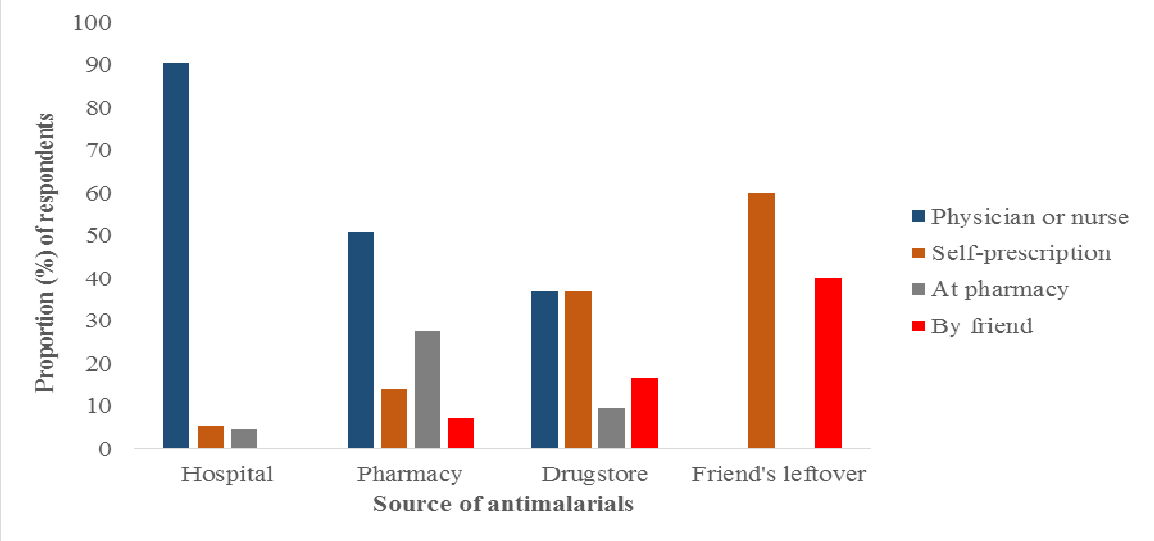

Figure 2. Association between Treatment Recommendation and Sources of Purchase of Antimalarials

In the context of the current study, adherence was defined as abiding to medical advice in terms of dosage interval (regular treatment) and the ability to complete treatment regimen (treatment completion). 50.9% of the respondents took antimalarials regularly and 57.2% completed the treatment regimen. There was no association between adherence and demographic factors of respondents ($p > 0.12$). It was observed that females adhere to treatment better than males. 51% of females took medications regularly of which 58.2% actually completed the treatment course whereas 50.8% of males took medications regularly 56.2% completed the treatment course. The degree of adherence was higher (57.1%) in people of age group > 44 years and among illiterate (56.0%).

Respondents whose treatments were based on laboratory diagnosis and upon recommendation by a physician adhere better than those whose treatments were based on self-prescription or recommended at the pharmacy ($p < 0.02$) (Figure 3).

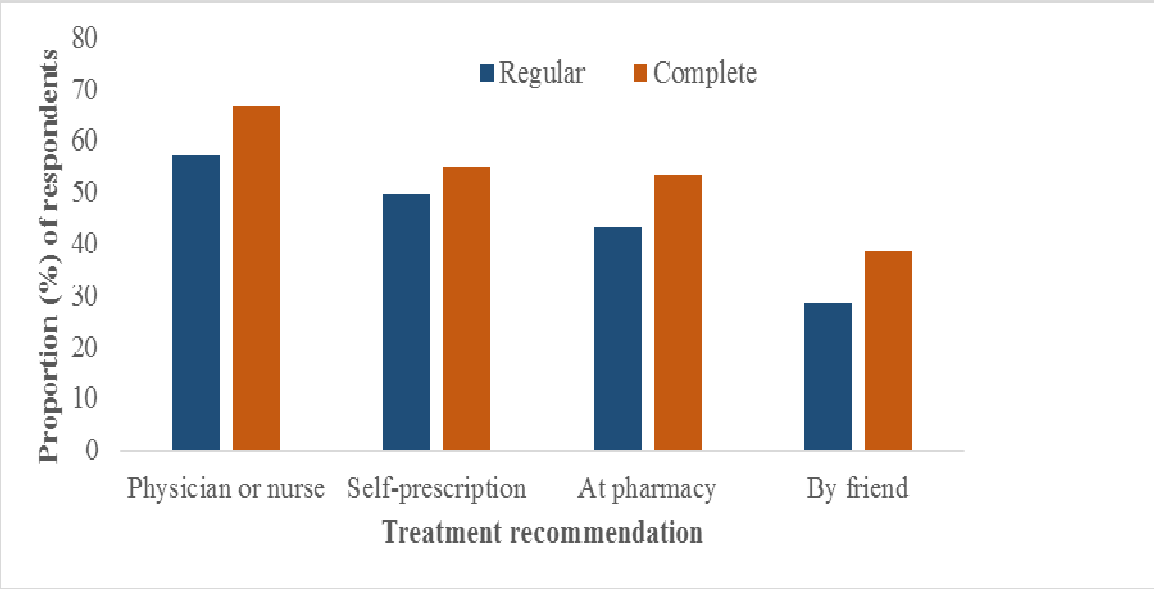

Figure 3. Association of Treatment Recommendation and Adherence

3.3 Profile of antimalarials frequently purchased by respondents.

A wide range of antimalarials was used by respondents; classified either as artemisinin combination therapy (ACT), monotherapy or non-ACT (Table 3). More than half of the antimalarials (56.9%) used by respondents were ACTs. These drugs are currently recommended for the treatment of uncomplicated malaria in Cameroon. The ACTs mostly used were artemether-lumefantrine (AL), artesunate-amodiaquine (AQ) and dihydroartemisinin-Piperaquine (DHAP). However, 34.9% of respondent used monotherapies such as artemether, quinine sulfate artesunate etc. An additional 8.2% used non-ACTs such as sulphadoxine-pyremethamine, atovaquone–proguanil. Herbal medicine was used by some respondents in treating malaria.

Table 3. Profile of Antimalarias Frequently Used by Respondents

Drug category	Name	n=523(%)	Total (%)
ACT	artesunate-amodiaquine (AL)	34(6.5)	
	Artemether-lumefantrine (AQ)	242(46.4)	56.9
	Dihydroartemisinin- Piperaquine (DHAP)	13(2.4)	
	artesunate	24(4.6)	
Non –ACT	artemether	100(19.1)	34.9
(Monotherapy)	Dihydroartemisinin	4(0.7)	
	Quinine sulfate	36(6.9)	
	Mefloquine	3(0.5)	
	Chloroquine	27(5.1)	
Non-ACT	Sulphadoxine-pyremethamine	14(2.6)	
(combination therapy)	Atovaquone -proguanil	1(0.1)	8.2
	Herbal medicine	23(4.4)	

It was established that majority of the respondents (72.1%) used ACTs when recommended, 23.5% used the medications because of past experience and 4.4% because of cost. On the other hand, majority of respondents

(68.2%) preferred using non-ACTs because they were less costly this was followed by 23.1% who preferred the non-ACTs due to past experienced, 8.7 % used non-ACT when recommended.
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4.0 Discussion

The emergence and spread of antimalarial drug resistance is one of the greatest challenges facing control nowadays. A contributing factor to this phenomenon is the widespread use of artemisinin compounds in the treatment of the disease, especially in endemic regions. Overuse of these medications coupled with inadequate treatment practices and patient noncompliance to treatment regimen have been the largest contributing factors to the trends reported in this study.
Results of this study showed that majority (80.6%) of the inhabitants of the Buea Health District BHD) had heard about malaria and demonstrate better knowledge of malaria signs and symptoms, treatment and preventive methods. These observations are typical in endemic regions including the BHD and it is expected that inhabitants of such areas would frequently experience malaria and should have an adequate knowledge of the disease. This finding is supported by other studies in the district (Kimbi *et a*l. 2014) including other endemic regions such as Southeast Iran, Malaysia and Africa (Mazigo *et a*l. 2010; Aborah *et al*. 2013; Soleimani-A *et al*. 2014). However, the study revealed a poor knowledge on the cause of malaria especially among illiterate and elderly people. Only few respondents (31.3%) associated a protozoan as the causative agent of malaria.
The findings of this study revealed that presumptive diagnosis was highly practiced by both the respondents and healthworkers in the district. Only 32.7% of the respondents took medications based on confirmed laboratory diagnosis. This is a common practice in endemic regions where people take antimalarials based on some noticeable signs and symptoms of malaria attack such as febrile and joint pains. This practice however, exposes them to dangers of treatment failure as symptoms may be indistinguishable from many other simple or serious conditions from viral illness or dengue fever (Bloland 2001). To minimize treating false positive cases for malaria, current World health organisation (WHO) protocol recommends a “test and treat” policy that permit diagnosis by means of microscopy or rapid diagnostic test (RDT) prior to treatment (WHO 2012). Similar findings have been reported in studies conducted in Ethiopia, Nigeria and Tanzania (Deressa *et al*. 2004; Akanbi *et al*. 2005; Chipwaza *et al*. 2013). The results further showed that only 52.9% of respondents took antimalarials upon recommendation by a physician or nurse indicating that the pattern of antimalarial drug prescription in the study area is poor. This therefore, implies that 47.1% of the respondents were exposed to a high probability of drug abuse or misuse thereby exposing them to the tendency of purchasing low quality drugs. The prevalence of self-medication in the study population was 18.4%. 63% of the respondent who practiced presumptive diagnosis was self-medicated with previously purchased or recommended antimalarials. This practice of self-medication or depending on medication from unlicensed practitioners is a serious problem in sub Saharan African. Studies conducted in Nigeria, Ghana and Kenya corroborated poor antimalarials prescription patterns (Santoshkumar *et al*. 2010; Aghahowa *et al*. 2014; Chipwaza *et al*. 2014). However, the treatment rate reported in this study is much lower compared to findings of studies conducted in Kenya with a reported 70.3% of self-treating respondents with ACTs (Kimoloi *et al*. 2013). There is therefore a need to discourage this practice as use of presumptive treatment for malaria has the potential for facilitating resistance by greatly increasing the number of people who are treated unnecessarily but will still be exerting selective pressure on the circulating parasite population (Graz *et al*. 2011).
It was observed that most of those who were self-medicated obtained their antimalarials from drugstore or community, some of them relied on leftover from previous malaria episodes, others obtained them from neighbors or friends whereas those who used medication prescribed based on laboratory findings obtained them from either hospital pharmacy or community pharmacy. Similar results were reported in studies conducted in Ethiopia, Kenya and Nigeria (Deressa *et al*. 2004; Osemene & Lamikanra 2012; Kimoloi *et al*. 2013). A contributing factor to this high purchase of self-medicated antimalarials in these retail areas is that drugs can be sold without prescription. Studies have shown that treatment through the medicine outlets is mostly based on clinical symptoms resulting to over 50% being non-malaria cases (Uzochukwu *et al*. 2010; Ezenduka *et al*. 2014), leading to wastage and inappropriate management of fevers and other complications. It has been reported that another contributing factor to the purchased of antimimalarials at these locations is due to lack of access to formal health services, inadequate services (shortage of drugs and long waiting time), couple to the fact that they are cheap and easily available as over-the-counter drugs in such locations (WHO 1998; Deressa *et al*. 2004). Moreover, it has been reported that medications sold in drugstores or chemist are of low quality thereby exposing individuals to dangers of treatment failure which can lead to drug resistance through increasing the likelihood of exposure of parasites to suboptimal drug levels (Bloland 2001; Onwujekwe *et al*. 2009).

Pattern of drug usage showed a preference for ACT (56.9%) over non-ACTs (43.1%), as the drugs of choice for the treatment of malaria. These drugs were recommended as the first- treatment of uncomplicated malaria since 2004 (Ali *et al*. 2014). The prevalence of ACTs reported in this study is in agreement with similar studies performed in Kenya (Kimoloi *et al*. 2013). Of the ACTs, AL also known as Coartem®, Lumartem®, Artefan® was frequently used especially among self-medicated individuals than AQ (Arsucam®) or DHAP (Cotecxin®). A reason given by some respondents regarding the choice of drug was that it was effective, cheap and easily available. However, 34.9% of respondents used non-ACTs such as artemether, artesunate and quinine sulfate. Alarming is the fact that these non-ACTs are dispensed as over- the-counter drugs in drugstores including the pharmacies promoting irrational drug use. Some of these drugs were misused. 3.1% of the respondents used propylaxis (SP, mefloquine, atovaquone/proproguanil) to treat malaria.

With regards to adherence to medication, findings from this study have shown that the degree of adherence defined as the extent to which patients take medications as prescribed was low as only 49.1% of the respondents took medication regularly with just 57.2% completing the treatment regimen. The practice of adherence to medication is important as it determines the treatment outcomes. Several studies have shown that poor adherence in terms of not taking the right dosage regularly and not completing the treatment regimen can lead to treatment failure as it exposes the parasites to suboptimal drug levels (Bloland 2001). A devastating consequence to this effect is that poor adherence can give rise to the development of drug resistant. Our study further revealed that adherence was lower in self-medicated individuals. 44.8% of these individuals took drugs regularly and only 55.6% completed the treatment regimen. Related studies have shown low degree of adherence to treatment regimen particularly in self-medicated individuals. In the Maheba refugee settlement of Zambia, 39.4% of patients were classified as probably adherent to a three-day course of the combination of artesunate and SP, 21.2% were certainly non-adherent, and 39.4% were probably non-adherent (Lawford *et al.* 2011). Similar result was obtained in a study by Gore-Langton *et al*. 2015. Of those who did not complete the treatment regimen, majority (76.2%) terminated when they felt better. This practice increases the likelihood of exposing the parasites to suboptimal drug level which may eventually lead to the development of drug resistance.

5.0 Conclusions

The findings of this study reveal a high awareness of malaria but poor practices regarding the use of antimalarials. Suggesting that efforts are needed to educate inhabitants of the Buea health district on good practices regarding the use of antimalarial to prevent early emergence of resistance to highly effective antimalarials.

Competing interests

The authors declare no competing interests in this work.

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Author Contributions

Conceived and designed the survey: MUA, TOA, CA, and SNA. Conducted the survey: MUA, TOA, and EAA. Analyzed the data: MUA, TOA, CA and MA. Wrote the paper: MUA, TOA, and SNA.

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