Economic burden of malaria in Burundian children: An evidence for disease management in resource limited settings

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ABSTRACT

In Burundi, malaria is the leading cause of morbidity and mortality, especially in children under five. This results in high clinical burden of the disease; however, its economic burden remains unknown. The aim of this study was to estimate the economic burden associated with malaria in Burundi and explore the factors that can affect the costs. This study was a prospective incidence-based cost-of-illness study analysed from the societal perspective. The study included children aged under five years with malaria infection, who visited and received treatment at any of the two study health facilities in the period of November to December 2019. Data collection was done by reviewing medical and financial records and by interviewing caregivers of the patients. Micro-costing approach was used to estimate the economic costs of malaria per episode. The cost was presented in international dollars (Int\$) for the year 2019. Stepwise multiple linear regression method was applied to examine the factors affecting the costs and to generate a cost model. Eighty-five children with the average age of 29 months were included in the study. Most of them (70.5%) were treated as in-patient. The out-patient visits costed Int\$23.5, while the in-patient hospitalization costed Int\$218.2. The types of medical services, health facilities, antimalarials used, and duration of fever before seeking appropriate medical care were found to affect the costs. The model indicates that up to Int\$18.76 can be saved per malaria episode if treated early (in less than 2 days). This can save up to Int\$24,257,748 per year at national level. This study demonstrated that malaria is associated with a considerable economic burden in Burundi. It will support decision makers in deciding an appropriate clinical management for malaria prevention like the community case management program.

Keywords: Malaria; Burundi; economic and cost of illness

INTRODUCTION

Malaria is a mosquito born infectious disease that can be cause of long term neurological sequalae or death (WHO, 2022). Worldwide, there has been a slow decrease in malaria cases and deaths since 2010 with 251 million cases and 585,000 deaths. In 2018, there were 228 million cases and 405,000 deaths (WHO, 2018). Majority of disease burden i.e., more than 90% of cases and deaths has been in Sub-Saharan Africa. Children aged under five years are the most vulnerable group of the cases in 2018 with accounted for more than 60% of all deaths (WHO, 2018). However, Burundi, a land-locked, low-income country in East Africa and one of

the poorest countries in the world (WFP, 2020), has seen a large increase of 51% in malaria cases and deaths (WHO, 2018). Malaria cases were accounted for 2.6 million cases and 2,609 deaths in 2012, to 5 million cases and 3,279 deaths in 2018 (USAID, 2022) and reached epidemic threshold in 2019 (Mark Nonkes, 2017; Pat Lok, 2019). The prevalence of malaria in children has increased in the country from 17% in 2012 to 27% in 2017 (DHS, 2017) resulting in 69% of all deaths in Burundi (Moise, 2018).

To decrease the high mortality rate caused by malaria in children under five, Burundian government has offered free healthcare services from all public health facilities to all children since 2006 (USAID, 2022). However, timely access to health care is limited. Hence, the community case management (CCM) program for malaria has been established since 2013 (USAID, 2014). This program provided training for community health workers (CHWs) to early diagnose and provide basic health care for the children at home within 24 hours from the onset of fever, according to WHO recommendation (USAID, 2014).

Malaria does not only pose a heavy clinical burden on health system of the affected countries, such as Burundi, but also the economic burden hindering sustainability of the public health and growth of those countries (Gallup & Sachs, 2001). This highlights the importance of investigating the economic burden of malaria including the associated factors to know the magnitude of the problem in Burundi, and to provide a basis for advocacy to increase funds and investment in malaria control programs. Hence, this study aimed to estimate costs of malaria in children aged under five years in Burundi from societal perspective, and to explore the factors that can affect the costs of malaria.

METHODOLOGY

Study design and study location

The study was an incidence-based cost of illness analyzed from a societal perspective. The economic costs were estimated for the whole episode covering from onset until 3 weeks after the outpatient or in-patient treatment. The costs were estimated in 2019 values. The study sites were from 2 levels of health facilities; hospital and primary health center. One of each level was purposively selected based on cooperation, i.e., Hospital Prince Regent Charles (HPRC) - a tertiary hospital with 600 beds having both out-patient and in-patient departments, and Centre de Medecine Communautaire de Buyenzi (CMC Buyenzi) - a primary health center having only outpatient department. Both selected study sites locate in Bujumbura Mairie province (the largest and economical capital city) in Burundi.

Study sample

The study population were children aged under five years diagnosed with malaria infection, who visited and received treatment (as out- or in-patients) at any of the two health facilities (HPRC and CMC Buyenzi) in 2019. The patients with severe chronic illnesses (e.g., HIV/AIDS or malnutrition) as well as the patients with incomplete medical records were excluded.

To calculate the sample size, we used a sample size calculation for multiple regression analysis to explore factors affecting the cost (Lwanga & Lemeshow, 1991):

n (at least) =
$$10 \times IV$$

where n is the sample size, and IV is the number of potential predictor variables. Based on characteristics of the study sample, it was hypothesized that the treatment costs of malaria are associated with 8 variables, i.e., age, type of service (out- or in-patient services), disease severity (uncomplicated or severe), type of health facility, duration of symptoms before treatment, and type of antimalarials. Therefore, a minimum sample size of 50 cases was determined.

Data collection

Prospective data collection was done during November-December 2019. The review of medical and financial records was employed to collect the patients' general characteristics (i.e., age, gender and insurance scheme), clinical characteristics (i.e., disease severity, type of service, and outcome on discharge), admission/discharge/visit date, health care resources and quantity of resources used during the malaria episode (i.e., drugs and other medical suppliers, laboratory tests, out-patient consultations, and length of stay for in-patient cases). The resources used and related costs incurred with patients' family were collected from a face-to-face interview of parents or caregivers. In addition, we interviewed the patients' caregivers or parents regarding the expenditures that related to malaria and time loss when caring for their sick child) as well as the duration of fever before seeking appropriate medical care

For out-patient (OPD) cases, we collected data for four times, i.e., week 0 (on the first visit date), week 1 (a week after the first visit), week 2 and week 3. While we collected in-patient (IPD) data from the IPD cases on the

admission and discharge date, and then interviewed their caregivers/parents every week after the discharge for three times.

Costing method

Activity based costing approach (Drummond et al., 2005) was applied to estimate the costs in this study. The cost was estimated for the year 2019 from a societal perspective covering costs of health care providers and patients' family. It consisted of: 1) direct medical cost (DMC), i.e., all related treatment costs in the health facilities; 2) direct non-medical cost (DNMC) included any out-of-pocket expenses on food, transportation, and accommodation before, during and after admission/visit due to the disease; and 3) indirect cost (IDC) which is the opportunity cost of time loss of parents and/or caregivers when giving care for their sick child.

To calculate DMC, the quantities of each clinical service received were multiplied with the unit cost of that service. Due to limitations to access and calculate unit cost of the health facilities, we used references from various sources. Unit costs of antimalarial drugs were derived from MSH international drug price guide (MSH, 2015), and added 10% to the price for the cost of shipment and delivery, as recommended. The unit cost of other drugs and medical suppliers were the health facilities' purchasing price or median price from drugstores. In case of investigations included all kinds of diagnostic tests, we used the median price (charge) of these tests from private health facilities. For routine services provided to the patients during their visits or admissions, i.e., consultation, administration of drugs, checking of medical parameters (e.g. temperature, and pulse rate), OPD cost and inhospitalization per day, the unit cost of these services were referred to the WHO-CHOICE (CHOosing Interventions that are Cost-Effective) database (WHO, 2012).

Indirect cost was calculated based on human capita approach (Drummond et al., 2005) by multiplying the caregivers time lost with the Burundi Gross National Income (GNI) per capita per time (World Bank, 2019). The total costs were first calculated from local currency (BIF) and then converted in the international dollar (Int\$) using purchasing power parity. Exchange rate used is Int\$1=751.7BIF (World Bank, 2019)

Statistical analysis

Demographics, clinical characteristics, and cost per episode in terms of total cost and cost components were statistically analyzed. Descriptive statistics were used to summarize the characteristics of the study samples and to present the costs. A stepwise linear regression was conducted, to analyze the factors affecting the cost and to predict cost of various conditions. The cost was first transformed to natural logarithm to make it normally distributed. The final model was investigated for normality, heteroscedasticity and multicollinearity (Belsley et a., 1980). Smearing factor (Belsley et al., 1980), which help to retransform the cost from natural logarithm to original scale was calculated.

RESULTS

Between November and December 2019, 93 children were diagnosed with malaria at the two health facilities. Five children were excluded because they had HIV/AIDS, malnutrition and sickle cell anemia conditions. Another three children were excluded as the caregivers did not give the consent. Finally, 85 children were included in this study. Two children were referred from the health center to the hospital and they received both OPD and IPD services.

Baseline characteristics of the study sample

Table 1 shows the baseline characteristics of the study population. The mean age was 29 months and 51.7% of the patients were male. Majority of the patients (95.2%) was covered by the government free health care insurance. Comparing between the health facilities, there was no statistically significant difference between the demographic characteristics. However, the clinical characteristics were statistically different between those who received cares from the two health facilities. Most of the cases (70.6%) were treated as IPD cases with the average length of stay of 7 days. About half of the cases (48.2%) were classified as severe malaria. Most of the caregivers (61.2%) sought appropriate medical treatment in less than 2 days from the onset of fever.

Major resources utilization

There is a difference between the resources used in the two health facilities (Table 2). Since the primary health center treats only OPD cases, they use mainly oral drugs. The tertiary hospital treats mainly IPD cases, thus parenteral artesunate was the most widely prescribed (71.6%). The investigations done included malaria rapid test, thick blood smear for malaria microscopy, full blood count, C reactive protein test, urea and creatinine test. At the primary health center, the most prescribed tests were malaria rapid test and thick blood smear for malaria microscopy. The tertiary hospital, dealing with complicated case; therefore, they prescribed a variety of tests.

Overall, 69.4% of the children received treatment before visit/admission, and 4.7% received treatment after visit/admission. The mean caregiver loss days is 10.3 days (1.7 days at the health center and 12.6 days at the tertiary hospital).

Table 1: Baseline characteristics of the study sample

Characteristics		All (n=85)	Health center	Tertiary hospital	p-value ^a
Demographic Ch	aractoristics		(n=18)	(n=67)	
Gender	Male	44(51.7%)	8(44.4%)	36(53.7%)	0.598 ^b
denuei	Female	41(48.3%)	10(55.6%)	31(46.3%)	0.590
Ago(montha)					
Age(months)	Mean (<u>+</u> SD)	28.8(±15.8)	25.8(<u>+</u> 15.2) 23	29.5(<u>+</u> 15.9)	0.420c
T	Median	25.0		29	0.438c
Insurance	Government	81(95.2%)	18(100%)	63(94%)	$0.484^{\rm d}$
	MFP	2(2.4%)	0 (0%)	2 (3%)	
	Personal payment	2(2.4%)	0 (0%)	2 (3%)	
Clinical Characte	eristics				
Type of service	OPD	25(29.4%)	18 (100%)	7(10.4%)	0.000 ^b
	IPD	60(70.5%)	0 (0%)	60 (89.6%)	
Disease severity	Uncomplicated	44(51.7%)	18 (100%)	26(38.8%)	0.000 ^b
-	Severe	41(48.3)	0	41 (61.2%)	
Outcome on	Alive	84(98.8%)	18 (100%)	66 (98.5%)	0.602b
discharge	Dead	1(1.2%)	0 (0%)	1 (1.5%)	
Time between	Mean (+SD)	2.5(+ 1.9)	1.7 (+ 1.5)	2.7 (+2)	0.039c
visit/admission	Median	2	1	2	
and onset of					
symptoms					
J 1	Less or equal to 2 days	52 (61.2%)	16(88.9%)	36 (53.7%)	0.007 b
	More than 2 days	33(38.8%)	2(11.1%)	31(46.3%)	0.007
Duration of	Mean (<u>+</u> SD)	10.4(± 6.7)	6 (± 8)	12 (<u>+</u> 6)	0.000c
episode (days)	Median	9	4	10	2.000
Length of stay	Mean (±SD)	7 (<u>+</u> 4)	-	7 (<u>+</u> 4)	_
(day)	Median	7 (<u>-</u> 1)		7	

Free HC= Free health care; MFP= Mutuelle de la fonction publique (Civil servant insurance scheme, ^ato compare between primary health center and tertiary hospital, significance level is <0.05 ^b chi-square test, ^c Mann Whitney U test and ^d Fischer exact test

Cost of malaria per episode by health facility and type of service

The total cost of treating a malaria episode as out-patient was Int\$23.5. The cost attributed to DMC (Int\$16.8) was the largest contributor of the total cost. The DNMC (Int\$3.4) and IDC (Int\$3.2) had nearly equal proportions. The costs between the two health facilities were statistically significant different, except for the IDC. The total cost of an OPD case at the tertiary hospital (Int\$43.9) was 2.8 times higher than those treated at the primary health center (Int\$15.6).

The total cost of an episode of malaria as IPD case at the tertiary hospital was Int\$218.2. Its DMC (Int\$148.0) was accounted for 67.8% of the total cost followed by IDC (Int\$28.4) and DNMC (Int\$27.0). (Table 3).

Factors influencing the costs

The potential variables affecting the costs of malaria used in the stepwise linear regression of this study are shown in Table 4. The type of services, the type of health facilities, type of antimalarials and duration of fever before seeking appropriate medical care were found affecting the cost of malaria per episode (with adjusted R2 was 0.898) (Table 5). The model passed the homoscedasticity test as scattered plot of residuals against predicted values and all independent variables shows no funnel shape. The condition indexes were less than 30 which indicates no multicollinearity between the predictors. The Durbin Watson constants was 2.2 which indicates the independence of the residuals. The cook's distance value was less than 1 showing that there is no influential observation. Leverage statistic was less than 3(k+1)/n (where, k = number of independent variables, n = sample size) which indicates no outlying independent variable observation. The studentized deleted residuals varied between -3.5 to 3 showing no outlying dependent variable observation.

According to the fitted model, the predicted treatment cost of an out-patient case at the primary health center in less than 2 days from fever onset (best case scenario) was Int\$15.09. The cost of the worst-case scenario i.e., inpatient case at the tertiary hospital admitted after 2 days from fever onset and in which there was treatment

failure and they used both parenteral quinine and artesunate were Int\$549.03. It increases by 3638% compared to the best-case scenario (Table 6).

It is recommended by WHO that the febrile children should receive appropriate medical care in less than 2 days to avoid malaria complication. In this study, we provide the evidence that delaying medical care in febrile children could increase the cost of treatment. From the fitted model, we estimated the cost of malaria for the patients who received medical care in less than 2 days and those who received medical care after 2 days, for the other predictors we used their mean values. The cost of malaria per episode was Int\$83.36 and Int\$102.13 for the patients who received medical care in less than 2days and those who received medical care after 2 days, respectively. Hence, early medical care can save up to Int\$18.76 per episode of malaria.

According to DHS (DHS, 2017), the total number of malaria cases in children under five years is estimated to be 2,751,185 per year and only 53% of these cases receive medical care in less than 2 days. If also the remaining cases would receive early treatment, the country would save up to: (2,751,185*47%)* Int\$ 18.76= Int\$ 24,257,748 per year.

Table 2: Major ressources utilisation

		All (n=85)	Health center (n=18)	Tertiary hospital (n=67)	p-value ^a
Antimalarial	Both Parenteral artesunate and quinine	2(2.7%)	0	2(3%)	$0.000^{\rm b}$
	Parenteral artesunate	51(60%)	0	51(76.1%)	
	Parenteral quinine	7(8.2%)	0	7(10.4%)	
	Oral antimalarials	25(29.1%)	18(100%)	7(10.4%)	
Glucose 5% IV	fluid	9(10.5%)	0	9(13.4%)	0.000^{c}
Whole human	blood for transfusion	19(22.3%)	0	19(28.4%)	0.009^{c}
Iron suppleme	ent	10(11.7%)	0	10(14.9%)	0.000^{c}
Dipyrone IV a	mp 5 ml	46(54.11%)	2(11.1%)	44(65.7%)	0.000^{c}
Paracetamol s	yrup 250mg/ml	18(21.17%)	12(66.7%)	6 (9%)	0.000^{c}
Investigation					
Malaria rapid	test	14(16.47%)	11(61.1%)	3(4.5%)	0.000^{c}
Thick blood sr	near	51(60%)	7(38.9%)	44(65.7%)	0.057^{c}
Urea test		27(31.7%)	0	27(40.3%)	0.000^{c}
Creatinine tes	t	27(31.7%)	0	27(40.3%)	0.000^{c}
Full blood count		56(65.88%)	0	56(83.6%)	0.000^{c}
C Reactive protein test (CRP)		39(42.9%)	0	39(58.2%)	0.000^{c}
Received treatment before visit/admission		59(69.4%)	7(38.9%)	52(77.6%)	0.606c
Received treatment after visit/admission		4(4.7%)	0	4(6%)	0.003c
Caregiver time loss in days		10.3(8, 8.7)	1.7 (1.3, 1.3)	12.6 (8.4,	0.000^{d}
Mean (Median, SD)				11.0)	
Length of stay (Median, SD)	in days Mean	7 (4, 7)	7 (4, 7)	-	-

Note: The proportion calculated is column percentage.

 $^{^{\}rm a}$ to compare between primary health center and tertiary hospital, significance level is <0.05, $^{\rm b}$ Fischer exact test, $^{\rm c}$ chi-square and $^{\rm d}$ Mann Whitney U test

Table 3: Cost of malaria per episode by health facility and type of service (Int\$, 2019 value)

Out-Patients	All (n=25) Primary Health center (n=18)		Tertiary Hospital (n=7)	p value ^a	
	Mean (<u>+</u> SD) Median (IQR)	Mean (<u>+</u> SD) Median (IQR)	Mean (<u>+</u> SD) Median (IQR)		
DMC	16.8(±13.9) 10.8 (15.3)	9.9(±4.8) 9.7 (5.3)	34.6(±14.2) 43.7 (24.6)	0.01	
Before admission/visit	1.9(±3.8) 0.0 (1.6)	1.9(±4) 0.0 (1.4)	1.9(±3.6) 0.0 (4.6)	0.836	
During admission/visit	14.9(±13) 9.5 (11.9)	8(±1.9) 9.2 (3.9)	32.6(±12.7) 36.3 (22.3)	0.000	
Drug& Medical suppliers	4.2 (<u>+</u> 4) 2.4 (2.2)	2.3(±0.3) 2.4 (0.6)	9.1(±5) 6.8 (7.4)	0.021	
Investigations	9.9(<u>+</u> 9.4)	5(±2.1)	22.6(<u>+</u> 9.3)	0.000	
Routine service	6.8 (8.9) 0.7(±0.1)	6.8 (4.1) 0.6(±0.0)	27.5 (13.7) 0.92(±0.0)	0.000	
After admission	0.6 (0.3) 0.0(±0.0)	0.6 (0.0) 0.0(<u>+</u> 0.0)	0.9 (6.6) 0.0(±0.0)	1.000	
/visit DNMC	0.0 (0.0) 3.4(<u>+</u> 3.8)	0.0 (0.0) 2.2(<u>+</u> 1.7)	0.0 (0.0) 6.5(<u>+</u> 5.8)	0.025	
Transport	2.2 (3.1) 2.5(<u>+</u> 3)	1.7 (2.5) 1.7(<u>+</u> 1.4)	4.6 (5.3) 4.7(<u>+</u> 4.6)	0.047	
Meal	1.8 (2.4) 0.8(±0.9)	1.4 (2) 0.4(<u>+</u> 0.5)	3.3 (1.3) 1.7(±1.2)	0.006	
Accommodation	0.6 (1.3) 0.0(<u>+</u> 0.0)	0.4 (0.8) 0.0(<u>±</u> 0.0)	1.3 (1) 0.0(±0.0)	1.000	
IDC	0.0 (0.0) 3.2(<u>+</u> 2.3)	0.0 (0.0) 3.4(±2.6)	0.0 (0.0) 2.7(±1.5)	0.701	
Total cost	2 (2) 23.5(<u>+</u> 16.4)	2.5 (2) 15.6(<u>+</u> 6.7)	2 (1.3) 43.9(±16.8)	0.000	
	16.7 (18.1)	14.7(6.5)	48.4 (29.6)		
In-Patients	All (n=60) Mean (<u>+</u> SD)	Primary Health center	Tertiary Hospital (n=60) Mean (± SD)	p value	
	Median (IQR)		Median		
DMC	162.7 (<u>+</u> 74.6) 148.5 (86.9)	n/a	162.7 (± 74.6) 148.5 (86.9)	n/a	
Before admission/visit	3.6(±8.4) 0.0 (1.9)	n/a	3.6(±8.4) 0.0 (1.9)	n/a	
During admission/visit	158.8(±72.9) 145.6 (81.4)	n/a	158.8(±72.9) 145.6 (81.4)	n/a	
Drug& Medical suppliers	94.8(±48.5) 86.1 (55.9)	n/a	94.8(±48.5) 86.1 (55.9)	n/a	
Investigations	41.2(±24.2) 36.2 (28.5)	n/a	41.2(±24.2) 36.2 (28.5)	n/a	
Routine service	22.8(<u>+</u> 8.3)	n/a	22.8(±8.3) 22.4 (7.7)	n/a	
After admission /visit	22.4 (7.7) 0.2(±1.7) 0.0 (0.0)	n/a	0.2(±1.7) 0.0 (0.0)	n/a	
DNMC	27(<u>+</u> 32) 18 (22)	n/a	27(±32) 18 (22)	n/a	
Transport	15.1(±27.8) 7.7 (10.3)	n/a	15.1(±27.8) 7.7 (10.3)	n/a	
Meal	11.8 (±12.4) 9.9 (14.3)	n/a	11.8 (±12.4) 9.9 (14.3)	n/a	
Accommodation	0.0(±0.0) 0.0 (0.0)	n/a	0.0(±0.0) 0.0 (0.0)	n/a	
IDC	28.4(<u>+</u> 16.2) 23.6 (17.9)	n/a	28.4(±16.2) 23.6 (17.9)	n/a	
Total cost	218.2(±96.1) 199.8 (95.7)	n/a	218.2(±96.1) 199.8 (95.7)	n/a	

^a to compare between outpatient cases at the two health facilities using Mann Whitney U test

Table 4: Potential variables used in stepwise linear regression

Predictors	Definition	code and values (n=85)
Dependent predictor		
Ln cost	Natural logarithm of cost	
Independent predictors		
Age	Age (months)	Mean age: 29 months
Service	Type of service	1=IPD (70.6%), 0=OPD (29.4%)
Health facility	Type of Health facility	1=Tertiary hospital (78.8%), 0=Primary Health center (21.2%)
Severity	Disease severity	1=Severe (48.3%), 0= uncomplicated (51.7%)
Antimalarials drugs	Type of antimalarials drugs used. Parenteral artesunate (60%) was taken as the reference group	
Oral antimalarials	Oral antimalarials (29.1%)	1= Oral antimalarials 0=other
Parenteral quinine	Parenteral quinine (8.2%)	1= Parenteral quinine 0=other
Mixed parenteral quinine and artesunate	Use both parenteral quinine and artesunate (2.7%)	1=Yes 0=No
Duration of fever before seeking appropriate medical care	Number of days	1= "> 2 days" (38.8%), 0= "≤ 2 days" (61.2%)

Table 5: Multiple linear regression of the cost of malaria per episode

Predictors	Unstandardized constant	SE	p Value	Smearing factor	Adjusted R ²
Constant	2.656	0.083	0.000	1.06	0.898
Service	1.527	0.141	0.000	_	
Health facility	0.998	0.157	0.000	_	
Mixed Parenteral	0.893	0.256	0.001	_	
quinine and artesunate				_	
Duration of fever before	0.203	0.083	0.017		
seeking appropriate					
Medical Care					

Table 6: Predicted direct medical cost

Patient	Service	Health facility	Duration of fever before the treatment	Use both parenteral quinine and artesunate	Predicted cost	Difference comparing to patient A
A	OPD	Health center	<u><</u> 2 days	No	15.09	n/a
В	OPD	Health center	<u>></u> 2 days	No	18.49	3.4
С	OPD	Hospital	<u><</u> 2 days	No	40.94	25.85
D	OPD	Hospital	<u>></u> 2 days	No	50.16	35.07
Е	IPD	Hospital	< 2 days	No	188.53	173.44
G	IPD	Hospital	>2 days	No	230.96	215.87
F	IPD	Hospital	< 2 days	Yes	460.47	445.38
Н	IPD	Hospital	>2 days	Yes	564.12	549.03

DISCUSSION

Our findings on cost of malaria provide evidence of substantial economic burden of malaria on societal perspective. The cost of out-patient treatment was Int\$ 23.53, which represent 8.58% of the GNI per capita; whereas the cost of in-patient treatment was Int\$ 218.28 which account for 79.66% of the GNI per capita (World Bank, 2019). A systematic review of cost of malaria studies in children aged under five years in Africa (El-Houderi et al., 2019) found that the cost per an out-patient case in Africa varies between Int\$ 7.9 and Int\$95 whereas the cost per in-patient case varies between Int\$122 and Int\$350. Although our findings were in the ranges, a direct comparison between our results and those of other studies was not possible as these studies presented differences on study design, cost components, perspectives, and type of healthcare facilities. For instance, one study in Nigeria conducted in 2013 (Onwujekwe et al., 2013) found that cost of OPD visit for uncomplicated malaria was Int\$95 whereas in our study the cost of OPD visit for uncomplicated malaria was Int\$23.5. The main difference was unit cost used. In this study, we used unit cost from WHO-CHOICE to estimate the cost of routine services, from different health facilities, which includes health personnel cost, whereas in the Nigerian study, they calculated the unit cost of medical services from a big national hospital, which may explain higher cost.

Even though, the healthcare services are provided for free in many public hospitals for children aged under five years in Burundi, parents/caregivers still face with high cost due to direct non-medical cost (such as transportation, and food) and productivity loss especially for IPD cases. Given the high transmission rate and high number of cases, malaria can represent a high economic burden not only to the provider (government) who pay for the health facility cost but to the caregiver/household. Majority of the population in Burundi are farmers or labors who need to work each day to gain daily bread (Sophie Lambert-Evans et al., 2009), hence for them losing 7-8 days caring for a sick child in addition of other cost like DNMC can represent a catastrophic burden. This highlight the need of preventive methods to control malaria which can also be cost saving.

To the best of our knowledge, this is the first study to conduct the regression analysis of the cost of malaria on societal perspective. The types of medical services, health facilities, antimalarials used, and duration of fever before seeking appropriate medical care were found to affect the cost. In-patient care and higher level of health facility increased the cost. Using both parenteral artesunate and quinine increased drastically the cost, even if it occurred in few patients. Finally, delayed treatment increased the cost, suggesting the implementation of program for early treatment like the community case management (CCM) program. The CCM program is a program that aims to diagnose and treat malaria case at home in less than 2 days from the onset of fever. We demonstrated that this program can be cost saving. For instance, for each malaria case treated early (in less than 2days), there is a saving of Int\$18.76 and at national level the savings can amount to Int\$ 24,257,748 per year. This study provides evidence that a program like the CCM program can save a lot of money, if implemented properly. The cost of malaria treatment through the CCM program is estimated to be Int\$3.5/malaria case treated (USAID, 2014). For better public health management, the implementation cost of the CCM program should be less than the savings generated by this program. Therefore, an economic evaluation of this program including cost utility analysis, cost benefit analysis and budget impact analysis is needed.

Moreover, better clinical management can save up to Int\$594.03 which is the difference between the worst-case scenario and best-case scenario. This can serve as advocacy in the implementation of malaria control program like the CCM program, and the vector control programs like the use of insecticide-treated nets and regular indoor residual spraying which has shown to decrease the prevalence of malaria in Burundi especially in young children (Protopopoff et al., 2008). However, this study has faced some limitations. Firstly, the data were collected during the minor wet season where the malaria cases are at lowest (Moise et al., 2016). Secondly, unit costs of routine services and laboratory tests were derived from WHO-CHOICE database and proxy price from private sector, respectively. These unit costs may not represent the actual economic cost of those resources compared to primary costing for calculation of the unit cost of medical services in a hospital.

Despite these limitations, this study is the first to be conducted on cost of malaria in Burundi. This study can also assist in the management of malaria in Burundian children as they are the most vulnerable. Moreover, the results of this study can be used in economic evaluation of malaria control programs.

CONCLUSION

This study demonstrated that malaria is associated with a considerable economic burden in Burundi. The cost of malaria per episode was Int\$23.5 and Int\$218.2 for out-patient and in-patient treatment, respectively; which represent a high share of the GDP. The regression analysis suggested that early treatment in less than 2 days can reduce the economic burden of malaria in Burundi. Hence, this study will support decision makers in deciding an appropriate clinical management for malaria prevention like the community case management program.

AUTHOR CONTRIBUTIONS

Nina Hezagira and Sitaporn Youngkong wrote the first draft of the manuscript with input from Arthorn Riewpaiboon. All authors interpreted the data and approved the final version to be published.

ETHICS APPROVAL

This study was approved by the Institutional Review Board, Faculty of Dentistry and Faculty of Pharmacy (DTPY-IRB), Mahidol University, Thailand (Project No. 2019/PY125, COA No. 2019/071.1810).

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest in this work.

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