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Malaria Related Deaths among Children with Manifestations of Fever Symptoms on Admission in a Secondary Health Care Institution in Western Region of Ghana - a Retrospective Study

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Authors' contributions

This work was carried out in collaboration between all authors. Authors VNO, AOS, CO, NCI designed the study, performed the statistical analysis, wrote the protocol and first draft of the manuscript. Authors VNO, AOS, CO and NCI managed the analyses of the study. Authors VNO, MF, BKS, OSO, AOS, CO, NCI managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Malaria is a major contributor to deaths in children especially in sub-Saharan Africa. Children less than five years of age are susceptible to malaria infection in endemic regions leading to serious complications. Malaria causes death in children either directly through Cerebral Malaria (CM) and Severe Malaria Anaemia (SMA) or indirectly through co-morbidity with pneumonia or a sequela like hypoglycemia.

Methods: This retrospective study examined malaria-related deaths among children at Effia-Nkwanta hospital within a study period of 3 years.

Results: A total of 1,416 medical records were reviewed, out of which 223 were medical records of children with fatal outcomes. Deaths over the study period due to all causes were 15.7% (223/1416) and confirmed malaria was 13.7% (40/292). Deaths due to all causes and confirmed malaria decreased from 21.6% and 24.3% in 2010 to 11.1% and 4.4% in 2012, respectively. Anti-malarial testing was done for 152 of the children with 40 positive and 112 negative results. Seventy-one children had no malaria testing done on them, with 23.4% in 2010 40.3% in 2011 and 35.5% in 2012. Anti-malarial treatment was administered to 83% of children who tested negative and 80% of children without anti-malarial testing.

Conclusion: Deaths in the children declined from 2010 to 2012 in this study. Despite this improvement, there was poor anti-malarial testing and improper use of anti-malarial treatment. National malaria programs should ensure improvement in anti-malarial testing and strict adherence to the anti-malarial treatment protocol.

Keywords: Malaria; children; mortality; anemia; death.

1. INTRODUCTION

Malaria remains a serious public health issue in malaria-endemic areas, with residents at the risk of infection and higher risks are often seen in children and pregnant women [1]. Children less than five years are susceptible to malaria infection leading to serious complications and death if not promptly and adequately treated with effective anti-malarial drugs [1]. Plasmodium falciparum is the predominant species in sub-Saharan Africa, the major cause of severe disease leading to death [1]. The exposure of children to sub-lethal P. falciparum infection leads to the gradual acquisition of clinical However, immunity [2]. some children unfortunately never live to develop this immunity as their infection progresses to severe disease leading to death before adulthood [3].

Malaria infection due to *P. falciparum* can cause mortality directly by being the underlying cause of death. Cerebral malaria and severe malaria anemia are very common direct causes of childhood mortality [4]. Cerebral malaria defined as confirmed *P. falciparum* infection with unrousable coma [5] causes death in children due to hypo-perfusion of brain cells as a result of sequestration of infected red cells within cerebral capillaries [6]. Another common direct cause of death in *P. falciparum* infected children is anemia, referred to as severe malaria anemia (SMA) [4]. World Health Organization (WHO) defines SMA as a hemoglobin level (Hb) below 5.0 g/dL in the presence of malaria parasites [7]. Indirect causes of death in malaria are cases in which malaria is only a contributing factor, such as in a child with malaria-related anemia developing pneumonia or hypoglycemia and dying from it [8].

There is a reported 18% global decline in malaria cases from 262 million in the year 2000 to about 214 million in 2015 [9]. It was estimated that 88% of the new cases in 2015 occurred in sub-Saharan Africa [9]. However, the region has recorded a tremendous progress in terms of reduction in the number of malaria deaths among children under 5 years of age, with the bulk of global decrease occurring in the region [9]. The estimated number of malaria deaths among children under 5 years of age fell from 694,000 in 2000 to 292,000 in 2015 [9]. These findings suggest that malaria is no longer the leading but the fourth leading cause of death among children, accounting for about 10% in 2015 [9]. This declining mortality in children from sub-Saharan Africa is due to the positive outcome from scale-up of malaria intervention programs deployed in the region [10]. These control programs have facilitated the reduction of childhood malaria morbidity and mortality in most parts of sub-Saharan Africa [11,12]. The control programs include household and community

activities such as the use of insecticide treated nets ITNs, indoor residual spraying IRS, larval control and health facilities activities including adequate case management for malaria [13].

Adequate case management of malaria is a veritable arm of the malaria control program. It is primarily carried out in healthcare facilities. Invariably, the quality of care in the facilities can impact greatly on malaria-related mortality especially among children. The generally dilapidated state of healthcare in many Africa countries negatively impacted on the quality of management and treatment of many diseases especially malaria in children [14]. However, there has been some improvement in malaria case management over the years with the improvement of diagnosis and treatment by the provision of tools for on the spot diagnosis like the rapid diagnostic test for malaria, effective drugs, and skilled healthcare personnel [14,15]. Despite this, quality of care in hospitals and clinics still needs improvement since avoidable malaria deaths have been reported [16].

In Ghana, childhood mortality is a serious public health issue as diseases like pneumonia, diarrhea, malnutrition, and malaria take their toll on children [17]. Malaria remains a constant threat to the life of children in Ghana especially those who live in rural areas [18]. In the first guarter of 2016, the country recorded a total of 2.2 million cases of malaria in all health facilities nationwide. The number of malaria confirmed deaths recorded was 379 which was a 15.2% drop from the value in the first guarter of 2015. Of these, there were 152 malaria deaths in children under 5 years of age compared to 182 recorded in 2015 [19]. However; this noted decline is not uniform within the country. It is very important to constantly review mortality figures and pattern in different parts of the country to assess the progress of malaria control programs and the dynamics of malaria infection. Hence, this retrospective study evaluated the trend in malaria-related deaths among children who died on admission for febrile illness in a referral hospital in Sekondi-Takoradi metropolis Ghana over a three-year period.

2. MATERIALS AND METHODS

2.1 Study Area

Effia-Nkwanta Regional Hospital is a secondary health-care institution and is the only referral hospital for the whole western region of Ghana. Ghana is bordered by Togo on the east and Ivory Coast on the west (Fig. 1). Effia-Nkwanta hospital is located at the Regional capital, Sekondi-Takoradi. It serves all other hospitals within the entire 22 districts of the western region and sub-divisions of 13 major districts. Details of the study area have been published previously [20].

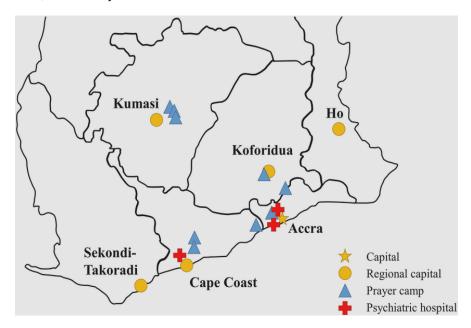


Fig. 1. Map of Ghana showing location of Sekondi-Takoradi [21]

2.2 Data Collection

This is a retrospective study that was carried out at the Paediatric Unit of Effia-Nkwanta Regional Hospital (ENRH). Before this study, Paediatric emergencies were seen and where necessary. were admitted to the children's ward of the hospital. The patients admitted were recorded in the admissions register. The admissions register of the Accident and Emergency Unit of the hospital was used to collect folder numbers of children who were recruited into the retrospective study. Children admitted with fever as one of the presenting symptoms with subsequent fatal outcome over the study period of 2010, 2011 and 2012 were included in the study. Their medical records were searched and retrieved. Information on the demographics (i.e. age and sex), clinical and laboratory findings were collected. Clinical information retrieved included other symptoms accompanying fever, the weight of the child and temperature as well as information on sickle cell trait and blood transfusion during admission. Reported laboratory findings included malaria parasite diagnosis, white blood cell counts, sickling status and hemoglobin concentration. Information on treatment histories was also collected as well as the number of days the patients spent in the hospital. Permission was granted for this work from the regional office Ghana Health Service and the medical director of the facility.

Patients with malaria admitted in the hospital were classified according to the WHO criteria for mild and severe malaria [7]. Diagnosis of malaria parasite was done using P. falciparum specific rapid diagnostic test kits, containing membrane strip, precoated with a monoclonal antibody which is specific to the histidine-rich protein 2 of the Plasmodium falciparum (First Response, Premier Medical Corporation Ltd) and microscopy using Giemsa staining. The rapid response kit detects P. falciparum antigens and the presence of two lines in the test kit well Ρ. falciparum positive. indicates Malaria parasites were confirmed with thick and thin peripheral blood smears stained with Giemsa and examined microscopically using 100 power fields under oil immersion. Two microscopists read the slides independently and a third microscopist was called upon to resolve discordant results. Hemoglobin estimation and white cell count were done as part of the complete blood count from an automated blood cells analyzer machine (Sysmex Haematology Analyser, Xuzhou Hengda, China). Certification

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and establishment of the cause of death were done mainly by using clinical judgment based on history, physical examination and laboratory findings. These were done by experienced medical officers or specialist pediatricians after proper review of patient's records.

Malaria was defined as the presence of any asexual blood stages form of P. falciparum species in thin smear blood film while malaria negative samples were confirmed when 100 high power fields have been examined using x100 oil immersion objective lens. Anemia was defined based on WHO criteria of hemoglobin (Hb) levels<11 g/dL [22,23], and categorized as mild anemia (Hb<11 g/dL), moderate anemia (Hb<10 g/dL) and severe anemia (Hb<7 g/dL. A febrile malarial episode in children was defined as a reported history of fever within the last 24-72 hrs of admission or a measured axillary temperature of 37.5°C or greater (or both), with a positive peripheral blood smear slide with asexual forms of P. falciparum at any level of parasite density at time of contact with ENRH clinic [24]. A malaria is death defined as one death per parasitologically diagnosed clinical episode [11]. We calculated malaria mortality (expressed as a percentage) with the formula: malaria deaths per year / Number of children in the population at midvear. We calculated case fatality rate (express as a percentage) with the formula: malaria deaths per year / Number of confirmed malaria cases among admitted children per year [25].

2.3 Statistical Analysis

Univariable analyses were performed and results were presented as proportions and mean \pm standard deviation (SD). Statistical significance for cross-tabulations was performed using Pearson χ^2 test for categorical variables. Oneway analysis of variance (ANOVA) was used for the comparison of the mean of continuous variables. All tests were two-tailed and P<0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS software version 21.0 (IBM Corporation, Armonk, NY, USA).

3. RESULTS

3.1 Characteristics of the Study Population

Table 1 describes the characteristics of the 223 children who died during the three year study

period. Severe anemia (Hb<7 g/dL) was seen in 34.1% of the children while 18.8% of the children that died were not anemic (Hb>11 g/dL). Malaria diagnostic test was not performed in about 31.9% of the children that died. However, 17.9% of the children were laboratory confirmed malaria positives while 50.2% were malaria negatives. Ninety-seven children (43.5%) died within the first 24 hours of admission, 37.2% died within 72 hours and 19.3% after 72 hours of admission.

Table 1. General characteristics of the study	
population	

Characteristics	Number (n=223)	Percentage (%)				
Sex	``					
Male	122	54.7				
Female	101	45.3				
Age (Years)						
<1	110	49.3				
2-5	63	28.3				
>5	50	22.4				
Hemoglobin						
<7 g/dL	76	34.1				
<10 g/dL	75	33.6				
<11 g/dL	30	13.5				
≥11 g/dL	42	18.8				
Sickle cell*						
HB (AS)	21	15.8				
HB (SS)	6	4.5				
HB (AA)	106	79.7				
Malaria parasite						
MP Seen	40	17.9				
No MP Seen	112	50.2				
Not done	71	31.9				
Death on admission in hospital (Hours)						
<24	97	43.5				
<72	83	37.2				
>72	43	19.3				

Fig. 2 describes the percentage mortality of the children admitted into the children's ward. During the study period, a total of 1,416 children were

the study period, a total of 1,416 children were admitted to the children unit of Effia-Nkwanta Regional Hospital. Out of this total number of admitted children, 1193 children were successfully treated and discharged home, while 223 children, unfortunately, died over the same period, with a percentage mortality of 15.7%. There was a progressive decline in the percentage of mortality from 21.6% in 2010 to 11.1% in 2012 (Fig. 2). Fig. 3 describes malaria case fatality in the study population. During the three year study period, 40 children died out of the 292 admitted with supposedly malaria cases

with a total case fatality rate of 13.7%. There was also a steady decline in the case fatality rate for laboratory-confirmed malaria cases from 24.3% in 2010 to 4.4% in 2012 (Fig. 3).

Table 2 shows the characteristics of the study population stratified against malaria laboratory investigations. A significant proportion of malaria diagnosis was done without malaria testing and some were negative on malaria test. Antimalarial treatments were accurately given to all of the children with confirmed malaria test, while 83% and 80% of the children that tested negative and those without malaria test respectively were incorrectly prescribed anti-malarial drugs. Children without malaria testing significantly decreased as they stayed longer in the hospital (>24hrs, 63.4%; <72hrs, 28.2%; >72hrs, 8.4%).

Fig. 4 shows that malaria testing rate worsened over time with 23.4% of children not tested in 2010, 40.3% in 2011 and 35.1% not tested in 2012.

Table 3 summarizes the combination of the prescribed medications during the study period stratified by year. Apparently, patients without laboratory-confirmed malaria diagnosis or patients with negative malaria diagnosis were given a parenteral anti-malarial treatment of either quinine or artemether.

3.2 Other Non-Malaria Causes of Death

Fig. 5 shows the distribution of other non-malaria causes of death. Among these children that died from non-malaria causes, 12.1% were diagnosed with sepsis, 9.4% were diagnosed with bronchopneumonia, 8.5% were diagnosed with gastroenteritis, and 7.2% were diagnosed with severe anemia. Children who died without a specific diagnosis were 19.7%.

4. DISCUSSION

This study evaluated the contribution of malaria to the mortality of children in the children ward of Effia-Nkwanta Regional Hospital over a 3 year study period. There was a steep decline in malaria deaths from 2010 to 2012. This is a drastic drop and an interesting finding indeed. Firstly, there was a high case fatality rate for malaria in 2010 compared to the subsequent years, which might be due to both in the hospital and out of hospital factors. These factors have contributed to poor and fatal treatment outcomes in children with malaria [26]. Late arrival to the hospital is one major out of hospital factor responsible for malaria mortality in children in many countries in sub-Saharan Africa especially Ghana [27]. This is due to; poor health-seeking behavior caused by poor understanding of the symptoms of malaria, over-reliance on home and herbal remedies and financial constraints [27,28]. In hospital factors, especially in Ghana are hinged majorly on the poor quality of care for the sick child, including poor and delayed diagnosis, lack of appropriate medications and treatment and lack of well-trained health care personnel [29,30]. Poor quality of care has been reported in regional hospitals similar to the facility where the present study took place [30,31].

In 2011 there was a tremendous reduction in malaria confirmed deaths despite an increase in admitted confirmed malaria cases. An improvement in the arrival time of the sick children to the hospital and improvement in the

quality of care in the hospital might have been responsible for this. Parents and caregivers would have become better educated on the early recognition of symptoms and signs of malaria, the dangers of herbal medication and the importance of coming early to the hospital with their sick children. This is the likely outcome of the various forms of health education carried out by the National Malaria Control Program [19]. More so, the improved enrolment of patients to the National Health Insurance scheme would have overcome the barrier of financial constraint allowing more patients to assess health care in the hospital [29,32]. Also, increase in the confirmed malaria cases on admission, might be due to an improvement in malaria diagnosing capacity of the regional hospital based on the massive deployment of rapid diagnostic test kits as well as training of health care personnel on the use of the test kits [19,33]. This improvement in case identification and the diagnosis was

Clinical and demographic characteristics	Malaria positive n = 40 (%)	Malaria negative N=112(%)	Not done N=71(%)	P-value
Age (Mean ± SD)	3.1 ± 3.1	2.9 ± 3.2	2.5± 3.5	0.6
Age (Years)				
<1	15(37.5)	57(50.9)	38(53.5)	0.01
2-5	20(50)	28 (25.0)	15(21.1)	
6-11	5(12.5)	27 (24.1)	18(25.4)	
Sex				
Male	24 (60)	66 (59)	32(45.1)	0.23
Female	16 (40)	46 (41)	39(54.9)	
Hemoglobin				
<7g/dL	22 (55)	36 (32.1)	18(25.4)	0.18
<10g/dL	10 (25)	43 (38.4)	22(31.0)	
<11g/dL	4 (10)	12 (10.7)	14(19.7)	
≥11g/dL	4 (10)	21 (18.8)	17(23.9)	
Death on admission in hospital (Ho	ours)			
<24	12 (30)	40 (35.7)	45(63.4)	
24-72	25 (62.5)	38 (33.9)	20(28.2)	0.001
>72	3 (7.5)	34 (30.4)	6 (8.4)	
Blood transfusion				
Yes	22 (55)	36 (32.1)	17(23.9)	0.02
No	18 (45)	76 (67.9)	54(76.1)	
Presumptive diagnosis for malaria				
Severe malaria anemia	12 (30)	30 (26.8)	10(14.08)	0.004
Cerebral malaria	16 (40)	29 (25.9)	14(19.7)	
Severe malaria	10 (25)	19 (16.9)	7(9.9)	
Bronchopneumonia +malaria	2 (5)	17 (15.2)	811.3)	
Epilepsy + malaria	0 (0)	17 (15.2)	3(4.2)	
Anti-malaria treatment given				
Yes	40(100)	93(83.0)	57(80.3)	0.05
No	0(0)	19(17)	9(12.7)	

Table 2. Patients' characteristics stratified by malaria laboratory diagnosis

*Significant P-value= (P<0.05); SD=Standard deviation

invariably followed by prompt, adequate and successful treatment outcomes for the majority of the children that was admitted in 2011. This success in treatment was perhaps due to better training of the healthcare personnel as well as the availability of appropriate therapeutic drugs and effective therapy with strict adherence to standard treatment guidelines [19]. Ghana adopted the WHO artemisinin-based combination treatment (ACT) policy in 2004 with artesunateamodiaguine as first-line treatment and a subsequent review in 2009 involving the inclusion of artemether-lumefantrine and dihydroartemisinin-piperaquine as alternative first-line drugs for children who cannot tolerate artesunate-amodiaquine combination therapy. Parenteral treatment includes artemether and quinine injection for severe malaria. This study showed that these anti-malarial drugs were basically used in the management of malaria in the children in this hospital, but the details of how they were used and administered were not available. Studies, however, showed that there were challenges in the practicality of this policy as it took some time for health workers through frequent training to fully acquire the necessary skills to use these treatments effectively [31,34,35].

In 2012, there was further improvement in the case fatality rate coupled with a decline in admitted malaria confirmed cases despite an overall increase in admitted children. The decline in the admitted malaria confirmed cases might be a reflection of the overall decline in the global and regional malaria burden noted in the country [9,19], or a dividend of activities of National Malaria Control Program involving continuous campaign on the use of ITNs and IRS [19]. Another possible reason for the decline might be that most parents or caregivers have well-improved knowledge in the home management of uncomplicated malaria with an affordable ACT, thereby preventing complication that will warrant admission in hospital [36,37]. More so, many primary health centers and clinics in the area are now well equipped with RDTs and ACTs to handle malaria in children [37,38]. The lowest case fatality for malaria recorded in 2012. was perhaps the result of progressive improvement in case management and strict observance of the standard treatment guideline for malaria in the hospital [38].

It is important to highlight the ever-nagging problem of poor laboratory diagnosis of malaria

observed in this study; as 31.9% of children who died never had malaria test done on them. This is a very common problem seen in many hospitals and clinics in developing countries and it has been blamed on the incessant break down of the diagnostic machine and frequent stock out of reagents [39,40]. In all, the situation worsened between 2010 (23%) to 2012 (35%). Another study that was done among discharged children over the same period in the same hospital also reported a significant proportion of children who were not tested for malaria [20,41]. However, in this study, time spent on admission before death may have played a role in the number of children who died without malaria test done on them, since the majority of children who died within the first 24 hours never had malaria test done on them. The chances of getting a malaria test done in the laboratory increased if the child survived beyond 72 hours before death. The presumptive diagnosis of malaria was woefully inaccurate in this study as significant proportions of the case diagnosed were not confirmed by laboratory investigation. This is really an important finding for clinicians to be reminded that in all cases, their clinical judgment should always be supported by laboratory investigations.

As seen in most studies, children under five years of age remain the most vulnerable group for fatal consequences of diseases and infections [42,43]. The higher proportion of under-five children among those who died with malaria in this study further buttresses the age-specific severity of malaria morbidity and mortality as seen in malaria-endemic areas [19,42,43]. Taking a closer look at the specific diagnosis of children who tested positive for malaria in this study, CM and SMA were more common. CM and SMA are the most common complications of malaria linked with pediatric mortality [4,44].

Aside from malaria mortality, there was a progressive decline in overall mortality, despite the increased patient load over the study period. This decline is consistent with the declining trend in child mortality reported for sub-Saharan Africa over the years [42,43]. This can be attributed to the continuous improvement in the healthcare system and implementation of various preventive measures such as child survival programs and vaccinations as well as improvement in diagnostic methods and effective treatments that mitigate the impact of diseases responsible for child mortality in the region [45].

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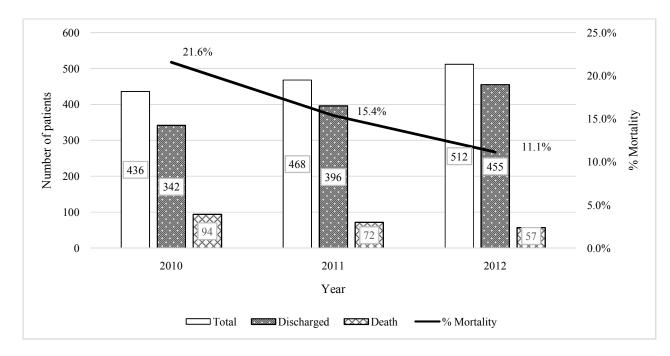
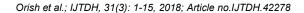


Fig. 2. Percentage mortality (all causes) from the year 2010 to 2012



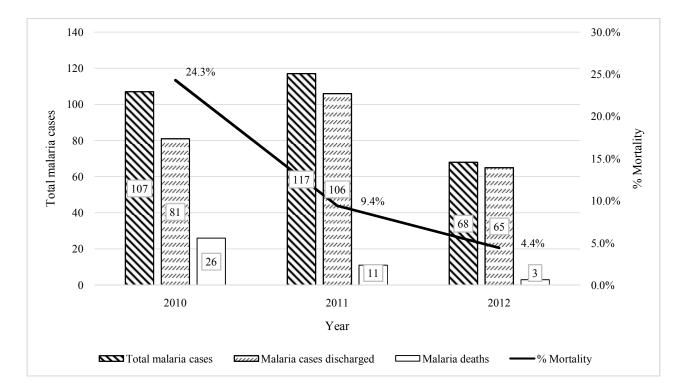
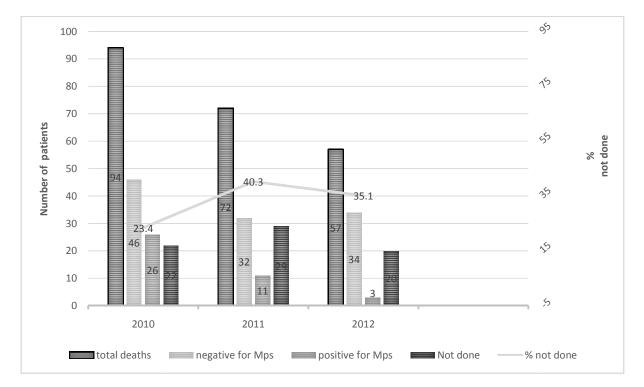


Fig. 3. Malaria case fatality rate



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Fig. 4. Malaria testing for the year 2010 to 2012

	2010			2011			2012		
List of prescribed medications	Malaria positive (%)	Malaria negative (%)	Not done (%)	Malaria positive (%)	Malaria negative (%)	Not done (%)	Malaria positive (%)	Malaria negative (%)	Not done (%)
Artemether injection, Antibiotics and Antipyrectics	2 (33.3)	3 (50)	1 (16.7)	1 (16.7)	3 (50)	2 (33.3)	3 (17.6)	10 (58.8)	4 (23.5)
Antibiotics	0 (0)	4 (66.7)	2 (33.3)	0 (0)	5 (62.5)	3 (37.5)	0 (0)	17 (65.4)	9 (34.6)
Antibiotics and Antipyrectics	0 (0)	5 (62.5)	3 (37.5)	1 (8.3)	4 (33.3)	7 (58.3)	0 (0)	6 (85.7)	1 (14.3)
Artemether-lumefantrine, Antibiotics and Antipyrectics	0 (0)	4 (66.7)	2 (33.3)	0 (0)	3 (100)	0 (0)	1 (6.6)	10 (66.7)	4 (26.7)
Artemether-lumefantrine and Antipyrectics	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
Artesunate-amodiaquine, Antibiotics and Antipyrectics	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)
Artesunate-amodiaquine and Antipyrectics	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Artemether Injection, artemether-lumefantrine and Antipyrectics	3 (33.3)	3 (33.3)	3 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Quinine and Antipyrectics	0 (0)	0 (0)	1 (100)	0 (0)	1 (50)	1 (50)	1 (12.5)	4 (50)	3 (37.5)
Antipyrectics	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	2 (66.7)	1 (33.3)
Artemether-lumefantrine and Antibiotics	0 (0)	0 (0)	1 (100)	3 (33.3)	3 (33.3)	3 (33.3)	0 (0)	3 (60)	2 (40)
Artemether injection, artemether-lumefantrine and Antibiotics	0 (0)	3 (100)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	8 (80)	2 (20)
Quinine, Antibiotics and Antipyrectics	1 (6.7)	4 (26.7)	10 (66.7)	1 (10)	5(50)	4 (40)	23 (37.7)	20 (32.8)	18 (29.5)
Artemether injection, Arthesunate Amodiaquinine and artemether-lumefantrine	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
Artemether injection, artemether-lumefantrine, Quinine and Antibiotics	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Artemether injection and Antipyrectics	0 (0)	1 (50)	1 (50)	1 (25)	1 (25)	2 (50)	2 (28.6)	2 (28.6)	3 (42.9)
Artemether injection, Quinine, Antibiotics and Antipyrectics	0 (0)	0 (0)	0 (0)	0 (0)	2 (50)	2 (50)	0 (0)	0 (0)	0 (0)
Artemether-lumefantrine, Quinine and Antipyrectics	0 (0)	2 (100)	0 (0)	0 (0)	1 (100)	0 (0)	1 (12.5)	6 (75)	1 (12.5)
Artesunate-amodiaquine, Quinine, Antibiotics and Antipyrectics	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)

Table 3. List of combination of the prescribed medications during the study stratified by year

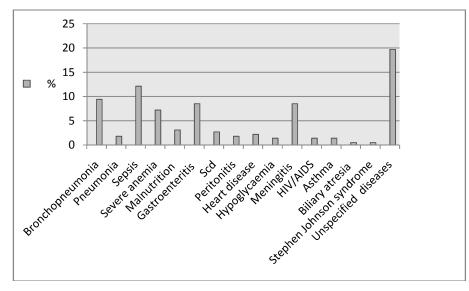


Fig. 5. Other non-malaria causes of death.

Other diseases were also responsible for child mortality in this study as more of these children that had malaria laboratory investigation done were negative. Bacterial and viral diseases, malnutrition, congenital abnormalities, intrapartum events, and injuries have all been implicated in child mortality [42,43,45]. This study noted a rather high number of children with missing/unknown diagnoses. The probable clinical explanation for this would have been that some children die within a few hours of arrival to the ward or arrive at a period where the doctors and laboratory personnel are not readily available on duty especially during the weekends. Weekend admissions would have probably contributed to the mortality due to lack of quality care, which is a common finding in hospitals in similar settings [46].

5. LIMITATIONS

Despite the fact that in this study the anti-malarial oral ACT and parenteral drugs used were all documented, a detailed audit of how these treatments were used vis-à-vis dosages, timelines, duration, ancillary treatment like infusions and correction of hypoglycemia, were not documented. Availability of this document would have revealed more information on the outcome of the treatment. There is a possibility that some discharged children died at home thereby making the mortality rate in this study a little conservative. Finally, it is possible that the children who had no malaria test done on them would have skewed the result in the comparison over time in this study.

6. CONCLUSION

This study noted a steep decline in all-cause mortality and malaria confirmed deaths despite an increase in admitted patients over a 3 years period in the pediatric department of Effia-Nkwanta hospital. There was however poor antimalarial testing among the children, a practice that worsens over the study period. There were incorrect diagnoses and treatments of malaria noted in this study with a significant proportion of children wrongly diagnosed with those negative for malaria and those not tested receiving antimalarial treatment. Despite the commendable decline of deaths in children noted in this study. there is room for improvement vis-à-vis improvement in anti-malarial testing, and strict adherence to proper anti-malarial treatment protocol to ensure adequate case management which will go a long way in reducing malaria mortality in children.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Hospital's Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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