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Evaluation of the Risk Factors and Prevalence of Cerebral Malaria in Children below 10 Years in Kiryandogo General Hospital.

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ABSTRACT

This study aimed at determining the prevalence and risk factors of cerebral malaria among children aged 10years and below in Kiryandogo General Hospital. The study was done in Kiryandogo General Hospital with target population of children diagnosed with cerebral malaria between February – December 2017 and constituted a sample size of 100 cases obtained using Kish and Leslie formula. The results were analyzed using descriptive method to calculate frequencies, proportions, means, measures of association and their 95% confidence intervals. Stepwise forward logistic regression was done for all variables that were significantly associated with cerebral malaria at the p=0.25 level on bivariate analysis to determine the independent factors associated with cerebral malaria. The results revealed that out of 100 cases that were enrolled into this study, the majority were male; 58.0% compared to females; 42.0%. the risk factors were found as follows; Caregiver factors associated with cerebral malaria among children were; having at least secondary education, being the mother of the child and female caregiver although not significant. Environmental factors that were significantly associated with Cerebral malaria were; staying in house under construction, staying in a house with open eaves or poorly covered windows, stagnant water within 10 meters from household and having received IRS 12 months preceding child's illness. Household related factors that were significantly protective of cerebral malaria were; sleeping under mosquito net every night and owning at least one ITN in the household. Patient related factors that were significantly associated with Cerebral malaria were; undernutrition and history of malaria illness. Health system factors that were significantly associated with Cerebral malaria among children were; distance between home and nearest health facility >10km, delayed diagnosis and having received antimalarial medicines at initial visit to a health facility. The study also revealed that children who were managed by a VHT were 1.53 times more likely to have cerebral malaria than those who were not. However, this finding was not statistically significant. A Stepwise forward logistic regression analysis revealed that patient related factors that were associated with mortality were; under nutrition and age <5 years. Caregiver healthcare seeking behavioural factors that were associated with mortality due to Cerebral malaria were; duration of child's symptoms before seeking medical care >2 days and first action taken was seeking medical care though not statistically significant. A bivariate analysis revealed the independent risk factors for Cerebral malaria as; distance >10km to the nearest health facility, duration of symptoms before seeking medical care >2 days, staying in a house under construction and duration of illness before receiving antimalarial medicines >24 hours. Owning at least one ITN in the household and having a mother as a caregiver were independent protective factors for cerebral malaria. The prevalence of cerebral malaria was high among children aged 5 years and below with the median age being 3 years. Most of the age group of children affected with cerebral malaria that died was 0-3 years.

Keywords: prevalence, risk factors, cerebral malaria, children aged 10 years, under nutrition

INTRODUCTION

Cerebral malaria is the leading cause of seizures and encephalopathy and a major cause of death in African children. Manifestations of cerebral malaria differ in children and adults. Intravenous quinine remains the drug of choice for cerebral malaria treatment, but intramuscular quinine and artemisinin derivatives are excellent alternatives. Intrarectal treatment with these drugs also appears to be efficacious [1-5].

Plasmodium falciparum malaria is a leading infectious cause of morbidity and mortality in children worldwide [4, 6]. Each year, 300 to 500 million clinical cases of malaria occur, resulting in 1.5 to 2.7 million deaths. Most deaths caused by malaria occur in children younger than 5 years in sub-Saharan Africa [7, 8]. In the United States, approximately 1000 cases of malaria are reported to the CDC every year. Of these cases, approximately 39% are caused by *P falciparum,* and almost all occur in travelers returning from countries where malaria is endemic or in immigrants arriving from these countries [9, 11].

Death from cerebral malaria in children is most often caused by cerebral malaria, cerebral malarial anemia, acidosis with accompanying respiratory distress, or a combination of these factors [7, 11]. Cerebral malaria is associated with a particularly high mortality rate, which averaged 18.6% in a 1998 survey of studies of African children [12, 13]. Cerebral malaria is seen in children in the United States who have traveled to areas where malaria is endemic. In a review of 62 children admitted to a Washington, DC, hospital with malaria, 3 (4.8%) had cerebral malaria; 1 of the 3 had Cerebral neurologic sequelae [14].

The clinical manifestations of cerebral malaria differ in children and adults, suggesting that the pathogenesis of this syndrome may be different in the 2 populations [15, 16, and 17].

This study aimed at determining the prevalence and risk factors of cerebral malaria among children aged 10years and below in Kiryandogo General Hospital.

The present review will highlight recent advances in our understanding of the clinical presentation, pathogenesis, management, and outcome of cerebral malaria in children.

METHODOLOGY

Study Site

The study was hospital based, that was in Kiryandongo general hospital

Study Design

It was a cross sectional descriptive study.

Sample Plan

A probability random sampling technique was applied by including in the study any child who has been diagnosed with cerebral malaria in the hospital.

Sample Size Determination

Using Kish and Leslie formula, the sample size was

$$N = \frac{Z^2Pq}{d^2}$$

Where N = Sample size.

Z = Score at 95% confidence limit (interval).

P = Proportion of the population affected by cerebral malaria.

d = Required precision, 10%

q = 1-p

The proportion is taken as 50% which gave the maximum sample to obtain results required, 10% precision because the true proportion is not known

Therefore, $N = \frac{(1-96)^2 \times 0.5 \times 0.5}{(0.1)^2} = 96$

From the above calculation sample size N was taken as 100

Selection Criteria

Only registered children diagnosed with cerebral malaria in Kiryandongo General Hospital were considered.

Data Collection

Pretested interviewer administered questionnaires were used to collect data on socio-demographic

characteristics, household related factors, patient related factors, health system related factors and caregiver healthcare seeking behavioural factors. Patients' medical records at the health facility were also reviewed to assess eligibility for participation in the study. Parents/caregivers of cases were interviewed in the community.

Data Analysis

Data were analyzed using Epi info version 3.5.3 to calculate frequencies, proportions and means. The same statistical package was used to calculate measures of association and their 95% confidence intervals. Stepwise forward logistic regression was done for all variables that were significantly associated with cerebral malaria at the p=0.25 level on bivariate analysis to determine the independent factors associated with cerebral malaria.

RESULTS

A total of 100 cases were enrolled into the study. The majority of cases were male; 58.0% compared to females; 42.0%.

Table 1 presents the risk factors associated with cerebral malaria among children below ten years in Kiryandongo General Hospital, February - December, 2017

Caregiver factors associated with Cerebral malaria among children were; having at least secondary education [Odds ratio (OR) =0.73, 95% CI=0.37, 1.43], being the mother of the child [OR=0.41 95% CI=0.18, 0.91] and female caregiver [OR=0.36, 95% CI=0.07, 1.66].

Environmental factors that were significantly associated with Cerebral malaria were; staying in house under construction [OR=3.89, 95% CI=1.927.88>7.88], staying in a house with open eaves or poorly covered windows [OR=2.09, 95% CI=1.06, 4.12], stagnant water within 10 meters from household [OR=2.08, 95% CI=1.01, 4.28] and having received IRS 12 months preceding child's illness [OR=0.39, 95% CI=0-20, 0.77].

Household related factors that were significantly protective of Cerebral malaria were; sleeping under mosquito net every night [OR=0.33, 95% CI=0.16, 0.70] and owning at least one ITN in the household [OR=0.23, 95% CI=0.10, 0.51].

Patient related factors associated with Cerebral malaria were; malnutrition [OR=3.40, 95% CI=31.24, 9.34] and history of malaria illness [OR=0.48, 95% CI=0.24, 0.96].

Health system factors that were significantly associated with Cerebral malaria among children were; distance between home and nearest health facility >10km [OR=10.96, 95% CI=1.25, 96.41], delayed diagnosis [OR=5.24, 95% CI=1.29, 21.18] and having received antimalarial medicines at initial visit to a health facility [OR=0.19, 95% CI=0.05, 0.77].

Table 1: Factors associated with cerebral malaria among children below ten years, Kiryandogo General Hospital, February –December 2017

Variable	Cases (%)	OR (95% CI)	p-value
At least secondary education	64(64.0)	0.73 (0.37-1.43)	0.36
Being mother of the child	88(88.0)	0.41 (0.18-0.91)	0.02
Female caregiver	97(97.0)	0.36 (0.07-1.66)	0.17
Staying in a house under construction	36(36.0)	3.89 (1.92-7.88)	<0.01
Staying in a house with open eaves or poorly covered windows	43(43.0)	2.09 (1.06-4.12)	0.03
Stagnant water within 10 meters from household	74(74.0)	2.08 (1.01-4.28)	0.04
Received IRS 12 months preceding child's illness	68(68.0)	0.39 (0.20-0.77)	0.01
Own at least 1 ITN in household	91(91.0)	0.23 (0.10-0.51)	<0.01
Child sleeps/slept under mosquito net every night	52(52.0)	0.33 (0.16-0.70)	<0.01
Malnutrition	62(62.0)	3.40 (1.24-9.34)	0.02
History of malaria illness	59(59.0)	0.48 (0.24-0.96)	0.04
Distance between home and the nearest health facility >10km	65(65.0)	10.96(1.25-96.41)	<0.01
Delayed diagnosis	3(2.9)	5.24 (1.29-21.18)	0.01
Child managed by a VHT	25(24.0)	1.53 (0.74-3.20)	0.35
Received antimalarial at initial visit to a health facility	97(97.0)	0.19 (0.05-0.77)	0.01
Duration of symptoms before seeking medical care >2 days	4(4.0)	14.30(4.57-45.36)	<0.01
Duration of illness before child received antimalarial >24hrs	34(34.0)	5.59 (2.67-11.68)	<0.01
First action taken when child got sick was seeking medical care	84(84.0)	0.28 (0.13-0.58)	<0.01

Children who were managed by a VHT were 1.53 times more likely to have cerebral malaria than those who were not. However, this finding was not statistically significant [95% CI=0.74, 3.20].

Caregiver healthcare seeking behaviors that were significantly associated with Cerebral malaria were; duration of child's symptoms before seeking medical care >2 days [OR=14.30, 95% CI=4.57, 45.36], duration of illness before child received antimalarial >24hrs [OR=5.59, 95% CI=2.67, <11.68], and first action taken when child got sick was seeking medical care [OR=0.28, 95% CI=0.13, 0.58] of the 100 children with cerebral malaria, 20 died and 80 improved.

A sub-analysis was done to determine factors associated with mortality due to cerebral malaria. Table 2 summarizes the factors that were associated with mortality due to cerebral malaria among children below ten years in Kiryandongo General Hospital.

The patient related factors that were associated with mortality were; malnutrition [OR=10.13, 95% CI=1.04-98.49], and age <5 years [OR=2.35, 95% CI=0.67, 8.24].

Caregiver healthcare seeking behavioural factors that were associated with mortality due to Cerebral malaria were; duration of child's symptoms before seeking medical care >2 days [OR=2.70, 95% CI=0.79, 9.29] and first action taken

was seeking medical care [OR=0.45, 95% CI=0.13, 1.55] though not statistically significant.

Table 2: Factors associated with mortality due to cerebral malaria among children below ten years, Kiryandongo General Hospital, February –December 2017.

Variable	Category	Died n (%)	Recovered n (%)	OR(95%CI)	p-value
Child malnourished	Yes	9(90.0)	8(47.1)	10.13(1.04-98.49)	0.03
	No	1(10.0)	9(52.9)		
Delayed Diagnosis	Yes	2(15.4)	16(18.4)	2.75(0.49-15.53)	0.24
	No	11(84.6)	71(81.6)		
Duration of child's symptoms before seeking medical care >2 days	Yes	9(56.3)	14(16.7)	2.70(0.79-9.29)	0.11
	No	7(43.7)	70(83.3)		
Age <5 years	Yes	10(62.5)	19(41.5)	2.35(0.67-8.24)	0.18
	No	6(37.5)	65(59.5)		
First action taken was seeking medical care	Yes	5(35.7)	69(80.2)	0.45(0.13-1.55)	0.20
	No	9(64.3)	17(19.8)		
Sex	Female	5(33.3)	37(43.5)	0.27(0.08-0.96)	0.04
	Male	10(66.7)	48(56.5)		

Independent risk factors for cerebral malaria

The independent risk factors for Cerebral malaria were; distance >10km to the nearest health facility [Adjusted Odds Ratio (AOR)=14.35, 95% CI=1.30, 158.81], duration of symptoms before seeking medical care >2 days [AOR=9.03, 95% CI=2.21, 36.93], staying in a house under construction [AOR=4.51, 1.80, 11.32] and duration of illness before receiving antimalarial medicines >24 hours [AOR=3.82, 95% CI=1.44,10.12]. Owning at least one ITN in the household [95% CI=0.11, 0.95] and having a mother as a caregiver [AOR=0.23, 95% CI=0.09, 0.76] were independent protective factors for Cerebral malaria

Table 3: Independent factors associated with cerebral malaria among children below ten years, Kiryandongo General Hospital, February –December 2017.

Variable	AOR	95%CI	Coefficient	p-value
Distance between home and nearest health facility >10km	14.35	1.30-158.81	2.66	0.03
Duration of child's symptoms before seeking medical care >2 days	9.03	2.21-36.93	2.20	<0.01
Staying in a house under construction	4.51	1.80-11.32	1.51	<0.01
Duration of illness before child received antimalarial >24hrs	3.82	1.44-10.12	1.34	<0.01
Own at least 1 ITN	0.32	0.11-0.95	-1.14	0.04
Having mother as a caregiver	0.23	0.09-0.76	-1.36	0.01
Constant	+	+	-1.15	0.12

The study enrolled 100 cases of children aged 10 years and below. The highest proportion of cases, 87(87.0%), were aged 5 and below, whilst only 13(13.0%), were aged 6 and above. The median age of cases was 3 years (Q1=1; Q3=5).

Table 4: Shows the most affected age group of children with cerebral malaria

Age group	Cases Freq.	Cases Percent.	Cum.	p-value
0-5yrs	87	87.0%	87.00%	0.02
6-10yrs	13	13.0%	100.00%	
Total	**100**	**100.0%**		

The prevalence of cerebral malaria was high among children aged 5 years and below with the median age being 3 years. Most of the age group of children affected with cerebral malaria that died was 0-3 years.

The results above indicates that age group was significantly a risk factor for cerebral malaria since at 95% confidence level since the p-value=0.02 < p-value =0.05.

The Case Fatality Rate among cases was 28.8%. The CFR was high in this study. This can be attributed to the fact that the majority of the cases, were from IDP, Refugee camps and rural areas.

Table 5: Address of children with cerebral malaria

Area of residence	Case freq.	Cases percent.	Cum.	P-value
Bweyale (panyadole)	48	48.0%	48.0%	<0.01
Bududa (IDP camp)	36	36.0%	84.0%	
Other rural areas	16	16.0%	100.0%	
Total	**100**	**100%**		

Forty eight 48(48.0%) cases resided in Bweyale panyadole refugee camp, 36(36.0%) resided in Bududa Internally Displaced Persons (IDP) Camp and 16(16.0%) resided in other rural areas. It has been noted that about 50% of those who develop cerebral malaria especially in remote areas die. This is because health services are far away and are not well equipped to manage complications caused by the diseases. In this study the high CFR can be attributed to convulsions which was the commonest manifestation of cerebral malaria among cases in this study. The CFR of Cerebral malaria is dependent on the predominant manifestations that also have implications on the treatment.

DISCUSSION

Distance of more than 10km to the nearest health facility was an independent risk factor for cerebral malaria. Time spend travelling to a health facility and associated transport costs can influence the decision to seek treatment early for malaria and therefore result in delayed diagnosis and treatment as caregivers opt for initial treatment at home. In a study by Malik et al. [18] in Sudan, the choice of treatment for sick children among caregivers was highly dependent on accessibility and availability of health facilities. Most people in rural areas live further away from health facilities.

To address the issue of long distances between communities and health facilities which may result in delayed diagnosis and treatment, Uganda introduced community case management of malaria by Village Health Teams (VHTs) in 2012. VHTs were introduced to bring essential health services closer to the people, hence they should have adequate malaria commodities at all times if their existence is to make a difference. Duration of symptoms before seeking medical care for the sick child of more than 2 days was an independent risk factor for cerebral malaria. Duration of illness >24 hours before receiving antimalarial medicines and delayed diagnosis were also significantly associated with Cerebral malaria in children. This was consistent with findings in a study by Byakika-Kibwika *et al*. [19]. Malaria is an emergency because of its capability to progress to Cerebral, fatal illness if not treated appropriately and promptly [20, 21].

Quite a number of children die because of malaria within 24-72 hours of onset of symptoms [22, 23]. Timeous diagnosis and treatment is therefore crucial to prevent progression of disease to cerebral form and ultimately lower mortality. Presumptive treatment with antimalarial medicines of all fevers in children who live in malaria endemic areas is the main strategy for reducing malaria related child morbidity and mortality [24-26].

Staying in a house under construction was an independent risk factor for cerebral malaria in this study. A partially complete house without windows or a roof or with other openings may facilitate frequent and repeated exposure to parasite infected mosquitoes because mosquitoes gain access to the inside of the house through these openings thereby exposing the habitants to infective bites. Complete and good house construction is a barrier to malaria transmission because it limits access of mosquitoes to the household. Siri *et al*. [27] reported similar findings in Kenya. However, the results were not significant on multivariate analysis [27]. Owning at least one ITN in the household was an independent protective factor against cerebral malaria. Sleeping under a mosquito net every night was also significantly protective of cerebral malaria. Bed net use offers personal protection from getting mosquito bites. Widespread ITN use has been seen to reduce malaria morbidity and mortality in Kenya and Nigeria [28-30].

Having a mother as a caregiver was independently protective of cerebral malaria. Mothers tend to seek care immediately for their sick children and they pay particular attention to their children's needs. It therefore makes it easier for a mother to notice that their child is not feeling well. In rural settings most mothers are not employed, they spend most of their time at home with the children. This creates a bond between mother and child, hence children are most likely to tell their mother if they are not feeling well and the mother takes prompt action thereby decreasing chances of disease progression to cerebral form. Since child care is normally done by mothers, we suspect that having a caregiver who was not the mother may mean that the child is orphaned and this may lead to late identification of signs of disease and late presentation to health facilities for medical care.

Malnutrition was a significant risk factor for cerebral malaria and associated with mortality in children [31, 32]. In a study by Caulfield et al in 2004, improved nutritional status was seen to reduce malaria related deaths because it lessens the severity of malaria episodes [33]. Malnutrition reduces functionality of all systems of the body. This has great consequences especially in young children [33]. Underweight children have increased susceptibility to malaria through impairment in the function of the immune system. Undernourished children may be incapable to mount appropriate immune response to

parasites causing malaria because of reduced T-lymphocytes, impairment of antibody formulation and atrophy of the thymus and other lymphocyte tissues [34, 35]. History of malaria illness prior to the recent illness was significantly associated with reduced odds of cerebral malaria. Similarly, in a study by Phillips history of malaria was seen to be protective of developing cerebral disease, probably through acquired immunity [36]. Related findings suggest acquiring some form of protection following at least one infection [37]. The CFR was high in this study. This can be attributed to the fact that the majority of the cases, were from IDP, Refugee camps and rural areas. It has been noted that about 50% of those who develop cerebral malaria especially in remote areas die. This is because health services are far away and are not well equipped to manage complications caused by the diseases [38]. The CFR was higher (28.8%) compared to that in a study in Ghana by Mockenhaupt *et al.* [39] in 2004 (11.2%). In this study the high CFR can be attributed to convulsion which was the commonest manifestation of cerebral malaria among cases in this study. The CFR of Cerebral malaria is dependent on the predominant manifestations that also have implications on the treatment.

CONCLUSION

Cerebral malaria was characterized by a high proportion of convulsions and the Case Fatality Rate was high in this study. The factors associated with cerebral malaria and mortality due to cerebral malaria were identified. There is need for prompt treatment with antimalarial medicines of all high risk patients like malnourished children to avoid further progression of disease to severe form. There is need for stronger program linkages e.g Malaria, and Nutrition. There is need for training of health workers on manifestations of cerebral malaria to avoid delayed diagnosis. Scaling up community health education and promotion campaigns emphasizing on consistent and correct use of preventive strategies like ITNs is essential. A Prospective study is necessary to address some of the limitations of this study.

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