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MALARIA PARASITEMIA AMONG ASYMPTOMATIC INFANTS SEEN IN A MALARIA ENDEMIC REGION OF WESTERN KENYA

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ABSTRACT

***Background*: Sustainable Development Goal number three call for complete reversal in the incidence of malaria by 2030. Malaria however remains a health priority in sub-Saharan Africa, with children under five experiencing the highest morbidity and mortality. In clinical settings, management of malaria cases has primarily been centred on case definition, giving minimal consideration to the asymptomatic individuals who remain a major reservoir since they do not seek care. In malaria endemic areas, infants are likely to remain asymptomatic since they have partial immunity acquired from the mother.**

***Objective*: To determine the proportion of infants with positive parasitemia and describe their clinical and demographic characteristics.**

***Design*: A cross-sectional study.**

***Setting*: Webuye District Hospital, Western Kenya.**

***Subjects*: Three hundred and eighty four infants.**

***Results*: Prevalence of malaria parasitemia among enrolled infants was 61%. Infants born to housewife mothers, born to mothers who attended ANC during pregnancy; those weaned late or with family history of sickle cell disease were more likely to have malaria parasitemia with p-values of 0.031,0.015,0.007, and 0.025 respectively.**

***Conclusion*: Prevalence of malaria parasitemia among asymptomatic infants in Webuye (Western Kenya) remains high.**

INTRODUCTION

Millennium development goals call for a complete reversal in the incidence of malaria by 2015. Roll Back Malaria strategies has been a great step forward in achieving this ambitious goal with reported decline in malaria related morbidity and mortality (1). However, malaria still remains a major health priority in the sub –Saharan Africa. It is the most important parasitic disease in the tropics and sub-tropics with the greatest burden among the children under five and the pregnant women.

Asymptomatic carrier state for malaria has been reported in a number of studies. This has commonly been documented in the sub- Saharan region where malaria endemicity remains as high as 52% among adults (2). However, among the children, the proportion of those who harbor malaria and are asymptomatic is lower compared to adults (3, 4). This is largely due to the low immunity to malaria especially among the under five year old's. Some studies show that a number of children have some inherent protection against malaria due to presence of maternal antibodies or foetal haemoglobin (HbF). Infants therefore are likely to have high levels of asymptomatic parasitemia compared to the older children. Based on the current World Health Organization and Ministry of Health (MOH) Kenya policies, all children with fever are supposed to have a confirmatory malaria diagnosis (5,6). Therefore, health care workers tend to treat children with malaria only when patients present with fever and have a positive blood slide for malaria. However asymptomatic parasitemia which has been noted to be as high as 60-80% among children in high transmissions regions of sub–Saharan Africa is likely to remain untreated (7).

A longitudinal cohort study by Klein *et al*. found low incidence of both malaria and asymptomatic parasitaemia in infants under the age of three months in Lambaréné, Gabon where only 0.34% (3/878) had malaria and another 6% having asymptomatic parasitemia (8). Eliades *et al*. study in Togo observed a rapidly increasing parasite prevalence and clinical malaria in a random sample of children at community-level from the age of two months onwards. The parasitaemia prevalence increased from 18.2% in children aged 0-2 months to 43.0% in children aged 3-5 months. The prevalence of parasitaemia with documented fever remained stable from three

months onwards (9). Studies have shown that foetal haemoglobin was associated with delayed first episode of febrile malaria and spatial distribution models of malaria prevalence have been shown to be important in approximating endemicity levels in widely distributed areas and are useful in guiding interventions strategies (10,12,13). Anemia in infants is associated with increased parasite density (14) and malaria infection is associated with fever especially in children less than twelve months (15). Urbanization is a risk factor for surge in malaria among children (16).

This study therefore purposes to describe the level asymptomatic parasitemia in the Western region of Kenya and compare this with reports from other parts of the world.

MATERIALS AND METHODS

Study area: The study was carried out in Webuye (Bungoma East district) level IV hospital. It is located in western Kenya with a catchment population of about 500,000 people. This being a malaria endemic region, the highest transmission of Malaria is experienced during the two rainy seasons- March to May and October to November every year. The hospital has a maternal child health (MCH) unit that provides routine health services to children which include immunisation, vitamin supplementation, growth and weight monitoring as well as provision of other child health related services.

Study population: Comprised of well infants attending maternal child health clinic for routine immunisation and weight monitoring at the Webuye district hospital. An average of 30 children are seen in this clinic every day of whom 95%. More than 95% (of all children seen) have no clinical complains. The study targeted infants (less than 1 year olds) who had no clinical symptoms and were attending the clinic for routine immunisation or routine weight monitoring.

Study design: A cross-sectional descriptive study design was used. Each study participant was encountered once with no follow-up.

Sample size: The sample size was calculated using fisher *et al*., 1998 formulae below. The study assumed a malaria parasitemia prevalenceof 50% since there was no documented prevalence of asymptomatic parasitemia among infants in a similar setting at the time the study was being conducted.

$$n = \frac{Z^2 pq}{d^2}$$

Where, n- minimum sample size; z - Standard normal deviation at desired confidence interval, that is 1.96 for the 95% confidence interval; and p- expected malaria parasite prevalence among asymptomatic infants – 50% (assumed prevalence since no similar study was found especially for this age group-infants); p is 1-q; while d is accepted error =0.05

$$n = \frac{1.96^2 \times 0.5 \times 0.5}{0.05^2} = 384$$

Sampling Technique: A systematic sampling method was used during recruitment of participants. The well baby clinic receives approximately 30 infants each day for immunisation. Since the study was conducted over 3 months, with a month estimated to have 20 working days, approximately1800 children were expected to attend the clinic within this period. For the purpose of the systematic sampling, K interval was calculated as follow: Total number of children seen / minimum sample size translating to 1800/384=4.6. Every 4th child attending the clinic was recruited. In case the 4th child did not meet the inclusion criteria, the next child was picked. Well infants up to one year of age with axillary temperature of less than 37.5^0 c and whose guardian/ mother provided written consent were included in the study. However, any such child with presence of any clinical complains from the mother/ guardian or those already on antimalarial medication or any other medications except supplements were excluded from the study.

Data collection and Subject enrolment: Four research assistants were trained to assist in recruiting the study participants. The research assistants had basic medical training such as in clinical medicine or nursing. They were stationed at the well-baby clinic during working hours from Monday to Friday. Axillary temperature was taken for all babies using a calibrated digital thermometer. Those with temperature of <37.0^{0}c were identified and parent or guardian asked to give consent. Complete history and physical examination was performed as per the data collection sheet and secondary data recorded.

Peripheral blood sample for blood smear was obtained after cleaning the puncture site with 70% alcohol and used to prepare a thick peripheral blood film. Puncture site was protected using an adherent tape. The thick blood film was stained using Giemsa stain and examined under oil emersion power 100 for malaria parasites. For quality assurance, two laboratory technicians examined the samples separately and a third one was used to resolve discrepancies.

Data analysis: STATA version 12 Special Edition was used for data analysis. Descriptive statistics was used to summarise the data. Measures of central tendency (means, medians and modes) were calculated and presented using frequency histograms and tables. The dependent variable in this study was the malaria parasitemia. The independent variables were the various clinical and socio-demographic characteristics of the participants including but not limited to age, sex, mothers' level of education, use of Insecticide treated nets (ITNS), use of Intermittent Prophylactic

Treatment (IPT) by the mother during pregnancy, maternal parity and birth order. Relationship between the dependent and the independent variables was tested using the Pearson's correlations and Chi-square test. If the expected cell counts / values for some cells was less than five then Fisher's exact test was used. The linearity of the relationship was tested using linear regression while the ability of the continuous independent variable to predict the dependent variable was determined using the multiple logistic. A variable was included in the multivariable logistic regression model if it had a p-value of ≤ 0.25 and was only retained in the model if it was statistically significant at 5% level of significance. To test for differences between the group who were positive for the parasitemia and the one that was negative, a two-sample Wilcoxon rank sum test was used. We reported the adjusted and the unadjusted odds ratios (OR) and the corresponding 95% confidence limits.

Ethical considerations: Written consent was obtained from the parent or guardian. No subject names were used to ensure confidentiality. Laboratory results were communicated to the primary care giver as soon as they were obtained and those found to have parasitemia were advised to have a complete dose of anti-malarial. Pain experienced during the needle prick while obtaining the blood sample for malaria test was anticipated and usually lasts a few seconds hence didn't need any medication. However the mother was alerted about this during the consenting process. Pressure was applied at the site using dry cotton wool for about 30 seconds tostop bleeding. Approval for the research was obtained from The Moi University Institutional Research and Ethics Committee (IREC).

Limitations of the study: Due to limitation in time, the study may not reflect the variations in parasitemia during all the seasons of the year. However, the highest season of transmission was covered. Children above nine months were not sufficiently reached since immunisation is up to nine months and thereafter most of the children do not frequently attend the well-baby clinics

RESULTS

The study enrolled 384 infants out of whom 233 (61%) were found to have malaria parasitemia. The median age of the infants was five months with an interquartile range (IQR) of three days eight months while the male to female ratio was 1:1. The median age among the infants with parasitemia was five months (IQR) compared to six months for those without. The infants' anthropometrics measures were taken. The current median weight of the infants was 6.8 kilograms (IQR 5.3, 7.9), median birth weight was 3.4 (IQR 3.3, 8) kilograms, median length was 63 (IQR 56, 68) centimeters and head circumference was 42.8 (IQR 39-45) centimeters. Each of these variables was not statistically significant.

As indicated in Table 1, a majority (95%) of the respondents attended ANC. The test of association showed that infants of mothers who attended ANC tend to test positive for parasitemia than those who didn't attend ANC (P=0.015). Most mothers (89.6%) had normal delivery with few cases of breech delivery (0.5%) and Caesarean section (9.6%). There was no association between parasitemia status and mode of delivery (p>0.05). The study also showed that 75% of the mothers practiced exclusive breastfeeding for at least six months, with 21% on mixed feeding and 4% replacement feeding. There was no association between mode of feeding and parasitemia status (p>0.05). Seventy two percent of mothers were still breastfeeding during the time of the study while 13% stopped exclusive breastfeeding within six months. Majority (89%) of the respondents weaned their children after six months, and there was no association between weaning age and positive parasitemia status (p=0.07) as infants weaned within six months were less likely test positive for malaria parasites. History of travel to malaria regions, use of insecticide treated nets by infant, and use of mosquito repellants were not significantly associated with parasitemia.

The study also assessed the significance, if any, between clinical presentations of the participants based on previous history of malaria, febrile illness, congenital abnormalities and sickle cell disease and malaria parasitemia (Table 2). Majority of the respondents had no previous history of malaria (74%) and febrile illness (72%). Up to 2% of the infants were HIV infected and 5% were exposed indeterminate. Those with history of sickle cell disease were likely to test negative for parasitemia (p=0.025).

Further analysis of the infants' mothers' socio demographic characteristics (Table 3) did not reveal any significant association with parasitemia. Majority of the mothers had primary education (40%) and secondary education (41%). The main occupation was being housewife (55%) and farming (17%), with majority (52%) earning less than Kenya shillings 1,000 ($11.5) monthly. The types of housing they live in were equally distributed, with 29% and 34% living in temporary and permanent houses, respectively. Infants whose mothers were farmers had 45% reduced chance of testing positive parasitemia compared to housewives.

Table 1
Birth history, feeding and test of associations

Characteristic	Negative parasitemia	Positive parasitemia	Total		p-value
Birth order		2(1-3)	2(1-3)	2(1-3)	
Mother's Parity		2(1-3)	2(1-3)	2(1-3)	
IPT during pregnancy	Yes	135 (89%)	219 (94%)	354 (92%)	0.102
	No	16(11%)	14(6%)	30(8%)	
Maternal ITN	Yes	133(88%)	213(91%)	346(90%)	0.285
	No	18(12%)	20(9%)	38(10%)	
Febrile illness	Yes	67(44%)	97(42%)	164(43%)	0.596
	No	84(56%)	136(58%)	220(57%)	
ANC attendance	No	12(8%)	6(3%)	18(5%)	0.015
	Yes	139(92%)	227(97%)	366(95%)	
Mode of delivery	SVD	137(90.7%)	207(88.8%)	344(89.6%)	0.920
	C-Section	13(8.6%)	24(10.3%)	37(9.6%)	
	Breech	1(0.7)	1(0.4%)	2(0.5%)	
	C-Section				
	Breech	0	1(0.4%)	1(0.3%)	
Feeding mode (in the first 6 months)	Breast Feeding	114(76%)	174(75%)	288(75%)	0.976
	Mixed feeding	31(21%)	50(21%)	81(21%)	
	Replacement feeding	6(4%)	9(4%)	15(4%)	
Duration of breast feeding	<6 Months	22(15%)	27(12%)	49(13%)	0.631
	6 Months- 1 year	21(14%)	26(11%)	47(12%)	
	Still breastfeeding	104(69%)	172(74%)	276(72%)	
	Never breastfed	4(3%)	8(3%)	12(3%)	
Weaning age					
	<6 Months	25(17%)	18(8%)	43(11%)	0.007
	< 6 Months	126(83%)	215(92%)	341(89%)	
History of traveling outside the residence	No	138(91%)	212(91%)	350(91%)	0.892
	Yes	13(9%)	21(9%)	34(9%)	
Use of ITN by infant	No	6(4%)	10(4%)	16(4%)	0.8779
	Yes	145(96%)	223(96%)	368(96%)	
Use of insect repellants by infant	No	110(73%)	182(78%)	292(76%)	0.238
	Yes	41(27%)	51(22%)	92(24%)	
Presence of Mosquito breeding grounds near the home steads	Yes	109 (72%)	159 (68%)	258(67.2%)	0.411
	No	42 (28%)	74 (32%)	126 (32.8%)	

Table 2
Past Infants' medical history and their test of association

Past medical history	Negative parasitemia	Positive parasitemia	Total		p-value
Previous malaria treatment	No	110(73%)	174(75%)	284(74%)	0.69
	Yes	41(27%)	59(25%)	100(26%)	
Previous febrile illness	No	106(70%)	172(74%)	278(72%)	0.438
	Yes	45(30%)	61(26%)	106(28%)	
HIV status	Infected	6(4%)	2(0.9%)	8(2%)	0.132
	Exposed, indeterminate	10(7%)	10(4%)	20(5%)	
	Non-infected	118(78%)	197(85%)	315(82%)	
	Unknown	17(11%)	24(10%)	41(11%)	
Congenital abnormalities	No	151(100%)	231(99%)	382(99%)	0.522
	Yes	0	2(1%)	2(1%)	
Sickle cell disease	No	149(98.7%)	232(99.6%)	381(99.2%)	0.564
	Yes	2(1.3%)	1(0.4%)	3(0.8%)	
Family history of sickle cell disease	No	142(94%)	229(98%)	371(97%)	0.025
	Yes	9(6%)	4(2%)	13(3%)	

Table 3
Mothers socio-demographics and their relationship to the infants' parasitemia state

Variable	Levels	Negative (n=151; 39%)	Positive (n=233; 61%)	Total (n=384)	p-value
Education level	None	11(7%)	17(7%)	28(7%)	0.548
	Primary	54(36%)	100(43%)	154(40%)	
	Secondary	67(44%)	90(39%)	157(41%)	
	Post secondary	19(13%)	26(11%)	45(12%)	
Occupation	Housewife	70(46%)	140(60%)	210(55%)	0.031
	Farmer	30(20%)	34(15%)	64(17%)	
Income level (monthly)	Business Woman	51(34%)	59(25%)	110(29%)	
	<1000	74(49%)	126(54%)	200(52%)	0.430
	100-10,000	38(25%)	46(20%)	84(22%)	
	>10,000	39(26%)	61(26%)	100(26%)	
Type of Housing	Temporary	51(34%)	61(26%)	112(29%)	0.272
	Semi permanent	51(34%)	90(39%)	141(37%)	
	Permanent	49(33%)	82(35%)	131(34%)	

DISCUSSION

The prevalence of asymptomatic parasitemia among infants seen in this malaria endemic region was high (61%). Two third of all the infants had positive malaria parasitemia. This finding is similar to Dal-Bianco *et al.* study in Gabon that found the prevalence of asymptomatic parasitemia among Gabonese adults at 52 percent (2) although higher than that in a study in Mozambique where prevalence was 37 percent among asymptomatic children (7). However, studies focusing on infants are scarce. These study findings suggest that infants are a high risk group for asymptomatic parasitemia. This is similar to observation by Larru *et al.* that revealed positive asymptomatic parasitemia was increasing among the younger infants compared to older infants and children less than two years (9). A high rate in malaria parasitemia prevalence was also found by Eliades *et al*. in their study that found a prevalence of 18.2% among children aged 0-2 months and 43.0% among children aged 3-5 month (9). These findings contrast those of Afolabi who found a prevalence of 27.1% among admitted infants who were ≤ 6 months. It is also not consistent with findings by Baliraine who found a low prevalence of asymptomatic parasitemia among children because of their lower immunity status (3, 10).

The differences in the findings of these studies could be attributed to many factors including different geographic locations, different population socio-demographics and genetic variations among these populations. All these factors could affect the populations differently hence variations across the region in prevalence of asymptomatic parasitemia among infants. Also, the variation in the populations utilisation of preventive measures and the coverage of the various preventive strategies run by the roll back malaria initiatives may explain the differences. There also exist differences in nutrition status and immunity among infants in the different regions and populations. Children with better immunity and good nutrition status are more likely to have high asymptomatic parasitemia as compared to children with low immunity ad poor nutrition status.

The high asymptomatic parasitemia among infants could be responsible for the high malaria transmission rates in in Kenya that has been reported by Division of Malaria Control(DOMC) as 7% in Nyanza province, Western Kenya. The high prevalence of asymptomatic paraistemia has been explained in the literature by various authors. Young infants have maternal antibodies and HbF which is protective and causes poor parasite growth (11). New born infants in endemic areas such as Western Kenya are markedly resistant to *plasmodium falciparum* malaria hence rarely have severe disease. However, they are not protected against infection (12). Asymptomatic carriers do not seek treatment hence constitute a reservoir for parasites thus posing high a public health risk for transmission for plasmodium falciparum. There is need therefore to formulate interventions targeting this group to reduce the carrier states. This will be consistent with the aspirations of Millennium Development Goal number six that advocates for two third reductions in malaria deaths and morbidities by 2015. High prevalence of malaria parasitemia may be contributing to the high infant mortality rate in the sub-Saharan Africa (7) since a number of report reveal that most of these cases progress to clinical states later.

This study found ANC attendance by the mother and family history of sickle cell disease significantly associated with malaria parasitemia. This contrasts Gemperli *et al*. study conducted in Mali in 2004 that found that mother's education, birth order and interval, infant's sex, residence, and mother's age at infant's birth had a strong association with infant mortality risk and were attributed to positive malaria parasitemia (11). This could be explained by the fact that the history of travel may not be an exposure if there was no contact with *plasmodium falciparum* carrying mosquitoes. The use of ITN should be

protective from mosquito bites hence less risk for infection of *plasmodium falciparum*. However, this could not be associated with positive parasitemia since its use depends on social behaviour and adherence among the mothers. The history of previous febrile illness could be due to other conditions caused by bacterial infections and not necessarily by malaria hence its lack of association.

The finding on the repellants may not be conclusive due to the limited sample size. However, other studies have found them to be protective. It is also good to note that children with asymptomatic parasitemia had better overall nutrition status as seen by the median weight and height, their mothers were also more likely to have attended ANC, this points towards better health for those with positive parasitemia. This can be explained by the fact that good health means better immunity hence more likely to harbor parasites without manifesting disease.

The weaning age of the infant was significantly associated (p-value=0.07) with negative parasitemia, with an infant weaned before six months having 59 percent less chance for developing positive parasitemia compared with those weaned after six months of age. The higher likelihood of negative parasitemia could be attributed to presence of development of child own antibodies and general improvement in child's immunity, as they grow older in malaria endemic region without breast-feeding. However it could also mean that those children weaned later are healthier and hence less likely to develop symptoms even in the presence of infection this has been explained by various authors (14-16).
The Occupation of the mother was significantly associated with the level of parasitemia. This study found that an infant whose parents are farmers have 45% reduced chance of testing positive parasitemia compared to housewives. It further demonstrated that an infant with a mother who is a business woman also has 43% reduced chance of getting positive parasitemia compared to housewives. This could also be explained by the fact that businesswomen and farmers tend to travel along with their infants hence exposing them to plasmodium parasites. This finding is similar to Kenya Division of Malaria Control report that found economic factors to be contributing factors to positive malaria parasitemia among children including infants (17). This finding is also congruent with Wang *et al*. study in Tanzania in which they found that urbanisation was partly attributed to surge in malaria among children (16) while the Gemper listudy in Mali suggested that residence and occupation of the mother increased positive parasitemia prevalence among infants (11).

The family history of sickle cell disease was also associated with 76% less chance of positive parasitemia. This shows that sickle cell disease is protective of parasitemia and could be attributed mutation in a malaria parasite transporter pathway. Also the ongoing knowledge transmission to families with children with sickle cell disease and use of more protective ways are used in these families. The status of HIV was not significantly associated with positive parasitemia although literature has shown that HIVinfection is a risk factor for the development of malaria (16). This could probably be due to the small number of infants that were HIV positive in the study that could not help in making congruent conclusion on the association between HIV and malaria parasitemia.

In conclusion, there is a high prevalence of positive asymptomatic parasitemia among the asymptomatic infants in Western Kenya. This suggests that infants have high level of immunity and could be attributed to many factors including duration of breast feeding, nutritional status and endemic exposure to malaria. Demographic and clinical factors have been found to be associated with asymptomatic parasitemia and these include ANC attendance by the mother and family history of sickle cell disease. It is recommended that routine malaria testing and treatment for asymptomatic infants attending well baby clinic for immunisation should be done. This will help in lowering the parasites reservoir level in the community. Further studies that can elucidate the role of infant immunity in determination of parasitemia status are called for.

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