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Prevalence of Under Nutrition and Its Effects on Response to Malaria Treatments Among Children Under Five Years at Ahero and Homa Bay Hospitals, Western Kenya

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Abstract
Nutritional status of a person with malaria infection is thought to contribute to host treatment outcome. Limited studies have investigated the association despite the widespread concern with nutrition in malaria endemic areas. We evaluated the impact of under nutrition on the treatment outcome by Artemether Lumefantrine and Clindamycin plus Quinine. Sample of 384 children aged below five years diagnosed with uncomplicated *Plasmodium falciparum* malaria, were randomized to receive Clindamycin plus quinine or Artemether-lumefantrine (AL) for treatment. The children were followed up for 28 days to monitor body weight and height, clinical and parasitological parameters of treatment response.Outcomes included parasite clearance at days 2 and 3 and risk of recurrent parasitemia after 28 days of follow-up. Prevalence of underweight was 6 % (n=23) and stunting was 12% (n=45). Body weight increased over the 28 day follow up period. The initial mean weight was 13.03kg while the mean weight on day 28 was 13.7kg.The proportion of children with stunting was comparable between the female and male children: 40% verse 60%, p=0.06. Generally, the prevalence of underweight was comparable between the treatment arms (p=0.08). Similarly, the prevalence of stunting was not significantly different between the treatment arms (p=0.34). Cure rate was high in the Artemether group (96.5%) compared to the Clindamycin group (44.2%). Children who were underweight were 0.69 times less likely to be cured compared to those who were not underweight, but this difference was not significantly different from that of children were had no underweight (p = 0.429). Treatment outcomes were known for 43 of the 45 (95.6%) children with stunting. Overall, stunted children were 1.15 times more likely to be cured compared with children who were not stunted, but this difference was not statistically significant (p=0.704). No association between under nutrition (underweight and stunting) and treatment outcome was observed. Further research is suggested on the impact of under nutrition on response to malaria treatment using Artemether Lumefantrine alone on children less than five years. Ministry of health and other policy makers may formulate guidelines to improve management of children with malaria taking into consideration their nutritional status, and to integrate nutrition in malaria programmes.

1. Introduction.

Malaria is a disease of global public health importance, caused by protozoan parasites of the genus *Plasmodium.* The largest malaria burden is borne by populations in Sub-Saharan Africa where *Plasmodium falciparum* is predominant and the high risk groups include young children and pregnant women (6). In 2010, a total of 214 million malaria cases and 438,000 malaria-related deaths were reported globally (10).

The burden of malaria persists in many parts of Africa despite the availability of many interventions that are focused on preventive and therapeutic strategies. For instance, the Roll-Back Malaria (RBM) initiative is working to improve prevention efforts in affected countries, through insecticide-treated nets (ITNs), indoor residual spraying (IRS) of pesticides, and intermittent preventive treatment (IPT) for pregnant women. Other interventions focus on effective anti-malarial regimens like Artemisinin-Based Combination Therapy (ACT) and improving home management of the disease. (11)

Nutrition plays a major role in maintaining health, and malnutrition appears to generate vulnerability to a wide variety of diseases and general ill health. Nutrition helps determine the height and weight of an individual; it can affect the body's ability to resist disease, the length of one's life, and the state of one's physical and mental well-being (5). Malnutrition is a condition that results when the cells do not receive adequate supply of the essential nutrients because of poor diet or poor utilization of food. Sometimes it occurs because people do not or cannot eat enough of the foods that provide the essential nutrients to satisfy body needs. At other times people may eat well-balanced diets but suffer from diseases that prevent normal usage of the nutrients. Improved nutritional status lessens the severity of malaria episodes and results in fewer deaths due to malaria.

In Sub-Saharan Africa, malaria and malnutrition are major causes of morbidity and mortality in children less than five years of age. Global estimates indicate that between 300 and 500 million clinical cases of malaria occur annually. (4).

Although malaria and malnutrition coexists (9), the relationship between malnutrition and response to malaria treatment in young children is under debate. Limited studies have been published that evaluated the association between malnutrition and response to Artemisinin based combination therapies (ACTs), (8).

With respect to Malaria's contribution to under nutrition, randomized controlled trials suggest that malaria has a detrimental effect on nutritional status in children under five years old.(6) However, whether the presence of under nutrition places children at higher or lower risk for malaria related morbidity is unclear. It is not clear whether being under nourished means poor response to malaria treatment and well nourished means good response to malaria treatment. It is also not clear whether chronic malaria infections predisposes one to malnutrition because of poor appetite or malnutrion predisposes one to malaria infection due to impaired immunity. (7). Malaria contributes significantly in morbidity and mortality burden at all ages and is a main confounder of other conditions and causes of deaths in children such as low birth weight, malnutrition and anemia (6). Malaria itself is a major health problem in the tropics, with 300 to 500 million new clinical cases annually, most of the cases are of uncomplicated malaria.World Health Organization estimates that globally, in 2012, there were two hundred and seven million malaria cases and about six hundred and twenty seven malaria-related deaths. 80% of the malaria cases and 90% of deaths occur in Africa.

Under nutrition is the underlying cause of more than half of all deaths in children aged less than five years worldwide. There are 143 million children under five who are underweight in the developing world. In sub-Saharan Africa, about 20% of all deaths occurring in under-fives are attributed to malaria (4).

As under nutrition has been linked to increased risk of morbidity (especially in children) it is crucial to address these issues in order to combat malnourishment and the risk of death in malaria sufferers. (2).

Data are also lacking on the effect of malnutrition on response to antimalaria therapy (8).Vulnerable groups such as very young children, HIV infected and malnourished are typically excluded from or underrepresented in the studies of malarial drug efficacy (3).World health Organization currently recommends Artemisinin Based Combination Therapies in the treatment of uncomplicated malaria (9).

Nutritional issues that are involved with malaria includes Malaria in children below five years, others are Malaria in pregnancy, malaria and iron deficiency anemia and protein energy malnutrition.

1.1 Materials and Methods.

1.1.1 Study area and population.

The study was conducted at Ahero sub district and Homa Bay County Referral Hospitals, located respectively, in Kisumu and Homa Bay Counties, along the shore of Lake Victoria in Western Kenya. The catchment populations of these hospitals are ethnically homogenous and exposed to intense year round malaria transmission. The predominant malaria species is the *Plasmodium falciparum* and the area is categorized as holoendemic transmission area. Malaria in these regions accounts for about 40% of out-patient visits, and about 40% of hospital in-patient admissions (WHO 2000). The study population was children below five years of age diagnosed with uncomplicated malaria, who were enrolled in a clinical trial designed to compare the efficacy and safety of two malaria treatment regimens; Artemether-Lumefantrine (AL) and Clindamycin plus Quinine, for the treatment of malaria. Eligibility included: age of 6 to 59 months with weights more than 5 kg and residents of Ahero and Homabay. Slide confirmation of monoinfection with *Plasmodium falciparum* malaria, with parasitemia level of between 2000 and 200,000 parasites per microlitre and ability to take oral medication with parent or guardian's informed consent. They were randomized to receive either of the two treatment regimes and were admitted to the pediatric ward for 3 nights to ensure compliance and for close clinical observation. They were discharged home on the third day after starting treatment and followed up as outpatients for 28 days to monitor the response rate, weight and height.

1.1.2 Instrument and data collection

The following data were collected on paper-based case-record forms: Demographic data (name, age, and sex), clinical data (symptoms, temperature), treatment data (study drugs received), anthropometric measurements (weight and height) and parasitological data (parasite density) were obtained on the day of enrollment and on during follow-up done on day 7, 14, 21, and 28 after enrolment. Data was collected using an interviewer administered questionnaire, by health workers under the supervision of the researcher.

At screening, a blood smear was taken using a finger prick to confirm presence of malaria parasites. Those who had a positive smear for malaria and met the inclusion criteria were enrolled into the study. At enrollment, body weight and height measurements were taken. Body weight was measured in kilograms, using a digital weighing scale (for those who were able to stand) or a Salter weighing scale for smaller children. Height was measured in centimeters, using a height board.

Treatment response was evaluated using a combination of clinical data (symptoms and temperature), parasitological data (presence and density of malaria parasites) and molecular data (genotyping, to differentiate new from recrudescent malaria infections). Axillary temperature was taken using a digital thermometer. Thin and thick malaria blood smears were taken, stained (using Giemsa stain) and evaluated under the microscope for

presence of malaria parasites. When malaria parasites were found, they were read against 200 white blood cells. At enrolment and during follow up, blood spots were collected on filter paper and used to perform parasite genotyping using the Polymerase Chain Reaction (PCR) test. For those who developed recurrent parasitemia during follow up, the PCR test enabled the differentiation between those who had acquired new *Plasmodia* infections or those with a resistant malaria infection.

1.1.3 Data management and analysis

Raw data was cleaned and entered into Ms Access database and later exported into SPSS (statistical Package of Social Sciences, version 16.0) and Epi info software for analysis. Anthropometric indices were computed from the age, weight and height data, using Epi Info. A weight-for age Z-score (WAZ) less than -2 below the standard deviation was classified as underweight, while a height-for-age Z-score (HAZ) below -2 was classified as stunting. Prevalence was computed as percentage of children who had malnutrition (underweight or stunting). Proportions of treatment outcome were compared using Fisher's exact test and odds ratios (together with 95% confidence intervals) were computed. P values <0.05 was considered statistically significant.

1.1.4 Ethical Consideration

The study was conducted according to Good Clinical Practice guidelines and declaration of Helsinki. Ethical standards for conducting the study were maintained through the following measures: The ethical approval was provided from the Ethics Review Committee of the Kenya Medical Research Institute. Permission to conduct the study was obtained from the respective Hospital management committees. Parents or guardians of eligible children signed the informed consent before enrolment. Anonymity of participants was maintained at all times by not using any identifiers or personal information in the questionnaires. Participation was voluntary and participants were informed that they could withdraw from the study at any stage if they desired without any penalty.

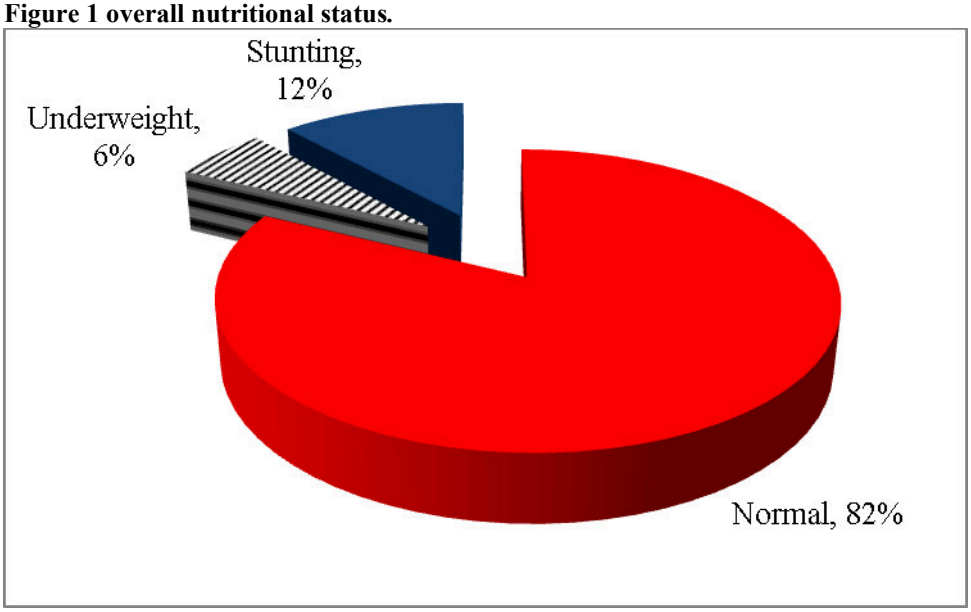
1.2 Results.

Table 1: Background Characteristics

Variable	**Overall**	**Clindamycin plus quinine**	**Artemether-lumefantrine**
Number	384	192	192
Study centre			
HomaBay Hospital	108	57	51
Ahero hospital	276	135	141
Age (months)	32.5 (14.5)	31.8 (14.7)	33.2 (14.4)
Sex: Male	199	98	101
Female	185	94	91
Body temperature (C)	37.5 (1.2)	37.6 (1.0)	37.5(1.3)
Body weight (Kg)	13.0 (2.94) 6.0-24.0	12.8 (2.9) 6.0—20.0	13.3 (2.9) 6.5—24.0
Body height (cm)	90.23(11.70) (58-117.2)	89.46(11.56) (65-115)	92.69(11.81) (58-117.2)
Malaria parasitemia (geometric mean)		54,173	56,951

A total of 384 children aged 6-59 months were enrolled in the study and randomized in equal proportions to the two arms of the study. A higher proportion of children were enrolled at Ahero County Hospital compared with Homa Bay County Referral hospital. A total of 199 children were male and 185 were female. The mean age in months (±Standard Deviation) was 32.5 (±14.5 SD). The mean body weight was 13kg (± standard deviation of 2.94) while the mean height was 90.2cm with a standard deviation of 11.7. All the children had malaria parasites at enrollment. 82% of the children enrolled in the study were well nourished (no underweight and no stunting), while 23 (6%) children were classified as underweight at enrolment, and 45 (12%) were stunted as shown in the figure 1 below.

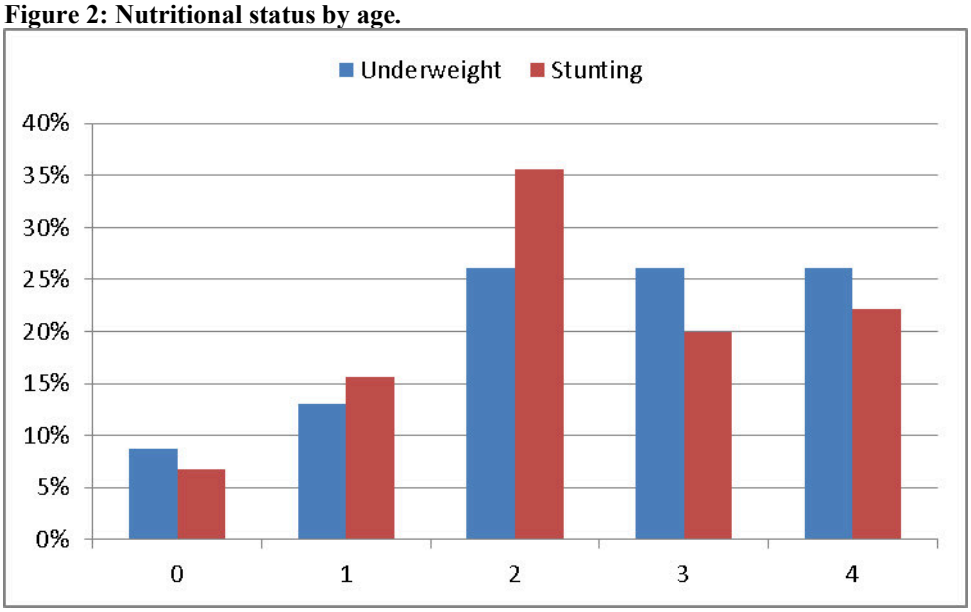
Figure 1 overall nutritional status.



1.2.1 Nutritional Status by Age

There was an increasing trend in the prevalence of both underweight and stunting that peaked at age 2 years and then decreased but was generally still higher than the prevalence in those below 2 years of age as shown in figure 3 below. The trend of underweight prevalence was not significantly different between the age groups (p = 0.605). The prevalence of underweight was higher among those above 2 years of age but this was not significantly different from the prevalence of underweight among those below 2 years of age (OR=2.18; 95% CI 0.79 to 5.99, p= 0.124). Similarly, the trend of stunting was not significantly different between the age groups (p =272), but those aged above 2 years were 2.2 times more likely to be stunted compared with those below 2 years of age (OR=2.20; 95%CI 1.06 to 4.60, p = 0.032).

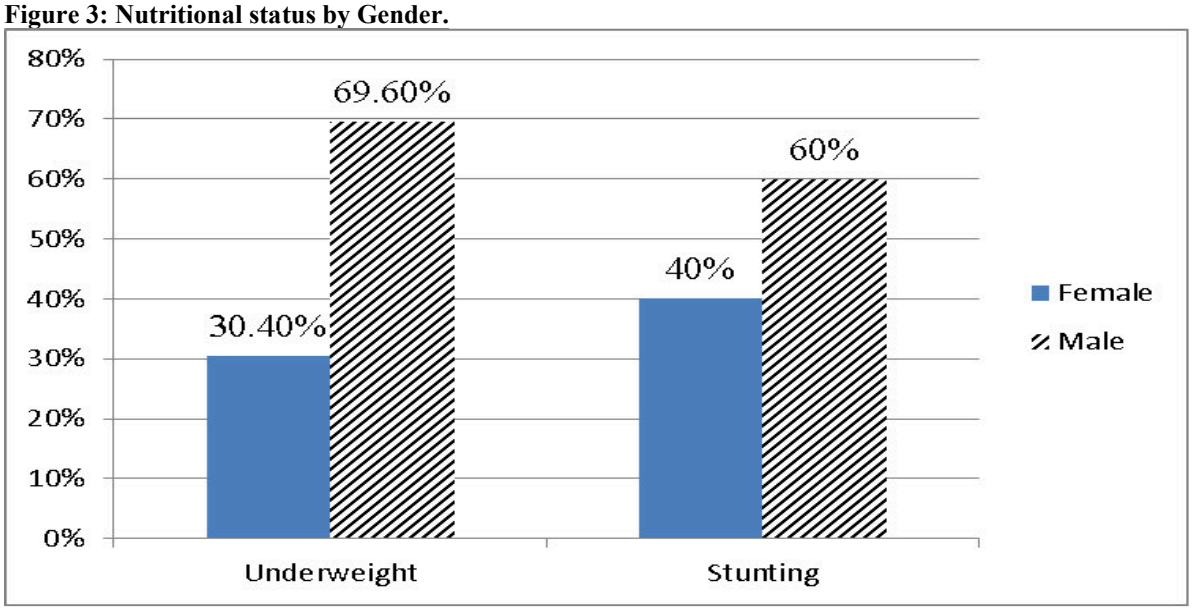
Figure 2: Nutritional status by age.



1.2.2 Nutritional Status by Gender.

A total of 7 (30.4%) female children were underweight compared with 16 (69.6%) male children. This difference was statistically significant (p=0.008). On the other hand, the proportion of children with stunting was comparable between the female and male children: 40% vs. 60%, p=0.06.

Figure 3: Nutritional status by Gender.



Prevalence of malnutrition by Study Arm

1.2.3 Underweight and Stunting by Study Arm.

Table 2 below showed that out of the 192 who received Clindamycin and Quinine, 16 (8.3%) were underweight while 26 (13.4%) were stunted. Of the 192 who received Artemether- lumefantrine, 7 (3.7%) were underweight and 19(9.9%) were stunted. The prevalence of underweight was comparable between the treatment arms (p=0.08). Similarly, the prevalence of stunting was not significantly different between the treatment arms (p=0.34).

Table 2.Showing nutritional status by study arms.

NUTRITIONAL STATUS	TREATMENT GROUP		P value
	Clindamycin plus Quinine	Artemether-lumefantrine	
Underweight	16/192 (8.3%)	7/192 (3.7%)	0.08
Stunting	26/192 (13.4%)	19/192 (9.9%)	0.34

1.2.4 Changes in Mean body Weight by Study Arm over time.

Table 3 below showed that generally, the body weight increased over the 28 day follow up period. The initial mean weight was 13.03kg while the mean weight on day 28 was 13.7kg. This indicates a statistically significant overall mean increase of 0.7kg (p = 0.005) over the study period. The mean increase in body weight was comparable between treatment groups over the follow up period but significantly different within the treatment groups. Among those who received Clindamycin plus quinine, the mean increase in body weight was 1.0kg, which was statistically significant (p = 0.017). However, among those who received Artemether-lumefantrine, the mean increase in body weight was only 0.41kg (p = 0.204).

Table 3: Mean body weight by study arm.

WEIGHT	N	Overall	Clindamycin plus quinine	Artemether-lumefantrine	P VALUE
DAY 0	384	13.02	12.73	13.31	0.055
7	272	13.33	13.32	13.33	0.98
14	266	13.34	13.25	13.38	0.73
21	258	13.51	13.36	13.57	0.60
28	217	13.72	13.73	13.71	0.98

1.2.5 Changes in Mean body Height by study arm over time.

Table 4 below shows the changes in body height over the 28 day follow up period. At enrollment, the mean height was 90.23cm and this increased to 92.2cm by day 28. This indicates an overall mean increase in height of 1.97cm, and this was statistically significant (p=0.047). The mean increase in height was comparable between and within the treatment groups over the follow up period. Those who received Clindamycin plus quinine had a mean increase of 3.0cm (p 0.067), while those who received Artemether-lumefantrine had a mean increase of 1.08cm (p=0.400).

Table 4: Mean body height by study arm

HEIGHT	N	Overall	Clindamycin plus quinine	Artemether-lumefantrine	P VALUE
DAY 0	384	90.23	89.46	91.00	0.20
7	272	90.94	91.03	90.90	0.92
14	266	90.66	90.92	90.53	0.81
21	258	91.54	92.37	91.15	0.50
28	217	92.2	92.47	92.08	0.82

1.2.6 Overall Treatment Outcome by Study Arm

Table 5 below shows that out of the 384 children enrolled in the study, treatment outcomes were known for only 352 (92%) children. Overall, treatment outcomes were known for 171 children who received Artemether-lumefantrine and for 181 children who received Clindamycin plus quinine. A total of 32 children (11 on Clindamycin plus quinine arm and 21 on the Artemether-lumefantrine arm) had no treatment outcomes because they were either lost to follow up or had withdrawn their consent from the study. Children who received Artemether-lumefantrine had a higher cure rate (96.5%) compared to those who received Clindamycin plus quinine group (44.2%). A significantly higher proportion of children who received treatment with Clindamycin plus quinine (53.6%) experienced early treatment failure compared with those who were treated using Artemether-lumefantrine. The rate of late treatment failure was comparable between the two treatment groups.

Table 5: Overall Treatment Outcome by Study Arm.

Treatment Outcome	**Treatment Group**	
	Clindamycin plus quinine (n=192)	**Artemether-lumefantrine (n=192)**
Cure	80	165
Early Treatment failure	97	2
Late Treatment failure	4	4
No treatment outcome		
Lost to follow up	5	12
Withdrawn consent	6	9

1.2.7 Association between Nutritional Status and Treatment Outcome

Overall Nutritional Status and Treatment Outcome

Out of the 23 children who had underweight, table 6 below shows treatment outcomes for 21 (91.3%) that was known. Out of these, 13 were cured (61.9%). Children who were underweight were 0.69 times less likely to be cured compared to those who were not underweight, but this difference was not significantly different from that of children were had no underweight (p = 0.429). Treatment outcomes were known for 43 of the 45 (95.6%) children with stunting. Overall, stunted children were 1.15 times more likely to be cured compared with children who were not stunted, but this difference was not statistically significant (p=0.704).

Table 6: Nutritional status and treatment outcome.

Nutritional status	**Cured**	**Crude Odds ratio (95%CI)**	**P value**
Underweight	13/21 (61.9%)	0.69 (0.257 to 1.99)	0.429
Stunted	31/43 (72.1%)	1.15 (0.54 to 2.56)	0.704

1.2.8 Nutrition status and Treatment outcome adjusted for Confounding factors

In this study, treatment outcome was strongly determined by the treatment received. Similarly, nutritional status was influenced by age and gender. In a logistic regression analysis, we evaluated the association between nutritional status after adjusting for these variables. Children with underweight were 0.85 times less likely to be cured compared to children without underweight (OR=0.846, 95% CI 0.291 to 2.463, p = 0.760). Similarly, compared to children without stunting, those who were stunted were 1.25 times more likely to be cured, but this difference was not statistically significant (OR=1.246, 95%CI 0.538 to 2.885, p = 0.608).

Table 7: Nutritional status and treatment outcome adjusted for confounding factors.

Nutritional status	**Cured**	**Adjusted Odds ratio (95%CI)**	**P value**
Underweight	13/21 (61.9%)	0.846 (0.291 to 2.463)	0.760
Stunted	31/43 (72.1%)	1.246 (0.538 to 2.885)	0.608

1.3 Discussion.

1.3.1 Prevalence of malnutrition (underweight and stunting).

This study has established that the prevalence of malnutrition in children below five years with malaria was: underweight, 6 % while stunting was 12 %. According WHO (2013), about 178 million children under five years worldwide are too short for their age group; while 115 million are underweight. The report also shows that stunting rate among children is higher in Africa and Asia than elsewhere. In Africa 16% of children are

underweight (low weight-for age).In Kenya, 35% of children under five are stunted, while the proportion severely stunted is 14%; (KNBS,).According to KDHS 2014 prevalence of stunting in Kenya is 26%, and underweight is 11%. Prevalence of stunting and underweight in Homa Bay for children below five years is 22.6%and 8%, and for Kisumu County where Ahero is situated are 24.9% and 10.4%, for Stunting and underweight. Study results for underweight and stunting are not consistent with other studies .The results of the study showed that prevalence for underweight and stunting is lower than that of Kenya, reason may be the life style situation for the children in the study areas have improved in the past year, due to introduction of health projects for children below five years like Integrated Management of Child hood Illnesses (IMCI), which has nutritional counseling as a component.

We had more males with underweight and stunting than the females, 21.6% and 13.5%. According to a study carried out by Henry et al 2007, we have more males who are undernourished than the females. The study revealed that 40% of the male children were stunted against 36% for the females. (OR 1.118 (95%CL 1.14-1.22) The study concluded that in sub-Saharan Africa, male children under five years of age are more likely to become stunted than females, which might suggest that boys are more vulnerable to health inequalities than their female counterparts in the same age groups. In several of the surveys, sex differences in stunting were more pronounced in the lowest social economic status groups.

1.3.2 Impact of Combination of Anti-malarial drug on Malaria Treatment Outcome.

Our study has established that cure rate is high in the Artemether group (96.5 %) compared to the Clindamycin plus Quinine group (44.2 %). Artemether is an Artemisinin based combination therapy. This is in consistent with current studies and recommendations from World Health Organization- WHO. *Plasmodium falciparum*, which causes the most life threatening malaria has developed resistance to almost every class of antimalaria compound (10) as a result of which World health organization (WHO) has recommended Artemisinin based combination therapy (ACT) as first line treatment of *Plasmodium falciparum*. ACT is the combination of artemisinin or an artemisinin derivative (Artesunate, Artemether, dehydraartemisinin) and partner drug (Amodiaquine, Mefloquine, Piperaquine, Lumefantrine, Sulphadoxine, Pyremethamine) ACT is about 90% effective when used to treat uncomplicated malaria (3). The rationale for ACT is that the Artemisinin precipitously reduces the parasitemia, and the less potent but longer- acting partner drug kills any residual parasites over 1 – 2 weeks (9).

1.3.3 Impact of Nutritional Status on Treatment Outcome

Our study showed that there was no association between under nutrition and treatment outcome. The study replicates one that had been done by Verret and Arinaitwe (8), that evaluated the association between malnutrition and response to artemisinin-based combination therapies (ACTs) in Uganda among children treated with ACTs for repeated episodes of malaria and found no significant association between height-for-age or weight-for-age z scores and a positive blood smear 2 days following treatment. However, existing evidence strongly suggests that micronutrient deficiencies and general under nutrition increase the burden of malaria morbidity and mortality, attributable fractions calculated by the CRA project (15; 8; 35), demonstrated that large numbers of children less than five years old suffer and die of malaria due to nutritional inadequacies in terms of protein energy, zinc, and vitamin A.

1.4 Conclusion

The study has established that the prevalence of malnutrition in children below five years with uncomplicated malaria in Ahero Sub County Hospital and Homa Bay county hospital in underweight was 6% and Stunting was 12%. Cure rate was high in Artemether group (96.5%) compared to Clindamycin plus Quinine group (44.2) %. The study has not identified under nutrition (Underweight and Stunting) as a factor that compromises malaria treatment response in children less than five years. Future research on the impact of under nutrition on response to malaria treatment among children with uncomplicated malaria using Artemether Lumefantrine is recommended, the Ministry of health and other policy makers to formulate guidelines to improve management of children with malaria taking into consideration their nutritional status and integrate nutrition in malaria programmes.

1.5 Acknowledgement

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REFERENCES

1. Barnes, K.I, .et al 2007.World Antimalaria Resistance Network (WARN)IV:clinical pharmacology.Malar.J.6:122
2. Caulfield LE, Richard SA Black RE, (2004).Under nutrition as an underlying cause of malaria morbidity and mortality in children less than five years old. *Am J Trop Med Hyg 71: 55-63?*
3. Howitt P, Darzi A, Yang GZ, Ashrafian H, Atun R, Barlow J, Blakemore A, Bull AM, Car J, Conteh L, Cooke GS, Ford N, Gregson SA, Kerr K, King D, Kulendran M, Malkin RA, Majeed A, Matlin S, Merrifield R, Penfold HA, Reid SD, Smith PC, Stevens MM, Templeton MR, Vincent C, Wilson E (2012). "Technologies for global health". *The Lancet* **380** (9840): 507–35. doi:10.1016/S0140-6736(12)61127-1. PMID 22857974.
4. Korenromp EL, Arnold F, Williams BG, Nahlen BL, Snow RW. Monitoring trends in under-5 mortality rates through national birth history surveys. Int J Epidemiol. 2004;33:1293–1301. doi: 10.1093/ije/dyh182. [PubMed] [Cross Ref].
5. Ruth A Roth, 2011, Nutrition and diet therapy 10th Edition, Delmar Cengage Learning, Indiana University Indiana.
6. Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI,(2005) The global distribution of clinical episodes of Plasmodium falciparum malaria. Nature. 2005;434:214–217. doi: 10.1038/nature03342. [PMC free article] [PubMed] [Cross Ref]
7. Shankar AH, 2000.Nutritional modulation of malaria morbidity and mortality .*J Infect Dis 182 (suppl 1):S37-S53.*
8. Verret, W. J., E. Arinaitwe,. (2012 MARCH). "Effect of nutritional status on response to treatment with artemisinin-based combination therapy in young Ugandan children with malaria." Antimicrob Agents Chemother **55**(6): 2629-35.
9. World Health Organization's 2010. Global Report on Antimalaria Efficacy and Drug Resistance: 2000-2010. Geneva: World Health Organization.
10. World Health Organizations .2010.Guidelines for the treatment of malaria, 2nd ed.World HealthOrganisations,Geneva.Switzerland.http//whqlibdoc.who.int/publications/2010/9789241564106_eng.pdf.
11. World Health Organizations :(2005) World Malaria Report: Rollback Malaria, Geneva. 2005.
12. World Health Organizations: 2000 The use of antimalaria. Report of WHO informal consultations 13-17,