

Original Research Article

Association between the RTS,S/AS01 malaria vaccine and under-nutrition in children aged 10 to 59 months in Siaya County, Kenya

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ABSTRACT

Background: Under-nutrition is a global problem associated with infectious diseases including malaria. In this study, we explored the association between the newly introduced malaria vaccine, RTS,S/AS01 and measles vaccine with under-nutrition in children.

Methods: We conducted a case-control study using anthropometric data for children aged between 10 and 59 months in Siaya County, Kenya collected from September to December 2021. Malaria and measles vaccines were the exposure variables, and under-nutrition, which is a composite variable including stunting and/or underweight was the outcome. Chi-square was used to test association between under-nutrition and the two vaccines. Further, a binary logistic regression was used to assess association between the vaccines, and independent variables with a confidence interval set at 95%.

Results: From a total of 1,701 children, 185 (16.8%) were undernourished. Among the undernourished children, 121 (11.0%) were stunted and 64 (5.81%) were underweight. The undernourished children were matched with children of normal nutritional status at a ratio of 1:1 giving a total of 370. Malaria vaccine coverage was low at 21.1% (39/370) and 17.3% (32/370) among undernourished and children with normal nutritional status respectively. Similarly, the measles vaccine coverage was 30.8% (57/370) and 36.2% (67/370) among cases and controls respectively. Neither exposure to malaria nor measles vaccines showed a statistically significant difference between the cases and controls.

Conclusions: We found no statistically significant association between malaria vaccine and under-nutrition in children. While malaria vaccine is important in protecting children from the malaria disease effects, it is not a proxy intervention for under-nutrition.

Keywords: Kenya, Malaria vaccine, RTS,S/AS01, Siaya County, Under-nutrition

INTRODUCTION

Under-nutrition and malaria are major causes of child morbidity and mortality, a global challenge that has shown very little progress especially in Asia and Africa.¹ In 2022, more than half of all under five children lived in Asia while two out of five hailed from Africa.¹ Almost all

countries worldwide are affected by at least one form of malnutrition but Low and Middle Income Countries (LMICs) bear the biggest burden.² Under-nutrition, which comprises wasting, stunting, underweight and micronutrient deficiencies is prevalent in areas with high prevalence of malaria.³ Under-nutrition is associated with about 45% of deaths among under five and research

studies conducted in sub-Saharan Africa and Asia reported that under-nutrition is responsible for 60.7% deaths from diarrhea, 52.3% deaths from pneumonia, 44.8% deaths from measles, and 57.3% of deaths from malaria.⁴ Eastern Africa experiences the highest levels of under-nutrition, especially stunting, in the continent.^{5,6} In the first half of 2022, Kenya reported 942,000 cases of acutely under-nourished children aged between 6 and 59 months.⁷

Under-nutrition is disproportionately distributed based on demographic, social and geographical location.⁸ Rural areas have been observed to experience a higher burden; for example, a research study conducted in a rural area of Kenya reported stunting at 26% and 11% underweight children.² In Siaya County, which is largely rural, the prevalence of stunting is 25%, wasting 3% and underweight 9%.⁹ The causes and factors associated with under-nutrition are well documented and poverty is cited as the main underlying cause.¹⁰⁻¹³ The risk factors for malnutrition in children include, inadequate dietary intake, low birth weight, feeding problems, diarrhea, frequent illness, measles, pertussis and malaria parasite.^{12,14} Undernourished children are vulnerable to infections and can easily die from common illnesses.^{15,16} Proper feeding on a balanced diet, drinking potable water and observing good hygienic standards prevent diseases and hence protect children from under-nutrition.

On the other hand, a disease condition such as malaria can adversely influence the host nutrition by restricting food intake through anorexia and vomiting, malabsorption of nutrients, and loss of nutrients through diarrhea or vomiting, and there is a greater risk for malnutrition if the body's metabolism is altered.¹⁷ Furthermore, malaria in particular has immunosuppressive impacts that can increase the risk for infection with other pathogens that result in nutritional deterioration.¹⁸ Consequently, in a malaria endemic zone such as Siaya County, it is possible that malaria disease is one of the underlying causes for under-nutrition. A research study conducted in Asembo, Siaya County reported that for every episode of malaria there is a 6% increased chance for stunting.¹⁹ The relationship between malaria and under-nutrition is not clear and some researchers have reported that it is bi-directional while others have reported no association. For example, a study conducted in the coastal part of Kenya reported no association between malaria and subsequent development of protein-energy malnutrition, except with age as a modifier where the youngest and oldest children experienced the highest incidence of under-nutrition.²⁰ Also, a study conducted in rural Gambia reported no malaria effect on children's nutritional status from the beginning to the end of malaria season.²¹ On the other hand, some research studies have reported an association.^{3,18,22,23}

Children in Siaya County and other lake regions experience the highest incidence of clinical malaria at

24.3 cases per 1000/month.²⁴ Furthermore, malaria is the main cause for under-five year old morbidity and mortality in the region.²⁵ Most of these hospitalized children are usually under-nourished.²⁶ Although the evidence on the association between malaria and under-nutrition is still inconclusive and based on the fact that malaria coexist with under-nutrition in endemic areas, it is imperative to investigate whether the RTS,S/AS01 malaria vaccine can help reduce under-nutrition cases. In 2019, the World Health Organization (WHO) sponsored a phased implementation of the RTS,S/AS01 vaccine in three African countries (Kenya, Malawi and Ghana).²⁷ In Kenya, the first, second and third doses of the malaria vaccine is administered to children at 6, 7 and 9 months respectively. Thereafter, a booster dose is given at 24 months. Vaccines have been proven to be cost effective in preventing most childhood diseases and a few research studies have investigated associations of childhood vaccines and nutritional status.^{28,29} In Siaya County, a cross-sectional survey reported that a child who had received all the recommended childhood vaccines had a protection against stunting.³⁰ Measles vaccine can be used as an indicator for a fully vaccinated child because is the last to be received at 9 and 18 months in the Kenya Expanded Program for Immunization (KEPI).

Consequently, in addition to the malaria vaccine, we evaluated an association between the measles vaccine and under-nutrition in children. In this study, under-nutrition refers to either stunting or underweight. Stunting is a consequence of chronic or recurrent under-nutrition and is related to poverty, poor maternal health and nutrition, frequent illness and/or inappropriate feeding and care in early life.¹² Stunting prevents children from reaching their physical and cognitive potential, which in turn affects their academic performance and productivity in adulthood.³¹ Besides, underweight indicates a history of poor health or nutritional insult to the child, including recurrent illness and/or starvation. An underweight child may be stunted, wasted or both and hence a composite of wasting and stunting.³²

METHODS

Study design and population

This was a nested case-control study conducted in three sub-Counties (Gem, Rarieda/Asembo and Karemo) of Siaya County in Kenya (Figure 1). The study area is covered by a Health and Demographic Surveillance System (HDSS) established by the Kenya Medical Research Institute (KEMRI) in collaboration with the Centers for Disease Control and Prevention (CDC) from 2002 to 2007.^{33,34} The Lake Victoria region has the highest malaria transmission in Kenya and remains the most important source of malaria transmission nationally at 24.3 cases per 1000/month.²⁴

Apart from the high prevalence of under-nutrition and malaria, Siaya County has the leading cases of HIV and

Tuberculosis (TB). In 2021, the County notified the highest proportion (34%) of new drug-sensitive TB cases.³⁵ Luo community dominates the study area and they undertake subsistence farming, fishing and small-scale trading as their main economic activities. The residents cultivate land twice a year during long rains (March to June) and short rains (October to December) and they plant: maize, beans, millet, and sorghum.

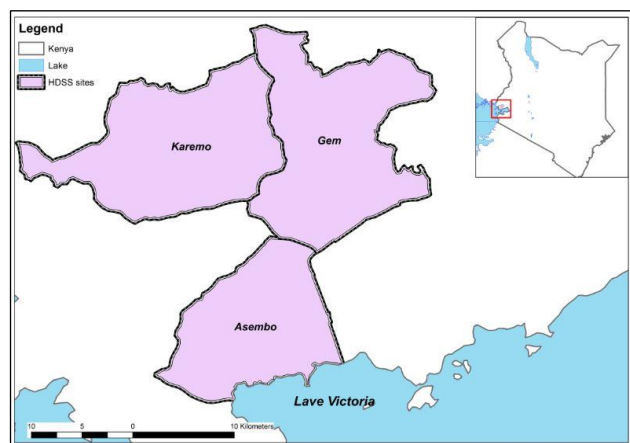


Figure 1: Study area in Siaya County, Kenya.

Data collection

This analysis was nested on a research study, conducted in the area to determine the potential of an integrated home gardening and nutrition counseling program as a possible climate change adaptation strategy to improve child health in rural Burkina Faso and Kenya.³⁶ Through the research study, baseline examinations of 683 children aged 6 to 24 months were performed between September and December 2021 in Kenya.

In addition to the quantitative surveys, anthropometric measurements were obtained in light clothes. Length and height were measured to the nearest centimeter (cm) and weight to the nearest 100g. For children who were <85cm, recumbent length was obtained. For mothers and children who could stand and were ≥ 85 cm, standing height was measured. Body weight was measured on a mother-and-child weighing scale. Based on the WHO growth standards, anthropometric indices, stunting, wasted and underweight were calculated. A Z-score of height-for-age (HAZ) <-2 SD of the WHO Reference 2007 was defined as stunting and A Z-score of weight-for-age (WAZ) <-2 SD of the WHO Reference 2007 is defined as underweight.³⁷⁻³⁹

Since wasting is an indicator of a recent and severe weight loss, and its prevalence is low in the study area, we used stunting and underweight to define under-nutrition in this analysis. The under-nutrition cases were matched on a 1:1 ratio with controls (children of similar demographic characteristics i.e., age and sex but with normal nutritional statuses). Explanatory variables

including age of participants and their parents, sex, birthweight, marital status, religion, and area of residence were collected during the baseline survey. For socio-economic status (SES)/wealth quartile, we used a previously validated scale that included occupation of the household head, primary source of drinking water, type of cooking fuel, household assets (lantern lamp, sofa set, radio, bicycles and television) and livestock possessions (poultry, pigs, donkey, cattle, sheep and goats).⁴⁰ As a result, the mother-child pairs were categorized to one of the following wealth quartiles: low, middle, and upper.

Exposure

Since first dose of malaria and measles vaccines are administered at 6 and 9 months respectively, we considered children who had attained the age of 10-59 months for the analysis. Exposed children are those who had received at least one dose of malaria or measles vaccines at the time of baseline health examination. Although children are expected to receive four doses of malaria vaccine and two doses of measles vaccine, a binary categorization of exposed or not exposed was used due to a small number of children who had received more than one dose of the vaccines. The vaccine records were verified using Maternal Health and Child (MCH) booklets and where documentation was missing, it was assumed that the participant did not receive the vaccine.

Data analysis

Data management and analysis was done using statistical analysis software, Stata (16.1, Stata Corp LLC, College Station, TX). Frequency Table was used to present vaccine coverage and other demographic and social characteristics. Chi-square was used to test the association between undernutrition and vaccine status. In addition, a logistic regression was used to assess association between the vaccines (malaria and measles) and nutritional status with a confidence interval set at 95%. To control the effect of confounding variables, a backward stepwise logistic regression technique was performed to select variables to the final model with a p value threshold of 0.25, variables were eliminated based on the p values and those that satisfied the elimination criteria were used in the final model.

Ethical approval was sought from KEMRI Scientific and Ethics Research Unit (SERU) and from the University of Hiedenberg Ethics Committee in Germany. In addition, as per the requirement of the Kenyan government, permission to conduct research activities was obtained from the National Council of Science and Technology Institute (NACOSTI). A written informed consent was administered to all potential participant's parents and signing of a consent form was required before recruitment. Data confidentiality was maintained using password protected computers and also anonymized prior to the analysis.

RESULTS

Out of the 1,701 children examined during the baseline survey, we obtained 1,100 eligible for our analysis as shown in Figure 2. Out of the 1,100 eligible children, 121 (11.0%) and 64 (5.81%) were stunted and underweight respectively, giving a total of 185 cases.

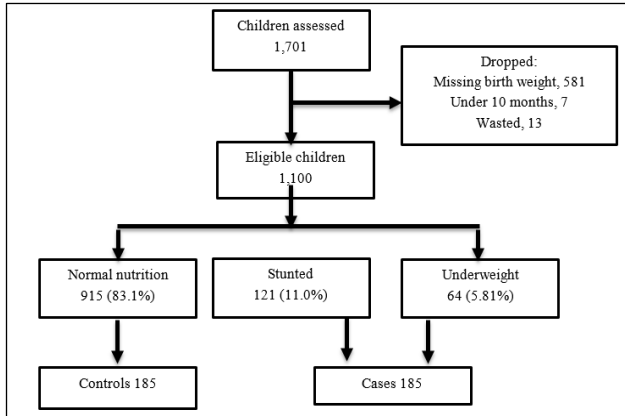


Figure 2: Flow diagram of the number of children included in the analysis.

Based on a ratio of 1:1, 185 children with normal nutritional status were matched with cases giving a total of 370. The mean ages of participants were 31 and 32 months for cases and controls respectively. Besides, mean ages for the participants' mothers/caregivers were 31 years for both cases and controls groups. Malaria vaccine coverage was low at 21.1% and 17.3% among undernourished and children with normal nutritional status respectively (Figure 3). Similarly, the measles vaccine coverage was low at 30.8% and 36.2% among

undernourished and children with normal nutritional status respectively (Figure 4).

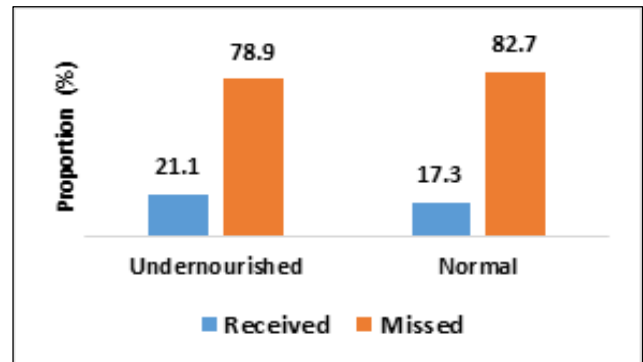


Figure 3: Malaria vaccine coverage.

Table 1 presents characteristics between undernourished children (cases) and those with normal nutritional status (controls). The case and control populations had no significant statistical differences on all factors assessed.

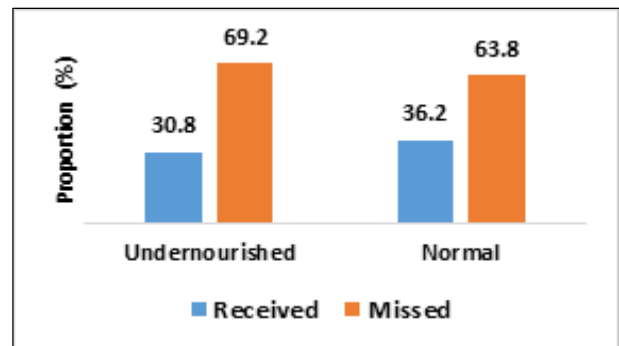


Figure 4: Measles vaccine coverage.

Table 1: Participants' demographic and social characteristics.

Characteristic	N	Cases, n=185 (%)	Control, n=185 (%)	P value
Education level	370			0.99
None		13 (7.0)	13 (7.0)	
Primary		145 (78.4)	145 (78.4)	
Secondary/high		27 (14.6)	27 (14.6)	
Gender of child	370			0.99
Male		103 (55.7)	103 (55.7)	
Female		82 (44.3)	82 (44.3)	
Area	370			0.62
Gem		77 (41.6)	79 (42.7)	
Karemo		61 (33.0)	53 (28.6)	
Asembo		47 (25.4)	53 (28.6)	
Marital status	370			0.99
Married		113 (61.1)	112 (60.5)	
Missing		35 (18.9)	35 (18.9)	
Single		32 (17.3)	33 (17.8)	
Divorce/separated		5 (2.7)	5 (2.7)	
Orphan hood	370			0.52
Not orphaned		144 (77.8)	149 (80.5)	
Orphaned		41 (22.2)	36 (19.5)	

Continued.

Characteristic	N	Cases, n=185 (%)	Control, n=185 (%)	P value
Weight at birth	370			0.10
<2.5 kg.		21 (11.4)	12 (6.5)	
2.5+ kg.		164 (88.6)	173 (93.5)	
Mother's age	370			0.99
<25 yrs.		37 (20.0)	38 (20.5)	
25-34 yrs.		89 (48.1)	89 (48.1)	
35+ yrs.		59 (31.9)	58 (31.4)	
Religion	370			0.28
African		105 (56.8)	92 (49.7)	
Catholic		48 (25.9)	50 (27.0)	
Protestants		32 (17.3)	43 (23.2)	
Child's age	370			0.24
10-23 months		64 (34.6)	62 (33.5)	
24-47 months		95 (51.4)	85 (45.9)	
48-59 months		26 (14.1)	38 (20.5)	
Wealth quartile	370			0.23
Low		64 (34.6)	56 (30.3)	
Middle		101 (54.6)	98 (53.0)	
Upper		20 (10.8)	31 (16.8)	
Malaria vaccine	370			0.36
0 dose		146 (78.9)	153 (82.7)	
At least 1 dose		39 (21.1)	32 (17.3)	
Measles vaccine	370			0.27
0 dose		128 (69.2)	118 (63.8)	
At least 1 dose		57 (30.8)	67 (36.2)	
Mean (SD); n (%)				
Pearson's Chi-squared test				

Table 2: Determinants of under-nutrition in children aged between 10 and 59 months in Siaya County, Kenya.

Characteristic	Unadjusted OR			Adjusted OR		
	OR	95% CI	p-value	OR	95% CI	P value
Malaria vaccine						
0 Dose	-	-		-	-	
At least 1 dose	1.47	0.76, 2.86	0.30	1.42	0.74, 2.74	0.30
Measles doses						
0 dose	-	-		-	-	
Either dose	0.75	0.46, 1.22	0.20	0.75	0.46, 1.20	0.20
Education level						
None	-	-		-	-	
Primary	0.93	0.38, 2.29	0.90	0.94	0.39, 2.27	0.90
Secondary/high	1.02	0.35, 2.96	0.90	1.01	0.37, 2.76	0.90
Gender of child						
Male	-	-		-	-	
Female	1.01	0.65, 1.56	0.90			
Marital status						
Single	-	-		-	-	
Divorce/separated	1.19	0.27, 5.24	0.80			
Married	0.98	0.52, 1.83	0.90			
Missing	0.95	0.40, 2.22	0.90			
Orphan hood						
Orphaned	-	-		-	-	
Not orphaned	0.80	0.45, 1.41	0.40			
Weight at birth						

Continued.

	Unadjusted OR			Adjusted OR		
<2.5 kg	-	-	-	-	-	-
2.5+	0.50	0.22, 1.07	0.08	0.50	0.22, 1.06	0.07
Mother's age						
<25 yrs.	-	-	-	-	-	-
25-34 yrs.	1.32	0.67, 2.61	0.40	1.27	0.71, 2.28	0.40
35+ yrs.	1.26	0.59, 2.72	0.50	1.23	0.65, 2.32	0.50
Area						
Gem	-	-	-	-	-	-
Asembo	0.86	0.47, 1.58	0.60	0.84	0.46, 1.53	0.60
Karemo	1.24	0.69, 2.24	0.50	1.21	0.68, 2.17	0.50
Child's age						
10-23 months	-	-	-	-	-	-
24-47 months	1.27	0.78, 2.08	0.30	1.27	0.78, 2.06	0.30
48+ months	0.76	0.39, 1.47	0.40	0.75	0.39, 1.46	0.40
Wealth quartile						
Low	-	-	-	-	-	-
Middle	0.88	0.55, 1.42	0.60	0.88	0.55, 1.41	0.60
Upper	0.50	0.25, 1.00	0.05	0.51	0.25, 1.00	0.05
Religion						
Catholic	-	-	-	-	-	-
African	1.23	0.74, 2.08	0.40	1.22	0.73, 2.03	0.50
Protestants	0.73	0.38, 1.37	0.30	0.72	0.38, 1.36	0.30
OR = Odds Ratio, AOR = Adjusted Odds Ratio, CI = Confidence Interval						

Determinants of under-nutrition in children

We assessed factors in Table 2 for their association with under-nutrition in children. Participants' birth weight and household's economic status (wealth quartile) showed a statistically significant association. Children born with normal birth weight of 2.5 Kg and above had a reduced chance of under-nutrition compared to those born with <2.5 Kg, AOR = 0.50, 95% CI: 0.22, 1.06; $p = 0.07$. Besides, children born in upper wealth quartile households had a 49% reduced chance of under-nutrition (AOR = 0.51, 95% CI: 0.25, 1.00; $p = 0.05$). Malaria vaccine showed a positive association with under-nutrition in children although not statistically significant OR = 1.47, 95% CI: 0.76, 2.86; $p = 0.30$. On the other hand, measles vaccine showed a negative association, also not statistically significant, OR = 0.75, 95% CI: 0.46, 1.22; $p = 0.20$.

DISCUSSION

Vaccines are the most cost effective public health interventions against infectious diseases such as measles.⁴¹⁻⁴³ Infectious diseases, malaria and measles are the leading cause of child morbidity and mortality particularly in malaria endemic zones.^{10,25,15} Infectious diseases can cause a delay in children's growth and development and consequently result in stunting and underweight. Given the high prevalence of malaria disease, stunting and underweight among children living in Siaya County in Kenya, and with the introduction of

malaria vaccine, we assessed associations between under-nutrition in children (either stunting or underweight) and two vaccines (malaria and measles). Extended benefits of vaccines in preventing other secondary conditions such as under-nutrition would be useful if included in messages meant to improve vaccine coverage.

Although under-nutrition and malaria are the leading causes for child morbidity and hospitalization in Siaya, our findings showed no statistically significant association between under-nutrition and malaria vaccine.² Given that under-nutrition and malaria disease coexist in malaria endemic areas, our findings beg for a further investigation using a more robust study design with sufficient sample size.⁴⁴ Our findings imply that at present, most of the under-nutrition cases in the County are not related to malaria disease. The low malaria coverage reported in our study is inconsistent with the facility based records.²⁷ Few studies have reported a positive association between malaria episodes and under-nutrition, especially stunting. As an example, a longitudinal observational study of children aged 0-2 years in Asembo, which is part of Siaya County indicated an increased chance for stunting by 6% for every episode of clinical malaria.¹⁹ Malaria vaccine is still new in the market and hence under-researched, nonetheless, the mixed findings require a systematic literature review to collate evidences. A research study conducted among under-five children in south west Ethiopia concluded that there was no association between malaria and under-nutrition.⁴⁵ These findings infer that the main intervention

for under-nutrition in children should continue targeting dietary intake despite the potential of infectious diseases to cause under-nutrition.⁴⁶

In the contrary, research studies have reported a negative association between measles vaccine and under-nutrition in children.^{47,46,48,29} Our findings on the association was not statistically significant but indicated the potential for the measles vaccine to reduce chances of under-nutrition in children. In general, vaccines help in the prevention of diseases that predispose children to under-nutrition.⁴⁹ In this regard, efforts to increase childhood vaccine coverage need to be stepped up. From our findings, the measles vaccine coverage was lower than the earlier reported rates i.e., 30% and 34% among the under-nourished children and those with normal nutritional status respectively vs. 80%.⁵⁰ This could be due to the fact that we analyzed data from children with vaccine records only and a possible negative impact of COVID-19 vaccine in the study area. Whichever is the case, there is a need to increase pro-vaccine uptake campaigns in the study area.

Apart from the recommendation for the vaccine uptake interventions, emphasis should be placed on promoting factors that have been shown to influence children's nutritional status positively. In this study, children's birth weight and household's wealth quartile are likely determinants of nutritional status. In order to improve chances of giving birth to children with weights within the recommended range i.e., 2.5 to 4 Kg, it is imperative that pregnant women are encouraged to visit antenatal care clinics for pregnancy health monitoring.^{51,52} Household's socio-economic status is dependent on several underlying factors and hence a complex issue to address. Nonetheless, interventions that aim to improve livelihoods are relevant in alleviating poverty and in turn improve wealth quartile.

To the best of our knowledge, our research study is the first to attempt investigating association between the newly introduced malaria vaccine and under-nutrition in children in a malaria endemic zone. The study findings report no significant association. We propose further research studies using robust study designs because our analysis apart from being a case-control, had a small sample size of 370. In addition, we combined stunting and underweight, which comprised under-nutrition outcome variable. Although the two variables, stunting and underweight, are closely related, it is possible that they relate differently with the exposure variables (malaria and measles vaccines). Finally, the proportion of children who received at least one dose of malaria and measles vaccines was low i.e., less than 50% which would be desirable for a comparison. While we are reporting important findings, which should inform public health practitioners to magnify efforts for increasing vaccine coverage in the study area, it denied this analysis power to detect presence or lack of association between the studied vaccines and under-nutrition in children.

CONCLUSION

In this research study, we investigated whether there is any association between malaria vaccine, measles vaccine and under-nutrition in children aged 10 to 59 months. Our findings indicate no statistically significant association between the two vaccines and under-nutrition. However, measles vaccine indicates a potential to reduce under-nutrition in children. Further, we assessed factors associated with under-nutrition. Birth weight, and household's wealth quartile (socio-economic status) showed a statistically significant association. Children with low birth weight and those from poor households had higher chances for under-nutrition compared to their counterparts.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Ethics Committee of EMRI Scientific and Ethics Research Unit (SERU) and the University of Hildenberg, Germany

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