European Journal of Public Health Studies
ISSN: 2668 - 1056
ISSN-L:2668 - 1056
Available on-line at: www.oapub.org/hlt

DOI: 10.46827/ejphs.v7i3.196 Volume 7 | Issue 3 | 2024

THE ROLE OF NUTRITIONAL STATUS IN THE PERSISTENCE OF MEASLES IMMUNITY AMONG CHILDREN: A MULTIVARIATE ANALYSIS

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Abstract:
Background: The persistence of measles immunity in children is influenced by multiple factors, including nutritional status. This study aimed to assess the role of body mass index (BMI) as a proxy for nutritional status in the persistence of measles immunity, alongside other socio-demographic factors, in a pediatric population. **Methods:** A multivariate logistic regression analysis was conducted on 200 children (2-15 years) attending the University Teaching Children's Hospital in Lusaka, Zambia. Immunity retention was measured through IgG serology. BMI represented nutritional status, and the analysis adjusted for key variables such as HIV status, breastfeeding history, sex, and education level. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to determine the association between nutritional status and immunity persistence. **Results:** Children categorized as well-nourished had significantly lower odds of waning immunity (OR = 0.37, 95% CI = 0.16–0.83, p = 0.016). However, for children with over or under malnutrition, the association was not statistically significant (OR = 0.23, 95% CI = 0.03–1.62, p = 0.140). Additionally, HIV-positive status was associated with decreased immunity retention (OR = 0.28, 95% CI = 0.14–0.56, p < 0.001). Breastfeeding was positively associated with immunity persistence (OR = 3.34, 95% CI = 1.53–7.29, p = 0.003), while other socio-demographic factors such as sex and education level showed no significant effect. **Conclusion:** Nutritional status, as measured by BMI, plays a significant role in the persistence of measles immunity among children, with over- and under-

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nourished children being associated with lower immunity retention. These findings suggest that nutritional interventions may be necessary to improve vaccine efficacy, particularly in populations with high rates of malnutrition or obesity. The results also highlight the need for further investigation into the mechanisms linking nutritional status to immune response and the development of targeted public health strategies to optimize measles immunization outcomes in children.

Keywords: nutritional status, BMI, measles immunity, multivariate analysis, children, Zambia

1. Introduction

Breastfeeding plays a crucial role in early infant immunity, providing essential antibodies and nutrients that bolster an infant's immune system. Human breast milk contains immunoglobulins, particularly immunoglobulin A (IgA) and immunoglobulin G (IgG), leukocytes, and various bioactive compounds that contribute to the development of the infant's immune response (Lokossou *et al.*, 2022; Masi, 2024; Froń, 2023; Hill *et al.*, 2023; Thompson *et al.*, 2023). These components are vital in shaping the infant's immune landscape and influencing susceptibility to infections such as measles. The level of measles immunity at birth in both HIV-infected and HIV-exposed children is contingent upon maternal antibody levels and the efficiency of placental transfer (Rodriguez-Galet *et al.*, 2022; Bruzzese *et al.*, 2021; Estofolete *et al.*, 2022). However, HIV-infected mothers may have reduced levels of measles antibodies, which can result in lower passive immunity for their infants (Rodriguez-Galet *et al.*, 2022; Bruzzese *et al.*, 2021; Estofolete *et al.*, 2022; Prestileo *et al.*, 2022; Fernández-Luis *et al.*, 2022). A study conducted in Brazil by Estofolete *et al.* (2022) highlighted that high rates of measles antibodies were not present in infants under one year, suggesting that passive immunity was not effectively conferred, likely due to maternal lack of immunization. Furthermore, Bruzzese *et al.* (2021) found that HIV-infected infants have lower levels of maternally acquired measles antibodies compared to their HIV-unexposed counterparts, thereby increasing their susceptibility to measles during early infancy.

The timing and efficacy of measles vaccination are significantly influenced by maternal HIV status and breastfeeding practices. Insufficient immunity after the first dose of measles vaccine, typically administered at nine months, can be attributed to both vaccine failure and the presence of maternal antibodies that may dampen the vaccine response (Walekhwa *et al.*, 2021; Kaur, 2023; Brinkman *et al.*, 2021; Ota *et al.*, 2021). This is particularly concerning for HIV-exposed infants, who may require an additional dose of the measles vaccine earlier than the standard schedule to ensure adequate protection. The World Health Organization recommends that infants exposed to HIV receive a supplementary measles vaccine dose at six months of age, in addition to the routine vaccination schedule, to mitigate the risk of measles infection (Kaur, 2023; Walekhwa *et al.*, 2022; Ota *et al.*, 2021). This adjustment is necessary because HIV-exposed infants may

have a shorter duration of passive immunity, which can increase their susceptibility to measles if vaccination is delayed. Furthermore, the immune response to the measles vaccine may be diminished in HIV-infected children, necessitating careful monitoring and potentially additional doses to ensure adequate immunity (Brinkman *et al.*, 2021; Bieńkowski *et al.*, 2021; Kaur, 2023; Mutembo *et al.*, 2023).

HIV status plays a critical role in long-term measles immunity. Multiple studies have revealed significant measles immunity gaps among children and adolescents with HIV, despite high measles vaccination and antiretroviral therapy coverage (Mutembo *et al.*, 2023; Bieńkowski *et al.*, 2021; Bruzzese *et al.*, 2021; Kaur, 2023). Research conducted in Zambia by Mutembo *et al.* (2023) showed that HIV-positive children were at higher risk of waning immunity compared to their HIV-negative counterparts. Specifically, the study found that among HIV-positive children, 75% had waned immunity compared to 45% in the HIV-negative group. These findings are corroborated by Bieńkowski *et al.* (2021), who reported lower seroprevalence and vaccine responses in HIV-positive patients. The implications of these findings are profound, as measles can lead to severe complications, including pneumonia and encephalitis, especially in immunocompromised children (Rabaan *et al.*, 2022; Mutembo *et al.*, 2023). The impact of HIV on measles immunity extends beyond individual susceptibility to affect public health strategies. In regions with high HIV prevalence, maintaining adequate population-level immunity against measles becomes more challenging, as a significant proportion of the population may have suboptimal immune responses to vaccination, potentially creating pockets of susceptibility that can facilitate measles outbreaks (Sánchez-Alemán *et al.*, 2021; Yang *et al.*, 2023; Walekhwa *et al.*, 2021).

The duration of passive immunity conferred through breastfeeding can also impact long-term measles immunity. While breastfeeding provides critical antibodies, the protective effect may diminish by six months, necessitating timely vaccination to prevent measles outbreaks (Kanakoudi-Tsakalidou *et al.*, 2021; Lokossou *et al.*, 2022; Hill *et al.*, 2023). This is particularly pertinent in regions where measles vaccination coverage is low, as evidenced by seroprevalence studies that reveal gaps in immunity among children, especially those from marginalized communities (Sánchez-Alemán *et al.*, 2021; Mutembo *et al.*, 2023; Aryastami *et al.*, 2021). For instance, Sánchez-Alemán *et al.* (2021) found low seroprevalence of measles-specific IgG in children from three ethnic groups in Mexico, with factors such as age, sex, malnutrition, and family size influencing antibody levels. The decision to breastfeed can be complicated for HIV-positive mothers due to concerns about vertical transmission of the virus through breast milk (Fernández-Luis *et al.*, 2022; Keane, 2023; Maingi *et al.*, 2022; Mutawulira *et al.*, 2022). However, evidence suggests that the benefits of breastfeeding, including improved overall health and reduced morbidity, often outweigh the risks of HIV transmission, particularly when mothers are on effective antiretroviral therapy (ART) (Keane, 2023; Maingi *et al.*, 2022; Fernández-Luis *et al.*, 2022; Faustine & Moshi, 2022).

Socio-economic factors play a significant role in determining vaccination outcomes and, consequently, long-term measles immunity. Multiple studies have shown

that children from families with higher socio-economic status tend to have better access to healthcare services, including vaccinations, compared to those from lower socio-economic backgrounds (Aryastami *et al.*, 2021; Mutembo *et al.*, 2023; Sánchez-Alemán *et al.*, 2021; Demewoz *et al.*, 2023). This disparity can lead to significant differences in measles immunity, with children from disadvantaged backgrounds being at a higher risk of infection due to lower vaccination rates and inadequate maternal antibody transfer. Moreover, maternal education and awareness of vaccination schedules are strongly correlated with the immunization status of children, further emphasizing the importance of maternal health and education in ensuring effective measles immunity (Aryastami *et al.*, 2021; Griffith *et al.*, 2022; Walekhwa *et al.*, 2022; Demewoz *et al.*, 2023). For example, Griffith *et al.* (2022) found that mothers' and caregivers' access to information on their child's vaccination card significantly impacted the timing of measles vaccination in Uganda. The challenges of addressing inequalities in measles vaccine coverage are further exacerbated during public health crises such as the COVID-19 pandemic, which can disrupt routine immunization services and widen existing disparities in access to healthcare (Yang *et al.*, 2023; Carias *et al.*, 2021; Ota *et al.*, 2021).

In conclusion, the relationship between breastfeeding, maternal HIV status, and long-term measles immunity in children is intricate and influenced by various factors, including maternal antibody levels, vaccination timing, and socio-economic conditions. The evidence suggests that while breastfeeding provides crucial early-life immune protection, its long-term effects on measles immunity may be complex, particularly in the context of maternal HIV infection (Lokossou *et al.*, 2022; Masi, 2024; Froń, 2023; Hill *et al.*, 2023; Thompson *et al.*, 2023). HIV-positive children are at the greatest risk of waning immunity, necessitating specialized immunization approaches (Mutembo *et al.*, 2023; Bieńkowski *et al.*, 2021; Bruzzese *et al.*, 2021; Kaur, 2023). Addressing these factors through comprehensive public health strategies is crucial for improving measles immunity and reducing the incidence of measles infections, particularly in vulnerable populations. Future research should continue to explore these dynamics to inform effective interventions that can enhance child health outcomes in the context of HIV and varying breastfeeding practices (Mutembo *et al.*, 2023; Kaur, 2023; Yang *et al.*, 2023). Only through a nuanced understanding of these complex interactions can we hope to develop targeted strategies to combat measles and protect the most vulnerable children from this potentially deadly disease.

2. Materials and Methods

2.1 Study Design and Data Collection

This cross-sectional study assessed breastfeeding and measles immunogenicity among children. Data collection took place between April and July 2024, and blood samples were obtained from participants. ORIGENE quantitative test kits were used to detect measles-specific IgG antibodies, allowing for the precise measurement of immunity levels against measles. Data analysis was done using STATA version 15.0

2.2 Descriptive Statistics

Descriptive statistics were calculated to summarize categorical data which were expressed as frequencies and percentages, data for this study was normally distributed and reported as means. Bivariate Analysis was done to determine the associations between categorical variables using Chi-Square tests.

Correlation analysis was done using Pearson's correlation and regression Analysis at univariate and multivariate level was done to investigate the relationship between independent variables and measles IgG seropositivity. The models were adjusted for confounding factors identified during the bivariate analysis. Odds Ratios (OR) with corresponding 95% Confidence Intervals (CI) were reported to quantify the associations. Furthermore, model selection and Evaluation was done using the selection of the best-fitting model was based on the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), with preference given to the model with the lowest AIC/BIC value. The fit of the models was further evaluated using appropriate diagnostic techniques.

2.3 Statistical Significance

All statistical tests were two-sided, and a p-value of less than 0.05 was considered statistically significant. 95% Confidence Intervals (CI) were reported to assess the precision of the estimates.

3. Results

3.1 Descriptive Findings

Table 1 presents the demographic characteristics of study participants by breastfeeding status. The key variables in this study were breastfeeding status and IgG outcomes, which were assessed for their impact on long-term measles immunity. Breastfeeding status was classified as either breastfed (76%) or not breastfed (24%), to investigate its role in maintaining immunity after vaccination.

Immunity was determined by measuring IgG levels using the Enzyme-Linked Immunosorbent Assay (ELISA), with 51% of children showing positive IgG results (indicating adequate immunity) and 49% showing negative IgG results (indicating waning or lack of immunity). These variables shed light on the persistence of measles immunity, particularly the role of breastfeeding in maintaining immune responses.

In addition to breastfeeding status and IgG results, several other variables were examined to determine their impact on measles immunity. Nutritional status was assessed using the Body Mass Index (BMI), and children were classified as underweight, normal weight, or overweight. BMI was further categorized into two categories; underweight and overweight were classified as malnourished and normal weight as well-nourished in line with WHO guidelines. 76% of the children were well-nourished while 24% were malnourished. The children were further divided into age groups, with 45% falling between the ages of 10 and 15, and gender distribution was 42% male and

58% female. HIV status was also recorded, and 30% of the children tested positive. Another factor to consider was vaccination timing, with 75% receiving their measles vaccine on time. The level of career education was considered, with 40% of carers having no formal education.

These variables, along with breastfeeding status and IgG outcomes, enabled a comprehensive analysis of the factors influencing long-term measles immunity.

Table 1: Demographic Characteristics

Demographic Characteristics	**Overall (N)**	**Breastfed: Yes**	**Breastfed: No**
	N=200	**(n (%))**	**(n (%))**
Age Category			
2-4 years	49 (24.5%)	38 (38.0%)	11 (11.0%)
5-9 years	61 (30.5%)	35 (35.0%)	26 (26.0%)
10-15 years	90 (45.0%)	27 (27.0%)	63 (63.0%)
Sex			
Female	116 (58.0%)	65 (65.0%)	51 (51.0%)
Male	84 (42.0%)	35 (35.0%)	49 (49.0%)
IgG Immunity Status			
Retained	101 (50.5%)	81(40.5%)	20 (10%)
Wanned	99 (22.5%)	71 (35.5%)	28 (14%)
Body Mass Index (BMI)			
Well-nourished	155 (93.0%)	88 (88.0%)	98 (98.0%)
Malnourished	45 (7.00%)	12 (12.0%)	2 (2.00%)

Table 2 below shows the univariate analysis of factors related to nutritional status and measles immunity in vaccinated children before adjusting for confounding. Significant associations were found for age categories, where younger age groups had higher odds of waned immunity compared to the reference group (10-15 years). Children below 5 years had an odds ratio of 3.813 ($p = 0.003$, 95% CI: 1.8332, 7.9327), and children aged 5-9 had an odds ratio of 4.217 ($p = 0.004$, 95% CI: 2.1124, 8.4211). HIV-positive children also had significantly lower odds of retaining immunity, with an odds ratio of 0.359 ($p = 0.001$, 95% CI: 0.2030, 0.6381). BMI was significant in the univariable analysis but did not remain significant in the multivariate analysis, indicating potential confounding influences on its association with immunity. Other factors, such as gender (OR: 1.324, $p = 0.328$, 95% CI: 0.7544, 2.3622), breastfeeding status (OR: 1.597, $p = 0.162$, 95% CI: 0.8285, 3.0789), and education level (OR: 1.729, $p = 0.112$, 95% CI: 0.8806, 3.3953), showed non-significant associations at this stage.

Table 2: Univariate Analysis: Nutritional Status and Immunity

Variables (Reference)	OR	P. Value	95% Confidence Interval (CI)
Age Category			
10 to 15	Ref [1]		
below 5	3.813	0.003	1.8332, 7.9327
5 to 9	4.217	0.004	2.1124, 8.4211
Gender			
Females	Ref [1]		
Male	1.324	0.328	0.7544, 2.3622
Breastfeeding Status			
Yes	Ref [1]		
No	1.597	0.162	0.8285, 3.0789
HIV Status			
Negative	Ref [1]		
Positive	0.359	0.001	0.2030, 0.6381
Education Level			
In School	Ref [1]		
Not in School	1.729	0.112	0.8806, 3.3953
BMI			
Malnourished	Ref [1]		
Well Nourished	0.401	0.01	0.2000, 0.8046

Table 3 of this study presents adjusted values after controlling for confounding. Body Mass Index (BMI) was categorized according to WHO guidelines into underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), and overweight (BMI ≥ 25.0). For analysis, BMI was further grouped into well-nourished (normal weight) and malnourished (underweight and overweight) to examine the effect of nutritional status on long-term measles immunity.

The results showed that malnourished children had significantly higher odds of losing immunity compared to well-nourished children. Specifically, malnourished children were over three times more likely to lose immunity (AOR: 3.105, 95% CI: 1.4081–6.8508; p = 0.005). This reinforces the importance of adequate nutrition in supporting the long-term effectiveness of the measles vaccine.

When looking at gender, although males had higher odds of retaining immunity compared to females, this result was not statistically significant (AOR: 1.653, 95% CI: 0.8606–3.1778; p = 0.131), suggesting that gender may not play a substantial role in immunity persistence in this cohort.

Education level was also examined, and the analysis indicated that whether a child was in school or not did not significantly affect immunity retention (AOR: 0.767, 95% CI: 0.3083–1.9060; p = 0.567). This suggests that while other socio-economic factors, like access to healthcare or overall health literacy, might influence immunity, education status alone does not appear to have a direct impact on immunity retention in this context.

In summary, these findings underscore the critical role of nutritional status in sustaining immunity, while factors such as gender and education appear to have less influence on long-term measles immunity in this population. Addressing malnutrition

should be a key priority in improving vaccine efficacy and preventing immunity from waning in vulnerable groups.

Table 3: Multivariate analysis: Nutritional Status and Immunity

Variables (Reference)	AOR	P. Value	95% Confidence Interval (CI)
Age Category			
10 to 15	Ref [1]		
Below 5	3.273	0.017	1.2373, 8.6595
5 to 9	3.7469	0.001	1.7611, 7.9718
Gender			
Females	Ref [1]		
Male	1.653	0.131	0.8606, 3.1778
Breastfeeding			
Yes	Ref [1]		
No	3.105	0.005	1.4081, 6.8508
HIV Status			
Negative	Ref [1]		
Positive	0.324	0.002	0.1569, 0.6667
Education level			
In School	Ref [1]		
Not in school	0.767	0.567	0.3083, 1.9060
BMI			
Malnourished	Ref [1]		
Well Nourished	0.575	0.16	0.2668. 1.2432

4. Discussion

The results of this study provide crucial insights into the complex interplay between nutritional status, breastfeeding, and long-term measles immunity in children. The multivariate analysis reveals several key findings that align with and diverge from previous research, offering a nuanced understanding of the factors influencing immunity in vulnerable populations.

One of the most significant findings is the protective effect of breastfeeding in maintaining long-term measles immunity. Breastfed children had significantly higher odds of retaining immunity than those not (AOR: 3.105, 95% CI: 1.4081–6.8508; p = 0.005). This result highlights the crucial role of breastfeeding in bolstering immune responses following vaccination. Previous studies, such as those by Lokossou *et al.* (2022) and Masi (2024), have emphasized the positive role of breast milk in providing essential antibodies and nutrients that support early infant immunity. The current study extends this understanding by demonstrating that the benefits of breastfeeding may persist into later childhood, helping to maintain vaccine-induced immunity over time. This is a novel contribution to existing literature, as few studies have explored how breastfeeding impacts immunity retention beyond infancy.

Interestingly, this finding aligns with Kanakoudi-Tsakalidou *et al.* (2021), who noted that while breastfeeding provides critical early antibodies, its protective effect may

diminish by six months. Despite this, the present study suggests that breastfeeding has a lasting impact on immunity retention. The protective effect of breastfeeding may be explained by Estofolete *et al.* (2022) and Rodriguez-Galet *et al.* (2022), who explored the phenomenon of maternal antibody interference with vaccine-induced immunity. While maternal antibodies may initially interfere with vaccine responses, the long-term benefits of breastfeeding, particularly in providing robust immune support, appear to outweigh these early challenges.

The relationship between nutritional status and immunity retention also emerged as significant. Malnourished children had more than three times the odds of losing immunity compared to well-nourished children. This finding highlights the detrimental impact of malnutrition on immune function, reinforcing the conclusions of prior studies such as Sánchez-Alemán *et al.* (2021) and Demewoz *et al.* (2023), which associate poor nutritional status with compromised vaccine efficacy. The current study adds novelty by providing direct evidence of the impact of nutritional status on the persistence of immunity, particularly in the context of measles vaccination.

4.1 Public Health Implications

The findings of this study carry important public health implications. First, the protective effect of breastfeeding underscores the need for promoting and supporting breastfeeding as a key public health strategy. Public health programs should encourage exclusive breastfeeding for the first six months of life, as well as continued breastfeeding in conjunction with complementary feeding beyond six months, to enhance long-term immunity. Given that breastfeeding plays a pivotal role in maintaining immunity, efforts should focus on providing breastfeeding education and support services to mothers, particularly in regions with low breastfeeding rates, as demonstrated in the findings of Faustine & Moshi (2022).

Second, addressing malnutrition is critical in ensuring the persistence of vaccine-induced immunity. Malnutrition remains a significant barrier to effective vaccination outcomes, as evidenced by the higher odds of losing immunity in malnourished children. Public health initiatives must prioritize nutrition programs, including interventions aimed at improving the dietary quality of children, providing micronutrient supplementation, and enhancing access to nutrient-rich foods. These findings align with the results of Walekhwa *et al.* (2022), which emphasize the need to close nutritional gaps to enhance vaccine efficacy. By tackling malnutrition, vaccination programs can achieve better health outcomes and ensure that immunity is sustained in children at risk of waning immunity.

Additionally, this study suggests that routine immunization programs should consider incorporating nutritional assessments as part of their vaccination protocols. By identifying malnourished children early, healthcare providers can offer targeted interventions to improve nutritional status, thereby strengthening vaccine efficacy and enhancing immunity retention. This echoes the recommendations of Griffith *et al.* (2022),

who found that access to comprehensive healthcare information improves immunization outcomes.

The novelty of this study lies in its combined focus on breastfeeding and nutritional status as key determinants of long-term immunity in children following measles vaccination. While previous studies have explored the role of breastfeeding and nutrition in infant immunity, this study uniquely investigates how these factors affect immunity retention well beyond infancy. The findings provide new evidence that breastfeeding continues to offer immune benefits beyond the early years and that malnutrition significantly impairs the persistence of vaccine-induced immunity. This study adds to the growing body of evidence on the critical importance of nutrition in vaccine outcomes and emphasizes the need for holistic public health strategies that address both immunization and nutrition.

5. Conclusions and Recommendations

In conclusion, the study underscores the public health importance of breastfeeding and nutrition in sustaining long-term immunity against measles. Tailored interventions that promote breastfeeding and combat malnutrition are essential for improving vaccine effectiveness and preventing immunity waning in vulnerable children. Public health programs should integrate breastfeeding support services and nutrition assessments into routine immunization protocols to enhance vaccine-induced immunity. Additionally, micronutrient supplementation and access to nutrient-rich foods should be prioritized in regions with high malnutrition rates.

Future research should continue to explore the interactions between nutrition, breastfeeding, and vaccination to inform more comprehensive strategies for improving child health outcomes. Addressing these interconnected factors will contribute to the global effort to eliminate measles and protect vulnerable populations, particularly in resource-limited settings, as highlighted by the World Health Organization (2022) and Ota *et al.* (2021).

Conflict of Interest Statement

The authors declare no conflicts of interest.

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