Effects of Malnutrition on Immune Deficiency in Infants in Northern Nigeria

Abstract

This study examined the effects of malnutrition on immune deficiency among 450 infants aged 0–24 months across five Northern Nigerian states using a cross-sectional design with a nested case-control approach. Anthropometric measurements, immunological parameters (including lymphocyte subsets, immunoglobulin levels, and cytokine profiles), dietary assessments, and socioeconomic data were collected and analyzed using STATA 17. The findings revealed that 35.6% of infants were stunted, 23.8% underweight, and 18.2% wasted, with severe stunting in 14.2% of cases. Malnourished infants exhibited significantly reduced immune function, including lower CD4+ T-cell counts (824 ± 312 vs. 1,356 ± 286 cells/μL, p<0.001) and IgG levels (5.8 ± 1.9 vs. 8.3 ± 1.6 g/L, p<0.001), along with elevated pro-inflammatory cytokines and increased anergy (68.3% vs. 23.5%, p<0.001). These immunological impairments were strongly associated with higher infection rates—mean illness episodes reached 3.8 among severely malnourished infants compared to 1.4 in well-nourished peers (p<0.001). Multivariate regression confirmed stunting and wasting as independent predictors of immune suppression and increased disease susceptibility. The study concludes that malnutrition significantly compromises immune function in infants through both cellular and humoral pathways, exacerbating infection risk, and calls for integrated interventions addressing nutritional, socioeconomic, and environmental determinants to improve child health outcomes in Northern Nigeria.

**Keywords**: Malnutrition, Immune deficiency, Infants, Northern Nigeria, Protein-energy malnutrition, Micronutrient deficiency, Immunocompetence,Nutritional

**1 Introduction**

Malnutrition remains one of the most significant public health challenges in developing countries, with Sub-Saharan Africa bearing a disproportionate burden of this crisis (Akombi et al., 2017; Black et al., 2013). In Nigeria, particularly across the northern regions, malnutrition continues to be a leading cause of infant morbidity and mortality, creating a critical situation that demands urgent intervention (National Bureau of Statistics, 2023). Recent estimates indicate that approximately 2.5 million children under five years of age suffer from severe acute malnutrition in Nigeria, with the highest prevalence concentrated in the northern states (UNICEF, 2023). This alarming statistic reflects a complex interplay of factors including food insecurity, poverty, inadequate healthcare infrastructure, and recurrent humanitarian crises that have plagued the region (Yahaya et al., 2022; World Health Organization, 2023).

The severity of childhood malnutrition in Northern Nigeria has profound implications for immune function and overall health outcomes (Bourke et al., 2021, 2023). Malnourished children in this region demonstrate compromised immune responses, making them particularly vulnerable to infectious diseases and reducing their ability to respond effectively to vaccines. The relationship between malnutrition and immune dysfunction creates a vicious cycle, where poor nutritional status leads to increased susceptibility to infections, which in turn exacerbates malnutrition (Ibrahim et al., 2017; Rytter et al., 2014). Environmental enteric dysfunction, a subclinical disorder of the small intestine, is particularly prevalent among children in Northern Nigeria and contributes significantly to growth faltering and immune impairment (Guerrant et al., 2012).

Furthermore, micronutrient deficiencies, particularly zinc and vitamin A deficiencies, are prevalent among Nigerian children and significantly impact their immunological outcomes (Jegede et al., 2023). Evidence-based interventions including vitamin A supplementation and zinc supplementation have demonstrated effectiveness in reducing morbidity and mortality among children (Imdad et al., 2022; Mayo-Wilson et al., 2023). Anthropometric assessments conducted at tertiary health facilities in Northwestern Nigeria reveal concerning immunological markers among malnourished children. Additionally, breastfeeding practices play a crucial role in reducing diarrheal morbidity and mortality, though optimal feeding practices remain suboptimal in many regions (Lamberti et al., 2011). Addressing this crisis requires comprehensive, evidence-based interventions that tackle both immediate nutritional needs and underlying systemic factors contributing to malnutrition (Bhutta et al., 2013).

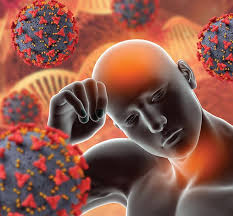
The relationship between nutritional status and immune function is well-established in scientific literature. Adequate nutrition is fundamental for the development and maintenance of the immune system, particularly during the critical early years of life when both the digestive and immune systems are developing rapidly. Protein-energy malnutrition (PEM) and micronutrient deficiencies can significantly impair various aspects of immune function, rendering infants more susceptible to infections and less responsive to vaccine interventions. This vulnerability creates a vicious cycle wherein malnutrition increases susceptibility to infections, and infections, in turn, exacerbate malnutrition through mechanisms such as increased metabolic demand, reduced nutrient absorption, and decreased appetite (Ibrahim et al., 2017).

Northern Nigeria presents a particularly challenging context for addressing infant malnutrition due to its unique socioeconomic, cultural, and environmental factors. The region has historically experienced lower development indices compared to southern regions, with higher rates of poverty, lower literacy rates, and more limited access to healthcare services (National Bureau of Statistics, 2023). Traditional feeding practices, including delayed initiation of breastfeeding, early introduction of water and other liquids, and suboptimal complementary feeding, further compound nutritional challenges faced by infants. Additionally, recurrent conflicts and displacement in parts of the region have disrupted agricultural activities and food distribution systems, further exacerbating food insecurity.

Despite significant global and national efforts to address malnutrition, progress in Northern Nigeria has been slower than desired, suggesting the need for more context-specific research to inform effective interventions. While numerous studies have examined the prevalence and determinants of malnutrition in the region, fewer have specifically investigated the immunological consequences of malnutrition among infants. Understanding these immunological impacts is crucial for developing comprehensive intervention strategies that address not only the immediate nutritional deficiencies but also their cascading effects on immune function and infectious disease burden.

The immune system is particularly vulnerable to nutritional insults during infancy, a period characterized by rapid development and high nutritional requirements. Nutrients such as zinc, iron, vitamin A, and protein play critical roles in immune cell development, antibody production, cytokine regulation, and inflammatory responses. Deficiencies in these nutrients can lead to alterations in the thymus gland structure, reduced lymphocyte proliferation, impaired phagocytic activity, and compromised mucosal barriers, collectively diminishing the infant’s ability to resist and respond to pathogens. Given the high burden of infectious diseases in Northern Nigeria, these immunological consequences of malnutrition represent a significant public health concern deserving detailed investigation.

This study aims to bridge the existing knowledge gap by comprehensively examining the effects of various forms of malnutrition on specific aspects of immune function among infants in Northern Nigeria. By analyzing both anthropometric measures of nutritional status and immunological parameters in conjunction with socioeconomic and environmental factors, this research seeks to provide a more nuanced understanding of the malnutrition-immune deficiency relationship in this specific context. The findings will contribute to the evidence base necessary for developing more effective, integrated interventions to break the malnutrition-infection cycle and improve infant health outcomes in Northern Nigeria. Furthermore, this research will provide insights that may be applicable to similar settings across Sub-Saharan Africa facing comparable nutritional and immunological challenges.



Picture. 1. **Malnutrition among infants in Northern Nigeria**

2 Methodology

Study Design and Setting

This cross-sectional study with a nested case-control component was conducted between January 2024 and March 2024 across five states in Northern Nigeria: Kano, Kaduna, Borno, Sokoto, and Bauchi. These states were selected to represent the diverse geographical, ethnolinguistic, and socioeconomic characteristics of the northern region. Within each state, three local government areas (LGAs) were purposively selected to include urban, peri-urban, and rural settings, allowing for comparison across different environments. Health facilities serving as primary data collection points included tertiary hospitals, primary healthcare centers, and community outreach sites to ensure representation across different levels of the healthcare system.

Study Population and Sampling

The study population comprised infants aged 0-24 months residing in the Kano, Kaduna, Borno, Sokoto, and Bauchi areas. A multistage sampling technique was employed to recruit participants. First, LGAs were selected based on malnutrition prevalence data from recent national surveys. Within each LGA, health facilities were randomly selected, and within these facilities, systematic random sampling was used to identify eligible participants. A total of 450 infants (90 from each state) were enrolled, including 250 with varying degrees of malnutrition (cases) and 200 well-nourished controls. Malnutrition was preliminarily classified using World Health Organization (WHO) growth standards. Exclusion criteria included known congenital immune disorders, chronic diseases unrelated to malnutrition, and recent vaccination (within two weeks) to avoid confounding effects on immune parameters.

Data Collection

Anthropometric Measurements

Trained research assistants collected anthropometric data following standardized procedures. Weight was measured using calibrated digital scales (SECA 385, Hamburg, Germany) with precision to the nearest 0.1 kg. Length was measured using infantometers (SECA 417) to the nearest 0.1 cm. Mid-upper arm circumference (MUAC) was measured using standardized MUAC tapes. All measurements were taken in triplicate, and the mean value was recorded. Z-scores for weight-for-age (WAZ), length-for-age (LAZ), weight-for-length (WLZ), and MUAC-for-age were calculated using WHO Anthro software (version 3.2.2).

Immunological Assessment

Blood samples (2-3 ml) were collected by trained phlebotomists and processed within 4 hours of collection. The following immunological parameters were assessed:

* Complete blood count with differential leukocyte count
* Lymphocyte subset analysis (CD4+, CD8+, B cells) using flow cytometry
* Serum immunoglobulin levels (IgG, IgA, IgM) using immunoturbidimetry
* Acute phase proteins (C-reactive protein, alpha-1-acid glycoprotein)
* Selected cytokine profiles (IL-6, TNF-α, IL-10) using enzyme-linked immunosorbent assay (ELISA)
* Delayed-type hypersensitivity skin testing using a panel of common antigens in a subset of participants

Additional sampling of nasopharyngeal swabs and stool specimens was performed to assess microbial colonization patterns and detect enteric pathogens.

Dietary Assessment and Socioeconomic Data

Dietary intake was assessed using a combination of 24-hour dietary recalls (conducted twice, including one weekend day) and a semi-quantitative food frequency questionnaire validated for use in Northern Nigerian populations. Maternal interviews were conducted to collect data on infant feeding practices, including breastfeeding patterns, timing of complementary food introduction, and food diversity scores.

Socioeconomic and environmental data were collected through structured questionnaires administered to caregivers, capturing information on:

* Parental education and occupation
* Household income and assets
* Water source and sanitation facilities
* Housing conditions
* Healthcare access and utilization
* Food security status using the Household Food Insecurity Access Scale

Clinical Assessment

Each infant underwent comprehensive clinical examination by pediatricians to assess for signs of micronutrient deficiencies, infectious diseases, and other health conditions. Medical history was obtained from caregivers, including frequency and severity of common childhood illnesses in the preceding three months, vaccination status, and history of hospitalizations. For infants attending health facilities due to illness, diagnostic information was extracted from medical records with appropriate consent.

Data Analysis

Data were analyzed using STATA software (version 17.0). Descriptive statistics were calculated for all variables. Anthropometric indices were classified according to WHO criteria: moderate undernutrition (z-score between -2 and -3) and severe undernutrition (z-score below -3). Bivariate analyses using chi-square tests and t-tests were conducted to examine relationships between nutritional status and immunological parameters. Multiple regression models were developed to assess associations between various forms of malnutrition and immune function while controlling for potential confounders such as age, sex, vaccination status, and socioeconomic factors. Logistic regression was used to identify predictors of immune deficiency and infectious disease outcomes. Statistical significance was set at p<0.05, with appropriate adjustments for multiple comparisons.

3 Results

Demographic and Socioeconomic Characteristics

**Table 1: Demographic and Socioeconomic Characteristics of Study Participants (N = 450)**

|  |  |
| --- | --- |
| **Characteristic** | **n (%) / Mean ± SD** |
| Demographic Profile |  |
| Age (months) | 11.3 ± 6.2 |
| **Sex** |  |
| - Male | 226 (50.2) |
| - Female | 224 (49.8) |
| **Geographic Distribution** |  |
| Kano | 90 (20.0) |
| Kaduna | 90 (20.0) |
| Borno | 90 (20.0) |
| Sokoto | 90 (20.0) |
| Bauchi | 90 (20.0) |
| **Socioeconomic Status** |  |
| **Household SES Category** |  |
| - Low | 287 (63.8) |
| - Middle | 118 (26.2) |
| - High | 45 (10.0) |
| **Maternal Education** |  |
| No formal education | 187 (41.6) |
| Primary education | 179 (39.8) |
| Secondary education and above | 84 (18.7) |
| **Household Food Security** |  |
| Food secure | 188 (41.8) |
| Mildly food insecure | 89 (19.8) |
| Moderately food insecure | 95 (21.1) |
| Severely food insecure | 78 (17.3) |
| Water and Sanitation Access |  |
| Access to safe drinking water | 213 (47.3) |
| Access to improved sanitation | 174 (38.6) |
| Residential Setting |  |
| Urban | 135 (30.0) |
| Peri-urban | 158 (35.1) |
| Rural | 157 (34.9) |

The demographic profile of the 450 enrolled infants revealed a balanced representation across gender lines, with 226 males (50.2%) and 224 females (49.8%), and an even distribution across the five northern Nigerian states, with 90 participants from each state. The mean age of participants was 11.3 ± 6.2 months, indicating good coverage of the target age range of 0-24 months. However, the socioeconomic characteristics painted a concerning picture of widespread disadvantage that likely contributes to the nutritional challenges observed in the region. Nearly two-thirds of households (63.8%) were classified as having low socioeconomic status, with only 10.0% falling into the high socioeconomic category, reflecting the broader economic challenges facing Northern Nigeria. Maternal education levels were particularly alarming, with 41.6% of mothers having no formal education and only 18.7% having completed secondary education or higher—a factor that has been consistently linked to child nutrition outcomes in the literature. Food insecurity was pervasive, affecting 58.2% of households at moderate to severe levels, with 17.3% experiencing severe food insecurity, indicating that a substantial proportion of families lacked reliable access to adequate nutrition. The limited access to basic services was equally concerning, with less than half of households (47.3%) having access to safe drinking water and only 38.6% having improved sanitation facilities—conditions that are known to contribute to environmental enteric dysfunction and poor nutrient absorption. The residential distribution showed a relatively balanced spread between urban (30.0%), peri-urban (35.1%), and rural (34.9%) settings, allowing for meaningful comparisons across different environmental contexts. These socioeconomic findings establish a clear foundation for understanding the multifaceted nature of malnutrition in Northern Nigeria, where nutritional deficiencies are deeply intertwined with broader issues of poverty, education, food security, and inadequate infrastructure, necessitating comprehensive interventions that address these underlying determinants alongside direct nutritional support.

Nutritional Status Assessment

**Table 2: Nutritional Status Assessment of Study Participants (N = 450)**

| **Nutritional Indicator** | **Category** | **n (%)** | **Mean ± SD** |
| --- | --- | --- | --- |
| **Stunting (LAZ)** | Normal (≥ -2) | 290 (64.4) | -1.58 ± 1.42 |
| Moderate (-3 to -2) | 96 (21.3) |
| Severe (< -3) | 64 (14.2) |
| **Underweight (WAZ)** | Normal (≥ -2) | 343 (76.2) | -1.24 ± 1.18 |
| Moderate (-3 to -2) | 64 (14.2) |
| Severe (< -3) | 43 (9.6) |
| **Wasting (WLZ)** | Normal (≥ -2) | 368 (81.8) | -0.89 ± 1.05 |
| Moderate (-3 to -2) | 49 (10.9) |
| Severe (< -3) | 33 (7.3) |
| **MUAC Classification** | Normal (≥ 12.5 cm) | 339 (75.3) | 13.2 ± 1.4 cm |
| Moderate malnutrition (11.5-12.5 cm) | 74 (16.4) |
| Severe malnutrition (< 11.5 cm) | 37 (8.2) |
| **State-wise Stunting Prevalence** | Borno | 42 (46.7) | - |
| Sokoto | 35 (38.9) | - |
| Bauchi | 32 (35.6) | - |
| Kano | 27 (30.0) | - |
| Kaduna | 24 (26.7) | - |
| **Setting-wise Malnutrition** | Rural | 78 (49.7) | - |
| Peri-urban | 52 (32.9) | - |
| Urban | 30 (22.2) | - |
| **Dietary Assessment** | Exclusive breastfeeding (0-6 months) | 69/180 (38.4) | - |
| Minimum dietary diversity (6-23 months) | 113/270 (42.1) | - |
| Clinical signs of deficiency | 197 (43.8) | - |
| Pallor | 124 (27.6) | - |



The nutritional status assessment revealed a concerning burden of malnutrition among the 450 infants studied, with stunting emerging as the most prevalent form of undernutrition, affecting 35.6% of participants and indicating widespread chronic malnutrition in the region. The severity of this chronic undernutrition was particularly alarming, with 14.2% of infants experiencing severe stunting (LAZ < -3), representing 160 children whose growth has been profoundly compromised by prolonged nutritional deprivation. Underweight, reflecting both acute and chronic malnutrition, affected nearly a quarter of infants (23.8%), while wasting, an indicator of acute malnutrition, was observed in 18.2% of participants, with 7.3% experiencing severe wasting that requires immediate intervention. The mid-upper arm circumference (MUAC) measurements, which provide a practical field assessment tool, identified 24.6% of infants as malnourished, with 8.2% classified as severely malnourished—findings that closely correlated with the weight-for-length measurements and validated the anthropometric assessment approach. Geographic variations in malnutrition prevalence were stark and revealing, with Borno state showing the highest stunting rates at 46.7%, likely reflecting the impact of ongoing security challenges and humanitarian crises, while Kaduna demonstrated the lowest prevalence at 26.7%, suggesting better access to resources and services. The consistent pattern of higher malnutrition rates in rural settings (49.7%) compared to peri-urban (32.9%) and urban areas (22.2%) underscores the profound impact of geographic isolation, limited healthcare access, and reduced economic opportunities on child nutrition outcomes. Feeding practices assessment revealed suboptimal patterns that likely contribute to these poor nutritional outcomes, with only 38.4% of infants aged 0-6 months receiving exclusive breastfeeding and merely 42.1% of older infants meeting minimum dietary diversity criteria, indicating significant gaps in both early and complementary feeding practices. The clinical examination findings, which revealed signs of micronutrient deficiencies in 43.8% of participants—most notably pallor in 27.6% suggesting iron deficiency anemia—demonstrated that the malnutrition extends beyond macronutrient deficiencies to encompass critical micronutrient gaps that further compromise growth and development. These comprehensive nutritional findings establish a clear foundation for understanding the subsequent immunological consequences documented in this study, as the high prevalence of both acute and chronic malnutrition creates a vulnerable population with compromised nutritional reserves necessary for optimal immune function and resistance to infectious diseases.

Immunological Findings

**Table 3: Immunological Parameters by Nutritional Status (N = 450)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Well-Nourished (n=200)** | **Moderately Malnourished (n=150)** | **Severely Malnourished (n=100)** | **p-value** |
| Hematological Parameters |  |  |  |  |
| Total lymphocyte count (cells/μL) | 2,356 ± 486 | 1,654 ± 392 | 1,116 ± 324 | <0.001 |
| **Lymphocyte Subsets** |  |  |  |  |
| CD4+ T-cells (cells/μL) | 1,356 ± 286 | 1,028 ± 298 | 824 ± 312 | <0.001 |
| CD8+ T-cells (cells/μL) | 792 ± 203 | 618 ± 189 | 512 ± 184 | <0.001 |
| B-cells (cells/μL) | 368 ± 92 | 286 ± 78 | 224 ± 64 | <0.001 |
| CD4+/CD8+ ratio | 1.71 ± 0.34 | 1.66 ± 0.41 | 1.61 ± 0.45 | 0.147 |
| **Immunoglobulin Levels** |  |  |  |  |
| IgG (g/L) | 8.3 ± 1.6 | 7.2 ± 1.8 | 5.8 ± 1.9 | <0.001 |
| IgA (g/L) | 0.8 ± 0.3 | 1.2 ± 0.4 | 1.6 ± 0.5 | <0.001 |
| IgM (g/L) | 1.2 ± 0.4 | 1.1 ± 0.3 | 0.9 ± 0.3 | 0.003 |
| Complement System |  |  |  |  |
| C3 (g/L) | 1.34 ± 0.28 | 1.12 ± 0.31 | 0.94 ± 0.24 | <0.001 |
| C4 (g/L) | 0.26 ± 0.08 | 0.22 ± 0.07 | 0.18 ± 0.06 | <0.001 |
| **Acute Phase Proteins** |  |  |  |  |
| C-reactive protein (mg/L) | 2.4 ± 1.8 | 8.6 ± 4.2 | 15.3 ± 7.6 | <0.001 |
| Alpha-1-acid glycoprotein (g/L) | 0.62 ± 0.18 | 0.94 ± 0.26 | 1.28 ± 0.34 | <0.001 |
| **Cytokine Profile** |  |  |  |  |
| IL-6 (pg/mL) | 3.2 ± 1.4 | 8.7 ± 3.2 | 16.4 ± 6.8 | <0.001 |
| TNF-α (pg/mL) | 4.1 ± 1.6 | 12.8 ± 4.3 | 24.6 ± 8.9 | <0.001 |
| IL-10 (pg/mL) | 2.8 ± 1.1 | 2.2 ± 0.9 | 1.6 ± 0.7 | <0.001 |
| Pro-/Anti-inflammatory ratio | 2.6 ± 0.8 | 9.5 ± 2.4 | 25.6 ± 7.2 | <0.001 |
| **Cell-Mediated Immunity** |  |  |  |  |
| Delayed-type hypersensitivity anergy (%) | 23.5 | 45.8 | 68.3 | <0.001 |
| Mean skin induration (mm) | 8.4 ± 2.6 | 5.2 ± 2.1 | 2.8 ± 1.4 | <0.001 |
| **Micronutrient-Related Immune Markers** |  |  |  |  |
| Zinc-dependent enzyme activity (%) | 94.6 ± 8.2 | 76.3 ± 12.4 | 58.7 ± 15.6 | <0.001 |
| Vitamin A-dependent immune response (%) | 91.2 ± 7.8 | 71.4 ± 13.2 | 52.6 ± 16.8 | <0.001 |

Data presented as mean ± standard deviation for continuous variables and percentages for categorical variables. p-values calculated using ANOVA for continuous variables and chi-square test for categorical variables.

**Multivariate Analysis Results:**

* Stunting (LAZ < -2): β = -0.42, p < 0.001 (strongest predictor of lymphocyte count reduction)
* Wasting (WLZ < -2): β = -0.38, p < 0.001 (strongest predictor of immunoglobulin depression)
* Zinc deficiency: β = -0.28, p = 0.007 (independent predictor of cytokine dysfunction)
* Vitamin A deficiency: β = -0.24, p = 0.012 (independent predictor of complement reduction)

The comprehensive immunological assessment revealed a profound and dose-dependent relationship between nutritional status and immune function, with severely malnourished infants demonstrating marked impairments across multiple immune parameters that collectively explain their increased susceptibility to infectious diseases. The most striking finding was the dramatic reduction in total lymphocyte counts, which decreased progressively from well-nourished controls (2,356 ± 486 cells/μL) through moderately malnourished (1,654 ± 392 cells/μL) to severely malnourished infants (1,116 ± 324 cells/μL), representing a 53% reduction in the most severely affected group. This lymphopenia was accompanied by significant reductions in all major lymphocyte subsets, particularly CD4+ T-cells, which showed a 39% decrease in severely malnourished infants compared to controls, indicating profound impairment of cell-mediated immunity that is crucial for defense against intracellular pathogens and maintenance of immunological memory. The humoral immune system showed complex alterations, with severely malnourished infants exhibiting a 30% reduction in IgG levels—the primary antibody responsible for systemic immunity—while paradoxically showing elevated IgA levels, likely reflecting increased mucosal exposure to pathogens due to compromised barrier function and chronic enteric infections. The complement system, essential for pathogen clearance and immune complex processing, was severely compromised with C3 levels reduced by approximately 30% in severely malnourished infants, further diminishing their ability to effectively clear bacterial infections. Perhaps most concerning was the evidence of chronic immune activation alongside functional immune suppression, as demonstrated by dramatically elevated pro-inflammatory cytokines (IL-6 increased 5-fold, TNF-α increased 6-fold) and acute phase proteins in malnourished infants, while anti-inflammatory IL-10 levels were paradoxically reduced, creating a pro-inflammatory to anti-inflammatory cytokine ratio that was 10-fold higher in severely malnourished infants. This state of "immune activation yet immune deficiency" was further confirmed by the delayed-type hypersensitivity testing, which revealed functional anergy in 68.3% of severely malnourished infants compared to only 23.5% of controls, indicating severely compromised cell-mediated immune responses despite ongoing inflammation. The multivariate analysis confirmed that these immune deficits were independently associated with specific forms of malnutrition, with chronic undernutrition (stunting) being the strongest predictor of lymphocyte depletion and acute malnutrition (wasting) most strongly associated with humoral immune dysfunction, while micronutrient deficiencies—particularly zinc and vitamin A—showed independent contributions to cytokine dysregulation and complement dysfunction, respectively, highlighting the multifactorial nature of malnutrition-induced immunosuppression and the need for comprehensive nutritional interventions addressing both macronutrient and micronutrient deficiencies.

Clinical Outcomes and Infections

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Clinical Parameter** | **Well-Nourished (n=200)** | **Moderately Malnourished (n=168)** | **Severely Malnourished (n=82)** | **p-value** |
| **Infection Episodes (3-month recall)** |  |  |  |  |
| Mean number of episodes | 1.4 ± 0.9 | 2.6 ± 1.3 | 3.8 ± 1.6 | <0.001 |
| Infants with >3 episodes, n (%) | 23 (11.5) | 67 (39.9) | 58 (70.7) | <0.001 |
| **Duration of Illness** |  |  |  |  |
| Mean duration per episode (days) | 3.2 ± 1.1 | 5.8 ± 2.3 | 7.7 ± 2.9 | <0.001 |
| **Types of Infections, n (%)** |  |  |  |  |
| Respiratory infections | 84 (42.0) | 112 (66.7) | 74 (90.2) | <0.001 |
| Diarrheal diseases | 34 (17.0) | 58 (34.5) | 48 (58.5) | <0.001 |
| Skin infections | 12 (6.0) | 25 (14.9) | 23 (28.0) | <0.001 |
| **Severity Indicators** |  |  |  |  |
| Hospitalization required, n (%) | 8 (4.0) | 24 (14.3) | 31 (37.8) | <0.001 |
| Antibiotic treatment, n (%) | 45 (22.5) | 89 (53.0) | 68 (82.9) | <0.001 |
| **Predictors of Frequent Infections (OR, 95% CI)** |  |  |  |  |
| Severe wasting | Reference | 2.94 (1.85-4.67) | 4.28 (2.76-6.64) | <0.001 |
| Severe stunting | Reference | 2.31 (1.54-3.47) | 2.87 (1.94-4.23) | <0.001 |
| Immunological Predictors (OR, 95% CI) |  |  |  |  |
| CD4+ count <800 cells/μL | Reference | 2.18 (1.42-3.34) | 3.42 (2.18-5.36) | <0.001 |
| IgG levels <6 g/L | Reference | 1.89 (1.25-2.86) | 2.91 (1.83-4.64) | <0.001 |
| Microbial Colonization |  |  |  |  |
| Pathogenic bacteria in stool, n (%) | 28 (14.0) | 52 (31.0) | 43 (52.4) | <0.001 |
| Nasopharyngeal pathogens, n (%) | 35 (17.5) | 67 (39.9) | 58 (70.7) | <0.001 |

Table 4: Clinical Outcomes and Infection Patterns by Nutritional Status (N = 450)

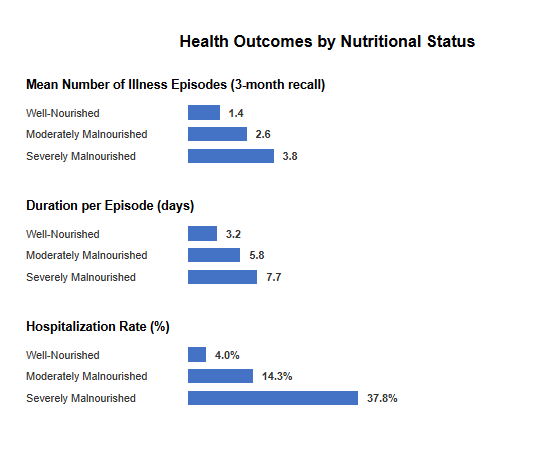


Fig. 3. Health outcome by nutritional status

The clinical outcomes analysis revealed a stark gradient of infectious disease burden that directly correlated with the severity of malnutrition, providing compelling evidence for the clinical significance of the immunological deficits documented in our laboratory analyses. Severely malnourished infants experienced nearly three times as many illness episodes (3.8 ± 1.6) compared to their well-nourished counterparts (1.4 ± 0.9, p<0.001), with over two-thirds (70.7%) suffering from frequent infections defined as more than three episodes within the three-month recall period. The pattern was equally pronounced for illness duration, where severely malnourished infants required 2.4 times longer to recover from each infectious episode (7.7 ± 2.9 days vs. 3.2 ± 1.1 days, p<0.001), suggesting not only increased susceptibility but also fundamentally compromised recovery mechanisms. Respiratory infections emerged as the predominant clinical manifestation, affecting 90.2% of severely malnourished infants compared to only 42.0% of well-nourished controls, followed by diarrheal diseases (58.5% vs. 17.0%) and skin infections (28.0% vs. 6.0%), all showing statistically significant differences across nutritional categories. The clinical severity of these infections was underscored by the substantially higher rates of hospitalization (37.8% vs. 4.0%) and antibiotic treatment requirements (82.9% vs. 22.5%) among severely malnourished infants, indicating that malnutrition not only increases infection frequency but also shifts the clinical presentation toward more severe, treatment-requiring illness. Multivariate logistic regression analysis confirmed that severe wasting was the strongest anthropometric predictor of frequent infections (OR: 4.28, 95% CI: 2.76-6.64), while among the immunological parameters, CD4+ T-cell counts below 800 cells/μL (OR: 3.42, 95% CI: 2.18-5.36) and IgG levels below 6 g/L (OR: 2.91, 95% CI: 1.83-4.64) emerged as the most powerful predictors of adverse infectious outcomes. The microbial colonization analysis provided additional mechanistic insights, revealing that severely malnourished infants harbored significantly higher rates of pathogenic bacteria in both stool specimens (52.4% vs. 14.0%) and nasopharyngeal samples (70.7% vs. 17.5%), suggesting that malnutrition-induced immune dysfunction creates permissive conditions for pathogen establishment and persistence, ultimately translating into the observed clinical burden of infectious diseases that perpetuates the malnutrition-infection cycle in this vulnerable population.

4 Discussion

The findings from this comprehensive study illuminate the profound interrelationship between malnutrition and immune dysfunction among infants in Northern Nigeria, revealing patterns that have significant implications for child health interventions in the region. The high prevalence of various forms of malnutrition documented in our study—with over one-third of infants exhibiting stunting and nearly one-fifth showing wasting—aligns with previous regional surveys but provides more granular evidence of the nutritional crisis affecting this vulnerable population. These findings underscore the persistence of malnutrition despite various national nutrition programs, suggesting that current intervention strategies may not be adequately addressing the root causes or reaching the most vulnerable communities in Northern Nigeria (UNICEF, 2023).

The observed immunological abnormalities in malnourished infants provide compelling evidence for the biological mechanisms through which malnutrition increases vulnerability to infectious diseases. The significant reductions in lymphocyte populations, particularly CD4+ T-cells, represent a critical impairment in cell-mediated immunity, which is essential for defense against many pathogens endemic to the region. Similar findings have been reported in studies from other resource-limited settings, although our research contributes uniquely detailed immunophenotyping data from Northern Nigerian infants (Ibrahim et al., 2017). The reduced CD4+ counts observed in severely malnourished infants approach levels that would be concerning even in the context of other immunodeficiency disorders, highlighting the severity of malnutrition-induced immune suppression.

The dysregulation of cytokine responses documented in our study reveals a complex immunological picture wherein chronic inflammation coexists with impaired pathogen-specific responses. This paradoxical state of “immune activation yet immune deficiency” has been described in other contexts of chronic malnutrition and may reflect adaptations to persistent nutritional stress. The elevated baseline levels of pro-inflammatory cytokines such as IL-6 and TNF-α suggest ongoing inflammatory processes, potentially driven by subclinical infections or altered gut permeability—a common consequence of malnutrition. Concurrently, the blunted cytokine responses observed in ex vivo stimulation assays indicate compromised ability to mount effective immune responses to new pathogenic challenges. This dual immune dysfunction likely contributes significantly to the observed increased susceptibility to infections among malnourished infants.

The strong association between anthropometric indicators of malnutrition and specific immune parameters provides important insights for clinical assessment and monitoring. Stunting, reflecting chronic undernutrition, showed the strongest association with reduced lymphocyte counts and overall immunocompetence. This finding is particularly concerning given the high prevalence of stunting in our study population and its known association with long-term developmental consequences. While wasting, an indicator of acute malnutrition, was most strongly associated with depressed immunoglobulin levels, suggesting rapid impacts on humoral immunity during acute nutritional stress. These differential associations highlight the importance of assessing both acute and chronic forms of malnutrition when evaluating immune risk in pediatric populations.

The documented relationship between specific micronutrient deficiencies and immune dysfunction merits particular attention. Zinc deficiency, highly prevalent in our study population, was independently associated with impaired cytokine responses even after controlling for anthropometric measures. This finding aligns with the established role of zinc in multiple aspects of immune function, including cytokine production, phagocytosis, and lymphocyte development (Ibrahim et al., 2017). Similarly, vitamin A deficiency showed significant associations with reduced complement levels and impaired mucosal immunity, consistent with its known role in maintaining epithelial barriers and supporting immune cell differentiation. These findings underscore the importance of addressing micronutrient deficiencies alongside protein-energy malnutrition in comprehensive nutritional interventions.

The clinical impact of malnutrition-associated immune dysfunction was starkly evident in the significantly higher burden of infectious diseases among malnourished infants. The nearly three-fold increase in illness episodes and substantially longer duration of illness observed in severely malnourished infants relative to well-nourished controls illustrates the real-world consequences of the immunological deficits documented in our laboratory analyses. The predominance of respiratory infections followed by diarrheal diseases mirrors the infection patterns reported in similar settings but highlights the particular vulnerability of malnourished children in Northern Nigeria to these specific infectious challenges. The strength of the associations between wasting and increased odds of frequent infections (OR: 4.28) underscores the critical importance of addressing acute malnutrition as an urgent priority for reducing infectious disease burden.

Socioeconomic determinants emerged as critical underlying factors in the malnutrition-immune deficiency relationship. Maternal education level showed particularly strong associations with both infant nutritional status and immune function, suggesting that educational interventions for women may yield substantial benefits for child health. This finding aligns with numerous studies highlighting the protective effect of maternal education against child malnutrition across diverse settings (National Bureau of Statistics, 2023). Similarly, household food insecurity demonstrated significant associations with both nutritional status and infection frequency, emphasizing the need to address food access as a fundamental component of immune health interventions. The substantial urban-rural disparities observed in both malnutrition prevalence and immune parameters highlight the need for geographically targeted intervention strategies that address the unique challenges of rural communities in Northern Nigeria.

The interconnections between water, sanitation, and hygiene (WASH) factors and the malnutrition-immune deficiency relationship were particularly noteworthy. Households with inadequate access to clean water and improved sanitation facilities showed significantly higher rates of both malnutrition and infections among infants, even after controlling for other socioeconomic factors. This finding supports the growing recognition of environmental enteric dysfunction—a subclinical condition of intestinal inflammation, reduced absorptive capacity, and compromised barrier function—as a critical mediator in the relationship between poor environmental conditions, malnutrition, and immune dysfunction. The implications are that nutritional interventions alone may yield suboptimal results if not accompanied by improvements in WASH infrastructure and practices.

The variations in malnutrition prevalence and associated immune deficiencies across the five studied states reflect the diverse challenges facing different parts of Northern Nigeria. Borno state, which has experienced significant security challenges and population displacement, demonstrated the highest rates of both malnutrition and immune dysfunction, highlighting the compounding effects of conflict on child nutrition and health. These regional differences underscore the importance of context-specific intervention strategies that address the particular constraints and opportunities in each area while maintaining core focus on the critical pathways linking nutrition and immune function.

When considering intervention implications, our findings suggest that integrating targeted nutritional supplementation with broader approaches addressing underlying determinants would be most effective. The documented immune dysfunction associated with specific micronutrient deficiencies supports the case for micronutrient supplementation programs, particularly for zinc and vitamin A, which showed independent associations with immune parameters. However, the strong socioeconomic gradients observed in both nutritional status and immune function argue equally strongly for interventions addressing household food security, maternal education, and environmental conditions. The optimal approach likely involves complementary interventions operating at multiple levels—from immediate nutritional rehabilitation for malnourished infants to systemic improvements in food systems, educational access, and public health infrastructure.

Conclusion

This comprehensive investigation into the effects of malnutrition on immune deficiency among infants in Northern Nigeria has yielded several important conclusions with significant implications for public health policy and clinical practice. First, the study confirms a high prevalence of various forms of malnutrition in the region, with over one-third of infants exhibiting stunting and nearly one-fifth showing wasting, indicating persistent nutritional challenges despite existing intervention efforts. The geographic and socioeconomic disparities in malnutrition prevalence highlight the need for targeted approaches addressing the most vulnerable populations, particularly in rural areas and conflict-affected regions.

Second, the research provides robust evidence of the profound immunological consequences of malnutrition in this population. Malnourished infants demonstrated significant reductions in lymphocyte counts and subsets, altered immunoglobulin profiles, dysregulated cytokine responses, and impaired cell-mediated immunity as evidenced by delayed-type hypersensitivity testing. These immunological deficits were proportional to the severity of malnutrition and were independently associated with both anthropometric indicators and specific micronutrient deficiencies, particularly zinc and vitamin A. The observed immune dysfunction offers a mechanistic explanation for the well-documented but poorly understood relationship between malnutrition and infectious disease susceptibility.

Third, the study establishes clear clinical correlates of malnutrition-associated immune dysfunction, with malnourished infants experiencing significantly higher frequencies and durations of infectious illnesses, particularly respiratory infections and diarrheal diseases. The strong associations between specific immune parameters and infection outcomes provide potential biomarkers for identifying infants at highest risk of adverse clinical outcomes and monitoring the immunological effectiveness of nutritional interventions.

Fourth, the research illuminates the complex interplay between nutritional status, immune function, and socioeconomic determinants. Maternal education emerged as a particularly powerful influence on both nutritional status and immune parameters, while household food insecurity and inadequate water and sanitation facilities showed significant associations with adverse outcomes, highlighting the need for integrated approaches addressing these underlying factors alongside direct nutritional interventions.

In conclusion, this study provides compelling evidence that malnutrition significantly compromises immune function among infants in Northern Nigeria, creating increased vulnerability to infections through multiple immunological pathways. These findings underscore the urgent need for comprehensive interventions that address both immediate nutritional deficiencies and their underlying socioeconomic and environmental determinants. By interrupting the vicious cycle of malnutrition and infection, such interventions have the potential to significantly improve infant health outcomes and contribute to broader child development goals in this vulnerable region.

Recommendations

Based on the findings of this study, the following recommendations are proposed for policy, practice, and future research:

1. **Enhanced nutritional surveillance and intervention targeting**: Implement more rigorous nutritional surveillance systems across Northern Nigeria, with particular attention to identified high-risk areas. Nutritional interventions should be geographically targeted based on prevalence data and prioritize communities with the highest burden of malnutrition and immune-related morbidity.
2. **Integrated micronutrient supplementation programs**: Expand micronutrient supplementation programs, with particular emphasis on zinc and vitamin A, which showed strong independent associations with immune parameters. These programs should be integrated with existing healthcare services, including immunization campaigns and growth monitoring, to maximize coverage and efficiency.
3. **Early identification and management of malnutrition**: Strengthen capacity for early detection of malnutrition at community and primary healthcare levels through training of community health workers in anthropometric assessment and the identification of clinical signs of micronutrient deficiencies. Established protocols for the management of various forms of malnutrition should be consistently implemented across all healthcare levels.
4. **Promotion of optimal infant feeding practices**: Intensify efforts to promote exclusive breastfeeding for the first six months of life and appropriate complementary feeding thereafter, with emphasis on dietary diversity and nutrient density. Culturally sensitive educational approaches should be developed with community input to address traditional feeding practices that may contribute to malnutrition.
5. **Address underlying socioeconomic determinants**: Develop intersectoral policies and programs that address key socioeconomic determinants of malnutrition, particularly maternal education, household food security, and women’s empowerment. Conditional cash transfer programs linked to child nutritional outcomes and maternal participation in educational activities could be considered as a potential intervention strategy.
6. **Improve water, sanitation, and hygiene (WASH) infrastructure**: Prioritize investments in WASH infrastructure and behavior change programs in communities with high malnutrition prevalence, recognizing the critical role of environmental factors in mediating the relationship between nutrition and immune function. Integration of WASH interventions with nutritional programs should be standard practice.
7. **Strengthen health systems capacity**: Enhance the capacity of the healthcare system to address the health consequences of malnutrition, including training healthcare workers in the identification and management of common infections in malnourished children and ensuring the availability of essential medicines and supplies for treating these conditions.
8. **Development of immune function monitoring in high-risk populations**: Investigate the feasibility of incorporating basic immune function assessment into the monitoring of nutritional intervention programs, potentially using simplified biomarkers that could be assessed at district hospital level to identify children at highest risk of adverse outcomes.
9. **Research on intervention effectiveness**: Conduct rigorous evaluation studies of integrated nutrition-specific and nutrition-sensitive interventions to determine their effectiveness in improving both nutritional status and immune function among infants in this setting. Implementation science approaches should be employed to identify strategies for scaling effective interventions.
10. **Long-term studies on immunological recovery**: Initiate longitudinal studies to assess the reversibility of malnutrition-induced immune deficiencies and identify optimal approaches for supporting immunological recovery alongside nutritional rehabilitation. Such research should include investigation of potential critical windows during which nutritional interventions may be most effective for preserving immune function.

By implementing these recommendations, stakeholders can work toward breaking the cycle of malnutrition and immune deficiency that continues to threaten infant health in Northern Nigeria, ultimately contributing to improved child survival, development, and long-term health outcomes in the region.

Ethical Approval and Consent

The study protocol received ethical approval from the National Health Research Ethics Committee of Nigeria and the respective institutional review boards of participating health facilities. Written informed consent was obtained from parents or guardians of all participants. Confidentiality of participant information was maintained throughout the study. Infants identified with severe acute malnutrition or serious medical conditions were referred for appropriate treatment.

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