

IMMUNE SYSTEM FORMATION IN CHILDREN UNDER 5 YEARS OF AGE: CLINICAL FEATURES, DEVELOPMENTAL PATTERNS AND PREVENTIVE STRATEGIES

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Abstract

This study investigates the formation and maturation of the immune system in children aged 0–5 years. The research analyzes key developmental stages of both innate and adaptive immunity, identifies critical windows of immune vulnerability, and presents epidemiological data on immunodeficiency-related morbidity in Uzbekistan. The article highlights the importance of breastfeeding, vaccination schedules, and micronutrient supplementation in supporting immune ontogenesis. Results demonstrate that targeted early-life interventions can reduce infectious morbidity by up to 40%. Scientific novelty lies in the comprehensive integration of clinical, laboratory, and epidemiological data within the Central Asian pediatric context.

Keywords

immune system ontogenesis; innate immunity; adaptive immunity; pediatric immunology; vaccination; breastfeeding; immunodeficiency; morbidity; early childhood; Uzbekistan

1. INTRODUCTION

The immune system of a child undergoes its most intensive and consequential developmental period during the first five years of life. During this interval, both innate and adaptive components of immunity transition from a state of relative immaturity at birth toward a progressively competent defense network capable of recognizing and neutralizing a wide spectrum of pathogens [1]. The vulnerability of infants and young children to infectious diseases is largely attributable to qualitative and quantitative deficiencies in immune effector mechanisms that persist throughout early childhood.

In Uzbekistan, respiratory tract infections, gastrointestinal infections, and vaccine-preventable diseases collectively account for approximately 62% of all pediatric hospital admissions in children under 5 years of age (Ministry of Health

of Uzbekistan, 2023). Understanding the precise developmental trajectory of pediatric immunity is therefore not merely an academic exercise but a prerequisite for the rational design of preventive and therapeutic strategies [2].

The scientific objective of this study is to provide a comprehensive, evidence-based characterization of immune system formation in children aged 0–5 years, with specific attention to: (1) the ontogenetic sequence of immune component development; (2) critical periods of immunological vulnerability; (3) the impact of nutritional, environmental, and vaccine-related factors; and (4) epidemiological patterns of immune-related morbidity in the Uzbek pediatric population [3].

2. LITERATURE REVIEW

The immunological immaturity of the newborn has been extensively documented in the scientific literature. Adkins et al. (2004) demonstrated that neonatal T-helper cells exhibit a marked bias toward a Th2 cytokine profile, with diminished capacity for Th1-driven cellular immunity [4]. This skewing is believed to reflect an evolutionary adaptation to the tolerogenic intrauterine environment, wherein robust Th1 responses could endanger the feto-maternal interface.

Hanson and colleagues (2003) established that human breast milk provides not only passive immunological protection through secretory IgA (sIgA), lactoferrin, and lysozyme, but also actively shapes the infant's developing immune system through cytokines, hormones, and microbiome-modulating oligosaccharides [5]. Cohort studies in low- and middle-income countries have consistently found a 40–50% reduction in infectious morbidity among exclusively breastfed infants during the first six months of life [6].

Central Asian and specifically Uzbek pediatric immunological research has gained momentum over the past decade. Rakhimova et al. (2021) published a cross-sectional study of 1,240 children in Tashkent province demonstrating that zinc deficiency — prevalent in 34% of children under 5 — was associated with a 2.3-fold increase in recurrent respiratory infections [7]. Simultaneously, Nazarov and Tursunov (2022) highlighted the impact of delayed vaccination schedules on community-level herd immunity thresholds in Uzbekistan [8].

International guidelines from the World Health Organization (WHO, 2023) and the American Academy of Pediatrics (AAP, 2022) converge on the importance of breastfeeding, timely vaccination, adequate vitamin D and zinc supplementation, and reduction of environmental pollutant exposure as primary determinants of healthy immune ontogenesis in early childhood [9].

3. RESEARCH METHODOLOGY

This study employed a multifaceted research design combining: (1) systematic literature review of 47 peer-reviewed publications (2015–2024) identified through

PubMed, Scopus, and CyberLeninka databases; (2) retrospective analysis of anonymized clinical records from the Department of Propaedeutics of Childhood Diseases No. 2, Tashkent State Medical University (n = 386 children, aged 0–5 years, 2021–2023); (3) secondary analysis of national epidemiological surveillance data from the Republican Center for Disease Control (RCDC, 2020–2023); and (4) comparative analysis of WHO immunization coverage statistics.

Inclusion criteria for the clinical cohort: age 0–5 years; complete vaccination history; two or more documented clinical visits; absence of congenital malformations. Exclusion criteria: diagnosed primary immunodeficiency; active malignancy; ongoing immunosuppressive therapy. Statistical analysis was performed using SPSS v.26.0; significance threshold was set at $p < 0.05$. Comparative methods, descriptive statistics, and correlation analysis were used.

4. ANALYSIS AND RESULTS

4.1 Stages of Immune System Development in Children (0–5 Years)

The immune system matures through a series of overlapping yet distinct developmental stages. Table 1 summarizes the key immunological characteristics and clinical implications of each phase.

Table 1. Developmental Stages of the Immune System in Children Aged 0–5 Years

Age Stage	Key Immune Components	Innate Immunity Features	Adaptive Immunity Features	Clinical Significance
0–28 days (Neonatal)	Maternal Ab, NK cells, neutrophils	Low complement activity; reduced TLR signaling; immature DCs	Near-absent B-cell memory; T-cell Th2 bias; limited sIgA	Highest susceptibility to gram-negative sepsis & HSV
1–6 months	Declining maternal IgG; emerging IgM	Improving phagocytosis; increasing cytokine diversity	First endogenous IgM production; Th1/Th2 imbalance persists	Physiological hypogammaglobulinemia trough; RSV risk
6–12 months	Own IgG rising; sIgA in mucosae	Near-adult NK function; better	T-cell memory beginning; improved	First immune memory; DTP vaccine optimal window

		neutrophil chemotaxis	vaccine responses	
1–3 years	Full sIgA; IgG subclasses maturing	Adult-level innate function for most parameters	IgG2 still low; polysaccharide Ag responses weak	Vulnerable to encapsulated bacteria; conjugate vaccines critical
3–5 years	Near-adult immunoglobulin levels	Mature innate system; robust inflammatory responses	Adult-pattern T and B cell memory; IgG2 approaching adult	Decreasing infection frequency; school-entry immunity stable

Source: Compiled by the author based on WHO (2023), Hanson (2003), Adkins (2004), and RCDC data (2023)

4.2 Immunoglobulin Dynamics in Early Childhood

Immunoglobulin (Ig) levels undergo dramatic and clinically consequential fluctuations during the first five years of life. The nadir of serum IgG – known as the physiological hypogammaglobulinemia of infancy – typically occurs between 3 and 6 months of age, coinciding with the waning of transplacentally acquired maternal antibodies before the child's own production reaches protective levels (Table 2).

Table 2. Reference Ranges of Serum Immunoglobulins by Age (g/L) – Uzbek Pediatric Cohort Data

Age Group	IgG (g/L)	IgA (g/L)	IgM (g/L)	IgE (IU/mL)	Total Ig (g/L)	Vulnerability Index*
Newborn (0–28d)	6.0–12.0	0.0–0.05	0.06–0.2	< 1.5	6.1–12.3	HIGH
1–3 months	2.5–7.5	0.01–0.1	0.1–0.5	< 3.0	2.6–8.1	VERY HIGH
3–6 months	1.5–5.0	0.02–0.2	0.2–0.7	< 5.0	1.7–5.9	MAXIMUM
6–12 months	2.5–6.5	0.1–0.5	0.3–1.0	< 10	2.9–8.0	HIGH
1–2 years	4.5–9.0	0.3–1.2	0.5–1.5	< 20	5.3–11.7	MODERATE
2–3 years	5.0–10.0	0.4–1.5	0.5–1.5	< 30	5.9–13.0	MODERATE
3–5 years	6.0–12.0	0.5–2.0	0.5–1.8	< 40	7.0–15.8	LOW-MODERATE
Adult (ref)	7.0–16.0	0.7–4.0	0.4–2.3	< 100	8.1–22.3	—

*** Vulnerability Index: author's composite score based on infection incidence correlation with Ig levels. Source: RCDC (2023); n=386 clinical cases, TSMU Department No.2**

4.3 Epidemiological Data: Infectious Morbidity in Uzbek Children Under 5 (2020–2023)

National surveillance data from the Republican Center for Disease Control (2020–2023) reveals a consistent pattern of infection-related morbidity concentrated in the 0–2 year age group. The data presented in Table 3 reflects incidence per 1,000 children per year across major categories of childhood infection.

Table 3. Infectious Disease Morbidity in Children Under 5 Years, Uzbekistan (per 1,000 children/year)

Disease Category	0–6 mo.	6–12 mo.	1–2 yr.	2–3 yr.	3–5 yr.	Trend
Acute Respiratory Infections (ARI)	124	186	220	168	112	↓ Peak at 1–2yr
Acute Gastroenteritis (AGE)	98	142	178	134	88	↓ Peak at 1–2yr
Pneumonia	22	34	41	28	14	↓ Declining
Otitis Media	18	42	67	54	31	↓ Peak at 1–2yr
Urinary Tract Infection	14	18	22	20	16	→ Stable
Chickenpox	2	12	44	56	38	↑ Peak at 2–3yr
Measles (unvaccinated)	1	3	8	5	2	↓ After vaccine
Meningitis (bacterial)	3.2	2.1	1.8	1.2	0.8	↓ Declining

Source: Republican Center for Disease Control, Uzbekistan (2020–2023 cumulative data)

4.4 Vaccination Coverage and Its Impact on Immune-Mediated Morbidity

Figure 1 below illustrates the vaccination coverage rates for key childhood vaccines in Uzbekistan across different regions and age cohorts (RCDC, 2023).

Figure 2 presents the observed reduction in morbidity correlating with vaccination coverage improvements between 2018 and 2023.

Figure 1. Vaccination Coverage by Age Group – Uzbekistan 2023 (%)

Age Group	V	Distribution Bar
BCG (birth)	98.2%	
DTP-3 (2 mo.)	4.6%	
OPV-3 (2 mo.)	5.1%	
Measle mumps (by 1 mo.)	96.7%	
Hep B (1 dose)		

Source: Ministry of Health of Uzbekistan, National Immunization Programme Report (2023)

Figure 2. Reduction in Vaccine-Preventable Disease Incidence (2018 vs 2023, per 100,000 children <5)

Age Group	Value (%)	Distribution Bar
Measles	78.4%	
Pertussis	65.2%	
Hib Meningitis	71.8%	
Hepatitis B	82.1%	
Tetanus (neonatal)	91.5%	

Source: WHO Country Immunization Profile – Uzbekistan (2023); RCDC surveillance data 2018–2023

4.5 Impact of Breastfeeding and Nutritional Factors on Immune Development

Breastfeeding remains the single most impactful nutritional intervention for supporting early immune ontogenesis. Table 4 summarizes the immunological components of human breast milk and their protective mechanisms.

Table 4. Immunological Components of Human Breast Milk and Their Protective Functions

Component	Concentration*	Mechanism of Action	Clinical Effect
Secretory IgA (sIgA)	High in colostrum (4–10 g/L)	Luminal pathogen neutralization; prevents mucosal adhesion	↓ 50% rotavirus diarrhea; ↓ 40% ARI in first 6 months
Lactoferrin	1–7 g/L in colostrum	Iron chelation; direct bactericidal/antifungal; TLR4 modulation	↓ Neonatal sepsis; anti-inflammatory; microbiome shaping
Lysozyme	0.1–0.5 mg/mL	Bacterial cell-wall lysis (peptidoglycan cleavage)	Protection against gram-positive cocci; synergy with sIgA
Human Milk Oligosaccharides (HMO)	5–20 g/L	Prebiotic; pathogen receptor decoys; microbiome modulation	↓ Necrotizing enterocolitis; promotes Bifidobacterium colonization
Cytokines (IL-10, TGF-β)	Variable	Th1/Th2 balance modulation; oral tolerance induction	Reduced allergy/atopy risk; mucosal immune maturation
IgG (maternal)	0.02–0.15 g/L	Systemic pathogen neutralization; complement activation	Broad pathogen protection before infant's own IgG rises
Zinc, Selenium, Vit D	Trace amounts	Co-factors for immune enzyme systems; DC maturation	Reduced susceptibility during physiological hypogammaglobulinemia

* Concentrations are highest in colostrum and decline progressively in mature milk. Source: Hanson (2003); WHO (2023); Rakhimova et al. (2021)

4.6 Micronutrient Deficiency and Immune Impairment – Uzbekistan Data

Micronutrient deficiencies represent a major modifiable determinant of immune competence in early childhood. Table 5 presents data from the Uzbekistan

Demographic Health Survey (2022) and TSMU clinical cohort (2021–2023) on deficiency prevalence and immune correlates.

Table 5. Micronutrient Deficiency Prevalence and Immune Consequences in Uzbek Children Under 5

Micronutrient	Deficiency Prevalence (%)	Reference Level	Immune Impairment Observed	RR of Infection*	Recommended Intervention
Vitamin D	44.3%	< 50 nmol/L	Reduced TLR signaling; impaired macrophage function; decreased antimicrobial peptides	RR = 1.8	400–1000 IU/day supplementation
Zinc	34.1%	< 60 µg/dL	Impaired T-cell proliferation; reduced NK cytotoxicity; thymic atrophy	RR = 2.3	Supplementation 5–10 mg/day
Iron (IDA)	38.6%	Hb < 110 g/L	Impaired neutrophil oxidative burst; reduced T-cell counts	RR = 1.7	Iron drops + dietary counseling
Vitamin A	12.8%	< 0.7 µmol/L	Impaired mucosal integrity; reduced sIgA; CD4+ depletion	RR = 2.1	Semi-annual high-dose (100,000 IU)
Selenium	18.2%	< 60 µg/L serum	Reduced glutathione peroxidase; oxidative immune damage	RR = 1.5	Dietary diversification

Iodine	9.4%	UIC < 100 µg/L	Thyroid axis → secondary immune dysregulation	RR = 1.3	Iodized salt programs
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* RR = Relative Risk of infectious illness compared to replete children.

Source: Uzbekistan DHS 2022; TSMU cohort n=386; Rakhimova et al. (2021)

4.7 Key Statistical Findings Summary

Figure 3. Key Statistical Outcomes: Immune-Related Health Interventions in Children Under 5 (TSMU Cohort, 2021–2023)

Intervention / Parameter	Baseline (without intervention)	Post-intervention (6 months)	Reduction / Improvement	Statistical Significance
Exclusive breastfeeding (0–6 mo.)	ARI rate: 186/1000	ARI rate: 108/1000	↓ 41.9%	p < 0.001, CI 95%
Zinc supplementation (IDA + zinc)	Recurrent ARI: 4.2/yr	Recurrent ARI: 1.8/yr	↓ 57.1%	p < 0.001
Vitamin D supplementation	IgG mean: 3.8 g/L	IgG mean: 5.1 g/L	↑ 34.2%	p < 0.01
Complete DTP-3 vaccination	Pertussis incidence: 18/1000	Pertussis incidence: 4/1000	↓ 77.8%	p < 0.001
Measles-Rubella vaccination	Measles cases: 8/1000	Measles cases: 0.6/1000	↓ 92.5%	p < 0.001
Microbiome-protective feeding	Gut infections: 178/1000	Gut infections: 121/1000	↓ 32.0%	p < 0.05
Combined preventive programme	Total hospitalizations: 284/1000	Total hospitalizations: 170/1000	↓ 40.1%	p < 0.001

Source: TSMU Department of Propaedeutics of Childhood Diseases No. 2; Clinical cohort n=386; 2021–2023

5. CONCLUSIONS AND RECOMMENDATIONS

This study has demonstrated that immune system development in children under 5 years of age follows a highly structured ontogenetic sequence, characterized by predictable periods of relative vulnerability that are amenable to targeted clinical and public health intervention. The following conclusions and recommendations are drawn from the analysis:

1. The period of physiological hypogammaglobulinemia (3–6 months) represents the single highest-risk window for infectious morbidity, during which the cumulative reduction of maternal IgG reaches its nadir before endogenous synthesis achieves protective levels. Clinicians should exercise heightened vigilance and prioritize vaccination and breastfeeding support during this interval.

2. Exclusive breastfeeding during the first six months of life reduced acute respiratory infection rates by 41.9% in the TSMU cohort ($p < 0.001$). Given the prevalence of early cessation of breastfeeding in Uzbekistan (36% of mothers discontinue before 4 months; DHS 2022), lactation support programs should be integrated into all primary healthcare facilities.

3. Micronutrient deficiencies – particularly zinc (34.1%), vitamin D (44.3%), and iron (38.6%) – are highly prevalent in Uzbek children under 5 and are each independently associated with increased risk of recurrent infections (RR 1.5–2.3). Universal prophylactic supplementation programs aligned with WHO 2023 guidelines are warranted.

4. Vaccination coverage for core antigens (DTP, OPV, Measles-Rubella) remained above 91% nationally in 2023; however, regional disparities and schedule delays continue to create herd immunity gaps. Integrated supervisory mechanisms and community health worker outreach require strengthening.

5. The implementation of a comprehensive preventive program combining breastfeeding support, micronutrient supplementation, and complete immunization was associated with a 40.1% reduction in total pediatric hospitalizations within the study cohort – a finding with direct implications for healthcare resource utilization in the Uzbek health system.

6. Future research should focus on longitudinal immunological profiling of Uzbek children, genome-wide association studies to identify population-specific immune variants, and the potential role of the gut microbiome in modulating immune ontogenesis in the Central Asian dietary context.

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