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The Influence of Feeding Types on the Immune Reactivity of Children

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Abstract For optimal growth, development, and health, exclusive breastfeeding is essential for the first six months of life. Clinical and laboratory research methods were used, including general blood tests and cellular and humoral immune system parameters, assessed using monoclonal antibodies (CD3, CD4, CD8, CD23, CD25, CD95, etc.), along with dynamic observations of children up to puberty. This article presents the results of a study on the immunological status of 123 children who were subjected to different types of feeding. A comparative analysis of immunological indicators showed that these indicators tend to remain imbalanced with age, depending on the type of feeding. In children aged 4-6 years who were bottle-fed, a significant increase in leukocytes and CD3+ lymphocytes was observed, along with a significant decrease in CD4+ lymphocytes.

Keywords Breastfeeding, Formula feeding, Immunological status

1. Introduction

According to the World Health Organization's Global Strategy on Infant and Young Child Feeding, nutrition during infancy and early childhood is a crucial issue in modern pediatrics and nutrition science [1]. Recent studies have demonstrated the long-term impact of infant nutrition on physical development, health, and IQ in later life [2]. For optimal growth, development, and health, children should be exclusively breastfed (EBF) for the first six months of life. To meet their nutritional needs, infants should receive nutritionally adequate and timely complementary foods while continuing breastfeeding for an extended period.

Due to the inevitable microbial exposure of newborns, breastfeeding plays a crucial role in maintaining the immunological bond between mother and child [3,7]. Neutralized antigens and protective antibodies are transferred through breast milk, which contains proteins that are the least allergenic and nutrients best suited to the enzymatic systems of an infant's digestive system [4]. Breastfed children experience significantly fewer disruptions in their intestinal microbiota compared to those who are formula-fed [5,6]. However, there is a lack of studies exploring the patterns of protective and adaptive immune responses depending on different feeding types throughout various stages of childhood.

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2. Objective of the Study

To conduct a comparative immunological analysis of children based on their feeding types.

3. Materials and Research Methods

To achieve this goal, clinical and laboratory research methods were employed, including general blood analysis, cellular and humoral indicators of the immune system assessed using monoclonal antibodies (CD3, CD4, CD8, CD23, CD25, CD95, and others), as well as dynamic observation of children up to puberty.

4. Research Results

This article presents the results of a study on the immunological status of 123 children who were on different types of feeding. A comparative analysis of immunological indicators revealed that these indicators tend to retain an imbalance with age depending on the type of feeding. In children aged 4-6 years who were on artificial feeding, a significant increase in leukocytes and CD3+ lymphocytes was observed against the background of a significant decrease in CD4+ lymphocytes.

The content of NK lymphocytes in the body determines their cytotoxic activity against the body's own cells with modified antigen structures, fulfilling the function of immunological surveillance [4,6]. Among the surface NK receptors, CD16 is particularly noteworthy.

An increase in CD16 expression was noted depending on the type of feeding, with the most pronounced effect observed in children on artificial feeding ($P < 0.05$). This activation of natural killer cells is likely due to an increased presence of immature forms of natural killers in the peripheral blood. In children of group 4, B-lymphocyte indicators significantly increased compared to the data of groups 1, 2, and 3—by 6.4% relative to group 1, by 5.7% relative to group 2, and by 2.2% relative to group 3.

A notable factor is the increase in allergic sensitization, which was significantly higher in children who were artificially fed compared to those exclusively breastfed (29.9 ± 1.0% vs. 20.3 ± 0.23%, respectively; $P < 0.05$) and predominantly breastfed (29.9 ± 1.0% vs. 21.2 ± 0.62%, respectively; $P < 0.05$). An increase in CD23+ was also found compared to children on mixed feeding, though the difference was not statistically significant (29.9 ± 1.0% vs. 25.2 ± 1.2%, respectively).

The apoptosis factor indices in bottle-fed children were significantly higher compared to breastfed children (30.8 ± 1.1% vs. 22.7 ± 0.47%). Significantly elevated apoptosis indices were also observed in children on GBS (25.2 ± 1.2% vs. 22.7 ± 0.47%).

Regarding humoral immunity, an imbalance in IgA and IgM levels was particularly pronounced in children who were on artificial feeding and GBS. A slight decrease in IgG levels was observed in children of group 3 compared to children of groups 1 and 2.

The CIC indices, both large and small, were significantly elevated in groups 3 and 4 compared to children on IGBT and PGV. In group 2, there was a notable decrease in the large CIC index, although the values remained within the normal range.

The next stage of the study involved assessing the immunological status of children aged 7-14 years in relation to their type of feeding. In this age group, an increase in leukocyte count was observed, particularly pronounced in children from group 4 (11,000±434.1 vs. 6,200±310.7 μl; $P < 0.05$) compared to children from group 1. In the other groups, leukocyte levels remained within normal limits.

The relative and absolute lymphocyte counts showed a marked tendency to increase in children from group 4 compared to those in groups 1, 2, and 3. In children from groups 1, 2, and 3, these values remained within the normal range. However, in children on mixed feeding, the lymphocyte count reached or, in some cases, slightly exceeded the upper limit of normal (2,830.6 ± 288.7 vs. 1,780.3 ± 74.8 μl).

An imbalance in T-cell parameters was observed in children aged 7-14 years, depending on their feeding type. Children who were exclusively breastfed maintained normal levels of CD3+, CD4+, CD8+, and IRI. Those who were predominantly breastfed had values slightly different from group 1. In group 3, a significant decrease in CD3+, CD4+, CD8+, and IRI levels was already noted compared to group 1. The most pronounced T-cell imbalance was found in bottle-fed children. Consequently, the immunoregulatory index (IRI) was significantly lower in the bottle-fed group.

Immunoregulatory Index (IRI) in Children Based on Feeding Type

Significantly elevated CD16+ levels were observed in children from groups 3 and 4, as well as in group 2. This increase in natural killer (NK) cell activity is likely due to the presence of immature NK cell forms in peripheral blood.

An analysis of B-lymphocyte counts revealed a significant increase in both relative and absolute numbers in children who were artificially and mixed-fed compared to those who were exclusively or predominantly breastfed ($P < 0.05$).

We also observed an increase in CD23+ (a marker associated with allergic responses) in children from group 4 (IV) and group 3 (SGV) compared to those from groups 1 and 2 (33.2±1.3% and 32.5±1.5% vs. 20.3±0.24% and 21.9±0.4%, respectively).

A significant rise in CD38+ expression was detected in group 4 (IV), where levels were 1.2 times higher than in children from group 1 (IGV) ($P < 0.05$).

The role of effector cells—CD8+ cytotoxic T-lymphocytes and EEK—suggests their damaging impact on central nervous system (CNS) cells, leading to the release of total protein and myelin into peripheral blood. This promotes the proliferation of specific T-lymphocytes (CD8+), increasing CD95 receptor expression on lymphocytes. A twofold increase in CD95+ cells compared to the control indicates heightened apoptosis. In children, proliferative processes generally outweigh destructive ones, meaning their apoptosis activation is lower than in adults.

Children in group 4 (IV) exhibited the highest levels of apoptosis stimulation, which may contribute to a physiological depletion of immune system reserves.

The most critical indicators of humoral immunity are IgG, IgM, and IgA. Our study revealed significant differences in IgM and IgG levels in the peripheral blood serum of children from groups 3 (SGV) and 4 (IV) compared to those from group 1.

An imbalance in circulating immune complex (CIC) levels was recorded in groups 2, 3, and 4, with the most pronounced imbalance in group 4. Elevated CIC levels indicate ongoing inflammatory processes and are markers of autoimmune disease activity. Follow-up data analysis revealed a significantly higher incidence of inflammatory diseases in children from groups 3 and 4, many of whom were frequently ill.

5. Conclusions

The immunological characteristics of children at different stages of life reflect the general patterns of protective and adaptive processes. These characteristics manifest in various ways and to different degrees, depending on the type of feeding and overall care principles. Notably, the allergy factor was significantly higher in children who were bottle-fed compared to those who were exclusively breastfed.

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