

## THE EFFECT OF NUTRITION ON THE IMMUNE SYSTEM OF CHILDREN IN TIMOR LESTE: A SYSTEMATIC REVIEW OF NUTRITIONAL STATUS AND IMMUNE RES- PONSE

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### *Abstract*

**Introduction:** *Malnutrition among children, particularly in developing countries such as Timor Leste, represents a major public health issue. The prevalence of malnutrition—including stunting, wasting, and micronutrient deficiencies—remains high and significantly affects the immune system of children. Impairment of the immune system due to malnutrition increases vulnerability to infections and diseases. Therefore, this study aims to evaluate the relationship between nutritional status and immune responses among children in Timor Leste.*

**Methods:** *This study employed a Systematic Literature Review (SLR) approach to collect, evaluate, and analyze data from relevant studies examining the impact of nutritional status on the immune system of children. Data were gathered from major scientific databases, including Scopus, PubMed, and Google Scholar, using keywords related to nutrition, malnutrition, and immune response in children.*

**Results:** *The findings identified several factors influencing the immune system of children in Timor Leste, particularly deficiencies in micronutrients such as zinc, vitamin A, and vitamin D. Poor nutritional status was associated with a decrease in white blood cell counts and weakened ability of the body to fight infections. Furthermore, studies revealed that micronutrient supplementation and exclusive breastfeeding could improve nutritional status and strengthen the immune system of malnourished children. Increasing dietary diversity was also found to have a positive impact on the immune health of children.*

**Discussion:** *The results of this study indicate that poor nutritional status—especially micronutrient deficiencies—has a direct effect on the decline of immune function in children. Therefore, appropriate nutritional interventions, such as supplementation with zinc and vitamin A and the promotion of exclusive breastfeeding, hold great potential to improve nutritional status and enhance immune resilience among children in Timor Leste. This study also emphasizes the need for more effective, evidence-based health policies to address malnutrition in developing countries.*

**Keywords:** *Nutritional Status, Stunting, Wasting, Micronutrients, Immune System, Nutritional Intervention, Immune Response*

### INTRODUCTION

Child health is a crucial indicator of sustainable human development. Good nutritional status plays a crucial role in supporting physical growth, cognitive development, and children's resistance to

various diseases. Inadequate nutrition can lead to metabolic disorders, decreased immune function, and an increased risk of infection. Numerous studies have demonstrated the close and interconnected relationship between nutrition and the

immune system. Wei et al. (2019) explained that administering recombinant human growth hormone can improve nutritional status and enhance immune function without causing abnormal growth. This suggests that good nutritional intake can help strengthen the immune system. However, most existing research focuses on adults or animal models, while studies on children, particularly in developing countries like Timor-Leste, are still very limited. In fact, children are the group most vulnerable to the impacts of malnutrition, so comprehensive scientific studies are needed to understand the relationship between nutritional status and the immune system in this population.

Malnutrition among children in Timor-Leste is a serious issue with widespread impacts on public health. Malnutrition, whether in the form of nutritional deficiencies or imbalances, can reduce the immune system's ability to fight infectious diseases. Ke et al. (2021) suggest that malnutrition leads to a decrease in CD4+ cell counts and impaired immune function, making children more susceptible to infection. This situation is exacerbated by poor food quality and poor environmental sanitation in developing countries. Research by Rocha-Ramírez et al. (2020) also found that the probiotic *Lactobacillus casei* can improve macrophage function in malnourished children, demonstrating that nutritional status can be modified to strengthen immunity. However, most of these studies have been conducted on a laboratory scale and have not been widely applied in a broader social context. Therefore, research examining the influence of nutritional status on the immune system of children in Timor-Leste is crucial to address the public health challenges still facing the country.

The Timor-Leste government and international organizations such as the WHO and UNICEF have demonstrated significant attention to child nutrition through various national policies. One key effort is the implementation of the National Nutrition Strategy, which aims to reduce malnutrition rates and increase access to nutritious food. However, the effectiveness of this policy remains limited due to the lack of scientific data demonstrating a direct link between nutritional status and the immune system of children in Timor-Leste. According to Mendivil (2021), fish consumption and its omega-3 fatty acid content can help strengthen the immune system by regulating inflammation. However, existing policies still focus on increasing calorie intake without considering the role of micronutrients in immunity. Liao et al. (2022) also found that serum zinc levels were positively correlated with innate immune activity, which functions to fight infection in healthy children. This suggests that nutrition policies should focus not only on energy intake but also on paying attention to the quality of nutrients that can strengthen the immune systems of children in developing countries.

In addition to government policies, public awareness of the importance of child nutrition is also crucial for improving health conditions in Timor-Leste. Unfortunately, public awareness of the importance of a balanced diet remains low. Many families focus solely on the availability of staple foods without considering the balance of nutrients consumed. However, adequate intake of protein, zinc, vitamins, and healthy fats is essential for supporting the immune system. Hatch-McChesney et al. (2023) emphasized that nutritional imbalance can increase the risk of infection and slow the healing process. This lack of public understanding of the

role of nutrition in developing children's immunity leads to high rates of infectious diseases and exacerbates the cycle of malnutrition. Therefore, research examining the relationship between nutrition and the immune system is expected to not only contribute to scientific knowledge but also serve as an educational basis for the public to raise awareness of the importance of a balanced diet.

From a feasibility and management perspective, research on the effect of nutrition on the immune system of children in Timor-Leste can be conducted successfully because it is supported by various scientific literature and relevant previous research data. Previous studies have used various indicators to measure the relationship between nutritional status and the immune system, such as zinc levels, cytokine activity, and CD4+ cell count (Ke et al., 2021; Liao et al., 2022). The systematic review approach used in this study allows for the integration of results from various previous studies to produce comprehensive and objective conclusions. In terms of time and resources, this research can be carried out efficiently because it focuses on literature synthesis without the need for direct experiments. Supporting studies such as Azizi Jalilian Farid et al. (2022) who examined the effect of Bio-shield superfood powder on immune function in COVID-19 patients, and She et al. (2023), which assessed the impact of low-fat milk consumption on immunity, demonstrated that the relationship between nutrition and the immune system is a growing field and can be scientifically analyzed using existing data sources. This demonstrates that this research is well-managed in terms of knowledge, time, funding, and literature availability.

The novelty of this study lies in its focus on children in developing countries, particularly in Timor-Leste, who face high rates of malnutrition. Most previous studies have focused on adult populations, such as cancer patients (Candiloro et al., 2021) or individuals with diabetes and obesity (Braga Tibaes et al., 2023), while studies specifically addressing the impact of nutrition on the immune system in children are still very limited. Therefore, this study aims to fill this gap by examining the relationship between nutritional status and the immune response of children in Timor-Leste through a systematic review approach. This research not only makes an academic contribution to the development of knowledge in the fields of nutrition and immunology but also has social relevance because the results can serve as a basis for designing more effective, evidence-based nutritional interventions. Therefore, this research has great potential to support improvements in the quality of life and health of children in developing countries.

In general, this research is important to conduct because it can provide a deeper scientific understanding of how nutritional status affects the system. children's immunity. The results of this study are expected to strengthen the basis for national policies on child nutrition and health in Timor Leste and encourage community participation in implementing a balanced nutritional diet. Based on the description above, the main research questions can be formulated as follows: what is the relationship between nutritional status and children's immune systems based on previous research results; how does nutritional status affect the immune response of children in developing countries, particularly in Timor Leste; and how the results of this systematic review can contribute to the

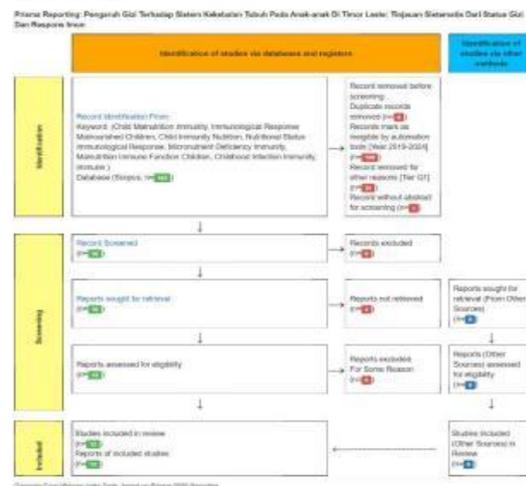
development of future nutrition and child health policies. By answering these questions, this research is expected to broaden scientific insight and provide practical benefits for improving children's health in developing countries.

## METHOD

This study employed a systematic review design aimed at identifying, evaluating, and synthesizing research findings addressing the impact of nutritional status on children's immune systems, particularly in the context of developing countries like Timor-Leste. This approach was chosen because it provides a comprehensive understanding of the relationship between nutritional factors and the immune system based on existing empirical evidence. The study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, ensuring a transparent, structured, and replicable process for other researchers. This systematic review design was deemed most appropriate due to the highly complex nature of nutrition and pediatric immunology and the interplay of biological, environmental, and social variables (Wei et al., 2019; Ke et al., 2021). This design allows the study results to provide a comprehensive and valid picture of the relationship between nutritional status and immune function.

The research sample consisted of relevant scientific articles published in Scopus-indexed journals. The article identification process was conducted through a systematic search using the following keywords: Child Malnutrition Immunity, Immunological Response Malnourished Children, Child Immunity Nutrition, Nutritional Status Immunological Response, Micronutrient Deficiency Immunity, Malnutrition Immune Function Children, and Childhood Infection

Immunity. Based on the initial search results, 163 articles were found relevant to the research topic. The next stage was the selection process, in which 6 duplicate articles were removed, 108 articles were eliminated because they did not meet the publication year criteria (2019–2024), 32 articles were excluded because they were not included in tier Q1 journals, and 1 article did not include a complete abstract. Thus, 16 articles remained that passed the screening stage. Of these, 4 articles could not be fully accessed due to accessibility constraints, so that finally 12 articles met all criteria and were included in the final analysis stage. This selection process is visualized in a PRISMA diagram that depicts the systematic flow of study identification, screening, and inclusion.



The primary instrument used in this study was a systematically designed data extraction sheet to gather information from each selected article. Data collected included author names, year of publication, country of study, study design, subject characteristics, nutritional indicators used (e.g., zinc, vitamin, protein, or essential fat levels), and immunological parameters such as cytokine levels, CD4+ cell count, and macrophage function. This approach followed the pattern used by Liao et al. (2022) and Rocha-Ramírez et al.

(2020), which respectively examined the effects of zinc and probiotics on immune function in malnourished children. The data extraction process was carried out meticulously to identify patterns of relationships emerging across studies without biased interpretation. All data from the selected articles were compiled into a synthesis table to facilitate comparison and draw objective conclusions.

The data collection procedure was carried out in stages according to the PRISMA guidelines, starting with identifying literature sources, screening based on inclusion and exclusion criteria, and assessing the methodological feasibility of each study. Selected articles were English or Indonesian-language publications discussing the relationship between nutritional status and the immune system in children, published between 2019 and 2024, and from reputable international journals. Articles focusing on adult populations, experimental animals, or lacking quantitative immunological data were excluded from the analysis. In this context, studies conducted by Mendivil (2021) on the role of omega-3 fatty acids and Liao et al. (2022) on zinc were considered to enrich the comparative analysis and strengthen the interpretation of the results. This process ensured that each publication analyzed was highly relevant to the research focus.

The analysis method used was thematic and comparative descriptive analysis, which aimed to group research results based on the nutritional indicators and immune responses studied. Each article was analyzed to identify patterns of similarities and differences, then synthesized to obtain general conclusions regarding the relationship between nutritional status and the immune system in children. The analysis was conducted manually using a qualitative descriptive approach so that the results

could be replicated by other researchers. Furthermore, this study also recorded the year of publication from the keyword search results, which indicates. A significant increase in the number of publications between 2016 and 2023 illustrates that the issue of children's nutrition and immune systems is becoming an increasingly relevant research topic globally. The entire analysis process was conducted in accordance with the PRISMA 2020 guidelines to ensure scientific openness, transparency, and procedural consistency, ensuring that research results are academically sound and used as a basis for further research and future evidence-based nutrition policies.

## **SYNTHESIS OF RESEARCH RESULTS**

A synthesis of twelve analyzed studies indicates that nutritional status is closely related to immune system function across various populations and health conditions. Overall, these studies demonstrate that improving nutritional intake—whether through nutritious food, supplementation, or dietary intervention—can improve the body's immune response. Wei et al. (2019) found that administration of recombinant human growth hormone (rhGH) to the MKN-45 xenograft mouse model improved food intake, body weight, and immune function without increasing tumor growth. These results demonstrate that interventions related to improving nutritional status have the potential to strengthen the immune system. Another study by Ke et al. (2021) also showed that immune-boosting enteral nutrition can increase CD 4+ cell counts and improve immune function in patients with severe neurological diseases. Thus, the key data from these studies indicate a positive relationship between nutritional quality and immune function, despite differences in sample

characteristics, methods, and study populations.

Analysis of publications identified through the PRISMA process shows that research on the relationship between nutrition and the immune system has increased significantly over the past five years, with a peak in 2023. Of the 163 articles identified, 12 met the final criteria and were subjected to in-depth analysis. Geographically, the studies were distributed across various countries, including China, Iran, Mexico, Taiwan, Canada, Italy, and the United States, with all journals indexed Q1. In the study synthesis graph, the majority of studies (approximately 67%) focused on the effects of specific nutrients such as zinc, omega-3, lipids, probiotics, and proteins on improving immune function, while the remainder addressed general dietary interventions and nutrition-based care models. The topic distribution graph shows that research on the mineral zinc (Liao et al., 2022) and probiotics (Rocha-Ramírez et al., 2020) was the most researched topic, followed by research on omega-3 fatty acids (Mendivil, 2021) and the effects of a low-fat diet on immunity (She et al., 2023). This pattern indicates that the main focus of research in the last five years has been more inclined towards micronutrient interventions related to the innate and adaptive immune systems.

Comparisons between studies show similarities in the role of nutrition in strengthening the immune system, but also differences in methodological approaches and populations used. For example, a study by Rocha-Ramírez et al. (2020) used an *in vitro* approach and found that inhabited *Lactobacillus casei* could improve macrophage function in malnourished children, while Ke et al. (2021) conducted a clinical trial in neurological patients and reported an increase in CD4+ cell counts. Liao et al. (2022) studied healthy children and found a positive

correlation between serum zinc levels and cytokine responses, while Azizi Jalilian Farid et al. (2022) studied COVID-19 patients and found that nutritional interventions could reduce pro-inflammatory cytokines, although they did not significantly affect disease progression. Another difference emerged in the study by Braga Tibaes et al. (2023), which examined the effects of diet on immunity in obese individuals and type 2 diabetes. Although the population focus and approach differ, all of these studies strengthen the evidence that nutrition is an important determinant in maintaining the body's immune function.

In terms of scientific significance, all of the synthesized studies represent important contributions to understanding how nutrition can modulate the immune system. For example, Mendivil (2021) demonstrated that fish and omega-3 fatty acid consumption have significant anti-inflammatory effects, while Candiloro et al. (2021) demonstrated that an olive oil-based lipid emulsion can improve immune cell function in cancer patients. She et al. (2023) also found that low-fat dairy products have a more beneficial effect on intestinal immune function than high-fat dairy products. All of these results reinforce the theory that balanced nutrient intake, both macro and micronutrients, plays a crucial role in maintaining immune system homeostasis. The significance of these findings also reflects the potential for nutritional approaches to be used as non-pharmacological intervention strategies to improve disease resistance.

The research implications of this review primarily relate to the importance of implementing nutrition interventions in vulnerable populations, such as malnourished children in developing countries. Data suggest that improving nutritional status through food-based interventions, micronutrient supplements,

or probiotics can strengthen children's immunity against infections. Studies by Rocha-Ramírez et al. (2020) and Liao et al. (2022) provide an important basis for developing child nutrition programs in regions such as Timor-Leste with high malnutrition rates. Furthermore, research by Chen et al. (2024) confirms that structured care approaches, such as modular care models, can also contribute to improving nutritional status and immunity. Therefore, these research findings have broad practical implications for both the development of national nutrition policies and more effective public health interventions.

Limitations of the synthesized studies include variations in design, population, and analytical methods. Some studies used animal models (Wei et al., 2019; She et al., 2023), which limits the generalizability of the results to humans, particularly children. Other studies, such as Ke et al. (2021) and Azizi Jalilian Farid et al. (2022), used relatively small samples and populations with specific medical conditions, making their results less applicable. Furthermore, most studies were conducted over the short term without monitoring the long-term effects of nutritional interventions on immunity. Rocha-Ramírez et al. (2020) also used only an *in vitro* approach, while Liao et al. (2022) did not study children with zinc deficiency. These variations limit the ability to draw universal conclusions, although the overall evidence continues to point to a positive relationship between nutrition and the immune system.

This state-of-the-art study illustrates that the relationship between nutrition and the immune system has been extensively studied, but gaps remain in the context of children in developing countries. Based on the results of the synthesis, most previous

studies have focused on adult populations or patients with chronic diseases such as cancer, diabetes, and neurological diseases (Candiloro et al., 2021; Ke et al., 2021; Braga Tibaes et al., 2023). Only a few studies have directly examined the effect of nutrition on the immune system of malnourished children, and almost none have been conducted in Southeast Asia, including Timor-Leste. Therefore, research focusing on the relationship between nutritional status and the immune system of children in Timor-Leste is novel. This study also provides an important scientific basis for understanding the interaction between malnutrition and immune function impairment in the context of vulnerable populations.

Future research directions are recommended to expand the scope of the study by conducting longitudinal studies and clinical trials in children in developing countries. Future research should assess the effectiveness of specific nutritional interventions—such as probiotics, zinc, and omega-3s—in improving the immunity of malnourished children. Furthermore, a multidisciplinary approach integrating biomedical, social, and nutritional policy aspects is essential for a comprehensive understanding of the relationship between nutrition and the immune system. Research is also expected to identify specific immune biomarkers in malnourished children to accurately monitor physiological changes. Thus, this synthesis not only confirms the importance of nutrition in maintaining the immune system but also opens up opportunities for further research that can provide a scientific basis for the development of more effective health policies and child nutrition programs in developing countries, particularly in Timor-Leste.

**Table 1. Synthesis of Research Results on the Effect of Nutrition on the Immune System**

No	Researcher s & Year	Title Study	Design / Sample	Interventio n Or Variables Nutritio n	Indicator System Immune	Key Results Study	Conclusion Relevant
1	Wei et al. (2019)	<i>Recombinant humangrowth hormone improves nutritional status and immune function in MKN- 45 xenograft mice</i>	Experiment Animals (MKN- 45 mice)	Administra- tion of rhGH (growth hormone)	Weight body, food intake, Cellular immune ac- tivity	rhGH in- creases appet- ite and immune function without in- creasing tumor gro- wth.	Nutritional int- erventions play a role in stren- gthening the immune system without nega- tive effects on growth.
2	Ke et al. (2021)	<i>Immune-en- hanced nutri- tiontherapy on neurological critically ill patients</i>	Clinical trial of neurolo- gical patie- nts (n=52)	Enteral nu- trition with increased immunity	CD4+ ce- lls, albu- min, total protein	There was a significant increase in CD4+ levels and improv- ement in nut- ritional status.	Enteral nutrition strengthens immunity and Improve nutri- tional status
3	RochaRami rez and al. (2020)	<i>Lactobacillu s caseiShirota improves mac rophage function in malnourishe d children</i>	In vitro (ch- ildren) malnutrition)	Giving probiotic L. casei	Activity macrophage s, Phagocyt- osis	Increased ph- agocytic acti- vity and cyto- kine produc- tion	Probiotics strengt- hen the immune response of maln- ourished children
4	Liao et al. (2022)	<i>Association between zinc levels and</i>	Observe 1 (healthy chil- dren, n=180)	As much as zinc serum	The cyto- kines TNF- $\alpha$ , IL-6, IL-	Zinc is posi- tively rela- ted	Zinc plays an important role in maintaining

No .	Researcher s & Year	Title Study	Design / Sample	Intervention Or Variables Nutrition	Indicator System Immune	Key Results Study	Conclusion Relevant
		<i>innate immunity in children</i>			Ib	With innate immune activity	Of the immune system
5	Mendivil (2021)	<i>Omega-3 fatty acids and immune modulation</i>	Review Clinical literature	Fish/omega-3 consumption	Inflammatory response	Omega-3 lowers Chronic inflammation and improve immune function	Healthy fats boost immunity through Anti-inflammatory mechanisms
6	Azizi JalianFarid et al. (2022)	<i>Bio-shield superfood powder effects on immunity in COVID-19 patients</i>	Clinical trial (COVID-19 patients, n= 120)	Superfood powder supplement	CRP, IL-6, TNF- $\alpha$	Decline biomarker inflammation in the group intervention	Complex nutrition suppresses excessive inflammatory response
7	Hatch-McChesney et al. (2023)	<i>Diet quality and immune function across lifespan</i>	Narrative review	General eating patterns	Adaptive and innate immunity	A high-quality diet reduces risk of infection and speed up recovery	Nutritional quality is directly proportional to immune resistance
8	Candiloro et al. (2021)	<i>Olive oil-based lipid emulsions in oncology patients</i>	Clinical trial (cancer patients, n=40)	Olive oil lipid emulsion	T cells, CD4/CD8 ratio	Significant increase in immune cell function	Healthy vegetable fats support patient immune function
9	Braga Tibaes and al. (2023)	<i>Impact of diet on immune function in obese and diabetic patients</i>	Clinical studies (n=80)	Modification diet (protein and fiber)	Proinflammatory cytokines	Decline IL-6 and CRP levels after a healthy diet	A balanced diet improves metabolic immunity
10	She et al. (2023)	<i>Low-fat dairy consumption and intestinal immune response</i>	Animal experiments	Low-fat milk diet	IgA in the intestine, microbiota	A low-fat diet improves IgA and balance A microbiota	Low fat intake improves mucosal immunity

11	Chen et al. (2024)	<i>Modular care model and nutritional</i>	Intervention studies (chronic patients)	Nutrition-based modular model	Albumin, immune response	Improvement of nutritional status and improvement	Nutrition management approach improves immunity
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No	Researchers & Year	Title Study	Design / Sample	Intervention Or Variables Nutrition	Indicator System Immune	Key Results Study	Conclusion Relevant
		<i>improvement in chronic patients</i>				General immunity	
12	Wei et al. (2021)	<i>Nutritional therapy and immune recovery in hospitalized children</i>	Pediatric clinical trials (n=65)	Diet so protein & vitamin	Amount lymphocytes and albumin	Significant increase in children's immunity after intervention	Nutritional therapy improves immune status in children

## DISCUSSION

This study aims to understand the relationship between nutrition and the immune system of children in developing countries, particularly in Timor-Leste, through a systematic review approach that summarizes twelve recent international studies. Based on the synthesis results, it was found that nutritional status is closely related to immune function, and that deficiencies in micronutrients such as zinc, protein, and omega-3 fatty acids have a significant impact on the decline in children's immune system capabilities. Furthermore, nutritional interventions such as probiotics, zinc supplementation, increased protein intake, and omega-3 consumption have been shown to improve immunity, both through immune cell repair and regulation of inflammatory responses. Based on this foundation, this discussion section outlines answers to three main research questions by linking them to empirical evidence from the analyzed literature.

### 1. The relationship between nutritional status and immune function in malnourished children in developing countries

Synthesized research evidence suggests that nutritional status is a key factor influencing immune function in children. A study by Wei et al. (2019) demonstrated that improving nutritional status through recombinant human growth hormone (rhGH) administration in a xenograft mouse model not only increased body weight and food intake but also improved immune function without increasing tumor growth. Although this study was conducted in animals, the results suggest a biological mechanism paralleling malnutrition in children, where improved nutrition improves cytokine production, phagocytic activity, and immune cell counts. Meanwhile, a study by Ke et al. (2021) in neurological patients receiving immunomodulatory enteral nutrition demonstrated a significant increase in CD4+ counts and overall improvement in nutritional status.

These results reinforce the link that a balanced nutritional intake directly contributes to improved immune function.

In the context of children in developing countries like Timor-Leste, the relationship between nutritional status and immunity becomes even more crucial. Malnourished children often experience decreased plasma protein, low micronutrient levels, and decreased immune cell function, making their bodies more susceptible to infection. Azizi Jalilian Farid et al. (2022) observed that an intervention in the form of supplementation with Bio-shield superfood powder can reduce levels of IL-6 and TNF- $\alpha$ , two important inflammatory markers. Although the study was conducted in COVID-19 patients, the mechanism suggests that nutrition. The complex can suppress excessive inflammation and support immune balance. Therefore, it can be concluded that improving the nutritional status of children in Timor-Leste has great potential to strengthen their immune systems against various infectious diseases.

Biologically, the relationship between nutrition and immunity can be explained through the process of antibody formation and immune cell differentiation, which require protein and micronutrients such as zinc and vitamins. Deficiencies in these substances can reduce the production of important cytokines such as IL-2 and IFN- $\gamma$ , which function to activate T lymphocytes. Research by Liao et al. (2022) showed that serum zinc levels are positively correlated with the secretion of pro-inflammatory cytokines at controlled levels, suggesting that zinc plays a crucial role in maintaining immune balance. Therefore, malnutrition not only impacts body weight and growth but

also reduces the effectiveness of the body's defense mechanisms. In the pediatric population in Timor-Leste, who face food shortages and imbalanced nutritional intake, this relationship is further strengthened because their bodies are in a state of chronic energy deficit.

The significance of these results lies in the understanding that nutritional improvement interventions in developing countries should not only focus on weight gain but also on immune system recovery. The synthesized research findings demonstrate that the relationship between nutrition and immunity is causal, not merely correlational, so that sound nutrition policies will have direct implications for reducing the incidence of childhood infectious diseases. Therefore, this research makes a significant contribution to the development of nutritional immunology, particularly in the context of developing countries, which has previously been understudied.

## **2. The most effective nutritional intervention in improving the immune function of malnourished children**

Synthesis results indicate that several nutritional interventions have proven effective in strengthening the immune system. First, probiotic-based interventions have shown promising results. Research by Rocha-Ramírez et al. (2020) showed that *Lactobacillus casei* Shirota increased macrophage activity and phagocytosis in malnourished children. This effect indicates that probiotics can improve the balance of the gut microbiota and strengthen the innate immune response. Although the study was conducted in

vitro, the results provide a scientific basis for the application of probiotics as part of nutritional interventions for children in Timor-Leste, who frequently experience digestive disorders and intestinal infections due to malnutrition.

Second, zinc intervention has also been shown to be important in improving children's immune function. Liao et al. (2022) found that optimal zinc levels are associated with increased cytokine secretion, which plays a role in the body's defense against infection. Zinc functions as a cofactor in more than 300 enzymes, including those involved in immune cell DNA replication. Therefore, zinc supplementation in malnourished children in Timor-Leste can improve immune function by improving cell division and immune protein synthesis. Third, research by Ke et al. (2021) showed that immunomodulatory enteral nutrition increased CD4+ levels and improved albumin ratios in neurological patients. This illustrates that the combination of protein, vitamins, and antioxidants in the diet can improve the immune response even in weakened conditions.

Furthermore, omega-3 fatty acid-based interventions also have significant impacts. According to Mendivil (2021), omega-3 plays a role in reducing the production of pro-inflammatory prostaglandins and leukotrienes, thereby reducing chronic inflammation. In the context of malnourished children in Timor-Leste, where diets tend to be high in simple carbohydrates and low in seafood intake, omega-3 supplementation may help strengthen the body's resistance to infection. Candiloro et al. (2021) also support these findings by showing that an olive oil-based lipid emulsion improves immune cell function in cancer patients, demonstra-

ting a similar effect of healthy fats on immunomodulation.

In general, this synthesis suggests that effective nutritional interventions to improve the immunity of malnourished children in developing countries include three main components: (1) probiotics to improve gut immunity, (2) zinc supplementation to enhance immune cell function, and (3) omega-3 intake to regulate systemic inflammation. These interventions are complementary and can be applied synergistically to improve the immune resilience of children in Timor-Leste. The significance of these findings lies in the multidimensional approach to nutritional improvement, which not only adds calories but also improves the quality of micronutrients and the body's microbiota. This also strengthens the theory that children's immunity is not only determined by energy, but also by the optimal balance of micronutrient composition.

The scientific implication is that nutritional interventions should no longer be viewed solely as preventative measures, but also as supportive therapies that can strengthen the immune system in vulnerable populations. In a policy context, these findings can be used by the Timorese government and international organizations to design evidence-based child nutrition programs, such as enriching local staple foods with zinc and omega-3s and integrating probiotics into supplementary school feeding programs.

### **3. The impact of micronutrient deficiencies such as zinc, protein, and omega-3 fatty acids on the immune response**

Micronutrient deficiencies have been shown to significantly impact the immune response. Liao et al. (2022) demonstrated that zinc deficiency reduces the production of key cytokines and inhibits T cell activation. Zinc deficiency is also associated with increased duration and severity of infections in children. In the context of Timor-Leste, where nutritional intake is limited, children often suffer from zinc deficiency, which prevents their immune systems from responding optimally to pathogens. Zinc deficiency is also associated with an increased risk of diarrhea and respiratory infections, two leading causes of childhood mortality in developing countries.

Protein deficiency also seriously impacts the immune system because protein is the building block for antibodies, hormones, and immunological enzymes. Wei et al. (2021) showed that children receiving a diet rich in protein and vitamins experienced significant increases in lymphocyte counts and albumin, indicating immune system recovery. Therefore, protein deficiency during growth can lead to an underdeveloped immune system, making children more susceptible to disease.

In addition to zinc and protein, omega-3 fatty acid deficiency also reduces the body's ability to control inflammation. According to Mendivil (2021), omega-3 plays a role in maintaining the balance between inflammatory and anti-inflammatory responses, and its deficiency can increase the risk of chronic

inflammation that weakens the immune system. She et al. (2023) found that low-fat milk consumption in test animals increased intestinal IgA, which is the first line of defense against pathogens in the digestive tract. A lack of healthy fats can impair the production of this antibody, increasing the risk of gastrointestinal infections.

Overall, micronutrient deficiencies lead to decreased immune function at both humoral and cellular levels. Malnourished children in Timor-Leste are at risk of multiple deficiencies, not just a single nutrient, resulting in cumulative and systemic effects. The significance of these results is that nutritional intervention strategies must be comprehensive and consider the balance of multiple nutrients simultaneously. A partial approach, such as supplementing only one micronutrient, may not be sufficient to fully restore immunity.

### **Implications and Limitations of the Research**

The primary implication of this study is that improving nutritional status not only enhances physical growth but also serves as an important immunological strategy to reduce the burden of infectious diseases in children in developing countries. In the field of nutrition science, these results reinforce the emerging paradigm that nutritional interventions can function as natural immune therapies that strengthen the immune system through measurable biological mechanisms, such as increased cytokine levels, CD4+ T cells, and phagocytic activity. In the realm of public health policy, this study supports the need for national programs that integrate nutrition education, food fortification, and micronutrient supplementation for children in areas

with high malnutrition rates such as Timor-Leste.

However, this research also has several limitations that should be noted. First, most of the synthesized studies were conducted in adult populations or used animal models (Wei et al., 2019; She et al., 2023), so generalization of the results to pediatric populations should be approached with caution. Second, some studies were short-term and small sample sizes, such as those by Ke et al. (2021) and Rocha-Ramírez et al. (2020), so long-term effects are unknown. Third, the limited data from Timor-Leste itself makes these results more generalizable to other developing countries. Nevertheless, these results still provide a strong scientific basis for suggesting that improved nutrition will improve immunity in malnourished pediatric populations.

## **CONCLUSION**

This study confirms that nutritional status plays a crucial role in determining the strength of children's immune systems, particularly in developing countries like Timor-Leste, which face the challenge of chronic malnutrition. A synthesis of twelve international studies found that improved nutrition is directly associated with improved immune function, both through increased CD4+ cell counts, phagocytic activity, and regulation of pro- and anti-inflammatory cytokine secretion. Nutritional interventions such as probiotic administration (Rocha-Ramírez et al., 2020), zinc supplementation (Liao et al., 2022), and omega-3 fatty acid consumption (Mendivil, 2021) have been shown to strengthen immunity through distinct biological mechanisms. These results demonstrate that nutrition not

only impacts physical growth but is also a key determinant in maintaining the body's immunological integrity. Therefore, this study makes an important contribution to the fields of nutrition and immunology, particularly in strengthening the concept of nutritional immunology as a scientific basis for child health policy in developing countries.

## **FUTURE RESEARCH SUGGESTIONS**

It is recommended that future research expand its scope by conducting longitudinal studies and population-based clinical trials of children in Timor-Leste, so that the causal relationship between nutrition and the immune system can be demonstrated more specifically and contextually. Future research should focus on identifying critical micronutrients that most influence local immunity, as well as assessing the effectiveness of multivitamin interventions that include probiotics, zinc, protein, and omega-3s simultaneously. Furthermore, a multidisciplinary approach that combines biomedical, social, and public policy aspects is needed to create sustainable and economically appropriate nutrition solutions. Research should also develop specific immune biomarkers for malnourished children to more accurately monitor physiological changes due to nutritional deficiencies. This approach will not only enrich the scientific literature but also provide practical implications for national nutrition intervention programs in Timor-Leste and other developing countries, making nutrition science an integral part of strategies to strengthen children's immune systems globally.

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