# THE EFFECT OF NUTRITIONAL INTERVENTIONS ON THE SUCCESS TREATMENT OF TUBERCULOSIS IN CHILDREN: LITERATURE REVIEW

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#### **ABSTRACT**

The incidence of tuberculosis in children is increasing and becomes a serious health problem because it can cause long-term effects such as death. TB can cause nutrient deficiencies and metabolic changes that delay recovery by suppressing immune function. Nutritional support is known to promote recovery in subjects treated for TB. The purpose of this study was to determine the effect of nutritional interventions on the success of childhood tuberculosis treatment. Literature review with three databases as literature search that are Pubmed, ProQuest, Ebsco with analysis conducted using PRISMA. Five research articles were obtained from three databases relevant to the topic. Tuberculosis infection causes anorexia, malabsorption of nutrients and metabolic disorders, also causing malnutrition characterized by a decrease in fat and muscle mass. Malnutrition can be addressed with nutritional interventions that can be provided in the form of macronutrient (high-protein diet) and micronutrients (vitamins and minerals). The combination of macronutrients and micronutrients can increase BMI, albumin levels, and improve fever and cough resolution. This can increase the ability of the child's immune response so that it can accelerate the recovery of children with TB. Improvement of nutrition in children is also supported by nutritional counseling that given to parents. Macronutrients and micronutrients are one of the factors supporting the success of TB treatment in children. Research on nutrition interventions is not enough, so it needs to be supported by further research on this topic so that it can provide better TB treatment results.

**Keyword:** children, nutritional intervention, treatment outcome, tuberculosis

#### **ABSTRAK**

Angka kejadian tuberkulosis pada anak semakin meningkat dan menjadi masalah kesehatan yang serius karena dapat menimbulkan dampak jangka panjang seperti kematian. Tuberkulosis dapat menyebabkan defisiensi nutrisi dan perubahan metabolisme yang menunda pemulihan dengan menekan fungsi kekebalan tubuh. Dukungan nutrisi diketahui mampu mendorong pemulihan pada subjek yang mendapatkan pengobatan TB. Tujuan penelitian ini adalah untuk mengetahui pengaruh intervensi gizi terhadap keberhasilan pengobatan tuberkulosis anak. Kajian literatur dengan tiga database sebagai pencarian literatur yaitu Pubmed, Proquest, Ebsco dengan analisis dilakukan menggunakan PRISMA. Lima artikel penelitian diperoleh dari tiga database yang relevan dengan topik. Infeksi tuberkulosis menyebabkan anoreksia, malabsorbsi nutrisi dan gangguan metabolisme, juga menyebabkan malnutrisi yang ditandai dengan penurunan massa lemak dan otot. Gizi buruk dapat diatasi dengan intervensi gizi yang dapat diberikan dalam bentuk makronutrien (diet tinggi protein) dan mikronutrien (vitamin dan mineral). Kombinasi makronutrien dan mikronutrien dapat meningkatkan BMI, kadar hemoglobin, dan memperbaiki resolusi demam dan batuk. Hal ini dapat meningkatkan kemampuan respon imun anak sehingga dapat mempercepat pemulihan anak penderita TBC. Perbaikan gizi pada anak juga didukung dengan penyuluhan gizi yang diberikan kepada orang tua. Makronutrien dan Mikronutrien merupakan salah satu faktor pendukung keberhasilan pengobatan tuberkulosis pada anak-anak. Penelitian terkait intervensi gizi belum cukup banyak, sehingga perlu didukung dengan penelitian lebih lanjut, sehingga dapat memberikan hasil pengobatan TB yang lebih baik.

Kata kunci: anak-anak, intervensi nutrisi, keberhasilan pengobatan, tuberkulosis

#### INTRODUCTION

Tuberculosis is an infectious disease caused by bacteria *Mycobacterium tuberculosis* and to this day is still a global burden disease (Roswati et al., 2022). World Health Organization reported that there will be an increase in the number of TB cases globally in 2021, that are 10.6 million TB cases. Deaths caused by TB are estimated to reach 1.6 million people in 2021 with a proportion of 1.4 million deaths with a negative HIV test and the remainder with a positive HIV test. The highest tuberculosis cases occurred in Southeast Asia at 44%, followed by Africa at 24% with the highest cases being in India (28%) and second in Indonesia (9.2%) (World Health Organization, 2022). Tuberculosis also continues to impact the lives and development of millions of children and adolescents. Tuberculosis cases in children and adolescents under 15 years of age represent approximately 11% of global adult TB cases. This means that around 1.1 million children and young adolescents under 15 years of age suffer from TB every year, and more than 225,000 of them die (World Health Organization, 2022).

Bacteria *Mycobacterium tuberculosis* can infect all age groups including children, however tuberculosis in children (under 15 years) is often considered a minor problem in the national tuberculosis program. World Health Organization stated that there would be more than 1.2 million cases of childhood tuberculosis in 2021 with the same proportion of women and men and dominated by children aged less than 15 years and more than half of them were undiagnosed and/or unreported. The proportion of "missing children" is highest among the youngest children, due to a lack of sensitive diagnostic tests and limited diagnostic capacity in the places where they seek care (World Health Organization, 2023). Childhood tuberculosis is a serious problem because it can cause long-term effects and one of the largest contributors to morbidity and mortality in children. The number of child TB cases in Indonesia in 2022 is 61,549, this figure has increased compared to 2021. In detail, TB cases occurred in children aged 0 - 5 years as many as 34,615 and 26,979 cases occurred in children aged 5 - 14 years (Yayasan KNCV Indonesia, 2022).

Children who have TB have a lower risk of infecting others than teenagers and adults, but they have a greater risk of disease and severe forms of TB, especially children under 5 years of age and without the BCG vaccine (Carvalho & Kritski, 2022). Tuberculosis infection is related to nutritional status and a decrease in the immune system. Tuberculosis disease causes an increase in energy requirements to maintain normal body functions, which is characterized by increased energy use at rest or resting energy expenditure (REE) of 10-30% of normal energy requirements, an increase in REE can cause an increase in leptin production which can cause eating disorders such as anorexia (Seneadza et al., 2021; Sudana, 2017). In addition, the protein that enters the body of children with TB is used more for energy production than for anabolism processes, thus triggering malnutrition. Malnutrition triggers a decrease in levels of IFN- $\gamma$  d, ILN-2, lymphocyte production and an increase in TGF- $\beta$ , this results in a decrease in lymphocyte production and the proliferation ability of the body's immune cells (Jaganath & Mupere, 2012; Seneadza et al., 2021b). Therefore, it is important for children with TB to have good nutritional status.

Poor nutritional status can reduce the immune system so that diseases can easily enter and infect the body, poor nutrition can also affect the disease healing process (Roswati et al., 2022). Poor nutritional status can affect the healing process of childhood tuberculosis because poor nutrition can inhibit the formation of antibodies and lymphocytes. The formation of antibodies and lymphocytes requires adequate nutritional intake such as protein and carbohydrates (Aulia Husna et al., 2016). Toddlers with stunted nutritional status have a three times greater risk of developing pulmonary tuberculosis compared to toddlers with normal nutritional status (Haerana et al., 2021). Children suffering from TB with poor nutritional status (malnutrition) have a risk of delayed healing, risk of relapse, incidence of hepatitis due to OAT, and even risk of death. Tuberculosis disease has an impact on decreased nutritional intake, malabsorption of

nutrients and changes in the body's metabolism which causes a decrease in muscle and fat mass or wasting, malnutrition can aggravate TB disease and can result in death (Pratomo & Burhan, 2012).

Previous research has suggested that malnutrition is known to be corrected with nutritional interventions such as a high-protein diet. High protein diet therapy is said to be able to support the healing process of tuberculosis. Adequate protein intake can help repair damaged cells, replace damaged tissue, and improve the body's metabolism. Energy intake combined with nutritional supplements can increase significant results in increasing body weight and muscle mass (Sudana, 2017). Other previous research shows that nutritional interventions in the form of macronutrients can improve the nutritional status of TB patients which has an impact on improving the immune system (Taslim et al., 2020). This study aims to determine the effect of nutritional intervention on the success of treating childhood tuberculosis.

#### **METHODS**

The research was conducted by Literature Review design, namely the method of identifying, evaluating and interpreting all research that is relevant to the topic under study. Analysis was conducted with the PRISMA method or Preferred Reporting Items for Systematic Reviews. The topic of this research is the effect of nutritional interventions on the success of treatment of childhood tuberculosis. Literature was taken from three databases, namely ProQuest, PubMed, and Ebsco with the keywords used, there are: "tuberculosis OR TB" AND "Children OR Child" AND "Nutritional Intervention." The inclusion criteria for this study were that the article had a title and content that was relevant to the topic discussing the effect of providing nutritional interventions on the recovery of tuberculosis treatment in children, the article was in Indonesian or English, the article could be accessed in full and there was no year limit because there are not enough research topics related to this research, as well as articles using intervention study designs such as experimental or as quasi experimental, randomized controlled trial (RCT), and non-randomized controlled trial. Meanwhile, the exclusion criteria are articles in book form, seminar results, conferences, and incomplete article structures. The data collection process was adapted to the PICO method with population criteria, namely children with tuberculosis, intervention in the form of nutritional intervention, the comparison was the child's nutritional status, and the outcome criterion was the success of tuberculosis treatment. The review was conducted by three reviewers with tasks, two reviewers screened the title and abstract to determine the relevance of the research, while the third reviewer resolved differences. All authors studied the manuscript, collected, synthesized data, and summarized conclusions using narrative synthesis.

#### **RESULTS**

A search for articles from three databases resulted five articles that were relevant to the topic and met the inclusion criteria. The identification phase resulted in 191 research articles (Figure 1) and there were twenty-two duplicate articles, so the remaining 170 articles could be continued in the second phase, namely searching. At the search phase, 135 articles excluded, the first was to exclude articles based on titles and abstracts that were not relevant to keywords with the following details, 70 articles did not have a suitable population (population not children), 15 articles did not use experimental study design, and 50 articles had backgrounds that did not focus on PICO research. Second, exclude research articles that cannot be accessed overall (n = 5 articles). Third, exclude articles that do not met the inclusion criteria (n = 20) with the following details: 9 articles in the form of final assignments, 6 articles that do not conduct nutritional interventions and 5 articles that do not measure nutritional status. The result of the article is obtained and can be done literature review that are five articles (figure 1).

Articles come from various countries, the most article distribution comes from developing countries with the highest proportion of articles from Indonesia that are two articles, while the other three articles come from India, South Africa and Tanzania, Africa. All articles included in literature review is an article with an observational study design. A summary of five articles discussing the influence of nutritional interventions on the success of treating children tuberculosis can be seen in Table 1.

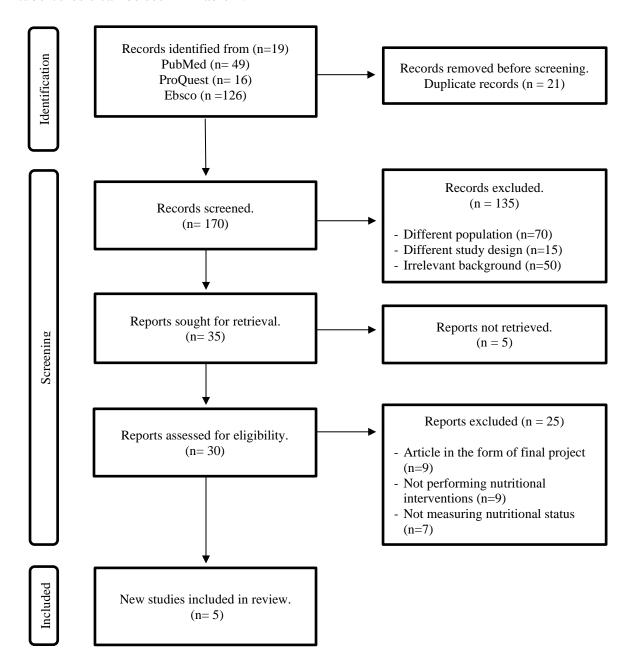


Figure 1. Flow diagram of search results for research articles

Table 1. Summary of articles included in the research.

No.	Title	Writer	Year	Study Design	Location	Results
1.	Effects of Vitamin D supplementation on resolution of fever and cough in children with pulmonary tuberculosis: A randomized double-blind controlled trial in Indonesia.	Lianda Tamara, Cissy B Kartasas mita, Anggrai ni Alam, Dida A Gurnida	2022	Randomized controlled trial (RCT)	Indonesia	<ul> <li>There were two intervention groups, namely the placebo intervention group and the vitamin D supplement intervention group with a dose of 1000 IU.</li> <li>The statistical results (median) of nutritional status in the Vit.D intervention group were greater than those in the placebo intervention group. In addition, clinical trials showed that the vitamin D intervention group had a shorter duration of fever and cough.</li> <li>Vitamin D is useful for increasing the resolution of fever and cough, as well as improving nutritional status in children with pulmonary TB and vitamin D insufficiency.</li> <li>Faster resolution of fever and cough indicates the child's excellent clinical improvement response. This plays a role in improving children's quality of life in carrying out daily activities, going to school, interacting with friends, and completing TB treatment.</li> </ul>
2.	Vitamin D supplementation to prevent tuberculosis infection in South African schoolchildren: multicentre phase 3 doubleblind randomized placebocontrolled trial (ViDiKids)	Keren Middelk oop, Justine Stewart, Neil Walker, Carmen Delport, David A., Anna K. Cousse, James Nuttall, Jonathan C.Y. T., William D, Christopher J., Geeta Trilok, Suzanne Filteau, Richard L. H., Robert J. W.,	2023	Double- blind randomized placebo- controlled trial	Afrika Selatan	<ul> <li>Research subjects were divided into nutritional intervention and placebo groups. The nutritional intervention was provided in the form of soft gel capsules containing 0.25 mg (10,000 UI) cholecalciferol (vitamin D3) in olive oil and olive oil without vitamin D content for the placebo group.</li> <li>The results of the intervention showed an increase in serum concentrations of 25-hydroxyvitamin (25[OH]D3 but does not reduce the risk of QFTPlus conversion. Average height-for-age z-score intervention group was higher.</li> <li>Increasing vitamin D concentrations can increase the ability of whole blood to limit the growth of mycobacteria.</li> </ul>

		Linda- Gail B., Adrian R. M.				
3.	Effect of tempeh dates biscuits on nutritional status of preschool children with tuberculosis	Fatmah, H.	2013	Quasi experimenta l	Indonesia	<ul> <li>The intervention was carried out by providing tempeh date biscuits (high in energy, fat, Fe and Vit C) for 6 weeks. After 6 weeks of tempeh date biscuit intervention, the intervention group experienced the highest weight gain (1 kg) compared to the control group, and experienced an increase in haemoglobin of 0.4 points.</li> <li>The highest change in nutritional status (BB and TB) occurred in the group with nutritional intervention in the form of date tempeh biscuits. Apart from that, it is also influenced by the mother's knowledge about TB and nutrition. Improving nutrition in children can help the success of the TB treatment process.</li> </ul>
4.	A randomized trial of multivitamin supplementation in children with tuberculosis in Tanzania.	Saurabh Mehta, Ferdinan d M Mugusi, Ronald J Bosch, Said Aboud, Anirban Chatterj ee, Julia L Finkelst ein, Maulidi Fataki, Rodrick Kisenge and Wafaie W Fawzi	2011	Randomized controlled trial (RCT)	Tanzania, Afrika	<ul> <li>The intervention given was in the form of a multivitamin capsule consisting of vitamin B1 0.5 mg, B2 0.6 mg, Niacin 4 mg, B6 0.6 mg, Folate 130 μg, B12 1 μg, C 60 mg, and E 8 mg.</li> <li>The results of the intervention showed an increase in haemoglobin levels, but there was no significant increase in average weight in the intervention group (average weight was 1.08 kg compared to the control/placebo group, namely 0.46 kg) and there was no increase in height.</li> <li>Increasing HB levels can help control anemia and iron deficiency in children so that it can help the process of treating children's TB and relieve symptoms of shortness of breath that children may experience. Short-term supplementation (8 weeks) can improve the haematological profile of all children with TB.</li> </ul>
5.	Effect of micronutrient supplementation on treatment outcomes in children with intrathoracic tuberculosis: a randomized controlled trial	Rakesh Lodha, Aparna Mukherj ee, Varinder Singh, Sarman Singh, Henrik Friis, Daniel	2014	Randomized controlled trial (RCT)	Delhi, India	• Children receive intervention in the form of syrup preparation with a daily dose of 5 mL for 6 months containing 1 of 4 regimens as follows: 1) only 20 mg zinc, 2) micronutrients such as vitamin A, thiamine, riboflavin, vitamins B6 and B12, folic acid, niacin, vitamins C, E, and D, selenium, and copper, 3) a combination of zinc and micronutrients (vitamin A, thiamine, riboflavin, vitamins B6

Faurholt	and B12, folic acid, niacin, vitamins
-Jepsen,	C, E, and D, selenium, and copper,
Shinjini	and 20 mg zinc, or 4) placebo.
В.,	• The results of the intervention
Savita	showed that children who received
Saini,	micronutrient supplements had an
Sushil K	increase in height (greater linear
Kabra,	growth). Increasing the HAZ or
Harleen	height can increase the
MS	improvement of a child's cough and
Grewal,	fever by as much as 94%, this can
	help speed up the process of treating
	children's tuberculosis.

#### **DISCUSSION**

In this study, we reviewed the relationship between providing nutritional interventions and the success of treating childhood tuberculosis. The success of nutritional intervention can be seen one way from the child's nutritional status, which is one of the supporting factors for successful treatment of childhood tuberculosis. Nutritional status is a valuable tool for predicting the success of treatment, outcomes and mortality of childhood tuberculosis. Several studies show that malnutrition is associated with worse treatment outcomes (Sinha et al., 2019). Improving nutritional status can be done with several nutritional interventions. Nutritional interventions can be divided into two, namely micronutrient and macronutrient interventions. Macronutrients can be provided in the form of a high protein, high energy diet. Meanwhile, micronutrients are vitamins and minerals. The combination of micronutrition and macronutrition interventions together with anti-TB therapy can speed up the recovery of TB patients, due to increased metabolic and immune system function (Hood, 2013).

#### **Micronutrients and Tuberculosis**

The micronutrient needs of children with TB should be able to meet 50-150% of daily needs (Pratomo & Burhan, 2012). Studies quasi experimental in Indonesia shows that micronutrient supplementation can increase children's weight, height and hemoglobin levels (Hutasuhut, 2013; Lodha et al., 2014). Micronutrient deficiencies are also considered to be a cause of secondary immune deficiency and morbidity in infectious diseases including tuberculosis (Gupta et al., 2009). Micronutrients in the form of vitamins A, C, E, D, B6. B12 and Zinc play a role in improving children's metabolism and immune response (Jaganath & Mupere, 2012; Pratomo & Burhan, 2012).

RCT studies in children show that vitamin D supplementation intervention can accelerate the duration of cough and fever in children with TB with a significant reduction in duration of only 2 weeks compared to the group without vitamin D supplementation intervention of up to 3 weeks. Apart from that, the vitamin D intervention group also had better nutritional status compared to the placebo group. Fever and cough are one of the physiological responses to TB infection. Research in Iran shows that adults with TB infection have an average duration of fever of 11.7 days and cough for more than 60 days (Tamara et al., 2022). Studies on the duration of fever in children with tuberculosis are still lacking, the mechanism of the relationship between nutritional intervention and the duration of resolution of cough and fever is unknown. Resolution of fever and cough may be due to Vitamin D's intervention on the immune system without excluding the possibility of other variables being involved (Fabbri et al., 2020; Tamara et al., 2022). However, there is another RCT study in India which showed that there was no significant difference in sputum conversion between subjects receiving micronutrient supplementation and no micronutrient supplementation. Vitamin D supplementation in the form of 2.5 mg tablets has a considerable effect on the immune system

and defense mechanisms against microorganisms, including *Mycobacterium tuberculosis* (Pratomo & Burhan, 2012). In tuberculosis ,vitamin D regulates the release of expression of specific endogenous antimicrobial peptides in macrophages and stimulates the production of cytokines and other inflammatory mediators (Tamara et al., 2022; Yani et al., 2017).

Micronutrients such as vitamin A play an immunocompetent role in human tuberculosis. Vitamin A has a key role in lymphocyte proliferation and is able to maintain epithelial tissue function. Vitamin A is also important in the normal function of T and B lymphocytes, macrophage activity, and the formation of antibody responses (Gupta et al., 2009). Vitamin C is useful as an antioxidant and contributes to increasing body immunity (Hutasuhut, 2013). Vitamin C is able to increase the proliferative response of T and B lymphocytes and reduce the concentration of proinflammatory cytokines (Jaganath & Mupere, 2012; Mehta et al., 2011). Vitamin E plays a role in increasing skin hypersensitivity responses, increasing IL-2 production, playing a role in phagocytosis of neutrophil, lymphocyte proliferation, and antibody responses to T cell-dependent vaccines, and reducing the production of inflammatory cytokines such as TNF-a and IL-6 (Mehta et al., 2011). Vitamin B plays a role in increasing lymphocyte production, cell-mediated cytotoxicity, hypersensitivity responses, and antibody production (Mehta et al., 2011). Vitamin B play a role in increasing lymphocyte production, cell-mediated cytotoxicity, hypersensitivity responses, and antibody production. (Mehta et al., 2011; Patti et al., 2021). Vitamin B6 (Pyridoxine) functions as an antioxidant while vitamin B12 (Cobalamin) has an ATP binding cassette which plays a role in MTB production (Patti et al., 2021). Vitamin E and selenium supplements can improve the antioxidant status of children with TB. In addition, vitamin B1, B6, and C supplementation can improve the immune response by increasing lymphocyte proliferation (Mehta et al., 2011; Pratomo & Burhan, 2012).

Analysis of a combined intervention between Indonesia, Peru, South Africa, and Vietnam among 1,134 infants showed that multiple micronutrient supplementation (Vitamins A, D, E, K, C, B1, B2, B6, and B12, niacin, zinc, folic acid, and copper) can effectively control anemia and iron deficiency (Smuts et al., 2005). Other research shows that micronutrient supplementation can increase hemoglobin levels in children with TB (Mehta et al., 2011). Measuring nutritional status using the delta body mass index (BMI) in children with TB produces a higher median of 0.5 or compared to the placebo group, namely 0.08 (Tamara et al., 2022).

Zinc is an essential element in protein function. Zinc plays a role in homeostasis and immune function. Zinc deficiency can reduce macrophage phagocytic function, the ability to fight intracellular pathogens, and the ability to recycle nutrients (Tellez-Navarrete et al., 2021). An increase in Zn is said to kill MTB. Zn also plays a role in thymus function by modulating the maturation of T lymphocytes T (Xiong et al., 2020). Zinc also contributes to the metabolism of vitamin A which is useful in the normal function of T and B lymphocytes, macrophage activity, and the formation of antibodies in children with TB (Hutasuhut, 2013). Studies conducted on pediatric patients provide evidence that Zn supplementation with vitamin A can increase sputum conversion within four weeks (Tellez-Navarrete et al., 2021).

#### **Macronutrients and Tuberculosis**

Macronutrients are known to have a role in increasing the body weight of children with TB. One form of macronutrient intervention is a high protein diet, such as an experimental study conducted in Indonesia by providing food in the form of date palm tempeh biscuits which can significantly increase the weight of children with TB. Date tempeh biscuits contain high amounts of energy (516 kcal), fat (27.5 g) and Zn (1.46 mg) and various nutrients, such as carbohydrates (66.1 grams), protein (8.44 g), Ca (49 mg), Fe (1.32 mg), and vitamin C. The Fe levels in dates help the formation of hemoglobin in red blood cells so that they can prevent

anemia in children (Hutasuhut, 2013). High protein diet therapy is said to be able to support the healing process of tuberculosis. Adequate protein intake can help repair damaged cells, replace damaged tissue, and improve the body's metabolism. Energy intake combined with nutritional supplements can increase significant results in increasing body weight and muscle mass (Sudana, 2017). RCT studies in India show that high energy and high protein diet interventions are able to provide significant results on CXR (Armijos et al., 2010; Lodha et al., 2014) Based on research, it can be interpreted that macronutrient interventions are more capable of providing an increase in CXR than micronutrients (Armijos et al., 2010). In line with research by Nurjanah and Sudana in 2017, nutrition had a direct effect on hemoglobin levels in TB patients by 23% (Sudana, 2017).

# Combination of Macronutrients, Micronutrients and Consultation

A detailed nutritional status assessment can manage the severity of children's TB disease. Nutrition counselors can help ensure that children with TB have adequate energy intake and encourage weight gain as well as provide education that supplements are only used as an addition, not as a substitute for diet (Wulandari & Karolina, 2023). Nutritional counseling given to parents and combined with giving supplements to children can result in significant increases in body weight, muscle mass and body function, thereby increasing the success of TB treatment in children (Paton et al., 2004). This is in line with an intervention study in Pakistan in 2021 which stated that providing education about nutrition to both TB patients and their parents could contribute to increasing the BMI index of TB patients (Khalid, 2021).

The combination of micronutrients, macronutrients and nutritional counseling indirectly influences the success of childhood tuberculosis treatment. Nutritional intervention in the form of macronutrients and micronutrients can help increase a child's weight and height or BMI index, increase hemoglobin levels, help cell regeneration, and improve the child's immune system so that it can prevent more severe TB disease. It is important for policy makers to include nutritional counseling services in the management of tuberculosis services in all health care facilities.

This research has several limitations, including that the article search was only conducted in three databases, so it is possible that there are articles that meet the inclusion criteria but are not included in the discussion of this research. Second, namely the number of articles conducted literature review a little to make it possible output different in other countries.

# **ACKNOWLEDGMENT**

The author sincerely grateful to the two reviewers from Public Health, Universitas Indonesia who were involved and participated in this literature review process.

### **CONCLUSION**

Based on the results literature review from five research articles it can be concluded that nutritional intervention in children has a significant influence on the success of treating childhood tuberculosis, although not directly. Nutritional intervention is a supporting factor in the success of pediatric TB treatment by being able to increase body weight, muscle mass, physical body function and a better immune system in children. Nutritional interventions can be provided in the form of vitamin supplementation, high protein foods, and providing counseling to parents of children with TB. There is not enough research on nutritional interventions, so it needs to be supported by further research on this topic, so that it can provide better treatment results for TB control programs.

#### **REFERENSI**

- Armijos, R. X., Weigel, M. M., Chacon, R., Flores, L., & Campos, A. (2010). Adjunctive micronutrient supplementation for pulmonary tuberculosis. *Salud Pública de México*, 52(3), 185–189. https://doi.org/10.1590/S0036-36342010000300001
- Aulia Husna, C., Fitry Yani, F., & Masri, M. M. (2016). Gambaran Status Gizi Pasien Tuberkulosis Anak di RSUP Dr. M. Djamil Padang. *Jurnal Kesehatan Andalas*, 5(1). https://doi.org/10.25077/jka.v5i1.474
- Carvalho, A. C. C., & Kritski, A. L. (2022). What is the global burden of tuberculosis among children? *The Lancet Global Health*, 10(2), e159–e160. https://doi.org/10.1016/S2214-109X(21)00548-9
- Fabbri, A., Infante, M, & Ricordi, C. (2020). Editorial Vitamin D status: A key modulator of innate immunity and natural defense from acute viral respiratory infections. *Eur Rev Med Pharmacol Sci.*, 25.
- Gupta, K. B., Gupta, R., Atreja, A., Verma, M., & Vishvkarma, S. (2009). Tuberculosis and nutrition. *Lung India*, 26(1).
- Haerana, Bs. T., Prihartono, N. A., Riono, P., Djuwita, R., Syarif, S., Hadi, E. N., & Kaswandani, N. (2021). Prevalence of tuberculosis infection and its relationship to stunting in children (under five years) household contact with new tuberculosis cases. *Indian Journal of Tuberculosis*, 68(3), 350–355. https://doi.org/10.1016/j.ijtb.2020.10.011
- Hood, M. L. H. (2013). A narrative review of recent progress in understanding the relationship between tuberculosis and protein energy malnutrition. *European Journal of Clinical Nutrition*, 67(11), 1122–1128. https://doi.org/10.1038/ejcn.2013.143
- Hutasuhut, F. (2013). Effect of tempeh dates biscuits on nutritional status of preschool children with tuberculosis. *Malaysian Journal of Nutrition*, 19, 173–184.
- Jaganath, D., & Mupere, E. (2012). Childhood Tuberculosis and Malnutrition. *Journal of Infectious Diseases*, 206(12), 1809–1815. https://doi.org/10.1093/infdis/jis608
- Khalid, S. (2021). The Effect of Nutrition Education on Nutritional Status of Tuberculosis Patients. *Biomedical Journal of Scientific & Technical Research*, 33(3). https://doi.org/10.26717/BJSTR.2021.33.005391
- Lodha, R., Mukherjee, A., Singh, V., Singh, S., Friis, H., Faurholt-Jepsen, D., Bhatnagar, S., Saini, S., Kabra, S. K., & Grewal, H. M. (2014). Effect of micronutrient supplementation on treatment outcomes in children with intrathoracic tuberculosis: A randomized controlled trial. *The American Journal of Clinical Nutrition*, *100*(5), 1287–1297. https://doi.org/10.3945/ajcn.113.082255
- Mehta, S., Mugusi, F. M., Bosch, R. J., Aboud, S., Chatterjee, A., Finkelstein, J. L., Fataki, M., Kisenge, R., & Fawzi, W. W. (2011). A randomized trial of multivitamin supplementation in children with tuberculosis in Tanzania. *Nutrition Journal*, *10*(1), 120. https://doi.org/10.1186/1475-2891-10-120
- Paton, N. I., Chua, Y.-K., Earnest, A., & Chee, C. B. (2004). Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. *The American Journal of Clinical Nutrition*, 80(2), 460–465. https://doi.org/10.1093/ajcn/80.2.460
- Patti, G., Pellegrino, C., Ricciardi, A., Novara, R., Cotugno, S., Papagni, R., Guido, G., Totaro, V., De Iaco, G., Romanelli, F., Stolfa, S., Minardi, M. L., Ronga, L., Fato, I., Lattanzio, R., Bavaro, D. F., Gualano, G., Sarmati, L., Saracino, A., ... Di Gennaro, F. (2021).
  Potential Role of Vitamins A, B, C, D and E in TB Treatment and Prevention: A Narrative Review. Antibiotics MDPI, 10(11), 1354. https://doi.org/10.3390/antibiotics10111354

- Pratomo, I. P., & Burhan, E. (2012). Malnutrisi dan Tuberkulosis. *Jurnal of The Indonesian Medical Association*, 62(6).
- Roswati, R., Ruhdiana, T., & Arfania, M. (2022). Literature Review Article: Faktor Hubungan Status Gizi Pada Penderita Tuberkulosis. *Jurnal Pendidikan dan Konseling*, 4(6).
- Seneadza, N. A. H., Antwi, S., Yang, H., Enimil, A., Dompreh, A., Wiesner, L., Peloquin, C. A., Lartey, M., Lauzardo, M., & Kwara, A. (2021a). Effect of malnutrition on the pharmacokinetics of anti-TB drugs in Ghanaian children. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union against Tuberculosis and Lung Disease*, 25(1), 36–42. https://doi.org/10.5588/ijtld.20.0301
- Seneadza, N. A. H., Antwi, S., Yang, H., Enimil, A., Dompreh, A., Wiesner, L., Peloquin, C. A., Lartey, M., Lauzardo, M., & Kwara, A. (2021b). Effect of malnutrition on the pharmacokinetics of anti-TB drugs in Ghanaian children. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union against Tuberculosis and Lung Disease*, 25(1), 36–42. https://doi.org/10.5588/ijtld.20.0301
- Sinha, P., Davis, J., Saag, L., Wanke, C., Salgame, P., Mesick, J., Horsburgh, C. R., & Hochberg, N. S. (2019). Undernutrition and Tuberculosis: Public Health Implications. *The Journal of Infectious Diseases*, 219(9), 1356–1363. https://doi.org/10.1093/infdis/jiy675
- Smuts, C. M., Lombard, C. J., Benadé, A. J. S., Dhansay, M. A., Berger, J., Hop, L. T., López De Romaña, G., Untoro, J., Karyadi, E., Erhardt, J., & Gross, R. (2005). Efficacy of a Foodlet-Based Multiple Micronutrient Supplement for Preventing Growth Faltering, Anemia, and Micronutrient Deficiency of Infants: The Four Country IRIS Trial Pooled Data Analysis,. *The Journal of Nutrition*, 135(3), 631S-638S. https://doi.org/10.1093/jn/135.3.631S
- Sudana, I. M. (2017). Analisis Pengaruh Fase Pengobatan, Tingkat Depresi dan Konsumsi Makanan Terhadap Status Gizi Penderita Tuberkulosis (TB) Paru Di Wilayah Kerja Puskesmas se- Kecamatan Genuk Kota Semarang. *Public Health Perspective Journal*, 2(3).
- Tamara, L., Kartasasmita, C. B., Alam, A., & Gurnida, D. A. (2022). Effects of Vitamin D supplementation on resolution of fever and cough in children with pulmonary tuberculosis: A randomized double-blind controlled trial in Indonesia. *Journal of Global Health*, *12*, 04015. https://doi.org/10.7189/jogh.12.04015
- Taslim, N. A., Rasyid, H., Atmanegara, M. K., Angriavan, S., & Amelia, R. (2020). Effect of Chocolate Soybean Drink on Nutritional Status, Gamma Interferon, Vitamin D, and Calcium in Newly Lung Tuberculosis Patients | Open Access Macedonian Journal of Medical Sciences. *Open Access Macedonian Journal of Medical Sciences*, 8(T2), 210–214.
- Tellez-Navarrete, N. A., Ramon-Luing, L. A., Muñoz-Torrico, M., Osuna-Padilla, I. A., & Chavez-Galan, L. (2021). Malnutrition and tuberculosis: The gap between basic research and clinical trials. *The Journal of Infection in Developing Countries*, *15*(03), 310–319. https://doi.org/10.3855/jidc.12821
- World Health Organization. (2022). *Global Tuberculosis Report 2022*. World Health Organization.
- World Health Organization. (2022). WHO consolidated guidelines on tuberculosis. Module 5, Management of tuberculosis in children and adolescents. World Health Organization.
- World Health Organization. (2023). *Tuberculosis (TB)*. https://www.who.int/news-room/fact-sheets/detail/tuberculosis

- Wulandari, P. S., & Karolina, M. E. (2023). The Relationship Between Treatment Phase And Nutritional Status In Adult Tuberculosis Patients At Public Health Centers In Jambi City. JMJ. 360-366.
- Xiong, K., Wang, J., Zhang, J., Hao, H., Wang, Q., Cai, J., & Ma, A. (2020). Association of Dietary Micronutrient Intake with Pulmonary Tuberculosis Treatment Failure Rate: ACohort Study. *Nutrients*, *12*(9), 2491. https://doi.org/10.3390/nu12092491
- Yani, F. F., Lipoeto, N. I., Supriyatno, B., Darwin, E., & Basir, D. (2017). Vitamin D status in under-five children with a history of close tuberculosis contact in Padang, West Sumatra. *Asia Pacific Journal of Clinical Nutrition*, 26(Suppl 1), S68–S72. https://doi.org/10.6133/apjcn.062017.s2
- Yayasan KNCV Indonesia. (2022). Apa Itu Tuberkulosis / TBC? *Apa Itu Tuberkulosis / TBC*? https://yki4tbc.org/tuberkulosis-tbc/