Nutritional supplementation, combined with a balanced diet and environmental health education, improved the conversion of LTBI and daily nutrient intake

Suparman Samsidi[1*], *Sukmal* Fahri[2], *Roro* Nur Fauziyah[1], *Maryati* Dewi[1], *Fakhrida* Khairat[2], *Egy* Sunanda Putra[2], and *Aditya* Juliastuti[3]

[1]Department of Nutrition, Bandung Health Polytechnic, 40514 Pasirkaliki, Indonesia
[2]Department of Environmental Health, Jambi Health Polytechnic, 36129 Paal Lima, Indonesia
[3]Department of Medical Laboratory Technology, Bandung Health Polytechnic, 40514 Pasirkaliki, Indonesia

Abstract. Latent tuberculosis infection showed an iceberg phenomenon and it is also an early form of tuberculosis. This disease remains prevalent in many countries and has become a public health problem. Integration-based approaches in the form of nutritional supplement intervention combined with a balanced diet and environmental health education, may be effective in addressing latent tuberculosis. This study evaluates the efficacy of an integrated intervention model in improving specific immune responses and nutrient intake among subjects. This study employed field experimental design and random allocation techniques. This study was conducted in two HCs (Health Centers) in Bandung and Jambi, Indonesia. A total of 36 samples were taken from Garuda HC in Bandung and 36 samples from Paal Merah II HC in Jambi. Each group consisted of 36 treatment and 36 control group samples. The intervention lasted for 30 days. The control group received a balanced diet and environmental health education and the treatment group received both education-based intervention and nutritional supplementation. The results showed that the proportion of the treatment group with reduced latent tuberculosis status was higher than that of the control group ($p>0.05$). The treatment group also had an increase in daily nutrient intake compared to the control group ($p<0.05$).

1 Introduction

According to the Indonesia National Basic Health Research (INBHR) 2018, the national incidence rate of tuberculosis disease in 2019 was 245 per 100,000 population. In contrast, WHO Global data reported a lower rate of 130 per 100,000 population in 2019 [1]. Nationally, the prevalence of tuberculosis among individuals above15 years old has remained stable compared to the previous five years, including several provinces in Java and Sumatra, such as West Java and Jambi [2].

* Corresponding author: suparmansamsidi@gmail.com

· The iceberg phenomenon of Tuberculosis shows that a bigger size of the population with Latent Tuberculosis Infection (LTBI) may develop into tuberculosis disease under certain conditions. Weak host resistance, along with decreased nutritional status will trigger conversion from closed contact to LTBI and from LTBI to Tuberculosis disease [3]. The Indonesia National Strategy for LTBI focuses on increasing screening coverage and prevention through health education and promotion [4]. However, specific nutritional interventions are not included.

Tuberculosis infection, caused by the bacterium called Mycobacterium tuberculosis (Mtb), is transmitted through air, with a transmission rate of 20% -40% [5]. For family members living with active tuberculosis patients, the risk of transmission is higher, due to the intensity of contact with Mtb germs through airborne droplets. Contact history with pulmonary TB patients in the respondent's household is a risk factor for incident pulmonary tuberculosis [6].

Family members infected with mycobacterium tuberculosis (latent tuberculosis) are at great risk of developing active tuberculosis disease. One of the factors that facilitates the conversion from latent tuberculosis to active tuberculosis is weak resistance or immunity deficiency, along with decreased nutritional status. Based on epidemiological data, as many as 10-30% of those infected are 90% becoming latent TB and 10% being active TB [7].

Based on this situation, developing a specific intervention is needed to control and prevent the increasing positive conversion rates among household members. Combination interventions, including nutritional supplementation, balanced diets-based education, and improvement in housing conditions, offer a promising strategy to enhance nutrient intake, immune response, better housing conditions, and nutritional status among individuals at risk of latent tuberculosis. This study aims to evaluate the efficacy of nutritional supplementation, combined with a balanced diet and environmental health education, in improving the negative conversion of LTBI, increasing daily nutrient intake, body weight, Body Mass Index (BMI), and better housing conditions among individuals with close contact to TB patients.

2 Materials and methods

Balanced diet-based education is an individual education method to deliver a model of daily diet for subjects identified with latent tuberculosis infection. Nutritional supplements-based interventions consists of 50 g whey protein isolate (milk-based), 15 mg of elemental zinc in the form of zinc-sulfate, 5000 IU Vitamin A as retinyl palmitate, and 2000 IU of vitamin D3 as cholecalciferol to address specific nutrients deficiencies. Improving housing ventilation-based education focuses on improving the air quality by improving ventilation and air circulation. To evaluate the effect of nutritional supplements, the treatment group and control group received similar intervention: balanced diet education and environmental health education.

This study used a field experimental design. Calculation of sample size was based on a minimum sample size formula for estimating the mean difference in IFN-γ titer between groups [8]. Using α=0.05, 1–β=0.842, and population means from the previous study (77.5 pg) with the standard deviation of 75 pg/mL [9], a minimum of 15 subjects for each group was required. To anticipate dropout during the 30 days of intervention due to unmet exclusion criteria, such as low adherence to nutritional supplements, illness, or relocation, 18 subjects were recruited for each group in Garuda HC in Bandung and Paal Merah II HC in Jambi. Random allocation techniques were used to assign samples to the treatment and control group.

The study was conducted in two health centers: Garuda in Bandung City and Paal Merah II in Jambi City, representing a high-density and a low-density population, respectively. A

field experimental design was used with 18 subjects for each group at each HC (each HC consisting of a treatment and a control group), who were in close contact with Tuberculosis patients. The treatment group received 30 days of an integrated intervention, including 30 days for nutritional supplementation, four visiting times for a balanced diet education, and environmental health education. The control group received only a balanced diet and environmental health education. Adherence to nutritional supplementation consumption was carried out. Daily nutrient intake was collected using the SQ-FFQ method, body weight, height, and BMI were measured using anthropometrics [10], and housing conditions were evaluated based on the observational method and environmental health equipment [11]. The identification of LTBI was identified using a standardized QuantiFERON TB Gold test [12]. Statistical analyses were performed using Student's t-tests in the SPSS application [13]. Ethical approval was granted by the Health Research Ethical Committee No.10.1/KEPK/PE/XI/2019 of Bandung Health Polytechnic. Explained informed consent was delivered to all accepted subjects before the study began.

3 Results and discussion

Table 1. Characteristics of samples in two groups

Parameters	n	Treatment (n=36)	Control (n=36)	p
Age (Yrs) (mean±sd)	72	33.8 (9.4)	34.2 (8.3)	p>0.05[1]
Sex (%)				
Male	22	22.5	35.0	p>0.05[2]
Female	50	77.5	65.0	
Households member (mean±sd)	72	5.2 (2.3)	4.9 (2.0)	p>0.05[1]

Note: not significant at p>0.05, [1] analyzed using independent t-test and [2] chi-square test

The demographic data of the two groups were not significantly different ($p > 0.05$) at baseline. The average age in the treatment group was 33.8 years, and it was 34.2 years in the control group. The proportion of women was 77.5% in the treatment group and 65.0% in the control group. The average number of household members was 5.2 in the treatment group and 4.9 in the control group.

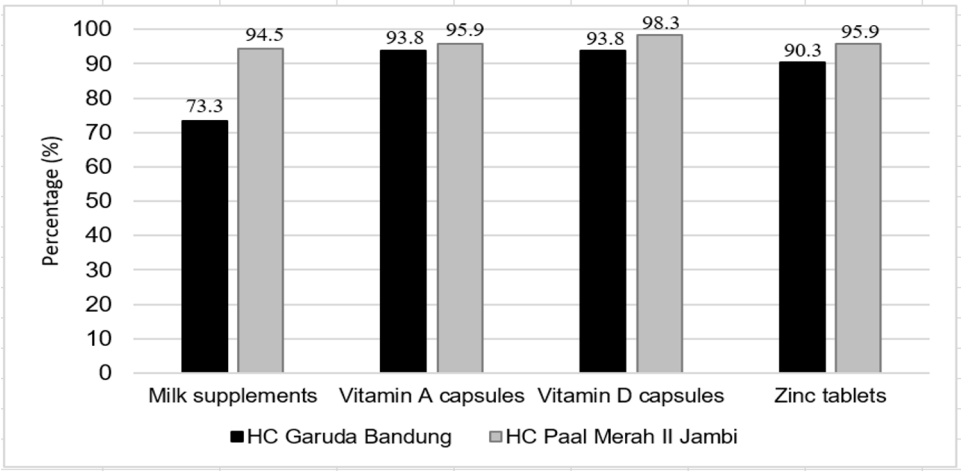

Fig. 1. Adherence rate consumption of nutritional supplements

The adherence rate for consuming nutritional supplements among subjects in the treatment group at two locations is shown in Figure 1. Subjects at Garuda HC in Bandung had lower adherence than those at Paal Merah II HC in Jambi. Furthermore, the average adherence rate at Garuda HC in Bandung was 87.8% of packages, or lower than those at Paal Merah II HC in Jambi with 96.2% of packages.

Table 2. The difference in daily nutrient intake between treatment and control groups (before and after intervention)

Parameters	Before	After	p
Energy (kcal)			
Treatment	1533.8 (751.5)	1644.3 (623.9)	<0.05*
Control	1371.6 (499.9)	1397.4 (530.6)	
Protein (g)			
Treatment	61.9 (27.7)	71.4 (27.4)	<0.05*
Control	56.2 (22.7)	57.3 (20.0)	
Vitamin A (ug)			
Treatment	485.6 (449.9)	869.9 (1019.3)	<0.05*
Control	494.2 (479.2)	538.9 (709.9)	
Zinc (mg)			
Treatment	6.5 (3.3)	7,8 (3,0)	>0.05
Control	6.1 (3.7)	7,0 (2,6)	

Note: *significant at p <0.05, analyzed using independent t-test for difference between treatment and control group after intervention.

After 30 days of intervention, daily dietary nutrient intake was significantly higher in the treatment group than in the control group ($p < 0.05$) at both locations (Bandung and Jambi). However, zinc intake increased, but there were no significant differences between the treatment and control groups (Table 2).

Table 3. Change in healthy housing indicators between two groups

Parameters	Before	After	p
Sunlighting (lux)			
Treatment	119.9 (57.3)	149.9 (49.1)	>0.05[2]
Control	94.0 (44.8)	146.7 (51.4)	
Humidity (%)			
Treatment	63.4 (12.3)	65.8 (8.3)	>0.05[2]
Control	66.4 (9.6)	72.4 (10.6)	
Room ventilation (m^2)			
Treatment	36.9 (77.5)	36.9 (77.5)	>0.05[1]
Control	17.7 (17.1)	17.7 (21.0)	
Housing density (person/hh)			
Treatment	7.4 (4.0)	7.4 (4.0)	>0.05[1]
Control	8.4 (4.6)	8.4 (4.6)	

Note: not significant at p>0.05, [1] analyzed using independent t-test (room ventilation and housing density) and [2] dependent t-tests (sunlighting and humidity)

Two parameters, sunlight exposure and humidity, slightly changed after conducting environmental health education (Table 3). However, room ventilation and housing density were not changed. All parameters had no significant differences ($p > 0.05$). These results suggest that the impact of environmental health education on housing requires more time, especially to improve the structure of the house building.

Table 4. Change in nutritional status between groups

Parameters	Before	After	p
BMI (kg/m2)			
Treatment	24.1 (4.3)	24.1 (4.3)	>0.05[1]
Control	24.1 (5.1)	24.0 (5.0)	
Body weight (kg)			
Treatment	58.2 (10.4)	58.2 (10.4)	>0.05[1]
Control	59.2 (13.0)	59.4 (12.9)	

Note: not significant at p>0.05, [1] analyzed using independent t-test (BMI and body weight)

After the intervention, BMI and body weight data showed no significant differences between the treatment and control groups ($p > 0.05$). Before and after the intervention, neither group had subjects with low BMI. Typically, LBTI subjects maintained normal nutritional status, in contrast to subjects with Tuberculosis disease, who had lower nutritional status [14].

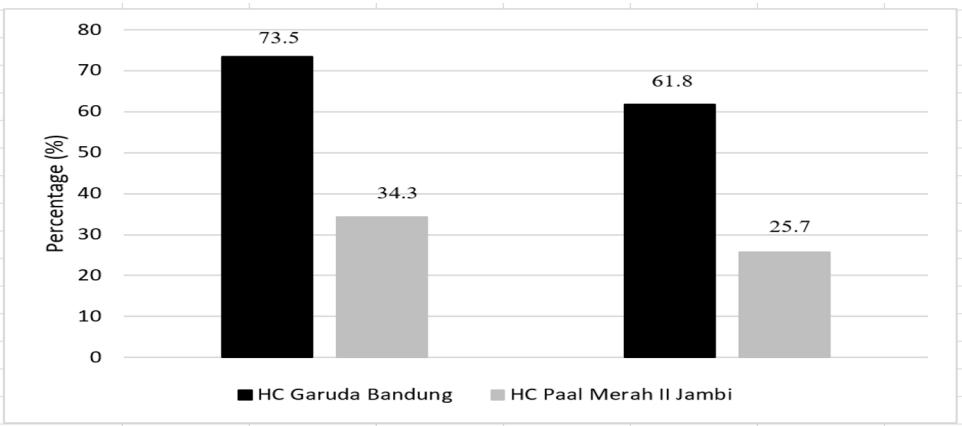

Fig. 2. Changed the proportion of LTBI status between research locus

The proportion of LTBI among close-contact subjects at Garuda HC in Bandung was higher (73.5%) than at Paal Merah II HC in Jambi (34.3%). This is probably related to the higher population density in Bandung City compared to Jambi City [15,16]. The population density at Garuda HC in Bandung was higher (2.9 m^2/person), while at Paal Merah II HC in Jambi was 12.9 m^2/person. The average number of household members at Garuda HC in Bandung was 5.4, compared to 4.6 at Paal Merah II HC in Jambi. Sunlight exposure at Garuda HC in Bandung (53.2 lux) was also lower than at Paal Merah II HC in Jambi (160.7 lux). A study in Surabaya found that house lighting below 60 lux significantly increased the odds ratio (OR = 21.3) of TB incidence compared to lighting above 60 lux, along with population density [17].

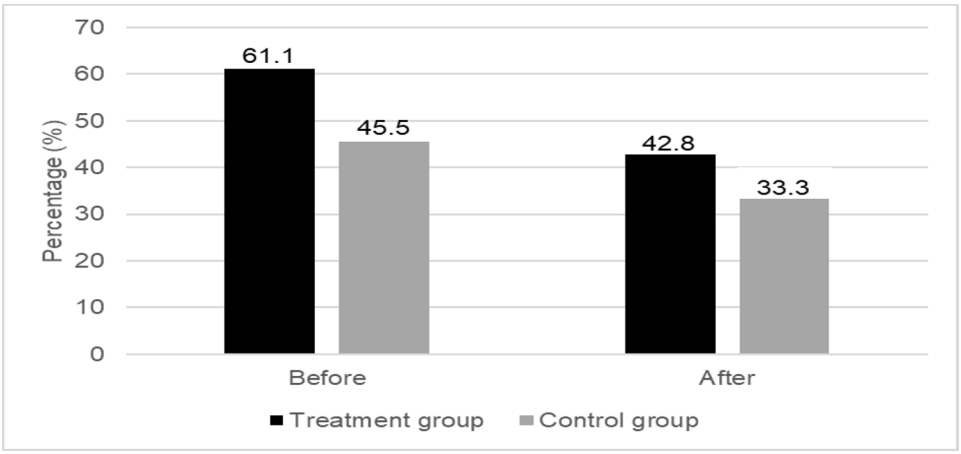

Fig. 3. Changed the proportion of LTBI status between research group

Before the intervention, the proportion of LTBI was higher in the treatment group (61.1%) than in the control group (45.5%). A trend of reduced LTBI proportions was observed in both groups and locations, but no significant difference was found ($p > 0.05$) (Fig.3). The low effect of the intervention on LTBI conversion may be due to the shorter duration of the intervention. A similar study using nutrition education, micronutrient supplementation, and fortification yielded similar results [18].

4 Conclusion

The model-integrated intervention partly improved daily nutrient intake, although no significant improvements were observed in other research parameters, despite overall progress. The low conversion rate of latent tuberculosis infection in the treatment group may be due to the shorter duration of the intervention. Future studies should extend the period of intervention to two or three months to observe changes in housing conditions and body weight. Additionally, LTBI status should be assessed at least three times or more to track progression.

References

1. WHO. Global Tuberculosis Report. Available from: https://iris.who.int/bitstream/handle/10665/274453/9789241565646-eng.pdf?sequence=1. (2020)
2. Ministry of Health of Republic of Indonesia. Basic Health Survey. Jakarta (2018). https://repository.badankebijakan.kemkes.go.id/id/eprint/3514
3. S. Yu et al., The association of dietary patterns with latent tuberculosis infection among young adults: A case-control study in Shanghai, J Infect Dev Ctries.**18**(1):93-100 (2024). https://doi.org/10.3855/jidc.18465
4. T. Lestari, A. Fuady, F.F. Yani, I.W.G.A.E. Putra, I.S. Pradipta, L. Chaidir, D. Handayani, A. Fitriangga, M.R. Loprang, I. Pambudi, R. Ruslami, A. Probandari, The development of the national tuberculosis research priority in Indonesia: A comprehensive mixed-method approach, PLOS ONE. February 9 (2023). https://doi.org/10.1371/journal.pone.0281591
5. D. Greenwood, R.C.B. Slack and J.F. Peutherer, Medical microbiology, (Edinburg,

ELBS, 1995)

6. A.N. Mamo, et al., Household contact tuberculosis screening adherence and associated factors among pulmonary tuberculosis patients on follow-up at health facilities in Shashamane Town, Southeast Ethiopia, Patient Preference and Adherence.**17,** 1867–1879 (2023). https://pmc.ncbi.nlm.nih.gov/articles/PMC10392788/pdf/ppa-17-1867.pdf
7. WHO. The Global Plan to Stop Tuberculosis. Available from: https://iris.who.int/bitstream/handle/10665/68582/WHO_CDS_STB_2003.23.pdf?sequence=1&isAllowed=y. (2003)
8. S.K. Lwanga, S. Lemeshow, Sample size determination in health studies: A practical manual. Available from: https://iris.who.int/bitstream/handle/10665/40062/9241544058_%28p1p22%29.pdf?sequence=1&isAllowed=y. (1991)
9. S. Samsidi, H. Hardinsyah, C.M. Kusharto, A. Sulaeman, B. Alisjahbana, V. Ulaganathan, Synbiotics and nutrient supplements improved of secretory immunoglobulin A (sIgA) in treated pulmonary tuberculosis patients, Annals of Tropical Medicine & Public Health. **23**, 8 (2020). http://doi.org/10.36295/ASRO.2020.23815
10. Y. Siyu et al., The association of dietary patterns with latent tuberculosis infection among young adults: A case-control study in Shanghai, J Infect Dev Ctries. **18 (**1), 93-100 (2024). https://jidc.org/index.php/journal/article/view/38377095
11. J.Y Lee, N. Kwon, G. Goo and S. Cho, Inadequate housing and pulmonary tuberculosis: a systematic review, BMC Public Health. **22:**622 (2022) https://doi.org/10.1186/s12889-022-12879-6.
12. H. Masoumi, A. Alborzi, B. Pourabbas, M. Kalani, QuantiFERON-TB gold and tuberculin skin test for the diagnosis of latent tuberculosis infection in children, Iran J Med Sci. **40** (5), 411-7 (2015). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4567600/pdf/IJMS-40-411.pdf
13. G. Liang, W. Fu and K. Wang, Analysis of t-test misuses and SPSS operations in medical research papers, BMC.**7**:31 (2019). https://doi.org/10.1186/s41038-019-0170-3
14. J. Ockenga et al., Tuberculosis and malnutrition: The European perspective, Clinical Nutrition. 42,486-492 (2023). https://doi.org/10.1016/j.clnu.2023.01.016
15. Bandung Regional Statistic Board. Demographic Profile of Bandung City. Available from: https://bandungkota.bps.go.id/id/publication/2019/08/16/bd52ff3d885d75c04ddcfb17/kota-bandung-dalam-angka-2019.html. (2019)
16. Jambi Regional Statistic Board. Demographic Profile of Jambi City. Available from: https://jambi.bps.go.id/id/statisticstable/3/V1ZSbFRUY3lTbFpEYTNsVWNGcDZjek53YkhsNFFUMDkjMw==/penduduk--laju-pertumbuhan-penduduk--distribusi-persentase-penduduk--kepadatan-penduduk--rasio-jenis-kelamin-penduduk-menurut-kabupaten-kota-di-provinsi-jambi--2019.html?year=2019. (2019)
17. A.J. Muhammad, P. Lestari, A.D.W. Widodo, The Ventilation-to-area ratio and house lighting relate to the incidence of pulmonary tuberculosis, AMJ. **7**(1), 1–5 (2020). https://journal.fk.unpad.ac.id/index.php/amj/article/view/1821
18. R.A. Salam, J.K. Das, W. Ahmed, O. Irfan, S.S. Sheikh and Z.A. Bhutta, Effects of preventive nutrition interventions among adolescents on health and nutritional status in lowand middle-income countries: a systematic review and meta-analysis, Nutrients. **12**(1), 49,1-22 (2020). https://doi.org/10.3390/nu12010049